# "EFFICACY OF PRE-EMPTIVE ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK WITH DEXAMETHASONE ADDED TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA AFTER LAPAROSCOPIC SURGERIES- A RANDOMISED CLINICAL STUDY"


**By**

## DR. SHREYAS. S


**Dissertation submitted to**

**BLDE (Deemed to be university),**

**VIJAYAPUR, KARNATAKA.**

In partial fulfillment of the requirements for the degree of

**DOCTOR IN MEDICINE**

**IN**

**ANAESTHESIOLOGY**

**UNDER THE GUIDANCE OF**

**DR. D. G. TALIKOTI** MD

**Professor & Head**

Department of Anaesthesiology

**SHRI B.M. PATIL MEDICAL COLLEGE, VIJAYAPUR, KARNATAKA**

**2019**

**B. L. D. E. (Deemed to be university)**

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Date:

Place: Vijayapur **Dr. Shreyas S**

## LIST OF ABBREVIATIONS USED

**(in alphabetical order)**

| | | |
|---|---|---|
| ASA | : | American society of anaesthesiologists |
| BP | : | Blood pressure |
| CNS | : | Central nervous system |
| $CO_2$ | : | Carbon dioxide |
| COX | : | Cyclooxygenase |
| CRPS | : | Complex regional pain syndrome |
| DBP | : | Diastolic blood pressure |
| EO | : | External oblique(muscle) |
| EtCO2 | : | End-tidal carbon dioxide |
| FRC | : | Functional residual capacity |
| HR | : | Heart rate |
| H/h | : | Hours |
| IAP | : | Intra abdominal pressure |
| IO | : | Internal oblique(muscle) |
| IV | : | Intravenous |
| IVPCA | : | Intravenous patient controlled analgesia |
| IVRA | : | Intravenous regional anaesthesia |
| MAP | : | Mean arterial pressure |
| Na | : | Sodium |
| NRS | : | Numeric Rating Scale |
| NO | : | Nitric oxide |

| | | |
|---|---|---|
| $N_2O$ | : | Nitrous oxide |
| No. | : | Number |
| NSAID's | : | Non steroidal anti inflammatory drugs |
| NS | : | Normal Saline |
| PaCO2 | : | Partial pressure of arterial carbon dioxide |
| PACO2 | : | Partial pressure of alveolar carbon dioxide |
| PACU | : | Post anesthesia care unit |
| PCEA | : | Patient controlled epidural analgesia |
| PONV | : | Post-operative nausea & vomiting |
| PR | : | Pulse rate |
| QoR | : | Quality of recovery |
| RR | : | Respiratory rate |
| SB | : | Systolic blood pressure |
| SPSS | : | Statistical presenting system software |
| TAP | : | Transversus Abdominis Plane |
| USG | : | Ultrasound Guided |
| VAS | : | Visual analogue scale |
| VRS | : | Verbal rating scale |
| WDR | : | Wide dynamic range neurons |

# ABSTRACT

**Introduction:** Undertake clinical trial to evaluate effect of dexamethasone as an adjuvant to local anaesthetic in TAPB.

**AIM:** To observe and compare the analgesic effect of ultrasound guided TAP block comparing 0.25% bupivacaine with dexamethasone and 0.25% bupivacaine with normal saline.

**OBJECTIVES:**

1. Evaluate efficacy of TAP block in providing post-operative analgesia in laparoscopic surgeries.
2. Evaluate pain severity using VAS Score (Visual Analog Score)
3. Evaluate need for rescue analgesia.
4. Evaluate safety and adverse effects of TAP block.

**Material and Methods:**

ethical committee permission: yes

patient consent: attached

**Randomization** done by computer generated random numbers.

Group I — Dexamethasone with 0.25% bupivacaine.

Group II— Normal saline with 0.25% bupivacaine.

Statistical tests: **Chi squire test, ANOVA test**

**INCLUSION CRITERIA:**

1. Patients between 18-60 years of age
2. ASA 1 & 2
3. Either male or female
4. BMI<30kg/m2

**EXCLUSION CRITERIA:**

1. Patient refusal.
2. Infection at local site
3. Chronic opioid use
4. Pregnancy

**Results:** The timing of first shot of rescue analgesic was significantly shorter in group I compared to group II. Significantly lower visual analogue scores were observed in group I verses group II during the initial 24 hours

**Conclusion**: Addition of dexamethasone to bupivacaine in TAP block prolonged the duration of the block and decreased the incidence of nausea and vomiting.

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# INTRODUCTION

Despite availability of numerous analgesic modalities, management of postoperative pain continues to be a challenge. Data has shown that 70% of patients undergoing surgical procedures reported postoperative pain and it is often inadequately treated in the hospital setting. [1] Untreated or semi-treated postoperative pain is associated with decreased patient satisfaction, delayed patient recovery, longer hospitalizations and increased medical care costs. [2]

Laparoscopic surgeries are commonly performed surgical procedures in day to day practice. These patients require a multimodal postoperative pain treatment regimen that provides high quality analgesia with minimal side effects. Opioids, such as morphine, delivered using a patient-controlled analgesia (PCA) device, remain the mainstay of postoperative analgesic regimens for such patients. However, the use of opioids can result in significant adverse effects including sedation, nausea and vomiting. Alternative approaches which reduce the postoperative requirement of strong opioids are required. Multimodal analgesic techniques that use regional anaesthesia and non-opioid pain medications in addition to opioids have shown to decrease opioid consumption as well as its adverse effects. [3] Some patients are not candidates for regional anaesthesia due to patient refusal, adverse psychological elements, type of surgical procedure, infection at site, preexisting neurological deficits and bleeding diathesis. Non-opioid pain medications include acetaminophen, aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) and selective cyclo-oxygenase inhibitors. [4] Use of intravenous NSAIDs, such as ketorolac, has been limited due to side effects including bleeding, gastric mucosal damage and renal toxicity. [5]

Transversus abdominis plane (TAP) block is a regional anaesthetic technique that first appeared in the anaesthesia literature in 2001 and has been applied as one segment of a multimodal pain regimen in abdominal surgeries including caesarean sections. The injection of local anaesthetics in the neuro fascial plane in the anterior abdominal wall has proven itself to be an effective adjunct to central neuraxial narcotic administration. With the untoward and undesirable side effects of narcotics, regional techniques such as the TAP block offers greater pain relief with less side effects and increased patient satisfaction. The duration of TAP block is limited to the effect of administered local anaesthetics (LAs). However, recently adjuvants such as epinephrine, ketamine and clonidine are added to LA solution in concentrations advocated for other peripheral blocks to prolong the effect of TAP block with promising results. Evidence supporting the presence of N-methyl-D-aspartate (NMDA) receptors in skin and muscles have led to the use of magnesium sulphate ($MgSO_4$) a NMDA antagonist through different routes for peripheral nerve blocks and the role of $MgSO_4$ as an adjuvant to bupivacaine in ultrasound-guided TAP block for post-operative analgesia in patients scheduled for TAH under subarachnoid block (SAB) has now been studied. [6]

Although the use of local anaesthetics administered centrally (eg: epidural or intrathecal) is effective, hypotension and reduced mobility are common and the potential for harm is great. Administering local anaesthetics more peripherally on the pain pathway such as with transversus abdominis plane (TAP) blocks, rectus sheath blocks, intraperitoneal instillation, wound catheters, is considered safer in this regard. However, some of the techniques use large amounts of local anaesthetic and the risk of high plasma levels of local anaesthetic and the concomitant cardiac toxicity and neurotoxicity should not be underestimated. The location of lipid emulsion in clinical

areas and knowledge of its administration to treat local anaesthetic toxicity should be readily available to hand.

The introduction of ultrasound (US) guidance in anaesthesia has permitted an indirect vision of internal structures (muscle, vessels, nerves) and ultrasonography has become an indispensable tool for anaesthesiologist and a gold standard for truncal and peripheral blocks, such as several international guidelines recommend. TAP blocks were popularized nearly 10 years ago and has a growing evidence base to support its use. Local anaesthetic is instilled between internal oblique and transversus abdominis muscles, preferably using ultrasonography. TAP block was initially performed as a blind technique, in which a double-pop technique was employed where a blunted needle was passed through the external and internal oblique muscles, a pop was heard as the needle pierced through the fascia overlying the muscle. The needle is inserted in the lumbar triangle of Petit, the borders of which are the external oblique muscle anteriorly, the latissimus dorsi muscle posteriorly and the iliac crest inferiorly. Main principle of TAP block is to deposit local anaesthetic in plane between internal oblique muscle and transversus abdominis muscle to block the sensory-motor innervations of the anterior abdominal wall which is supplied by anterior rami of the spinal segments T7-T11. A large volume (20 mL) of local anaesthetic provides block of the T10 to L1 dermatomes and covers incision for specimen and some port sites. TAP blocks have been used in open and laparoscopic surgery for which reductions in pain scores and morphine use (in the first 24 hours), time to tolerating diet, PONV and LOS have been described. [7,8] Results from recent meta-analysis showed that preoperative TAP blocks provide greater analgesia than postoperative TAP blocks. [9]

It is generally safe, although liver trauma has been described with inexpert clinicians. [10] Laparoscopy-guided TAP block has also been successfully used

recently. [11-13] Subcostal TAP blocks are performed to provide analgesia in the upper quadrants of the abdominal wall. [14,15] The analgesic efficacy of TAP blocks can be prolonged by intermittent boluses or continuous infusion of local anaesthetic through multi-hole catheters placed between the internal oblique and transverses abdominis muscle. [16-18]

Continuous wound infusion of local anaesthetic has been successfully used in one feasibility study. Transversus abdominis plane (TAP) block can be used for Pfannenstiel or midline incisions. A meta-analysis of 5 studies reported reduction in 24-hour pain scores and opioid consumption (reduced morphine equivalents by 5–19 mg) in patients who received a TAP block compared with no block for major open gynaecologic surgery. [18] In a meta-analysis of 10 studies in all-types of laparoscopic surgery three of which were gynaecologic, TAP blocks were shown to be effective in reducing postoperative pain scores and opioid consumption, particularly when administered preoperatively. The TAP block has shown conflicting data with regard to improvement in quality of Evidence-Based Anaesthesia for Gynaecologic Surgery recovery scores or opioid consumption after laparoscopic gynaecologic surgery but in line with the conclusions of the meta-analysis it may be that the timing of TAP block administration was the difference between benefit (preoperative) and no benefit (postoperative). [19,20] Some authors described the addition of dexamethasone which is an efficient glucocorticoid drug with anti-inflammatory properties has been proven to prolong effect of local anaesthetics. [21] In according to several works, [22-24] suggested the use of ropivacaine solution (a local anaesthetic that provides a longer postoperative analgesia, with a greater margin of safety for cardiotoxicity and neurotoxicity). Many studies have demonstrated that addition of clonidine to bupivacaine in single-shot TAP block for cesarean section under SA prolongs

analgesia by 10–12 hours and reduces overall postoperative analgesic requirements by more than 75 mg compared to bupivacaine alone. [25]

Further studies have demonstrated that addition of dexmedetomidine to bupivacaine in TAP block provides prolonged post-operative analgesia and better pain control than LA alone. The duration of LA was longer, VAS (visual analogue score) was lower and the need for rescue morphine doses was less when dexmedetomidine was added to bupivacaine. [26] Many studies have shown that the use of fentanyl as an adjuvant to bupivacaine has significantly reduced intraoperative fentanyl use in terms of both the amount and the number of patients who needed additional doses. [27] More studies occurred to evaluate the role and potential of dexamethasone and other adjuvants. Glucocorticoids have a prequisite to bind to ligands within the cell and be transported into the nucleus, where they have their effect on DNA transcription. Steroids may potentiate the action of local anaesthetics through modulation of the function of potassium channels in the excitable cells.

Although some articles suggest a superiority of local wound infiltration rather than TAP block in Caesarean section, cholecystectomy and radical prostatectomy in terms of pain reduction in the first four to six hours post-operative period. [28-32] Few complications have been reported especially when the TAP block is performed under direct US guidance. These include intrahepatic and intraperitoneal injections. Local anaesthetic toxicity should also be considered especially when multiples or continuous TAP blocks are performed. In accordance to pain, there was reduced static pain score and opioid consumption but there was inconclusive evidence in reduction of opioid side effects. This study is aims to compare the efficacy of the ultrasound guided Transversus Abdominis Plane (TAP) block by using 0.25% bupivacaine with dexamethasone versus 0.25% bupivacaine with normal saline.

# AIMS AND OBJECTIVES

## AIMS

To observe and compare the analgesic effect of ultrasound guided TAP (transverses abdominis plane) block using 0.25% bupivacaine with dexamethasone versus 0.25% bupivacaine with normal saline.

### OBJECTIVES

Comparison of effectiveness of ultrasound guided TAP block with 0.25% Bupivacaine with Dexamethasone and 0.25% Bupivacaine with normal saline.

#### A) PRIMARY OBJECTIVES

1. Evaluate efficacy of TAP block in providing post-operative analgesia in laparoscopic surgeries.
2. Evaluate pain severity using VAS (Visual Analogue Score).

#### B) SECONDARY OBJECTIVES

1. Evaluate need for rescue analgesia.
2. Evaluate safety and adverse effects of TAP block.

# REVIEW OF LITERATURE

## ANATOMY AND PHYSIOLOGY

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience which is primarily associated with tissue damage or describe in terms of such damage or both." This definition recognizes that pain is a perception and not a sensation. One influential model described pain in terms of three hierarchical levels: a sensory-discriminative component (e.g. location, intensity, quality), a motivational–affective component (e.g. depression, anxiety) and a cognitive-evaluative component. [34]

There is an important implication of both the IASP definition and the hierarchical model of pain: As a perception, pain may or may not correlate with an identifiable source of injury. The activity in the body's "nociceptive" system, which senses noxious stimuli and generates a physiological and behavioral response, can be initiated by injury and sustained by neuroplastic changes even after healing; activity in this system can occur in the absence of any discrete injury but in association with a recognizable disease.

In some cases, pain can develop and be unrelated to any identifiable physical process. In all cases, the reality that pain is a perception indicates the potential for profound influence of psychological and emotional factors, cognitions and varied external events.

There is another important implication of the concept of pain as perception. It is almost always best to believe that the patient is experiencing what is being reported. Because there is no objective indicator for pain, experts agree that the best clinical

approach in most circumstances is to assume that the patient is reporting a true experience, even in the absence of a clear explanation.

Importantly, accepting patient's complaint of pain as valid does not require clinical identification of a physical cause or demand the initiation of a specific treatment. Almost always, is a sound foundation for assessment and an important beginning in developing an effective physician patient dialogue.

## PATHOPHYSIOLOGY OF PAIN

### The "pain" system:

Precisely, the "pain system" should be called the "nociceptive system" because pain is a subjective result of nociception. Nociception is the encoding and processing of noxious stimuli in the nervous system that can be measured with electrophysiological techniques. A scheme of the nociceptive system is shown in Fig. 1. A noxious stimulus activates nociceptors (Aδ and C fibers) in the peripheral nerve. Their sensory endings are not equipped with corpuscular end organs, so-called free nerve endings. Most of the nociceptors are polymodal, responding to noxious mechanical stimuli (painful pressure, squeezing or cutting of the tissue), noxious thermal stimuli (heat or cold) and chemical stimuli. [35] Sensory molecules in the sensory endings of nociceptors transduce mechanical, thermal and chemical stimuli into a sensory potential and when the amplitude of the sensory potential is sufficiently high action potentials are triggered and conducted by the axon to the dorsal horn of the spinal cord or the brainstem.

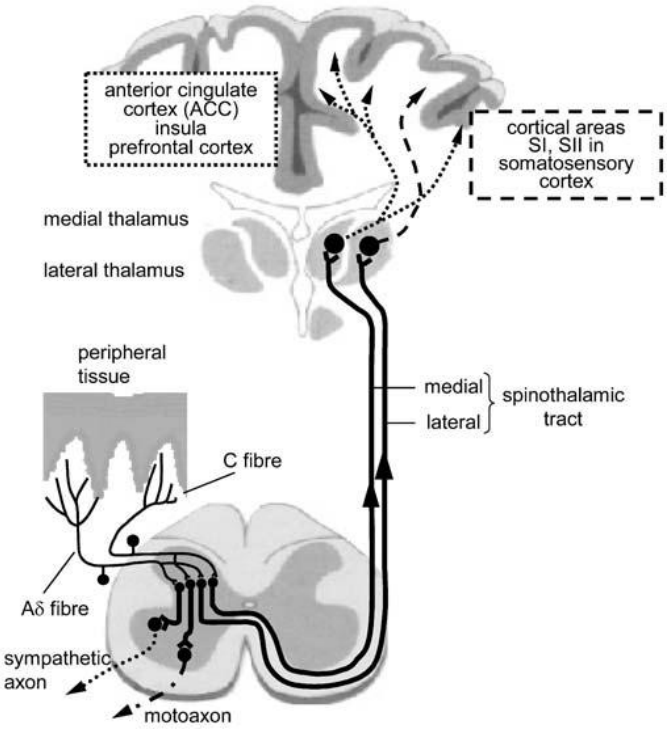



**Fig. 1:** Scheme of the nociceptive system with nociceptive free nerve endings in the peripheral tissue, afferent nerve fibers and their synapses in the dorsal horn of the spinal cord. From there the medial and lateral spinothalamic tracts ascend to the medial and lateral thalamus and interneurons project into motor and sympathetic reflex pathways. [36]

Nociceptors activate synaptically dorsal horn neurons (Fig. 1). The latter are either ascending tract neurons or interneurons that are part of segmental motor or vegetative reflex pathways. Ascending axons in the lateral spinothalamic tract activate the thalamocortical system that produces the conscious pain sensation. The pain sensation has a sensory discriminative aspect, i.e. the noxious stimulus is analyzed for its location, duration and intensity. This is produced in the lateral thalamocortical system which consists of relay nuclei in the lateral thalamus and the areas SI and SII in the postcentral gyrus. A second component of the pain sensation is the affective aspect i.e. the noxious stimulus feels unpleasant and causes aversive reactions.

This component is produced in the medial thalamocortical system, which consists of relay nuclei in the central and medial thalamus and the anterior cingulate cortex (ACC), the insula and the prefrontal cortex. [36]

The spinal cord is under the influence of descending tracts that reduce or facilitate the nociceptive processing. Descending inhibition is formed by pathways that originate from brainstem nuclei (in particular the periaqueductal grey, nucleus raphe magnus) and descend in the dorsolateral funiculus of the spinal cord. This system is able to suppress nociceptive information processing via interneurons in the dorsal horn of the spinal cord. [27] Nociceptors can also exert efferent functions in the tissue by releasing neuropeptides [substance P, calcitonin gene-related peptide (CGRP)] from their sensory endings. Thereby, they induce vasodilatation, plasma extravasation and other effects e.g. attraction of macrophages or degranulation of mast cells. The inflammation produced by nociceptors is called neurogenic inflammation.

**Types of Pain**

When a noxious stimulus is applied to normal tissue, acute physiological nociceptive pain is elicited (Fig. 2). This pain protects tissue from being further damaged so, withdrawal reflexes are elicited. Pathophysiological nociceptive occurs when the tissue is inflamed or injured. This pain may appear as spontaneous pain (pain in the absence of any intentional stimulation) and/or as hyperalgesia and/or allodynia. Hyperalgesia is a higher pain intensity that is felt upon noxious stimulation and allodynia is the occurrence of pain that is elicited by stimuli that are normally below the pain threshold. Some authors include the lowering of the threshold in the term hyperalgesia in non-neuropathic pain. While nociceptive pain is elicited by

noxious stimulation of the sensory endings in the tissue, neuropathic pain results from injury or disease of neurons in the peripheral or central nervous system (Fig. 2).

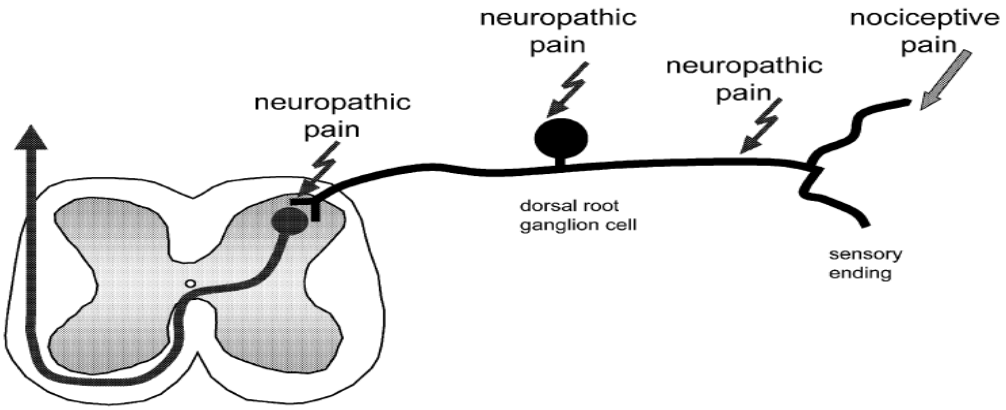



**Fig. 2:** Sketch of a nociceptive afferent with its synapse in the dorsal horn of the spinal cord. Noxious stimulation of the nociceptor at its sensory ending causes nociceptive pain. Pathological stimulation of the axon, the dorsal root ganglion or of neurons in the central nervous system causes neuropathic pain. [36]

This pain does not primarily signal noxious tissue stimulation and therefore feels abnormal. It often has a burning or electrical character and can be persistent or occur in short episodes (e.g. trigeminal neuralgia). It might be combined with hyperalgesia and allodynia. In the allodynic state even the touching of the skin with a soft brush can cause intense pain. Numerous pathological processes can cause neuropathic pain e.g. taxonomy, nerve or plexus damage, metabolic diseases such as diabetes mellitus or herpes zoster. The complex regional pain syndrome (CRPS) is a neuropathic pain syndrome that involves the sympathetic nervous system (one form was previously called sympathetic reflex dystrophy or Sudeck's disease). [37] Damage to central pain processing neurons (e.g. in the thalamus) can cause central pain. [38]

**Acute Pain**

A common definition of acute pain is "the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus associated with

surgery, trauma and acute illness". Yet patient's attitudes, beliefs and personalities also strongly affect their immediate experience of acute pain. Acute pain should therefore be viewed as the initiation phase of an extensive, persistent nociceptive and behavioral cascade triggered by tissue injury. [39] If suppression of pain responses was not mobilized along with processes of pain amplification, any minor injury could progress to chronic pain (unfortunately some do). An individual's responses for months after transient injury may be determined by processes that occur within the first day. As with other complex dynamic systems, small differences in the initial state of the host and in the intensity, quality and meaning of the nociceptive stimulus can produce major differences in the detailed manner in which this process unfolds.

**Chronic Pain**

Originally pain was called "chronic" when it lasted longer than 6 months. More recently, chronic pain is often defined by its character. In many chronic pain states the causal relationship between nociception and pain is not tight and the pain does not reflect tissue damage. Rather, psychological and social factors seem to determine the pain e.g. in many cases of low back pain. However, chronic pain might also result from a chronic disease and might then actually result from persistent nociceptive processes. It may be accompanied by neuroendocrine dysregulation, fatigue, dysphoria and impaired physical and even mental performance. [40]

**Peripheral Mechanisms of Nociceptive Pain**

During inflammation, polymodal nociceptors are sensitized (Fig. 3). In the normal tissue these fibers have relatively high mechanical and thermal thresholds and high intensity stimuli are required to excite the neurons. In the course of inflammation, the excitation threshold drops such that even light a normally innocuous stimuli activate the fibers. Thus when sensitized "pain fibers" are activated

by normally non-painful stimuli these stimuli cause pain. Noxious stimuli evoke stronger responses than in the non-sensitized state. [41] In addition, inflammation is also able to recruit so called silent nociceptors. These are C-fibers that are unexcitable by noxious mechanical or thermal stimuli in normal tissue. However, during inflammation these primarily mechanosensitive fibers are sensitized and then they are activated by stimuli. Both the enhanced activity of sensitized polymodal nociceptors and the recruitment of silent nociceptors generate the pathophysiological nociceptive input to the spinal cord.

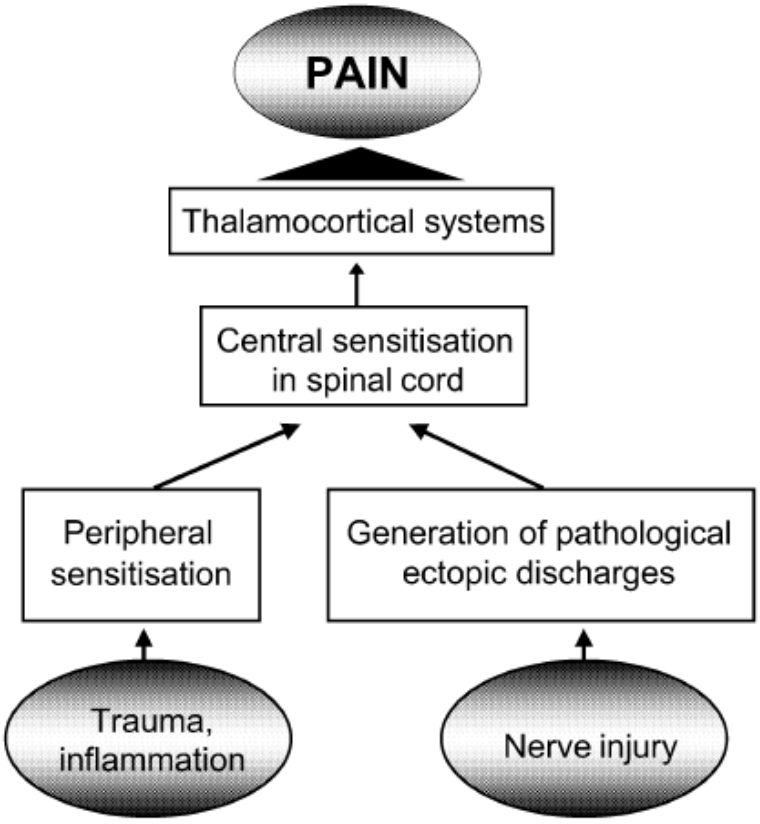



**Fig. 3:** Flowchart of the generation of pain in different pain states. Central sensitization can result both from peripheral sensitization and from pathological discharges in the afferent nerve fiber. [41]

The sensitization during inflammation is evoked by the action of inflammatory mediators on the nociceptors. Numerous inflammatory mediators are produced and

released in the course of inflammation and they cause the classical signs of inflammation i.e. swelling, redness, hyperthermia and pain. As mentioned, nociceptors express receptors for the transduction of mechanical, thermal or chemical stimuli into electrical potentials. In Fig. 4 a scheme of a sensory ending of a nociceptor is shown with a variety of ion channels and receptors. [41,42]

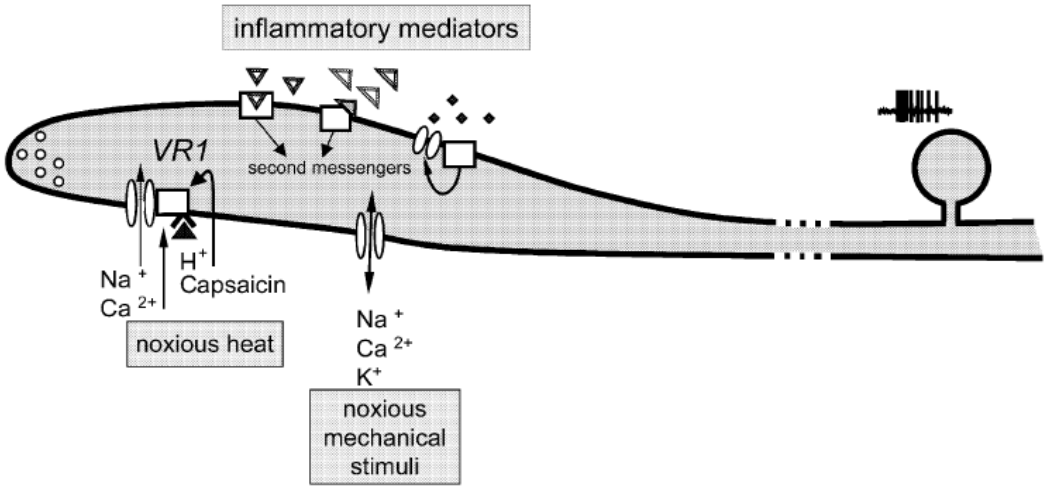



**Fig. 4:** Sketch of the enlarged ending of a nociceptor in the tissue and its axon and cell body. At bottom, the proposed ion channel that is activated by mechanical stimuli and the TRPV1 receptor complex that is activated by capsaicin, protons and by noxious heat. The circles in the cone symbolize vesicles filled with neuropeptides (substance P, CGRP) that can be released from the ending. [41]

Mechanoreception is thought to result from an opening of cation channels leading to a depolarization of the ending. During inflammation the swelling may more effectively open these channels than under normal conditions. Heat sensitivity and thermal hyperalgesia during inflammation are at least in part mediated by the activation of an ion channel that is part of the capsaicin sensitive vanilloid 1 receptor (TRPV1). This receptor is also activated by capsaicin, the compound in the hot pepper that causes pain. [43]

Inflammatory mediators (prostaglandins, bradykinin, histamine, ATP and acetylcholine and others) interact with specific receptors on the sensory endings. They either activate the neurons directly or sensitize them for other stimuli. The mediators activate second messenger cascades which then influence ion channels in the membrane. This process leads to enhanced excitability of the neuron with lowered threshold and increased action potential frequency elicited during suprathreshold stimulation.

Up to now, drug treatment interferes only with the synthesis of prostaglandins but many other important molecules are not directly targeted.

Primary afferent neurons also express receptors for neurotrophins. Neurotrophins are survival factors during the development of the nervous system but during inflammation of the tissue, the level of nerve growth factor (NGF) is substantially enhanced. By acting on the tyrosine kinase A (trk A) receptors, NGF increases the synthesis of substance P and CGRP (calcitonin related gene peptide) in the primary afferents. The release of these peptides from the endings produces neurogenic inflammation (see above). NGF may also act on mast cells and thereby, activate and sensitize sensory endings by mast cell degranulation.

The sensitization of nociceptors is rapidly induced i.e. the changes mentioned can be observed within a few minutes. If noxious stimuli persist, changes in the expression of receptors in the primary afferents are induced. For example, the expression of neurokinin 1 receptors (activated by substance P) and bradykinin receptors is enhanced in rat dorsal root ganglia and in peripheral nerve fibers during persistent inflammation. [44]

**Peripheral Mechanisms of Neuropathic Pain**

While in healthy sensory nerve fibers action potentials are generated in the sensory endings upon stimulation of the receptive field impaired nerve fibers often show pathological ectopic discharges. These action potentials are generated at the site of nerve injury or in the cell body of impaired fibers in dorsal root ganglia. The discharge patterns vary from rhythmic firing to intermittent bursts. [45,46]

Ectopic discharges do not only occur in Aβ-fibers and C-fibers but also in thick myelinated Aβ-nerve fibers that encode innocuous mechanosensory information. This has led to the idea that after nerve injury both low threshold Aβ fibers and C-fibers are involved in the generation of pain. In particular two mechanisms have been proposed as to how impaired Aβ-nerve fibers might cause pain. First, Aβ-fibers might evoke exaggerated responses in spinal cord neurons that have undergone the process of central sensitization. Second, Aβ-fibers might sprout into spinal cord layers that are usually only a target of C-fibers and thus, these fibers might activate the "wrong" neurons. These hypotheses are currently being further explored. However, recently the hypothesis was put forward that pain is not generated by the injured nerve fibers themselves but by intact nerve fibers in the vicinity of injured nerve fibers. After an experimental lesion had been introduced in the L5 dorsal root, spontaneous action potential discharges were observed in C-fibers in the uninjured L4 dorsal root. These fibers might have been affected by the Wallerian degeneration. [47]

Different mechanisms are thought to produce ectopic discharges i.e the changes in the expression of ionic channels, pathological activation of axons by inflammatory mediators and pathological activation of injured nerve fibers by the

sympathetic nervous system. At least six different types of sodium channels were found in primary afferents, two of them being tetrodotoxin (TTX)-insensitive. Sodium influx through TTX-sensitive sodium channels into the neuron inactivates it very quickly but sodium influx through TTX-insensitive sodium channels inactivates it more slowly. After nerve injury the expression of TTX-sensitive sodium channels is increased and the expression of TTX-insensitive sodium channels is decreased. These changes are thought to alter the membrane properties of the neuron, such that rapid firing rates (bursting ectopic discharges) are favored. Changes in the expression of potassium channels of the neurons have also been shown.

Injured axons of primary afferent neurons might be excited by inflammatory mediators e.g. by bradykinin, NO [46] and by cytokines. The source of these inflammatory mediators might be white bloods cells and Schwann cells around the damaged nerve fibers. The sympathetic nervous system does not activate primary afferents in normal tissue. Injured nerve fibers, however, might become sensitive to adrenergic mediators. This cross-talk might occur at different sites. Adrenergic receptors might be expressed at the sensory nerve fiber ending. A direct connection between afferent and efferent fibers (so-called ephapses) is considered. Sympathetic endings are expressed in increased numbers in the spinal ganglion after nerve injury. The cell bodies of injured nerve fibers are surrounded by “baskets” consisting of sympathetic fibers. Currently, the best treatment is the application of drugs that reduce the excitability of neurons (e.g. carbamazepine or gabapentin).

**Central Sensitization**

Pathological nociceptive input often causes central sensitization. This is an increase of excitability of spinal cord neurons. Hyper excitable spinal cord neurons are more susceptible to peripheral inputs and respond more strongly to stimulation.

Central sensitization amplifies the processing of nociceptive input and is thus an important mechanism that is involved in clinically relevant pain states (Fig. 3).

It consists of the following phenomena: (a) increase of the responses to input from the injured or inflamed region; (b) increase of the responses to input from regions adjacent to and even remote from the injured/inflamed region, although these areas are not injured/inflamed; (c) expansion of the receptive fields of the spinal cord i.e. the total area from which the neuron is activated, is enlarged. Presumably the latter accounts for secondary hyperalgesia i.e. hyperalgesia in normal tissue surrounding the injured/inflamed area (Fig. 5)

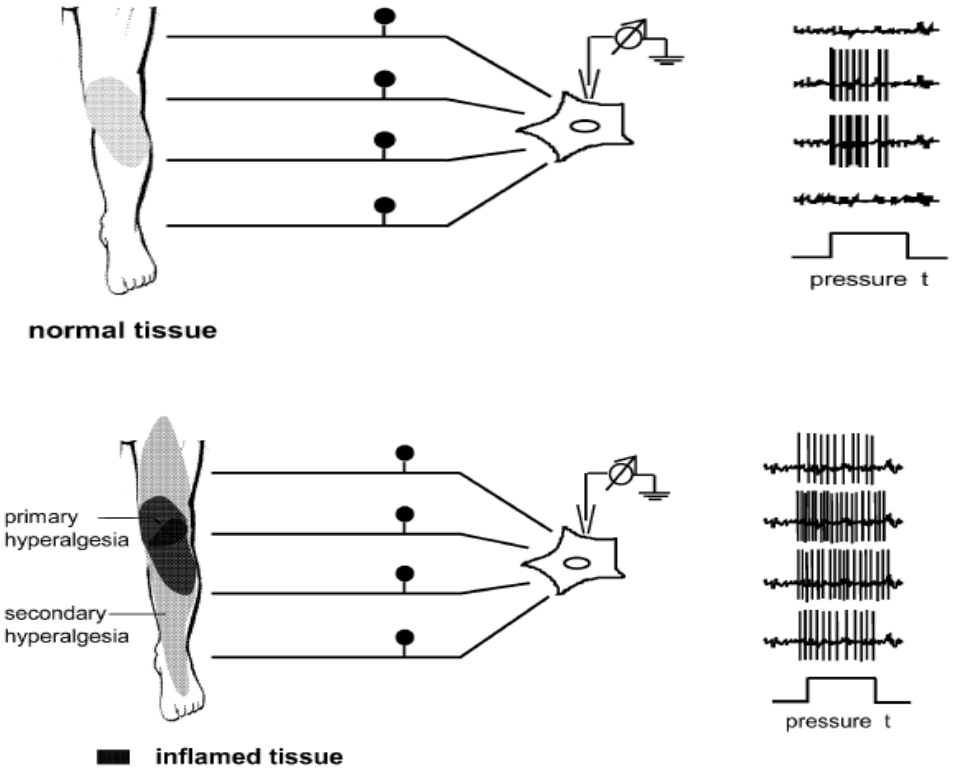



**Fig. 5:** Development of central sensitization in a spinal cord neuron. In normal tissue (top) this spinal cord neuron is activated (see action potentials at the right) only by pressure on its normal receptive field (shaded area) but not by pressure on adjacent or remote tissue (no action potentials elicited). During inflammation in the receptive field (bottom) stronger response. [48]

Fig 5. shows a model of how central sensitization could work. The top graph shows the original receptive field in the leg (hatched area) of a spinal cord neuron. Pressure on this area causes a response of the neuron. Stimulation of the surrounding adjacent area does not cause a response, although some afferent fibers from this fringe area project to the same neuron. Under normal conditions, synaptic activation by these afferents is too weak to evoke a suprathreshold response. During injury, nociceptors in the receptive field are sensitized and their increased activity causes activation and sensitization of the spinal.

When the spinal cord neuron is rendered hyper excitable, the weak inputs from the adjacent regions outside the original receptive field are sufficient to excite the spinal cord neuron hence, the receptive field shows an expansion. Another consequence of peripheral inflammation and spinal sensitization is that, in the spinal segments with input from the lesion / injured regions a higher proportion of neurons respond to stimulation of peripheral tissue. [48]

In many cases, central sensitization persists for as long as the nociceptive input persists and it disappears when the peripheral input is reduced. However, in other cases central sensitization may outlast the peripheral nociceptive process. Possibly nociceptive inputs have triggered a so-called long-term potentiation that causes a persistent increase of synaptic efficacy. Such a process could account for pain states that persist even when the peripheral nociceptive process has disappeared.

**Assessment of Pain:**

Assessment of pain can be a simple and straightforward task when dealing with acute pain and pain as a symptom of trauma or disease. Assessment of location and intensity of pain often suffices in clinical practice. However, other important aspects of acute pain in addition to pain intensity at rest needs to be defined and

measured when clinical trials of acute pain treatment are planned. If not meaningless data and false conclusions may result. Assessment of long-lasting pain and the effects of treatment is more challenging both in patients suffering pain from non-malignant causes and in patients with cancer pain. Numerous instruments have been developed for different types and subtypes of chronic pain conditions in order to assess qualitative aspects of chronic pain and its impact on function. The long list of published instruments indicates that pain assessment continues to be a challenge. Because pain is such a subjective, personal and private experience, assessing pain in patients with whom we cannot communicate well is difficult, most of all in patients suffering cognitive impairment and dementia.

**Assessment of pain intensity and Pain Relief in Acute Pain**

For acute pain caused by trauma, surgery, childbirth, or an acute medical disease determining location, temporal aspects and pain intensity goes a long way to characterize the pain and evaluate the effects of treatment of the pain condition and its underlying cause.

**Assessment of Intensity of Acute Pain**

The well-known visual analogue scale (VAS) and numeric rating scale (NRS) for assessment of pain intensity agree well and are equally sensitive in assessing acute pain after surgery and they are both superior to a four-point verbal categorical rating scale (VRS). They function best for the patient's subjective feeling of the intensity of pain right now-present pain intensity.

They may be used for worst, least, or average pain over the last 24 hours or during the last week. There are some limitations with this such as memory of pain is not accurate and often coloured by changing context factors. They are also used to assess unpleasantness of pain and to grade impact of pain on function. The indicated

ranges of the categories of the VRS scale on the NRS are approximate, with significant variation both between patients and in individuals at different time points (Fig 6): a study using simultaneous recordings of pain intensity on VAS, NRS and VRS scales in a large number of patients demonstrated the superiority of the VAS and NRS over VRS. [49]

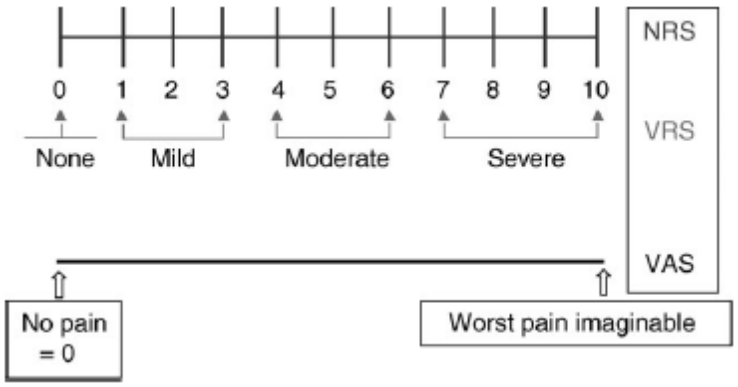



**Fig 6:** Commonly used one-dimensional pain intensity scales: the 11-point NRS, the VAS from no pain (=0) to worst pain imaginable [=10 (or 100)] and the four-point categorical verbal rating scale (VRS). [49]

A computerized simulation study from simultaneous observations of VAS, NRS and VRS, documented that the power to detect a difference in pain intensity was higher with the NRS and the VAS data compared with the VRS data. [49] This also means that if baseline pain is high before pain relief is initiated, an effective treatment will be able to cause a larger change in pain intensity than a less effective treatment.

The power of a trial to detect a large difference is high compared with a trial where the baseline pain intensity is low and even a very effective treatment will cause only a small change in pain intensity [49] (Fig. 7). When comparing a simple, weak analgesic with a potent analgesic drug in patients with only mild baseline pain, they will both relieve the mild pain and appear to be equally effective.

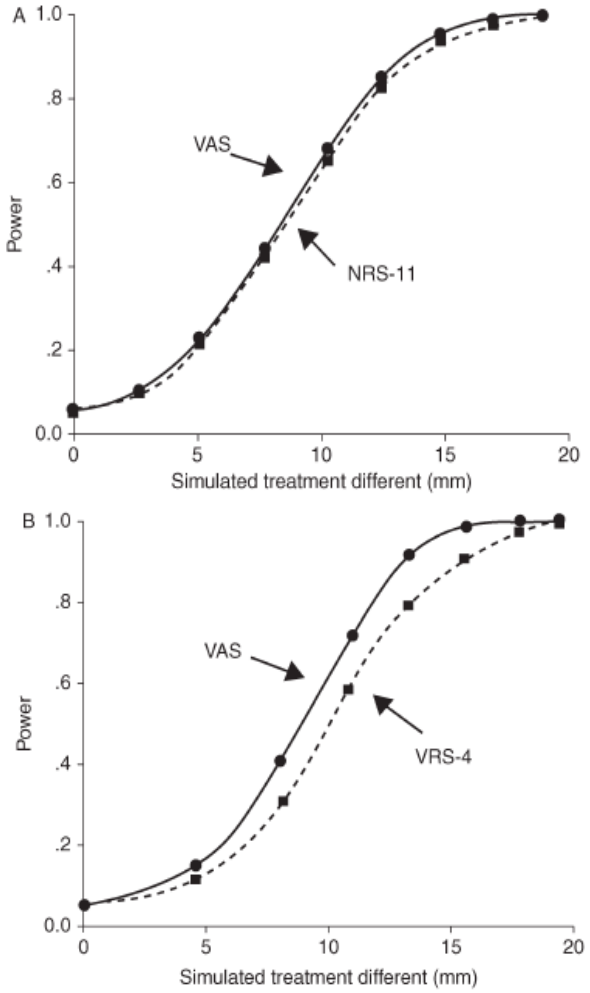



**Fig 7:** (A) The power to detect a difference in pain intensity observed with the VAS compared with simultaneously observed NRS values. Results from computer simulation of samples of 10 000 from simultaneously observed NRS and VAS pain intensity scores. The power to detect a difference increases with the magnitude of the difference in pain intensities before and after pain treatment. Differences less than about 15 (on a 0–100 VAS) or 1.5 (on a 0–10 NRS) are also clinically less meaningful. (B) The power to detect a difference in pain intensity observed with the VAS is higher than with the simultaneously observed four-point categorical VRS values. Results from computer simulation of samples from simultaneously observed VRS. [49]

The verbal categories mild, moderate and severe pain may correspond to different values on the VAS in the same patient on different occasions, whereas the NRS and VAS values generally agreed well. [49] Thus, a categorical pain scale should be used only as a coarse screening instrument and more accurate pain intensity assessment should rely on an NRS or VAS, even in routine clinical assessment.

For younger children, from about 3 years, pain scales with happy and unhappy faces are well validated for example, the faces pain scale [50] (Fig. 8).

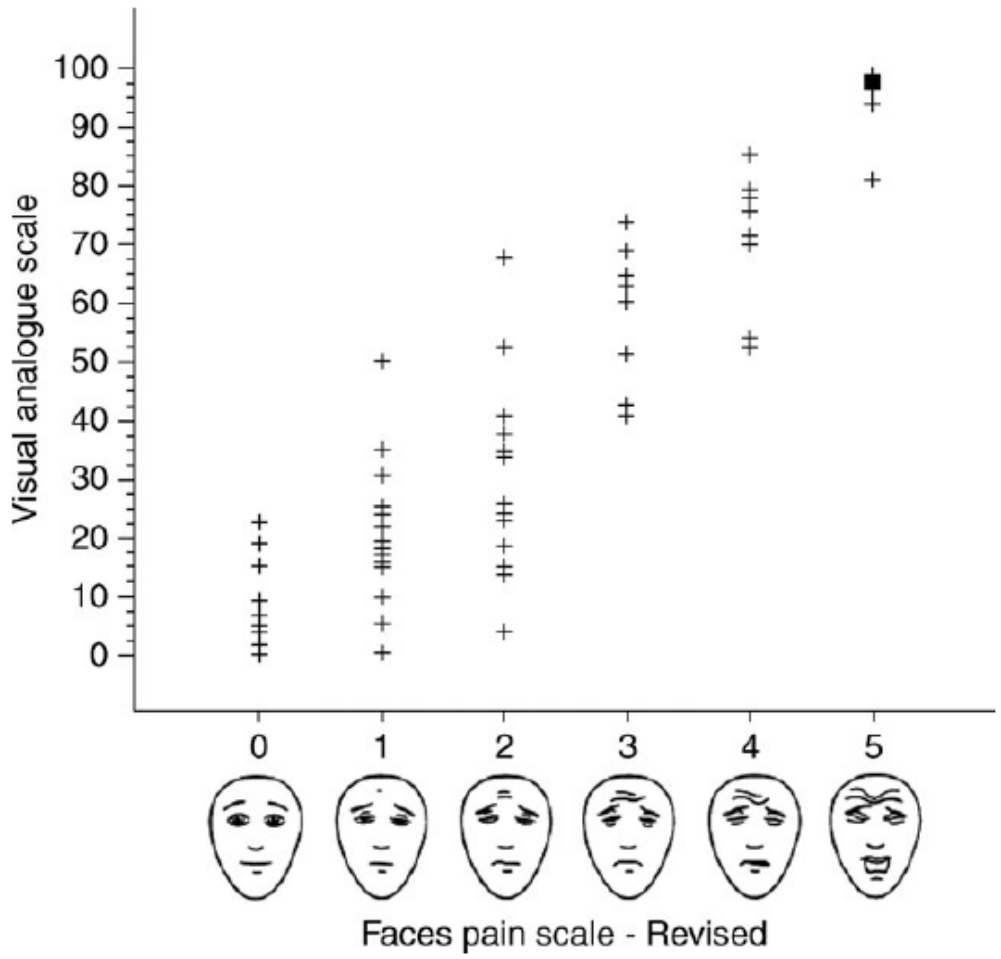



**Fig 8:** Agreement between simultaneously recorded pain intensity on a VAS and on a six-point faces pain scale: experimental pain: earlobe pinching in 4–12-yr-old children. [50]

**Assessment of Acute Pain during Movement (Dynamic Pain) is more important than pain at rest**

Assessment of the intensity of acute pain at rest after surgery is important for making the patient comfortable in bed. However, adequate relief of dynamic pain during mobilization, deep breathing and coughing is more important for reducing risks of cardiopulmonary and thromboembolic complications after surgery. Immobilization is also a known risk factor for chronic hyperalgesic pain after surgery becoming a significant health problem in about 1%, a bothersome but not negligible problem in another 10%. Effective relief of dynamic pain facilitates mobilization and therefore may improve long-term outcome after surgery. [51] Assessment of pain only at rest will not reveal differences between more potent pain-relieving methods such as optimal thoracic epidural analgesia, compared with less effective epidurals or systemic opioid analgesia. Systemic opioids can make the patient comfortable even after major surgery, when resting in bed. However, severe dynamic pain provoked by movements necessary to get the patient out of bed and mobilizing bronchial secretions by forceful coughing cannot be relieved by systemically administered potent opioids without causing unacceptable adverse effects.

**Assessment of Neuropathic Components in Acute Pain after Surgery**

Recently, awareness of the changes in central nervous system pain modulating mechanisms caused by surgical trauma has increased. The possibility that such central sensitization of the spinal cord may develop into chronic neuropathic pain after surgery in many patients makes it important that we assess and treat signs of central sensitization in acute pain. [51] Assessment of mechanical allodynia with Von Frey filaments has shown that central sensitization of pain transmission mechanisms after surgery can be suppressed by low-dose ketamine, a glutamate receptor antagonist.

The same effect occurs with glucocorticoid administration and may be the reason for a reduction of dysesthesia discomfort from 60% to 30% in patients 1 yr. after breast augmentation surgery when methylprednisolone was given before skin incision.

**Postoperative Pain**

Postoperative pain is considered a form of acute pain due to surgical trauma with an inflammatory reaction and initiation of an afferent neuronal barrage. It is a combined constellation of several unpleasant sensory, emotional and mental experience precipitated by the surgical trauma and associated with autonomic, endocrine-metabolic, physiological and behavioral responses. [52]

Pain being a subjective phenomenon is perceived only by the sufferer. In no symptom are the patients more inconsistent and unreliable as they are while describing pain. [53] The intensity of pain may not be constant even in a given individual but will wax and wane in a cyclical pattern. Women require less analgesia than men probably due to difference in neuro-endocrine mechanism of pain relief. Neurotic patients suffer greater postoperative pain than less neurotic patients. Smokers metabolize analgesics considerably faster than non-smokers and need more as a result.

**Postoperative Pain Management**

Postoperative pain is both distressing and detrimental for the patient. The management of postoperative pain involves assessment of the pain in terms of intensity at rest and activity associated pain, treatment by pharmacological and non-pharmacological means as well as monitoring induced side-effects. Besides being physically and emotionally disabling, the pain is associated with various physiological effects involving the increased perioperative stress response. The pain causes the

patient to remain immobile, thus becoming vulnerable to DVT, pulmonary atelectasis, muscle wasting and urinary retention. Poor control of postoperative pain could be due to various reasons which may include uniformed prescribing without taking into consideration the individual patient's physical status, the surgery that has been performed or the site and intensity of pain. Besides, the poor compliance of orders in administrating the analgesics prescribed and the fact that optimal pain relief is not aimed for may also contribute to the inadequate management of the pain occurring in the postoperative period. Thus, despite all efforts, there continues to be inadequate pain relief in a large majority of patients. The introduction of multimodal analgesia including opioids and non-opioids delivered through various routes, neuraxial use of local anaesthetics either alone or in combination with other drugs, nerve blocks, anti-hyperalgesics and techniques such as patient controlled analgesia and pre-emptive analgesia have greatly improved the efficacy of pain-control while minimizing the side-effects of any one modality. The recent recommendation of planning the pain services in an organized manner and implementation of Acute Pain Services (APS) has proven to be beneficial and rewarding.

**Problems Associated with Postoperative Pain**

Severe postoperative pain may have physiological consequences increasing the stress response to surgery seen as a cascade of endocrine-metabolic and inflammatory events that ultimately may contribute to organ dysfunction, morbidity, increased hospital stays and mortality. The pain often causes the patient to remain immobile thus becoming vulnerable to deep venous thrombosis, pulmonary atelectasis and muscle wasting and urinary retention. Besides restlessness caused by it may contribute to postoperative hypoxemia. The peripheral neural activation, together with central neuroplastic changes, associated with postoperative pain may in some patients

continue into a chronic pain state. [54] Patients with moderate to severe pain during postoperative period and those having undergone operation with risk of nerve damage are more likely to develop chronic pain. Treatment of acute pain by pre-emptive analgesia may prove to be beneficial in avoiding this complication.

**Pharmacological Measures:**

Include administration of drugs like opioids and non-opioids by various routes including oral, intra-muscular, intra-venous, per-rectal, epidural, intrathecal, sublingual, intra-articular, subcutaneous, etc. [54]

Use of Opioids for Postoperative pain relief has been well known. Various factors may affect the absorption of opioids and the resulting clinical response. These include route of administration, presence of hepatic or renal disease, age of the patient, concurrent administration of other drugs, hypothermia, hypothyroidism, hypovolemia, hypotension, etc.

**Patient Controlled Analgesia (PCA)**

Introduced in 1966, PCA has been used both, as a means of treating pain and a means of quantifying analgesic deficit. It has been demonstrated to be better than conventional intramuscular analgesia having lower postoperative morbidity, faster recovery of minute ventilation, rapid ambulation and early discharge of the patient, though certain other studies have failed to demonstrate a similar benefit. It is shown to provide adequate pain relief in the postoperative period without appreciable respiratory depression. [55]

The patient can administer his own analgesia and so titrate the dose to his own end-point of pain relief using a small microprocessor - controlled pump. In theory the plasma level of the analgesic will be relatively constant and side effects caused by

fluctuations in plasma level will be eliminated. Patient compliance is critical to the effectiveness of PCA and so patients should be given a pre-operative demonstration as well as explanation of the entire procedure. Choice usually depends upon availability, personal preference and experience. Certain parameters need to be set including the size of the bolus dose, the minimum time period between doses (the lock-out period) and the maximum dose allowed. Some devices permit the use of a continuous background infusion. Morphine is the most commonly used drug, in the dose of 1-1.5 mg with a lock-out period of five to ten minutes. However, regular review is needed in every case to ensure that pain relief is adequate. Besides being administered intravenously, PCA may also be given by subcutaneous and epidural routes.

**Intrathecal and Epidural Analgesia**

This may be provided either by using opioids and local anaesthetics separately or a combination of both. Intrathecal opioids are easy to administer and effective in producing analgesia without any demonstrable motor, sensory or autonomic deficit. The intrathecal potency of opioids is inversely proportional to their lipid solubility with patients remaining comfortable for 24hrs or more after a single injection of intrathecal morphine.

The epidural route may be used for administration of single bolus or as a continuous infusion of the drug. It has demonstrated advantageous physiological effects including efficient activity-dependent pain relief, improvement in protein economy, reduction in ileus as well as improvement in postoperative pulmonary function and decrease in cardiac demands. [56] Drug used may be either an opioid alone or in combination with a local anaesthetic. The latter has shown better results in relieving postoperative pain.

Side-effects encountered using these routes of delivery include nausea, vomiting, itching and urinary retention. However, most concern as with any opioid, is the possibility of respiratory depression. Other problems encountered with epidural infusions are that there is no end-point between ineffective at too low an infusion rate and systemic toxicity at too high an infusion rate. Besides in slow infusions, "break-through" pain is a problem and needs treatment with an additional epidural bolus dose.

**Opioid Analgesic Agents**

Opioids act as agonists on those stereospecific opioid receptors occurring at presynaptic and postsynaptic sites within the CNS and in the peripheral tissues. These opioid receptors are classified as μ, δ and κ receptors. Opioids mimic the actions of endogenous ligands by binding to opioid receptors, thus resulting in the activation of pain modulating systems. Opioids administered by neuraxial routes act by diffusion across the dura to gain access to μ opioid receptors on the substantia gelatinosa of the spinal cord, as well as by systemic absorption to produce effects similar to those that would follow intravenous administration of the opioid. The opioid analgesics includes: morphine, pethidine, fentanyl, sufentanil, alfentanil, tramadol, pentazocine, nalbuphine, butorphanol, buprenorphine. [57]

**Non-opioid analgesics**

**Paracetamol:**

Intravenous acetaminophen (paracetamol) was first used in the United States in 1955. [58] Although the exact mechanism of action of acetaminophen is not completely understood, many have been described. It is a centrally working nociceptor antagonist. In a study evaluating healthy children and CSF levels of acetaminophen after an intravenous infusion, they found that acetaminophen can cross

an intact blood brain barrier and allowing for a fast analgesic and antipyretic effect. [59] The many hypothesis of acetaminophen's mechanisms of action include serotonergic pathways, inhibition of prostaglandin synthesis, cannabinoid receptor stimulation and NMDA receptor inhibition.

Bioavailability is a term used to indicate the fractional extent to which a dose of a specific medication reaches its site of action. As discussed earlier, oral medications must first pass through the gastrointestinal tract and be metabolized by the liver before reaching circulation. Thus, a portion of the drug will be inactivated by the intestine and liver before it reaches the systemic circulation and subsequently decreases the bioavailability. [60] This concept of first pass metabolism can greatly alter the bioavailability of certain medications. This variability can be avoided with intravenous administration of medications because it is not dependent on gastrointestinal absorption.

First pass metabolism of oral medications by the liver can limit the amount of the drug actually makes it into the systemic circulation. Larger doses of oral medications are sometimes needed as compared to intravenous dosages. Acetaminophen is nearly completely absorbed orally with an extensive bioavailability of at least 88%.

Therefore, intravenous acetaminophen requires the same dosage as oral acetaminophen due to this extensive bioavailability. Intravenous acetaminophen however has a quicker onset and more profound analgesic effects

## TRANSVERSUS ABDOMINIS PLANE BLOCK

The anterior abdominal wall is a significant source of pain after abdominal surgery. [61] Epidural analgesia is traditionally considered the gold standard after major abdominal surgery. However, when epidural analgesia is contraindicated or is not possible the analgesic options are limited. Large doses of intravenous opiates may be needed which may be poorly tolerated. The quest to find an alternative means of providing effective analgesia led to the development of the Transversus abdominis plane (TAP) block. [62-63]

TAP block is a relatively new technique used to provide somatic analgesia after abdominal surgery. The TAP block is a regional anaesthesia technique that provides analgesia to the parietal peritoneum as well as the skin and muscles of the anterior abdominal wall. [64] First described just a decade ago and later investigated with cadaveric studies, it has undergone several modifications which have highlighted its potential utility for an increasing array of surgical procedures. [65,69] Despite a relatively low risk of complications and a high success rate using modern techniques, TAP blocks remain overwhelmingly underutilized. [66] Although the block is technically straightforward, there is inertia regarding its adoption into clinical practice. In part this may be related to limited sources for anaesthesiologists to develop a comprehensive understanding of the Transversus abdominis plane. The introduction of ultrasound has renewed the interest in this block, as the muscle layers of the abdomen are visualized with ease using ultrasound and the block itself is simple to perform with improved success.

Like other field blocks, TAP block relieves only the somatic component of the post-operative pain. The visceral component of the pain should be managed in the usual way using oral and parenteral analgesics. When performed appropriately, this

block provides good somatic analgesia for most abdominal procedures and reduces opioid requirements. [67] Therefore, inclusion of TAP block in the multi-modal approach to manage post-operative pain provides superior analgesia with reduced opioid related side effects.

**History**

Rafi first described the TAP block in 2001. He portrayed it as a refined abdominal field block, with a targeted single shot anaesthetic delivery into the Transversus Abdominis Plane (a site traversed by relevant nerve branches). This was a significant advance from earlier strategies that required multiple injections. In this approach, utilizing surface anatomical landmarks, the TAP was reached by first identifying the lumbar triangle of Petit (Fig 9), an area enclosed medially by the external oblique, posteriorly by the latissimus dorsi and inferiorly by the iliac crest. A 24-gauge, blunt-tipped, 2-inch needle was then advanced perpendicular to the skin through a preceding skin incision until a single confirmatory "pop" was appreciated. This sensation was thought to indicate proper needle depth for anaesthetic delivery. [68-69]

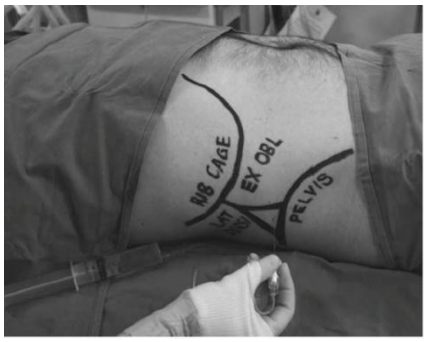



**Fig 9. Surface anatomical landmarks can be utilized to identify the triangle of Petit.**

In 2007, McDonnell *et al*. presented preliminary work on TAP blocks in cadavers and in healthy volunteers at the scientific meeting of the American Society of Anaesthesiologists. [65] Although referred to as the regional abdominal field infiltration (RAFI) technique, the authors brought forward preliminary evidence to support the anatomical basis for TAP blocks and demonstrated sensory loss spanning the xiphoid to the pubic symphysis following delivery of local anaesthetic to the TAP via the triangle of Petit. [69]

By the time the study was completed and published in 2007, McDonnell and his colleagues had already adopted the term TAP block and had demonstrated its analgesic utility in patients undergoing open retropubic prostatectomy.

**Anatomy**

The sensory nerve supply to the anterior abdominal wall is largely derived from the anterior divisions of the lower thoracic nerves (T7-T11, also called the thoraco-abdominal nerves), the sub-costal nerve (T12) and the first lumbar nerve.

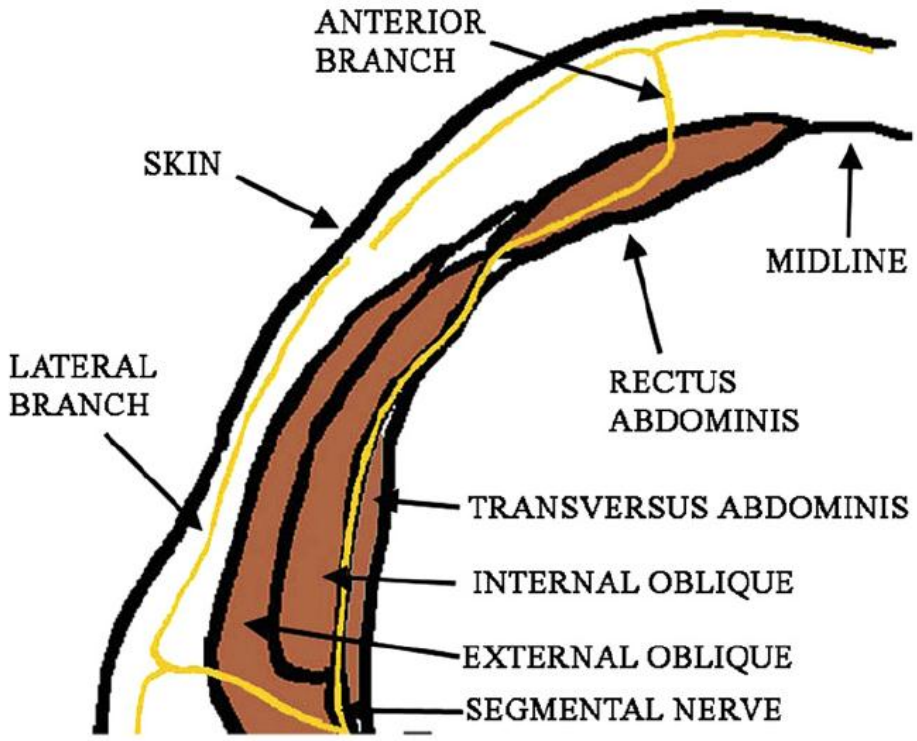



**Fig. 10:Cross sectional anatomy showing the nerves and muscles of the anterior abdominal wall**

A small area near the xiphoid process is supplied by T6. The thoracic nerves, after leaving the inter-vertebral foramina, divide into anterior and posterior divisions.

The posterior division divides further into medial and lateral branches and supplies the posterior trunk. The anterior division traverses along the intercostal space, along with the intercostal vessels in the intercostal groove (Fig. 10).

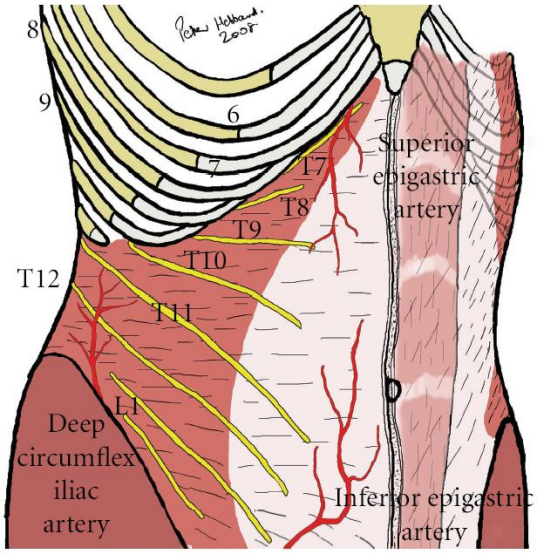



**Fig. 11: Typical distribution of nerves in the TAP**

Along its course, the anterior divisions of the thoracic nerves give lateral branches near the mid-axillary line and continue forward. Towards the end, the anterior divisions of the thoracic nerves pierce the rectus sheath and terminate as the anterior cutaneous nerves of the abdominal wall. [70] The thoraco-abdominal nerves, along with the sub-costal nerve and the first lumbar nerve (referred to as iliohypogastric and ilio-inguinal nerves) supply the skin of the entire antero-lateral abdominal wall, including the groin.

In the abdominal wall, the anterior division of the thoracoabdominal nerves traverses in the anatomic plane between the internal oblique and transversus abdominis muscles. [70] In this plane, there is extensive branching and cross-communication between the nerves. This plane is called the Transversus abdominis plane (TAP). This plane is roughly triangular in shape. The anterior border of the TAP is bounded by the linea semilunaris, formed by the aponeurosis of the internal oblique muscle. This is reinforced anteriorly by the external oblique aponeurosis and posteriorly by the transversus abdominis aponeurosis.

The linea semilunaris extends from the tip of the 9th costal cartilage to the pubic tubercle. The superior border of the TAP is the sub-costal margin, extending from the cartilages of the 9$^{th}$ to 12th ribs and continuing into the anterior border of the latissimus dorsi muscle and inferior lumbar triangle of Petit. The inferior border is formed by the inguinal ligament and the iliac crest. Local anaesthetic deposited in this plane blocks the lower thoracic nerves and the first lumbar nerve to provide useful analgesia of the anterior abdominal wall. [71]

**Human volunteer and cadaver studies**

Several authors have performed studies using human volunteers and cadavers to demonstrate the TAP and the spread of injected dye within the TAP. McDonnell and colleagues (2007) injected methylene blue into the TAP of un-embalmed cadavers using the 'two-pop' anatomic method via the inferior lumbar triangle of Petit. Dissection of the abdominal wall after embalming showed the spread of dye from the iliac crest to the costal margin in the TAP.

Injection of local anaesthetic and contrast solution in healthy volunteers (lignocaine and radio-opaque dye in three volunteers and bupivacaine mixed with MRI contrast in three volunteers) led to a sensory block from T7 to L1. Both CT and MRI scans after injection showed the distribution of contrast in the TAP extending from the iliac crest to the costal margin. Unlike McDonnell *et al*. (2007) Tran *et al*. (2009) [65,72] studied the spread of aniline dye injected under ultrasound guidance into the TAP of cadavers. In contrast to the findings by these two, Walter *et al.* found that the aniline dye only fixed T10 L1 nerves. [73] This inconsistency could be due to the differences in the technique between the two studies (ultrasound vs landmark, time allowed for the dye to spread, location of injection etc.). Although there is inconsistency with regards to the extent of spread, these two studies clearly

demonstrate the existence of this potential fascial plane and confirm the rostral and caudal spread of the injectate.

**Epidural analgesia vs TAP blockade**

Epidural analgesia is traditionally considered to be the analgesic technique of choice for abdominal procedures as it offers better analgesia, consistently superior results and improved patient comfort. [63] However, epidural analgesia may be technically difficult in patients with spinal abnormalities, morbid obesity and following spinal surgery. Similarly, epidural analgesia is contraindicated in the presence of systemic infection and coagulopathy. It is this group of patients that are best served with TAP block. In addition, when a previously working epidural fails for any reason or when the catheter has to be removed, TAP blocks can be useful as part of multi-modal analgesic regime.

Moreover, in a large number of abdominal procedures (e.g. appendicectomy, hysterectomy), the risks and side effects of epidural analgesia far outweigh the benefits. In such situations, post-operative pain management usually involves a balanced technique consisting of non-steroidal anti-inflammatory drugs and patient-controlled administration of opiates. Here, TAP blockade reduces the opiate requirement thereby minimizing potential side effects of opioids such as post-operative nausea and vomiting, sedation and constipation. However, TAP blockade serves to relieve only the somatic component of the post-operative pain and additional analgesia using oral or parenteral analgesics is needed to treat the visceral component of pain unlike epidural analgesia which covers both the visceral and the somatic components.

**TAP block methods/techniques**

**The landmark technique**

The original description of an abdominal field block by Rafi (2001) was a landmark method via the inferior lumbar triangle of Petit. [68,71] The triangle of Petit is bounded anteriorly by the external oblique muscle, posteriorly by the latissimus dorsi muscle and inferiorly by the iliac crest. This triangle is felt as a dip when a finger palpates posteriorly from the anterior superior iliac spine over the iliac crest (Fig. 11).

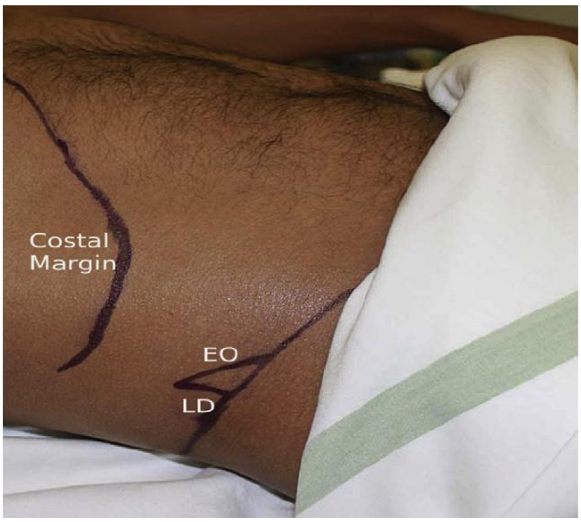



**Fig. 12: Inferior Triangle of Petit** (EO e External Oblique; LD e Latissimus Dorsi)

Occasionally, the anterior edge of the latissimus dorsi is easily palpated in thin individuals. The bed of this triangle is formed by external and internal oblique fascia. This inferior triangle of Petit gives easy access to the TAP, as a needle inserted at this site will traverse through the two fasciae only, giving two distinctive palpable pops before reaching the transversus plane (Fig. 12).

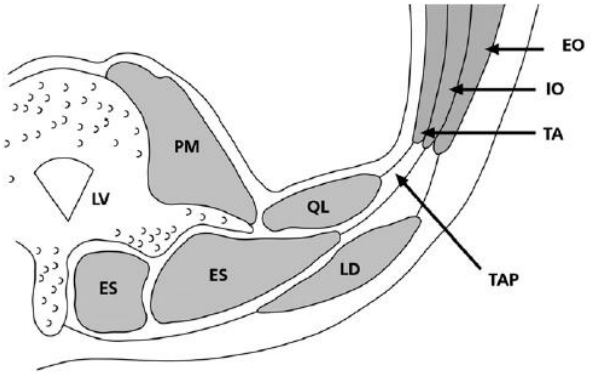



**Fig. 13:** Line diagram depicting the transverse section at the level of inferior triangle of Petit LV - Lumbar vertebra; PM - Psoas Major; EO - External oblique; IO - Internal Oblique; TA - Transversus abdominis; LD - Latissimus Dorsi; ES - Erector Spinae; QL - Quadratus Lumborum; TAP - Transversus abdominis plane

McDonnell (2004) assigned the current name to this block and demonstrated its use in patients who underwent open prostatectomy. If local anaesthetic is deposited in the right plane, in thin patients, a 'flank bulge sign' may be observed. This sign is an indication of local anaesthetic in the TAP leading to weakness of the muscles, thus producing a distinctive bulge above the iliac crests.[69]

Although easy to perform, the landmark method has several shortcomings. The inferior lumbar triangle of Petit is not always present in all individuals and its anatomic location may be inconsistent. [71] Ultrasound imaging has also revealed that the external oblique and latissimus dorsi muscles may overlap, leading to four muscle layers in this region. [73] This might explain the failure of the block when performed using the anatomic landmark technique. Therefore, ultrasound guidance is recommended to achieve an improved success rate.

**Ultrasound-guided posterior TAP block**

The anatomical inconsistencies of Pettit's triangle were highlighted by Walter and colleagues, [73] who suggested the use of ultrasound to visualize the transversus abdominis plane. A high frequency ultrasound probe placed transversely, approximately midway between the iliac crest and costal margin [74] (Fig. 13), shows the three muscle layers of the abdominal wall (Fig. 14).

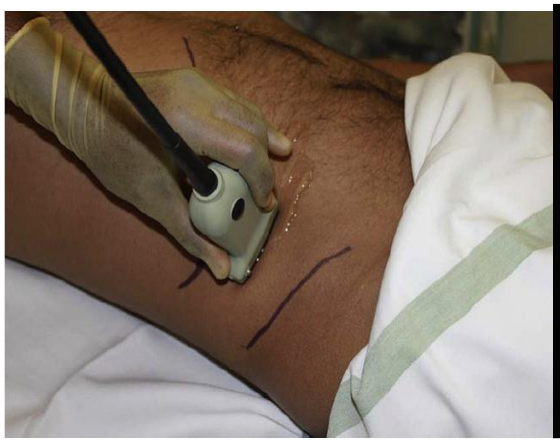


Fig. 14: Probe position for a posterior TAP block

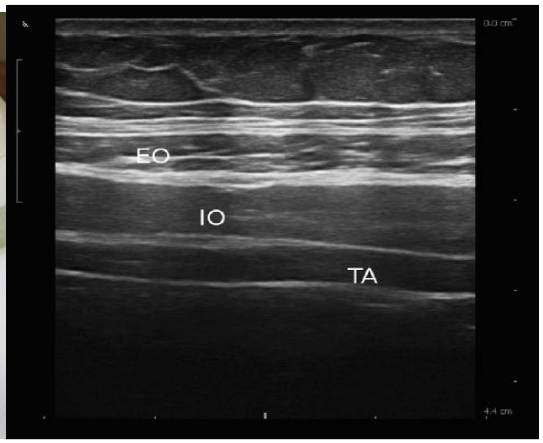



Fig. 15: Picture showing the sonoanatomy of the posterior TAP block EO – External Oblique; IO - Internal Oblique; TA - Transversus abdominis.

A regional block needle or an epidural needle can then be inserted anteriorly and slightly away from the probe and carefully advanced until it reaches the transversus plane. In this 'in-plane' technique (Fig. 15), the needle and its tip are visualized throughout the procedure, as it enters the transversus plane after piercing the fascial layer below the internal oblique muscle. A small volume of local anaesthetic is then injected to confirm the position of the needle before the full dose. The spread of local anaesthetic solution (Fig. 16) can then be visualized as a 'tear drop expansion'. If required, further hydro dissection may be performed or a catheter inserted to provide continuous instillation of local anaesthetic. Using this approach, both sides can be blocked with the operator standing on one side of the patient, alleviating the need for the operator to move from one side to the other to perform the block.

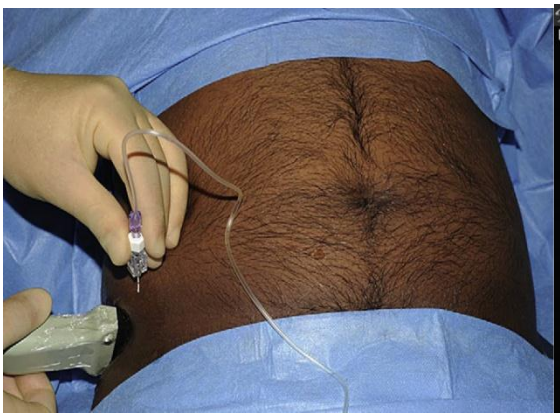


**Fig. 16:** Picture showing the needle position in relation to the ultrasound probe in an inplane technique.

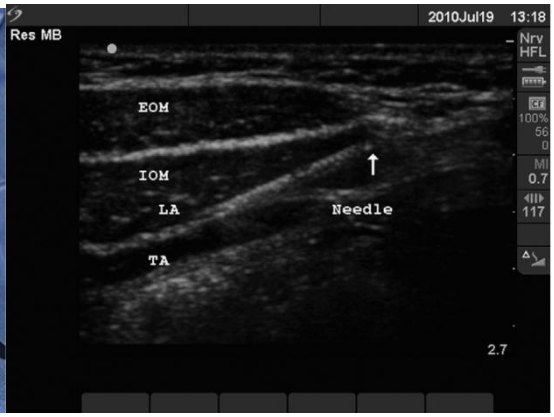



**Fig. 17:** Local anaesthetic injection producing the tear drop spread inside TAP EOM - External oblique muscle; IOM - Internal oblique muscle; TA - Transversus abdominis; LA - Local anaesthetic solution.

## Ultrasound-guided sub-costal TAP block

Originally described by Hebbard *et al*. (2008) this block is becoming increasingly popular for providing analgesia after upper abdominal procedures. [74] Using this approach, the ultrasound probe is placed parallel and close to the costal margin (Fig. 17). In this position, the rectus abdominis and transversus muscles are easily visualized. The transversus abdominis muscle is seen originating from the posterior aspect of the rectus muscle and the TAP is well-defined in this area (Fig. 18).

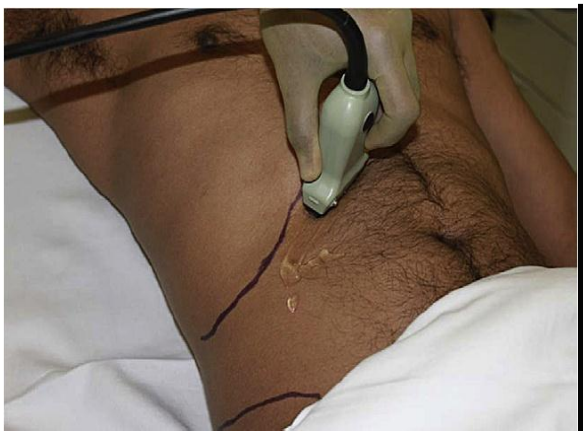


**Fig. 18:** Probe position for sub-costal TAP block

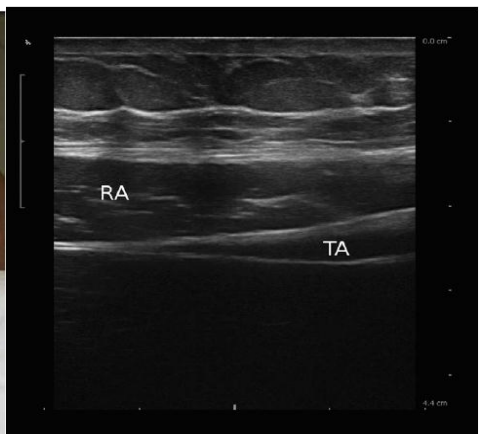



**Fig. 19:** Picture showing the sonoanatomy of the sub-costal TAP block RA e Rectus abdominis; TA e Transversus abdominis.

A 100-mm regional block needle or a Tuohy needle is carefully passed from a point close to the xiphoid process towards the probe. The needle should always lie parallel to the costal margin and should be advanced carefully until it reaches the transversus plane. With hydro-dissection, the needle can be advanced further in the plane and a catheter can be inserted to provide continuous analgesia. This block provides good analgesia for upper abdominal wounds. With this block, the lumbar segment (L1) is frequently spared. [74] Recently, some authors have described a new approach for the sub-costal TAP block called the oblique sub-costal block. In a brief technical report, they claim that the oblique sub-costal TAP block produces much wider sensory blockade than the anterior sub-costal block. [75]

**TAP catheters**

A single-shot TAP block can produce clinically-useful analgesia for up to 24 h after surgery. For effective analgesia for longer duration, a catheter must be inserted into the transversus plane and local anaesthetic should be injected at regular intervals (e.g. every 12 h) or infused continuously. [75]

Catheter insertion is generally performed under ultrasound guidance. An 18-g Tuohy needle can be used to enter the transversus plane and an epidural catheter can then be inserted into the plane.

**Surgeon-Assisted Approaches:**

While the majority of published literature on TAP blocks is purely from the perspective of anaesthesiologists, a growing number of reports have demonstrated that surgeons can help to facilitate these blocks. Chetwood *et al*. described a laparoscopic-assisted technique wherein a classic TAP block (based on anatomical landmarks) was performed while the injection area is observed with an intra-abdominal laparoscopic camera. [76] A peritoneal bulge at the area of injection was seen after local anaesthetic

was delivered within the TAP and this visual served as the desired endpoint for this technique. Such direct visualization may help to avoid intraperitoneal injection, one of the major potential risks of the TAP block. More recently, a surgical TAP block utilizing a trans-peritoneal approach was also described. Performed intraoperatively, a blunt tipped block needle was advanced from inside the abdominal wall through the parietal peritoneum, then the transversus abdominis muscle and into the TAP as indicated by a single pop sensation. [64,78] In addition, Araco *et al*. described a surgical TAP block in which blunt dissection through the external and internal oblique muscles leads to injection of local anaesthetic into the TAP under direct visualization. [79]

**Extent of analgesia**

Earlier studies by McDonnell *et al*. (2007) [65] showed that LA injection into the TAP resulted in a sensory block from T7 to L1. Many case reports and studies since been published show a block from T10 to L1, with a posterior TAP injection. If the sub-costal approach is used the block extends from T7 to T12. Hebbard *et al*. (2007) [74] conducted an audit comparing the block height following classical and subcostal TAP blocks. For upper abdominal incisions, a sub-costal TAP block is more appropriate than a posterior TAP block. For all lower abdominal procedures, a posterior TAP block will provide adequate analgesia and will reduce opioid requirements in the post-operative period. It should be remembered that a TAP block provides only somatic analgesia. The visceral pain needs to be treated in the usual way with standard analgesia. It is the reduction in opioid requirements (up to 70% reduction in the morphine requirement in some studies) [71] and the associated decrease in side effects such as nausea and vomiting, respiratory depression, that make TAP block an attractive technique.

While local anaesthetic's volume, concentration and delivery method differ between studies, these regimens have not yet been compared against each other. Therefore, there is insufficient evidence to support any particular combination in lieu of another. When duration of analgesia is an issue, there is good evidence to support using TAP catheters. This technique was first described in 2009 in a small case series. Two years later, the same group showed similar pain control between epidural and TAP catheter analgesia in a randomized study. In both reports, an intermittent bolus protocol was used. It remains unclear whether the use of a continuous infusion offers any advantage over intermittent blousing for TAP catheters. [75]

**Indications**

A posterior TAP block can be used to provide post-operative analgesia for any lower abdominal surgery (e.g: total abdominal hysterectomy, appendicectomy and caesarean section). A subcostal TAP block is useful to provide analgesia for upper abdominal procedures and full midline laparotomy wounds.[76]

**Lower abdominal surgery**

A unilateral posterior TAP block provides good pain relief and reduces the opioid analgesic requirement after appendicectomy and inguinal herniorrhaphy,[81] conducted a randomized controlled trial comparing ultrasound-guided TAP block with standard analgesia following open appendicectomy and found that TAP blocks significantly reduces the post-operative opioid requirement, pain scores and post-operative nausea and vomiting in the first 24 hours after surgery. Investigators in Copenhagen are currently conducting a randomized controlled trial comparing TAP block, ilio-inguinal block and local infiltration with saline controls in patients undergoing inguinal herniorrhaphy. The study results will hopefully help us choose

the right analgesic technique to provide optimal post-operative pain relief after open herniorrhaphy.

Bilateral posterior TAP blocks provide useful post-operative analgesia after abdominal hysterectomy, caesarean section, [82] and open retropubic prostatectomy. Carney *et al*. (2008) [62] conducted a prospective randomized study comparing the analgesic efficacy of TAP blocks using local anaesthetic with TAP blocks using saline in patients undergoing total abdominal hysterectomy. They concluded that local anaesthetic TAP blocks reduce the opioid requirements in the post-operative period for up to 48 hours. Ultrasound-guided TAP blocks are also effective in reducing pain following anterior iliac crest bone harvest in major orthopedic surgery. [83]

**Obstetric patients**

Two recent studies compared TAP blocks with standard treatment for post-operative pain relief following caesarean section under spinal anaesthesia. Belavy *et al*. (2009) [90] used fentanyl with bupivacaine for spinal anaesthesia and found that TAP block reduces the opioid requirement in the post-operative period, but there was no significant difference in the pain scores between the TAP and non-TAP groups.

Costello *et al*. (2009) [92] used morphine in spinal anaesthesia along with bupivacaine and found no beneficial analgesic effect from TAP blocks in patients receiving intrathecal morphine for caesarean section. In the UK, intrathecal diamorphine is routinely used along with bupivacaine in patients undergoing caesarean section under spinal anaesthesia. Diamorphine itself provides excellent post-operative analgesia for up to 18-24 hours in most cases. Thus, there is no possible advantage in using additional single-shot TAP block in patients undergoing caesarean section under spinal anaesthesia where intrathecal diamorphine has been administered. If TAP block is used as an additional technique in patients where epidural or spinal anaesthesia has

also been used the risk of local anaesthetic toxicity must also be borne in mind. However, in patients undergoing caesarean section under general anaesthesia, it will be an attractive option as it reduces the need for opioids and improves pain scores in the postnatal period.

**Laparoscopic surgery**

A prospective randomized study [84] compared TAP blocks with standard analgesia in patients undergoing laparoscopic cholecystectomy and found that TAP blocks provide effective analgesia and reduce both the intra-operative and post-operative opioid requirement. A case series reported by Mukthar *et al.* (2009) confirmed the findings of reduced analgesic requirements of in their studies with TAP block for renal transplant recipients. [85]

Currently, posterior TAP blocks are performed and found to be useful in laparoscopic procedures such as cholecystectomy, appendicectomy and herniorrhaphy. If the surgeon uses a supraumbilical port for cholecystectomy, a sub-costal TAP block should be considered.

**Paediatric and neonatal surgery**

Fredrickson *et al*. published two separate case series on TAP blocks in children and neonates. [86] Both of these publications strongly suggest that ultrasound-guided TAP blocks are feasible in children and neonates. The authors have successfully performed TAP blocks in neonates undergoing complex major procedures such as exomphalos major repair. This early success is likely to lead to further investigations comparing TAP blocks with traditional analgesic techniques in neonates. When performing TAP blocks in neonates and small children extreme care should be taken while advancing the needle as the liver surface may be less than 1 cm deep from the skin.

**TAP block in the intensive care unit**

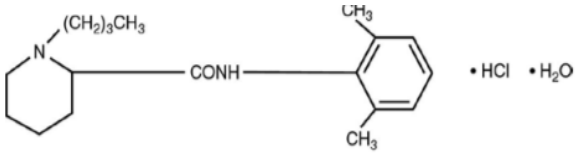
Niraj *et al*. (2009) [75] have successfully performed sub-costal TAP blocks, in the intensive care unit to provide analgesia and to facilitate chest physiotherapy in patients who underwent upper abdominal procedures. Although this was a case series, it is possible that TAP blocks performed in the intensive care setting have the potential to reduce morbidity and widen the analgesic options available to treat this group of patients where epidural analgesia may frequently be contraindicated because of coexisting clotting abnormality or systemic sepsis.

**Other indications**

Continuous TAP blocks have been used successfully in renal transplant recipients. They can also be used to provide analgesia after open and laparoscopic nephrectomy and laparoscopic prostatectomy. [76] Recent reports are also emerging describing the use of continuous TAP blockade for providing analgesia following thoraco-abdominal injury sustained in the battlefield in patients with coagulopathy associated with massive blood loss. Portable ultrasound machines were used in the austere battlefield hospital setting. [88]

## PHARMACOLOGY OF BUPIVACAINE

Bupivacaine was synthesized in Sweden by AF Ekenstam in 1957. Bupivacaine hydrochloride is 1-Butyl-2'/6'-pipecoloxylidide monohydrochloride, monohydrate, a white crystalline powder that is freely soluble in 95% ethanol, soluble in water and slightly soluble in chloroform or acetone. It has the following structural formula




Epinephrine is (-)-3,4-Dihydroxy-α-[(methylamino)methyl] benzyl alcohol. It has the following structural formula:

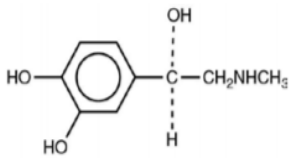



**Fig.20A:** Structural formula of bupivacaine.

Molecular weight of its chloride salt is 325. melting point is $258^0$C. Bupivacaine hydrochloride is related chemically and pharmacologically to aminoacyl local anaesthetics. It is a homologue of mepivacaine and is chemically related to lidocaine. All three of these anaesthetics contain an amide linkage between the aromatic nucleus and amino or piperidine group. They differ in this respect from the procaine- type local anaesthetics, which have ester linkage.

Bupivacaine Spinal is packaged as sterile, hyperbaric solution for subarachnoid injection (spinal block). Each 1ml of bupivacaine spinal contains 5 mg of bupivacaine hydrochloride anhydrous and 80 mg dextrose anhydrous. Bupivacaine spinal does not contain any preservatives.

**Mechanism of Action**

Like all local anaesthetics, Bupivacaine causes a reversible nerve conduction blockade by decreasing nerve membrane permeability of sodium. The binding of local anaesthetic to sites on voltage gated $Na^+$ channel prevents opening of channels by inhibition of conformational changes. This causes decrease in the rate of membrane depolarization, thereby increasing the threshold for electrical excitability. The blockade affects all nerves in the following sequence: autonomic, sensory and motor with effects diminishing in reverse order. Loss of nerve function clinically is as follows- pain, temperature, touch, proprioception and skeletal muscle tone. Direct nerve membrane penetration is essential for effective anaesthesia. During onset and recovery from local anaesthesia, impulse blockade is incomplete and partially blocked fibres are further inhibited by repetitive stimulation, which produces an additional use dependent binding to $Na^+$ channels.

**Pharmacokinetics**

Bupivacaine is a weak base and at physiologic pH, less than 50% of the drug exists in a lipid soluble non-ionized form. Absorption depends on the dose, concentration, site of administration and tissue vascularity.

The ultimate plasma concentration of local anaesthetic is determined by the rate of tissue absorption, distribution and rate of clearance of the drug. The tissue distribution of a drug in turn depends upon the tissue blood flow and lipid solubility of drug. The patient related factors such as age, cardiovascular status and hepatic function also influence the absorption and resultant plasma concentration. Lungs are capable of extracting bupivacaine from circulation. This limits the concentration of the drug that reaches the systemic circulation. This first pass pulmonary extraction is dose dependent and can be blocked by propranolol. Propranolol reduces plasma

clearance of the drug presumably by decreasing hepatic blood flow and competitive blockade at receptor site. After injection for peripheral nerve blocks, peak blood levels are achieved in 30-40 minutes. Bupivacaine's onset of action is rapid (1-10 minutes) and significantly longer than other local anaesthetics (3-9 hours). Bupivacaine is distributed to all tissues, with a high concentration in well perfused organs such as liver, lung, heart and brain.

**Pharmacokinetic properties of bupivacaine**

| Parameter | values |
|---|---|
| 1. Potency (as compared to lignocaine) | 4 |
| 2. pK | 8.1 |
| 3. protein binding | 95% |
| 4. Non-ionized fraction | 15% |
| 5. Lipid solubility | 2.8 |
| 6. Volume of distribution | 73 |
| 7. Clearance | 0.47 |
| 8. Elimination half time (min) | 210 |

**Metabolism**

Local amide anaesthetics undergo varying rates of metabolism by the microsomal enzymes in the liver. Initial step is conversion of amide bae to amino carboxylic and a cyclic aniline derivative. For complete metabolism additional steps such as dealkylation and hydroxylation are required. Possible pathways for

metabolism of bupivacaine include aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation. Only the N-dealkylated metabolite N-desbutyl-bupivacaine has been measured in urine or blood after epidural or spinal anaesthesia. The mean total urinary excretion of bupivacaine and its metabolite accounts for >40 % of total anaesthetic dose. Alpha 1 glycoprotein I the most important protein binding site for bupivacaine and its concentration is increased in many clinical situations, including post-operative trauma.

**Side Effects**

Principal side effects related to local anaesthetics use are allergic reactions and systemic toxicity due to excessive plasma and tissue concentrations of the drug, most common cause being accidental intravascular injection of drug. Allergic reactions are very rare and may be due to preservative methyl paraben. Occurrence of rash, urticaria and laryngeal oedema, with or without hypotension and bronchospasm is highly suggestive of an allergic reaction.

Systemic toxicity of bupivacaine is due to an excess in plasma concentration of the drug. Plasma concentration of local anaesthetics is determined by rate of drug entrance into the systemic circulation relative to their redistribution to inactive tissues and clearance by metabolism. Systemic toxicity of bupivacaine involves the central nervous system and cardiovascular system.

**CNS Toxicity**

At low concentrations of bupivacaine there is numbness of the tongue and circumoral tissues. On further increase in plasma concentration there is vertigo, tinnitus, restlessness and difficulty focussing. Further increase in concentration leads to slurred speech and skeletal muscle twitching followed by seizures (tonic clonic) at

a concentration of 1 mcg/mil. The seizures are classically followed by central nervous system depression accompanied by hypotension and apnoea. The explanation for the local anaesthetic seizures is as follows:

a) Selective depression of the inhibitory cortical neurons by the drug.
b) Inhibition of the release of neurotransmitters like gamma amino butyric acid (GABA)

There is an inverse relationship between PaCO2 levels and seizure threshold. This is due to increased cerebral blood flow and increased delivery of drug to brain. A decrease in arterial pH also decreases the seizure threshold probably due to ion trapping and subsequent decrease of drug in the brain. Treatment includes mechanical ventilation and benzodiazepines for supressing seizures.

**CVS Toxicity**

Local anaesthetics may produce profound hypotension due to relaxation of arteriolar vascular smooth muscle and direct myocardial depression. Hypotension reflects both decreased systemic vascular resistance and cardiac output. Part of cardiac toxicity that results from high plasma concentrations of local anaesthetic occur because of these drugs also block cardiac sodium channels. Cardio toxic plasma concentration of bupivacaine is 8-10 mcg/ml. When the plasma levels are excessive, sufficient cardiac sodium channels are blocked so that conduction and automacity is adversely depressed manifesting as prolongation of P-R interval and QRS complex on ECG. Effects on the calcium ion and potassium ion channels and local anaesthetic induced inhibition of cyclic adenosine monophosphate (cAMP) production may also contribute to cardiac toxicity. Accidental IV injection of bupivacaine may result in precipitous fall in blood pressure, cardiac dysarrythmias and atrioventricular heart block. After accidental IV administration, the protein binding sites for bupivacaine are

quickly saturated, leaving a significant amount of unbound drug available for diffusion into conducting tissues of the heart. Pregnancy may increase sensitivity to cardio toxic effects of bupivacaine. Threshold of cardiac toxicity produced by bupivacaine may be decreased in patients treated with drugs which inhibit myocardial impulse propagation (beta blocker, digitalis and calcium channel blocker). In presence of propranolol, cardiac dysarrythmias occurred at plasma bupivacaine concentrations of 2-3 mcg/ml. Epinephrine and phenylephrine increase bupivacaine concentration of 2-3 mcg/ml. Epinephrine and phenylephrine increases bupivacaine induced toxicity. Dissociation of highly lipid soluble bupivacaine from sodium channel receptor sites is slow, accounting for the drug's persistent depressant effect on cardiac action potential and subsequent toxicity. R enantiomer of bupivacaine is more toxic than S enantiomer. Tachycardia can enhance frequency dependent blockade of cardiac sodium channels by bupivacaine. Cardiac resuscitation is difficult in bupivacaine induced cardio vascular collapse.

**Indications**

1. Infiltration anaesthesia
2. Intravenous regional anaesthesia
3. Peripheral nerve blockade
4. Central neuraxial blockade

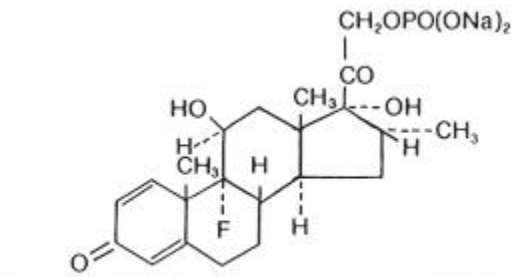
**Dosages**

The dose of local anaesthetics differ with the anaesthetic procedure, area to be anaesthetized, vascularity of tissues, number of segments to be blocked, duration of anaesthesia and individual tolerance. Maximum dosage limit:2-3 mg/kg body weight.


**Fig 20B:** Standard 0.5% vial used in our hospital

**Pharmacology of Dexamethasone**

Dexamethasone Sodium Phosphate Injection, IP is a water-soluble inorganic ester of dexamethasone which produces a rapid response even when injected intramuscularly. It occurs as a white to creamy white powder which is exceedingly hygroscopic, is soluble in water and its solutions have a pH between 7.0 and 8.5. It has the following structural formula:




$C_{22}H_{28}FNa_2O_8P$ M.W. 516.41

Cortisol is a glucocorticoid released by the adrenal gland which helps maintain homeostasis by regulating numerous enzymes throughout the body. During periods of stress, cortisol plays an important role in increasing blood glucose levels and elevating blood pressure. Clinically cortisol and its derivatives are often used for their immunosuppressive properties. They are also important for patients with adrenal deficiencies.

**Synthesis:** The limbic system ultimately controls cortisone production by regulating release of corticotropin releasing hormone (CRH) from the hypothalamus via serotoninergic, dopaminergic and cholinergic neurons. CRH stimulates release of adrenocorticotrophic hormone (ACTH) from the anterior pituitary. ACTH activates adenylate cyclase in the adrenal cortex. The resulting cAMP activates protein kinase which enhances cholesterol esterase activity. Cholesterol esterase increases the amount of cholesterol available to mitochondria where cortisone is made from cholesterol. ACTH also stimulates the conversion of cholesterol o pregnenolone, the first step in steroid synthesis.

**Transport to tissues:** Cortisol is secreted into the blood stream where it is 90% bound to cortisol-binding globulin (CBG) and albumin, Active cortisol (remaining 10%) freely diffuses into cells where it exerts its actions via intracellular receptors. CBG plays an important role in regulating cortisol delivery and clearance. Dexamethasone has low affinity for CBG. It is therefore more potent pharmacologically because a greater fraction is free in the bloodstream.

**Metabolism:** In the liver, cortisol is converted to dihydro and tetrahydro- derivatives which are subsequently conjugated with glucuronic acid of sulfates. The conjugates are water soluble and are rapidly excreted by the kidneys. Liver failure leads to decreased metabolism and decreased CBG synthesis. Thus, greater amounts of unbound (active) cortisol is present in the blood. This leads to hypercortism. Likewise renal failure increases the half-life of cortisol.

**Clinical indications:** Replacement therapy in adrenocortical insufficiency, salt-losing forms of congenital adrenal hyperplasia, autoimmune diseases, arthritis, asthma, dermatitis, cancer and sarcoidosis.

**Undesirable Effects:** Adrenal suppression (insufficiency upon withdrawal), Cushing's Syndrome (osteoporosis, skin atrophy, central fat distribution, abnormal glucose tolerance, behavioral abnormalities), suppression of somatic growth, osteopenia and bone fractures.

## CLINICAL PHARMACOLOGY

Dexamethasone sodium phosphate injection has a rapid onset but short duration of action when compared with less soluble preparations. Because of this, it is suitable for the treatment of acute disorders responsive to adrenocortical steroid therapy. Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties and are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs, including dexamethasone, are primarily used for their potent anti-inflammatory effects in disorders of many organ systems. Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli. At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium-retaining property of hydrocortisone and closely related derivatives of hydrocortisone.


**Fig 20C:** standard vial (2 ml) 4mg/ml used in our hospital.

# REVIEW OF CLINICAL STUDY

TAP blocks have been described as an effective component of multimodal postoperative analgesia for a wide variety of abdominal procedures including large bowel resection, open / laparoscopic appendicectomy, cesarean section, total abdominal hysterectomy, laparoscopic cholecystectomy, open prostatectomy, renal transplant surgery, abdominoplasty with / without flank liposuction and iliac crest bone graft [89]. Most reports demonstrate the efficacy of TAP blocks by highlighting some combination of reduced postoperative opioid requirement, lower pain scores and/or reduction in opioid-related side effects.

Several studies have revealed that when a TAP block is added to a multimodal analgesic regimen, postoperative pain following cesarean delivery is reduced. In a study by Mc Donnell *et al.*, researchers hypothesized that adding a TAP block to a common analgesic treatment for patients undergoing cesarean delivery would result in less opioid consumption and pain postoperatively. A randomized controlled study was performed in which one group of patients received a TAP block at the end of the surgery using 0.75% ropivacaine, while the control group received a placebo of normal saline. All patients received a standard spinal anaesthetic with 12 milligrams of 0.5% bupivacaine and 25 micrograms of fentanyl. The researchers located the transverse abdominis plane using the palpation technique, without ultrasound guidance. Postoperative orders called for 1 gram of oral acetaminophen every six hours, 100 milligrams of rectal diclofenac every 18 hours and patient-controlled analgesia (PCA) consisting of intravenous morphine. Pain assessments upon movement and at rest were performed using the visual analogue scale and categorical pain scoring system at 2, 4, 6, 12, 24, 36 and 48 hours postoperatively. The primary outcome measure was morphine consumption during the first 48 hours

postoperatively. The researchers found that patients who received a TAP block with ropivacaine had significantly less morphine requirements at every time point compared to the control group ($p<0.001$). It was concluded that when added to a multimodal analgesic routine, a TAP block provides reliable and effective analgesia. Ultimately, this leads to less morphine requirements postoperatively. [82]

In a similar study by Belavy *et al*. (2009) researcher's evaluated ultrasound guided TAP blocks in order to determine their effectiveness in providing analgesia post cesarean delivery. A randomized controlled study was performed in which one group received a TAP block using 0.5% ropivacaine under ultrasound guidance and the control group received placebo using normal saline. The TAP block was performed at the end of surgery. As in the previous study by McDonnell *et al*, each patient received a spinal anaesthetic with 12 milligram of 0.5% bupivacaine and 25 micrograms of fentanyl. Postoperative orders were to give 1gram acetaminophen every six hours, 100 milligrams of diclofenac at end of surgery, 400 milligrams of ibuprofen every eight hours and PCA morphine. The primary outcome measure of this study was total morphine requirements during the first 24 hours after surgery. Morphine consumption was recorded at 6, 12, 18 and 24 hours. Pain assessments were performed using the visual analogue scale upon movement and at rest. The patients who received a TAP block with ropivacaine required significantly less morphine at 24 hours following surgery than the patients who received a placebo with normal saline ($p=0.046$). Again, these results demonstrate that less morphine is required postoperatively when patients had received a TAP block using local anaesthetic. [90,82]

In 2009, Belavy *et al*., conducted a randomized, double blind, placebo-controlled study with 47 participants all receiving a hyperbaric 0.5% bupivacaine and fentanyl in spinal or spinal-epidural combination. Patients were excluded if the

epidural was utilized during the case, if they were regular opioid users, if they had a BMI > 35 or weight <50 kg. Utilizing the ultrasound guided technique either saline or ropivacaine 0.5%, 40 ml was administered. A standard postoperative pain regimen of acetaminophen 1 gram (g) and diclofenac 100 milligrams (mgs) at completion of surgery, as well as oral acetaminophen 1 gram four times a day and ibuprofen 400 mg three times a day after surgery was utilized. The outcome measures were assessed 24 hours after delivery for morphine usage (rescue analgesic), average pain score, nausea, vomiting, pruritus, drowsiness and satisfaction with pain relief. The results showed that the total morphine use in 24 hours was reduced in the ropivacaine group when compared to the placebo group. In addition, the TAP block group reported a decreased use of antiemetics and improved satisfaction with pain relief. The authors concluded the ultrasound guided TAP block reduces morphine requirements when used as a component of a multimodal analgesic regimen. [90]

Kanazi *et al*. (2010), with 57 patients, utilized subarachnoid 0.2 mg morphine in comparison to TAP blocks. Their hypothesis was that, subarachnoid morphine would provide more prolonged and superior analgesia than would TAP blocks in cesarean deliveries under spinal anaesthesia. The TAP block was given by using bupivacaine 0.375% plus epinephrine 5 mcg/ml. Inclusion criteria consisted of ASA I and II patients, with BMI <35 and no history of substance abuse or chronic pain disorders. The outcome measures were the time when patients first requested analgesia with secondary outcomes of pain scores at rest and with movement, analgesic requirements, pruritus, nausea and vomiting, sedation and respiratory depression seen at 2, 4, 6, 12, 24, 36 and 48 hours. The postoperative protocol for the first 24 hours was rectal diclofenac 100 mg every 12 hours and intravenous paracetamol 1g every 6 hours. The patients in the TAP group requested pain

medication at 4 hours compared to 8 hours in the subarachnoid morphine group. After 12 hours there was no statistically significant difference between the two groups. Postoperative VAS visceral pain scores at rest at 0, 2 and 4 hours and on movement at 2 and 4 hours were lower in the subarachnoid group than in the TAP group and were not significantly different at all other time points. Nausea scores were higher at 2, 4 and 6 hours in the subarachnoid morphine group with sedation being comparable between the two groups. Higher pruritus scores were recorded in the subarachnoid group at 2, 4, 6 and 12 hours postoperatively versus none in the TAP group. There was no difference in the satisfaction scores between the two groups. The authors concluded that as part of a multimodal analgesia, subarachnoid morphine provided better pain relief than did the TAP block. [91]

Costello *et al*. (2009), had the largest study population with 100 women who had a cesarean section under spinal anaesthesia. Inclusion criteria included ASA I-II, elective Cesarean delivery with a Pfannenstiel incision. Exclusion criteria included allergies to ropivacaine, morphine and ketorolac or acetaminophen consumption of any pain medications in the 24 hours before the surgery, failed or inadequate spinal anaesthesia and BMI > 40. All patients received a spinal anaesthetic of hyperbaric 0.75% bupivacaine with fentanyl 10 mcg or 100 mcg of morphine. A standard postoperative regimen consisted of 50 mg oral diclofenac every 8 hours and 1g of oral acetaminophen every 6 hours for the first 48 hours. Participants were randomly assigned to receive TAP blocks with either ropivacaine 0.375% or placebo. The primary outcome was the VAS pain score on movement at 24 hours after the TAP block procedure. Secondary outcome measures included the VAS pain scores at 6, 12, 24 and 48 hours after TAP block (both at rest and on movement), the total supplemental narcotic consumption in the first 48 hours, patient's satisfaction with the

pain management and the presence of abdominal pain 6 weeks postoperatively. Results showed that there were no statistically significant differences between the ropivacaine and placebo groups at 24 hours. Patient's satisfaction scores were high and similar in both groups. The authors concluded that when using a multimodal regimen inclusive of intrathecal morphine and oral diclofenac and acetaminophen the addition of a single-shot TAP block confers no benefit to the patient. [92]

Onishi *et al*. (2013), examined whether TAP blocks confer additional analgesic effects when compared to epidural morphine alone. They also examined the plasma levels of local anaesthetic after TAP blocks in a non-randomized study of 94 subjects. In this Japanaese study a combined spinal epidural anaesthesia technique was utilized after an injection of intrathecal hyperbaric bupivacaine 12 mg and fentanyl 10 mcg. Incremental doses of 2% lidocaine 5 ml were administered throughout the case, as assessed by hypoesthesia to ice to achieve a T4 level closing the peritoneum, morphine 2mg with 5 ml saline was administered through the epidural catheter. The TAP block was administered to patients who consented. The TAP block was given by using 20 ml of either 0.375% ropivacaine or 0.3% levobupivacaine injected into each side of the abdomen. The anaesthesiologist performing the procedure chose the local anaesthetic. Following the surgery, a standard postoperative patient controlled (PCA) regimen was used in both groups. The patient was instructed to call the nurse the first-time pain medication was obtained from the pump. The PCA was available for 24 hours post procedure. The results of this study showed the median time to first morphine request was longer in the TAP group at 555 versus 215 minutes in the control group. The cumulative morphine consumption within 24 hours was lower as well (5.3 versus 7.7 mg). The

conclusion by the authors of the study was that the TAP block did have additional analgesic effects to the epidural morphine alone. [94]

Lee *et al.* in 2013, conducted a randomized double blind, placebo-controlled study with 51 women undergoing elective cesarean delivery with a combined spinal-epidural technique that included intrathecal morphine. The primary outcome measure was the difference in verbal rating scale (VRS) pain scores with movement at 24 hours post surgery. Patients were excluded for a surgical approach other than a Pfannensteil, a BMI> 40, coagulation abnormalities, neuraxial block failure or major intraoperative complications, known history of chronic pain, allergy or contraindication to opioids, local anaesthetics, non-steroidal anti-inflammatory drugs, acetaminophen or the inability to tolerate oral medication. The spinal anaesthetic utilized was 9-12mg 0.75% hyperbaric bupivacaine, with fentanyl 15 mcg and preservative-free morphine 0.25 mg. The epidural was activated during the case if the spinal was inadequate or regressed. The patient could receive additional epidural boluses of 3-5ml of 2% lidocaine with 1:200,000 epinephrine if needed during the surgery. Patients receiving TAP blocks were administered either ropivacaine 0.5% or saline 0.9% 20 ml under ultrasound guidance to each abdominal side. In their postoperative pain regimen, patients were administered pain medication on request and according to severity of pain. Analgesics were administered according to severity of pain using the VAS. For mild pain (VAS 1-3) patients were given two acetaminophen 500 mg tablets every 6 hours as needed. For moderate severe pain (VAS 4-5) intravenous ketorolac 30 mg or oral ibuprofen 800 mg every 6 hours as needed. For severe pain (VAS 6-10) either intravenous morphine 2mg every 10 minutes as needed up to 6 mg as needed. The maximum cumulative acetaminophen dose allowed over 24 hours was 4000 mg. Patients were evaluated at 2, 24 and 48

hours for pain, at rest and with movement. Analgesic use during the 48-hour period after the block was recorded. Patient satisfaction and opioid side effects, quality of sleep, ability to ambulate and the ability to breastfeed/care for the newborn were assessed. The primary outcome measure was the difference in VAS pain scores with movement at 24 hours. Results showed at 2 hours the ropivacaine group reported significantly less pain at rest and with movement. At 24 and 48 hours no significant differences between groups were noted with respect to pain scores at rest or with movement. Analgesic use significantly differed between groups, 2 hours after the blocks. In the ropivacaine group there were no requests for supplemental analgesics in the PACU whereas 25% of patients in the saline group requested supplemental analgesics. There was no difference between groups in the time to first analgesic request following discharge from the PACU. By 24 hours there was no difference in the pattern of analgesic consumption. Pruritus was reported higher in the ropivacaine versus saline group but was not significant. The side effects of sedation, nausea and dizziness demonstrated no differences. The authors concluded that the TAP blocks in conjunction with intrathecal morphine provided superior early post cesarean analgesia to intrathecal morphine alone. [95]

A study was done in 2012 by Siddik *et al.*, comparing the efficacy and side effects of intrathecal morphine with an ultrasound guided TAP block in a randomized, controlled, double blinded trial but was terminated prematurely due to uncontrollable factors unrelated to the study itself. The primary outcome measure of the study was the morphine equivalent consumption in the 24-hour period after spinal insertion. Secondary outcome measures included pain scores at rest and movement and side effects related to the opioids such as nausea, vomiting, pruritus and sedation. Inclusion criteria were women scheduled for an elective Cesarean section with a low

transverse incision under spinal anaesthesia, ASA status I or II and a singleton fetus. Exclusion criteria were women in active labor, age <19 years, BMI >40 and women who had a history of opioid tolerance or insensitivity, inability to take non-steroidal anti-inflammatory or history of illicit drug use or prescribed opioids or benzodiazepines. In the study the woman were assigned to receive intrathecal morphine 100 mcg plus a placebo TAP block or a TAP block with 0.5% ropivacaine 1.5 mg/kg to each side to a maximum of 20 ml following a spinal anaesthetic of 0.75% hyperbaric bupivacaine 11.25 mg plus fentanyl 10 mcg. At the conclusion of the surgery all patients received rectal naproxen 500 mg and acetaminophen 975 mg. Postoperatively women received regular naproxen 500 mg (orally or rectally) every 12 hours and acetaminophen 1g orally every 6 hours. Women were assessed at 2, 6, 20 and 24 hours post-spinal for pain rating at rest and on movement, nausea and vomiting, sedation and pruritus. After one year and only 69 patients, the results demonstrated that the mean morphine equivalent dose consumed between 10 and 24-hour post-spinal in the TAP group was greater than the mean of the intrathecal fentanyl group. There was a difference between groups for postoperative pain scores at rest and on movement with the TAP block being higher but only statistically at 10-hours. The TAP block group experienced less nausea, vomiting, pruritus and sedation. The author's conclusions were that the ultrasound-guided TAP block did not provide analgesia as effective as intrathecal morphine 100 mcg in the first 24-hours postoperatively. [96]

In a study by Atim *et al.* in 2011, researchers assessed the efficacy of ultrasound guided TAP block in patients undergoing hysterectomy. The researchers compared ultrasound-guided TAP block with bupivacaine infiltration of the wound. A prospective, double-blind randomized controlled study was performed which included

sixty female patients undergoing elective total abdominal hysterectomy via Pfannensteil abdominal wall incision under general anaesthesia. The patients were divided into three groups: the TAP block group received bilateral TAP blocks with 20 milliliters of 0.25% bupivacaine on each side, a control group received bilateral placebos with 20 milliliters of 0.9% saline on each side and the infiltration group received 20 milliliters of 0.25% bupivacaine infiltrated to the skin and subcutaneous tissues of the surgical incision site at the end of surgery. All patients underwent standard general anaesthesia. Seventy-five milligrams diclofenac was given intravenously immediately before surgical incision. Before closure of the surgical incision, 0.5 milligrams per kilogram of tramadol was given. Patient controlled analgesia was used postoperatively with the patients receiving a 20 milligram bolus of tramadol, with a four hour maximum dose of 150 milligrams. Postoperative pain was measured at rest and upon movement using a visual analogue scale. The TAP group had significantly lower pain scores during rest at 1, 2, 4, 6 and 24 hours and lower movement-related pain scores than the control group at all times ($p=0.001$, $p=0.001$, $p=0.001$, $p=0.001$ and $p=0.018$, respectively). Comparison of the TAP and infiltration groups showed no difference in rest or movement-related pain scores at 1, 2 or 4 hours but significantly lower pain scores in the TAP group at 6 and 24 hours post-operatively ($p=0.003$ and $p=0.027$, respectively). Consumption of tramadol was significantly lowering the TAP group than both the control group and the infiltration group at all of the time points (p-values ranged from 0.001 to 0.012). The infiltration group showed significantly less consumption of tramadol than the control group at one hour only ($p=0.015$). This study showed that the TAP block was a more effective method of pain reduction than superficial wound infiltration. [97]

In 2010, Owen *et al*., conducted a study in which a TAP block was performed using a novel approach, termed the surgical TAP block. The approach involved performance of the TAP block under direct vision by the surgeon during cesarean section. After closure of the uterus, the rectus muscle was elevated superiorly by the surgeon. Access to the transversus abdominis plane was then achieved by the insertion of a blunt needle through the parietal peritoneum with further advancement until an appreciable loss of resistance was noted. After aspiration, the surgeon injected 20 milliliters of 0.25% bupivacaine on each side. The researchers claimed that if the surgeon was indeed in the transversus abdominis plane, there should be little to no resistance to injection. Sixteen women undergoing cesarean section under spinal anaesthesia received the surgical TAP block. The spinal anaesthetic included 12.5 to 15 milligrams of 0.5% bupivacaine and 25 micrograms of fentanyl. In addition to the spinal anaesthetic, each study participant was given 100 milligrams diclofenac rectally and 50 milligrams orally every eight hours. Also one gram of oral paracetamol was ordered every six hours. All participants could receive ten milligrams of intramuscular morphine as needed. Total morphine consumption and time to first request for morphine were the primary outcomes measured. The control group consisted of eighteen women who underwent cesarean section under spinal anaesthesia with the routine post-operative analgesic regimen, without the TAP block. The results showed that the TAP block group had a significantly longer time to first request for morphine ($p=0.004$) and significantly reduced morphine requirements ($p=0.011$) as compared to the control group. Furthermore, pain scores were significantly lower in women who received the surgical TAP block ($p=0.01$). In conclusion, the results of this study indicated less morphine was required

postoperatively when patients received a TAP block as part of a multimodal analgesic regimen. [78]

In a 2011 study by Adeline *et al.*, researchers conducted a prospective, randomized study to compare the efficacy of ultrasound-guided TAP blocks to conventional ilioinguinal/iliohypogastric nerve (IHN) blocks on both immediate postoperative pain and chronic pain after inguinal hernia surgery. Adult male patients undergoing elective unilateral open inguinal hernia repair under combined general anaesthesia and ultrasound guided TAP blocks or IHN blocks were enrolled in the study. A total of 1.5 milligrams per kilogram of 0.5% levobupivacaine was used for both the TAP block and the IHN block. Ultrasound was not used for the IHN blocks. After the regional anaesthetic technique was performed, patients underwent general anaesthesia. All patients received one gram of paracetamol and 100 milligrams of ketoprofen intravenously. In the post anaesthesia care unit (PACU), three milligrams intravenous boluses of morphine were given until visual analogue scale scores at rest were less than thirty (1-100 scale). After discharge from the PACU, patients received a combination of one gram of paracetamol every six hours and 150 milligrams of ketoprofen every twelve hours. Oral morphine tablets were given as a rescue analgesic. Pain assessments were taken at rest before discharge from the PACU and at four, twelve and twenty-four hours after surgery. A telephone interview was performed at three and six months following surgery to assess chronic pain. The TAP block group reported significantly less pain at rest at four hours ($p=0.04$), twelve hours ($p=0.0014$) and twenty-four hours ($p=0.0013$) postoperatively. Morphine doses given in the PACU were low and comparable between the two groups (median 0 to 3 milligrams and 0 milligrams in the IHN and TAP block groups, respectively, $p=0.15$). However, patients in the TAP block group required less oral morphine tablets during

the first two postoperative days. At three and six months after surgery, pain scores were comparable between the two groups (p=0.24). The researchers concluded that the TAP block provided higher quality immediate postoperative pain relief and reduced need for rescue morphine compared to the IHN block. However, the TAP block did not reduce the incidence of chronic pain. [98]

The aim of a study conducted by Sforza *et al.* in 2011, was to compare postoperative pain in patients undergoing abdominoplasty who received a TAP block versus those who did not receive the TAP block. The researchers hypothesized that the TAP block would reduce the amount of morphine required postoperatively, leading to earlier ambulation and fewer of the side effects associated with morphine. The study was a prospective, randomized, double-blind and controlled clinical trial in which 28 patients underwent abdominoplasty under general anaesthesia. A surgical TAP block similar to the technique described by Owen *et al.* [78] was performed by the surgeon. The TAP block group received a solution containing ten milliliters of 0.5% bupivacaine, ten milliliters of 1% lidocaine and 0.2 milliliters of 1:1000 epinephrine on each side. The control group received 20 milliliters of normal saline bilaterally. A standard analgesic regimen consisting of ten milligrams of morphine plus one gram of paracetamol was given. Pain scores at rest were assessed in the PACU 20 minutes after awakening and four, six and twelve hours following the surgery. The results of the study showed that patients in the TAP block group reported significantly less pain than the control group ($p<0.001$). In the control group, all patients were given fifteen milligrams of morphine compared with none given in the TAP block group. The patients in the TAP block group also demonstrated earlier ambulation times. At four hours postoperatively 81.8% of patients in the TAP block group had ambulated, compared with 18.2% in the control group. Ambulation rates were not significantly

different twelve hours following surgery. The results of this study demonstrated when a TAP block was added to a standard multimodal analgesic regimen, patients had reduced pain scores and received less morphine. Furthermore, patients were able to ambulate at an earlier stage, which may reduce the risk of complications such as deep venous thrombosis. [89]

In a study by Niraj *et al*. in 2009, the efficacy of TAP blocks in patients undergoing open appendicectomy was studied. In this randomized, double-blinded controlled study, a unilateral block was performed under ultrasound guidance on each patient in the experimental group prior to surgical incision. The local anaesthetic of choice in this study was bupivacaine 0.5%, of which twenty milliliters was injected into the right transversus abdominis plane. The control group did not receive a TAP block. Patients in both groups underwent general anaesthesia utilizing weight equivalent doses of thiopental, succinylcholine, atracurium and isoflurane. Each patient also received intravenous morphine and acetaminophen prior to incision. Each patient's postoperative pain control consisted of one gram of oral acetaminophen and 50 milligrams diclofenac as needed every six hours, together with patient-controlled morphine set at a bolus of one milligram with a five-minute lockout. An investigator blinded to group allocation assessed each patient for pain upon rest and coughing, morphine use and nausea at 30 minutes and 24 hours after surgery. The experimental group had significantly reduced morphine use at the 24-hour mark ($p=0.002$), significantly reduced pain scores at both intervals ($p<0.001$) and significantly reduced nausea at the 30minute mark ($p<0.05$). The researchers concluded that unilateral ultrasound-guided TAP blocks are a success when added to balanced postoperative analgesia for patients undergoing open appendicectomy. [75]

Research has been performed on the effectiveness of TAP blocks used for perioperative analgesia during laparoscopic cholecystectomies. In a 2009 study by El-Dawlatly *et al.*, researchers compare both intraoperative and postoperative anaesthesia opioid requirements in patients receiving general anaesthesia alone versus general plus TAP block. Each group underwent general anaesthesia using sufentanil, propofol and rocuronium for induction and sevoflurane for maintenance. After induction and fifteen minutes before surgical incision, bilateral TAP blocks consisting of fifteen milliliters of 0.5% bupivacaine were placed in the experimental group using ultrasound guidance. Sufentanil was to be administered if the patient's heart rate and/or blood pressure increased by fifteen percent of the baseline. This total dose of intraoperative sufentanil was recorded and compared between the two groups. For postoperative pain control each patient received a patient-controlled analgesia device set to give 1.5 milligrams of an intravenous morphine bolus dose with a fifteen-minute lock-out time between doses. A significant reduction in opioids both intraoperatively ($p<0.01$) and postoperatively ($p<0.05$) occurred in patients having received a TAP block. [84]

Anaesthesiologists play an important role in postoperative pain management. For analgesia after lower abdominal surgery, epidural analgesia and ultrasound-guided transversus abdominis plane (TAP) block are suitable options. The study aims to compare the analgesic efficacy of both techniques. Seventy-two patients undergoing lower abdominal surgery under spinal anaesthesia were randomized to postoperatively receive lumbar epidural catheter (Group E) or ultrasound-guided TAP block (Group T) through intravenous cannulas placed bilaterally. Group E received 10 ml 0.125% bupivacaine stat and 10 ml $8^{th}$ hourly for 48 hours. Group T received 20 ml 0.125% bupivacaine bilaterally stat and 20 ml bilaterally $8^{th}$ hourly for 48 hours.

Pain at rest and on coughing, total paracetamol and tramadol consumption were recorded. Analgesia at rest was comparable between the groups in the first 16 hours. At 24 and 48 hours, Group E had significantly better analgesia at rest ($P$ = 0.001 and 0.004 respectively). Patients in Group E had significantly higher number of patients with nil or mild pain on coughing at all times. Paracetamol consumption was comparable in both groups, but tramadol consumption was significantly higher in Group T at the end of 48 h ($P$ = 0.001). For lower abdominal surgeries, analgesia provided by intermittent boluses of 0.125% is comparable for first 16 hours between epidural and TAP catheters. However, the quality of analgesia provided by the epidural catheter is superior to that provided by TAP catheters beyond that both at rest and on coughing with reduced opioid consumption. [87]

Reducing postoperative pain from a midline incision following a large bowel resection was studied by McDonnell *et al*. in 2007. In this randomized controlled, double-blinded study, patients were allocated to undergo general anaesthesia only or general anaesthesia with bilateral TAP blocks. Following induction of anaesthesia using fentanyl and propofol, each patient received intravenous morphine, rectal diclofenac and rectal acetaminophen. After induction of anaesthesia, a bilateral TAP block using twenty milliliters of 0.375% levobupivacaine bilaterally, was administered to each patient in the experimental group. Patients in both groups received a postoperative analgesic regimen consisting of one-gram oral acetaminophen every six hours, 100 milligrams of rectal diclofenac every 18 hours and patient-controlled morphine set for bolus doses of one milligram with a six-minute lockout time and maximum dose of forty milligrams within four hours. An investigator, blinded to the group allocation, assessed for pain, nausea and sedation in the post anaesthesia care unit (PACU) at 2, 4, 6 and 24 hours postoperatively. Patients

rated their own pain, at rest and upon movement, using a visual analogue scale. Sedation scores were assigned by the investigator. The researchers found that patients in the experimental group had a longer time to first request of morphine and overall reduced morphine requirements. Postoperative pain scores were also reduced in the experimental group. Sedation scores were reduced at four and six hours postoperatively and postoperative nausea and vomiting was reduced at all times for the experimental group. Specific p-values were not included in the article. The researchers concluded that the TAP block holds considerable promise for decreasing pain and opioid use following abdominal wall incisions. [65]

Total abdominal hysterectomy is associated with substantial postoperative pain resulting from an abdominal wall incision. In 2008, Carney *et al*., studied the effectiveness of bilateral TAP blocks on postoperative pain following a total abdominal hysterectomy. Patients undergoing a total abdominal hysterectomy were allocated into one of two groups, TAP block using 1.5 milligrams per kilogram of 0.75% ropivacaine per side and TAP block using 0.9% saline all performed prior to surgical incision. Patients in both groups underwent general anaesthesia using fentanyl and propofol for induction. All patients also received intravenous morphine, rectal diclofenac and rectal acetaminophen immediately prior to surgical incision. Postoperative pain control consisted of one gram of rectal acetaminophen every six hours, 100 milligrams of rectal diclofenac every sixteen hours and intravenous patient-controlled morphine with a bolus dose of one milligram, a lockout time of six minutes and a maximum dose of forty milligrams within four hours. An investigator blinded to whether or not the patient's TAP block consisted of saline or ropivacaine assessed each patient for pain at rest or movement, sedation and nausea in the PACU and at 2, 4, 6, 12, 24, 36 and 48 hours postoperatively. The results revealed that

patients who received ropivacaine in their TAP blocks had significantly reduced cumulative morphine consumption at each time point, including 48 hours (p values ranged from 0.001 to 0.05). Pain scores as measured by a visual analogue scale were reduced at most time points and categorical pain scores were lower at 6, 36 and 48 hours in patients in the experimental group. A significant difference was not found in the incidence of nausea at any of the time points between both groups. The experimental group was also found to have reduced sedation scores. The researchers concluded that the TAP blocks provided reliable and effective analgesia in the first 48 hours postoperatively. [62]

In a 2011 study by Bharti *et al.,* researchers examined the effectiveness on bilateral TAP blocks on postoperative pain following colorectal surgery in a double-blind random controlled study. These researchers used a novel surgical approach to the TAP block in which they accessed the transversus abdominis plane from inside the abdominal wall just prior to wound closure. The experimental group received twenty milliliters of 0.25% bupivacaine per side and the control group received normal saline. All participants received proportionate doses of morphine and propofol for induction and were maintained throughout the case with a propofol infusion and nitrous oxide. In the postoperative period all patients received 1.5 milligrams per kilogram of intramuscular diclofenac every eight hours and 0.05 milligrams per kilogram of intravenous morphine every fifteen minutes as required. An investigator blinded to the group allocation monitored the patients for pain, sedation, nausea, vomiting and respiratory depression at 0, 0.5, 1, 2, 4, 6, 12 and 24 hours postoperatively. There was a significant decrease in total morphine use at 24 hours ($p<0.0001$) and at every other time point within the experimental group. The experimental group also showed significantly lower pain scores at each time point and

significantly lower sedation scores at 1,2, 4 and 6 hours postoperatively ($p<0.05$). There was no difference shown in the incidence of nausea and vomiting between the groups. The researchers concluded that TAP blocks provided effective analgesia for postoperative colorectal patients. [99]

In 2010, Conaghan *et al.*, studied the effectiveness of TAP blocks on pain control post colorectal surgery. This non-randomized comparative study sought to find if patients would require less morphine postoperatively by comparing a group of patients who received a TAP block with patient-controlled analgesia versus a group using patient-controlled analgesia alone. Following induction of general anaesthesia and prior to surgical incision, bilateral TAP blocks were placed under ultrasound guidance. Twenty milliliters of 0.25% levobupivacaine was injected bilaterally. Postoperatively, each patient received patient-controlled intravenous morphine. Postoperative data showed that the group with TAP blocks had a significant overall reduction of morphine use ($p=0.03$) as compared to the group receiving patient-controlled analgesia with morphine alone. [100]

A comparative study was performed by Gravante *et al*. 2011, that evaluated the efficacy of TAP blocks in post-bariatric patients and non-bariatric patients receiving abdominoplasty. In this retrospective study, the two groups received the same proportionate general anaesthesia consisting of propofol, fentanyl, nitrous oxide and sevoflurane, as well as bilateral TAP blocks. Bupivacaine was administered for the TAP blocks. Postoperative analgesic management for both groups consisted of intravenous morphine as needed within the first postoperative hour and oral paracetamol following the first hour. Overall, the non-bariatric patients required significantly less postoperative analgesia than the post-bariatric group ($p=0.01$). The researchers found that the significant parameter difference between the groups was

the weight of the flap resected. The conclusion by the researchers was the larger the flap, the less effective was the TAP block. [101]

In 2011, McMorrow *et al*., conducted a comparison study between TAP blocks and intrathecal morphine for pain relief after cesarean delivery. The researchers aimed not only to compare the TAP block with intrathecal morphine, but also to determine whether a TAP block provided any additional benefit when administered in conjunction with intrathecal morphine. The researchers hypothesized that a TAP block would result in less pain upon movement than spinal morphine at six hours following surgery. All patients received a standard spinal anaesthesia with 11 to 12.5 milligrams of hyperbaric bupivacaine and adjuvant. Along with the standard spinal anaesthetic, patients were randomly selected to receive either 100 micrograms of intrathecal morphine or an equivalent volume of saline. Bilateral TAP blocks were performed with two milligrams per kilogram of 0.375% bupivacaine or an equivalent volume of saline. Following surgery, all patients received one gram of paracetamol and 100 milligrams of diclofenac rectally. Immediately upon skin closure, TAP blocks were performed without the use of ultrasound. The standard analgesic regimen for all the patients included one-gram oral paracetamol every six hours, 100 milligrams of rectal diclofenac every eighteen hours and morphine PCA. The primary outcome measure was pain on movement secondary outcome measurements included pain at rest, morphine consumption, satisfaction, sedation, nausea and pruritus. A visual analogue scale of 1 to 100 was used and patients were assessed at 6, 12, 24, 36 and 48 hours after TAP block placement. The results showed early morphine consumption and pain on movement were lowest in groups receiving intrathecal morphine but were not improved by the addition of a TAP block. The researchers found an analgesic benefit with the addition of intrathecal morphine, but none with

the TAP block. Furthermore, no additional benefit was observed when TAP block and intrathecal morphine were given together. Therefore, the researchers concluded that the TAP block does not provide analgesic benefit when administered alone or in combination with intrathecal morphine. [93]

Albrecht *et al*. 2013, studied that despite the laparoscopic approach, patients can suffer moderate to severe pain following bariatric surgery. This randomized controlled double-blinded trial investigated the analgesic efficacy of ultrasound-guided transversus abdominis plane (TAP) blocks for laparoscopic gastric-bypass surgery. Seventy patients undergoing laparoscopic gastric-bypass surgery were randomized to receive either bilateral ultrasound-guided subcostal TAP block injections after induction of general anaesthesia or none. All patients received trocar insertion site local anaesthetic infiltration and systemic analgesia. The primary outcome was cumulative opioid consumption (IV morphine equivalent) during the first 24 h postoperatively. Interval opioid consumption, pain severity scores, rates of nausea or vomiting and rates of pruritus were measured during phase I recovery and at 24 and 48 h postoperatively. There was no difference in cumulative opioid consumption during the first 24 h postoperatively between the TAP (32.2 mg [95% CI, 27.6–36.7]) and control (35.6 mg [95% CI, 28.6–42.5]; $P$=0.41) groups. Postoperative opioid consumptions during phase I recovery and the 24–48-h interval were similar between groups, as were pain scores at rest and with movement during all measured intervals. The rates of nausea or vomiting and pruritus were equivalent. Bilateral TAP blocks do not provide additional analgesic benefit when added to trocar insertion site local anaesthetic infiltration and systemic analgesia for laparoscopic gastric-bypass surgery. [33]

The efficacy of ultrasound-guided transversus abdominis plane (USG-TAP) block as a part of multimodal analgesia was evaluated in morbidly obese patients undergoing laparoscopic bariatric surgery. Aparna Sinha *et al*., studied 100 patients with body mass index >35 kg/$m^2$. They were randomly allocated to study (USG-TAP) and control groups. Pain scores at rest and on movement at various time points up to 24 postoperative hours were compared. Other parameters evaluated were patients requiring Tramazac hydrochloride (TMZ) as rescue analgesic, sedation score, time to ambulate, any adverse events and patient satisfaction. The median visual analogue scale pain score of the study (USG-TAP) group was consistently lower at 1, 3, 6, 12 and 24 h at rest and on movement in the postoperative period. Number of patients requiring TMZ required in the first, third and sixth hour was significantly lower in the USG-TAP group. The prolonged sedative effect of the TMZ affected the time to ambulate. Patients in the control group remained more sedated. Four patients in the control group required BIPAP support postoperatively no adverse event was observed. Time to ambulate was 6.3±1.8 h in USG-TAP and 8±1.8 h in control groups; $P$<0.001. Patient satisfaction scores were significantly higher in the USG-TAP group; $P$<0.001. Concluded that the USG-TAP as part of multimodal analgesic technique in morbidly obese patients undergoing laparoscopic gastric bypass reduces opioid requirement, improves pain score, decreases sedation, promotes early ambulation and has greater patient satisfaction. [102]

Optimal analgesia following laparoscopic colorectal resection is yet to be determined, however, recent studies have questioned the role of postoperative epidural anaesthesia, suggesting other analgesic modalities may be preferable. The aim of this randomised controlled trial was to assess the effect of transversus abdominis plane (TAP) blocks on opioid requirements in patients undergoing

laparoscopic colorectal resection. Walter *et al.* 2013, studied all adult patients who were to undergo laparoscopic colorectal surgery at a single centre were randomised into the intervention group receiving bilateral TAP blocks or the control group (no TAP block). The blocks were administered prior to surgery after the induction of a standardised anaesthetic by an anaesthetist otherwise uninvolved with the case. The patient, theatre anaesthetist, surgeon and ward staff were blinded to treatment allocation. All patients received postoperative analgesia of paracetamol and morphine as a patient-controlled analgesia (PCA). Cumulative opioid consumption and pain scores were recorded at 2, 4, 6 and 24 h postoperatively and compared between the groups as were clinical outcomes and length of stay. The intervention (TAP block) group ($n = 33$) and the control group ($n = 35$) were comparable with respect to characteristics, specimen pathology and type of procedure. The TAP block group's median cumulative morphine usage (40 mg [IQR = 25–63]) was significantly less than that of the control group (60 mg [IQR = 39–81]). Pain scores and median length of stay (LOS) were similar between the two groups. Preoperative TAP blocks in patients undergoing laparoscopic colorectal resection reduced opioid use in the first postoperative day in this study. [103]

Laparoscopic cholecystectomy is associated with postoperative pain of moderate intensity in the early postoperative period. Recent randomized trials have demonstrated the efficacy of transversus abdominis plane (TAP) block in providing postoperative analgesia after abdominal surgery. Petersen *et al*. 2012 hypothesized that a TAP block may reduce pain while coughing and at rest for the first 24 postoperative hours, opioid consumption and opioid side effects in patients undergoing laparoscopic cholecystectomy in day-case surgery. In this randomized, double-blind study, 80 patients undergoing laparoscopic cholecystectomy in our day-

case surgery unit were allocated to receive either bilateral ultrasound guided posterior TAP blocks (20 mL 0.5% ropivacaine) or placebo blocks. Postoperative pain treatment consisted of oral acetaminophen 1000 mg, oral ibuprofen 400 mg, IV morphine (0–2 hours postoperatively) and oral ketobemidone (2–24 hours postoperatively). The primary outcome was postoperative pain scores while coughing calculated as area under the curve for the first 24 postoperative hours (AUC/24 h). Secondary outcomes were pain scores at rest (AUC/24 h), opioid consumption and side effects. Patients were assessed 0, 2, 4, 6, 8 and 24 hours postoperatively. Group-wise comparisons of visual analogue scale (VAS) pain (AUC/24 h) were performed with the 2-sample t test. Morphine and ketobemidone consumption were compared with the Mann-Whitney test for unpaired data. Categorical data were analyzed using the test. The primary outcome variable, VAS pain scores while coughing (AUC/24 h) was significantly reduced in the TAP versus the placebo group (P 0.04) group TAP: 26 mm (SD 13) (weighted average level) versus group placebo 34 (18) (95% confidence interval) (0.5–15 mm). VAS pain scores at rest (AUC/24 h) showed no significant difference between groups. Median morphine consumption (0–2 hours postoperatively) was 7.5 mg (interquartile range: 5–10 mg) in the placebo group compared with 5 mg (interquartile range: 0–5 mg) in the TAP group (P 0.001). The odds ratio of a random patient in group TAP having less morphine consumption than a random patient in group placebo was P (group TAP group placebo) 0.26 (confidence interval: 0.15, 0.37) where 0.5 represents no difference between groups. There were no between-group differences in total ketobemidone consumption, levels of nausea and sedation, number of patients vomiting or consumption of ondansetron. TAP block after laparoscopic cholecystectomy may have some beneficial effect in reducing pain while coughing and on opioid requirements but this effect is probably rather small.[104]

Kane *et al*. 2012, studied to determine whether transversus abdominis plane (TAP) block improves the early postoperative quality of recovery (QoR-40). The secondary objectives measured postoperative pain, length of stay and narcotic use. A randomized, single-blinded trial of TAP block versus no block on women undergoing laparoscopic hysterectomy was done. TAP block patients received 20 mL of 0.5% ropivacaine with epinephrine 1:200,000 placed under ultrasound guidance on each side. The outcomes were measured using validated quality of recovery questionnaires (QoR-40), visual analogue scales (VAS) for pain and documented narcotic use in the electronic medical record. In 58 women, no differences in demographics were noted between groups. Comparisons of pain and recovery between the 2 groups showed no differences. There was no decrease in narcotic use or length of stay among those who received the TAP block. TAP block does not improve post-operative QoR-40 scores or VAS pain scores following laparoscopic hysterectomy, nor does it decrease narcotic pain medication use. [21]

Postoperative pain can delay functional recovery after outpatient surgery. Multimodal analgesia can improve pain and possibly improve quality of recovery. De Oliveira *et al*. 2011 evaluated the dose-dependent effects of a preoperative transversus abdominis plane (TAP) block on patient recovery using the Quality of Recovery 40 (QoR-40) questionnaire after ambulatory gynaecological laparoscopic surgery. Global QoR-40 scores range from 40 to 200 representing very poor to outstanding quality of recovery respectively. Healthy women undergoing outpatient gynaecological laparoscopy were randomly allocated to receive a preoperative TAP block using saline, ropivacaine 0.25%, or ropivacaine 0.5%. Needle placement for the TAP blocks was performed using ultrasound guidance and 15 mL of the study solution was injected bilaterally by a blinded investigator. QoR-40 score and

analgesic use were assessed 24 hours postoperatively. The primary outcome was global QoR-40 score at 24 hours after surgery. Data were analysed using the Kruskal-Wallis test. Post hoc pairwise comparisons were made using the Dunn test with *P* values and 95% confidence intervals, Bonferroni corrected for 6 comparisons. Seventy-five subjects were enrolled and 70 subjects completed the study. The median (range) for the QoR-40 score after the TAP block was 157 (127–193), 173 (133–195) and 172 (130–196) for the saline group and 0.25% and 0.5% ropivacaine groups, respectively. The median difference (99.2% confidence interval) in QoR-40 score for 0.5% bupivacaine (16 [1–30], $P = 0.03$) and 0.25% bupivacaine (17 [2–31], $P = 0.01$) was more than saline but not significantly different between ropivacaine groups (−1 [−16 to 12], $P = 1.0$). Increased global QoR-40 scores correlated with decreased area under the pain score time curve during post-anaesthesia recovery room stay ($\rho = -0.56$, 99.2% upper confidence limit [UCL] = −0.28), 24-hour opioid consumption ($\rho = -0.61$, 99.2% UCL = −0.34), pain score (0–10 scale) at 24 hours ($\rho = -0.53$, 99.2% UCL = −0.25) and time to discharge readiness ($\rho = -0.65$, 99.2% UCL = −0.42). The aforementioned variables were lower in the TAP block groups receiving ropivacaine compared with saline. It concluded that the TAP block is an effective adjunct in a multimodal analgesic strategy for ambulatory laparoscopic procedures. TAP blocks with ropivacaine 0.25% and 0.5% reduced pain, decreased opioid consumption and provided earlier discharge readiness that was associated with better quality of recovery. [19]

To examine the effect of a preoperative transversus abdominis plane infiltration on postoperative quality of recovery and analgesia in patients undergoing laparoscopic hysterectomy. De Oliveira *et al*. 2011 conducted a randomized double-blinded, placebo-controlled trial. Seventy-five healthy women were randomized to

receive a preoperative infiltration with 0.5% ropivacaine, 0.25% ropivacaine, or saline. Postoperative quality of recovery score (QoR-40), pain and opioid consumption were assessed up to 24 hours after the surgical procedure. Data were analysed using Kruskal-Wallis test. Post hoc pair-wise comparisons were made using Dunn test. $P<.05$ was required to reject the null hypothesis. Sixty-six patients completed the study. Patient's baseline characteristics and surgical factors were not different between groups. The ropivacaine group experienced a better-quality recovery and less postoperative pain than the saline group. The median difference (99.2% confidence interval) in global recovery scores at 24 hours after surgery was 28 (QoR score 4–39, $P=.001$) for ropivacaine 0.5% and 28 (QoR score 10–43, $P<.001$) for ropivacaine 0.25% compared with saline respectively. The 0.5% ropivacaine group also had less pain, lower opioid consumption and faster post-anaesthesia care unit discharge than the saline group. Linear regression demonstrated an inverse relationship between opioid consumption and global quality of recovery at 24 hours ($P<.001$). It concluded that transversus abdominis plane infiltration improves quality of recovery. There was an inverse linear relationship between postoperative opioid consumption and quality of recovery. [105]

De Oliveira *et al*. 2014 conducted ten randomized clinical trials with 633 subjects were included in the analysis. The weighted mean difference (99% confidence interval) of the combined effects favoured TAP block over control for pain at rest (≤4 hours, −2.41 [−3.6 to −1.16]) and (at 24 hours, −1.33 [−2.19 to −0.48]) (0–10 numerical scale). Postoperative opioid consumption was decreased in the TAP block group compared with control, weighted mean difference (99% confidence interval) of −5.74 (−8.48 to −2.99) mg morphine IV equivalents. Publication bias was not present in any of the analysis. Preoperative TAP block administration resulted in

greater effects on early pain and opioid consumption compared with postoperative administration. Meta-regression analysis revealed an association between local anaesthetic dose and the TAP block effect on late pain at rest and postoperative opioid consumption. None of the studies reported symptoms of local anaesthetic toxicity. They concluded that TAP block is an effective strategy to improve early and late pain at rest and to reduce opioid consumption after laparoscopic surgical procedures. In contrast, the TAP block was not superior compared with control to reduce early and late pain during movement. Preoperative administration of a TAP block seems to result in greater effects on postoperative pain outcomes. We also detected a local anaesthetic dose response on late pain and postoperative opioid consumption. [8]

Laparoscopic surgery reduces pain after donor nephrectomy however, most patients still require a significant amount of postoperative parenteral opiate analgesia. Therefore, there is a need to investigate techniques that might further reduce postoperative pain. This study assessed the safety and efficacy of using a transversus abdominis plane (TAP) block in a randomized, double-blind, placebo- controlled trial. Hosgood *et al*. 2012, in their study forty-six patients were analysed in the trial and were randomized to undergo the TAP block procedure with either bupivacaine (n=24) or saline placebo (Control n=22) injected into the muscle plane. Prefilled syringes were dispensed with the group allocation concealed to maintain blinding. After surgery, the amount of morphine, level of pain and measures of recovery were recorded. The amount of morphine used 6 hr after surgery was significantly lower in patients receiving TAP block with bupivacaine compared with the control (presented as mean [SD], 12.4 [8.4] vs. 21.2 [14.0] mg; $P$=0.015). However, the total amount of morphine used was similar in both groups 45.6 [31.4] vs. 52.7 [28.8] mg; $P$=0.771. Patients in the bupivacaine group experienced significantly less pain on postoperative

days 1 (score: 19 [15] vs. 37 [20]; *P*=0.003) and 2 (score: 11 [10] vs. 19 [13]; *P*=0.031). Recovery and postoperative hospital stay were similar in both groups. There were no complications associated with the procedure. The TAP block procedure is beneficial in reducing postoperative pain and early morphine requirements in laparoscopic live-donor nephrectomy. [106]

Ra *et al*. 2010, studied Fifty-four patients undergoing laparoscopic cholecystectomy were randomized into three groups. The patients in Group Control did not receive the US-TAP block. The patients in Group B0.25 and Group B0.5 received the US-TAP block with 0.25% and 0.5% levobupivacaine 30 ml respectively. After the general anaesthesia, a bilateral US-TAP block was performed using an in-plane technique with 15 ml levobupivacaine on each side. Intraoperative use of remifentanil and postoperative demand of rescue analgesics in PACU were recorded. The postoperative verbal numerical rating scale (VNRS) was evaluated at 20, 30 and 60 min thereafter at 6, 12 and 24 hours. Postoperative complications, including pneumoperitoneum, bleeding, infection and sleep disturbance were also checked. Results were the intraoperative use of remifentanil, postoperative VNRS and the postoperative demand of rescue analgesics were lower in the groups receiving the US-TAP block (Group B0.25 and Group B0.5) than Group Control. There were no statistically or clinically significant differences between Group B0.25 and Group B0.5. No complications related to the US-TAP block were observed. Conclusions: The US-TAP block with 0.25% or 0.5% levobupivacaine 30 ml (15 ml on each side) significantly reduced postoperative pain in patients undergoing laparoscopic cholecystectomy. [107]

Nurçin Gülhaş *et al*. (2015), demonstrated that the addition of dexamethasone to ultrasound guided TAP block was decreased postoperative pain scores, increased

the time to first analgesic requirement, reduced postoperative narcotic requirements and adverse events. The rate of nausea or vomiting were also reduced with shorter length of hospital stay in patients undergoing total abdominal hysterectomy. [108]

Ammar *et al*. (2012), studied sixty adult patients undergoing elective open abdominal hysterectomy receiving TAP block using 20 mL of bupivacaine hydrochloride 0.25% + 2 mL saline0.9% or 20 mL of bupivacaine hydrochloride 0.25% + 2 mL dexamethasone "8 mg". TFA was significantly longer in the dexamethasone group, with lesser morphine requirements in the postoperative period.[109]

Sooyoung Cho *et al*. (2013), studied postoperative analgesic effects of ultrasound-guided TAP block for open appendectomy, using 20ml of 0.5% Levobupivacaine. The TAPB group with Levobupivacaine compared to the control group reduced VNRS (verbal numerical rating scale) significantly upto 12 hrs postoperatively. There were no significant differences in time to first analgesia, number of rescue analgesic demands, nausea, vomiting, pruritis and drowsiness between the groups. There were no complications attributable to the TAP block. USG guided TAP block provided effective postoperative analgesia for the duration of 12 hrs. [110]

Sharnouby *et al*. 2014, studied a total of 111 bariatric patients, scheduled for laparoscopic vertical banded gastroplasty under ultrasound-guided TAP block, were randomized blindly into three parallel groups: Group BC that received TAP block using 20 ml of isobaric bupivacaine hydrochloride 0.25%+2 ml saline 0.9%; low-dose dexamethasone group (Group DB4) that received TAP block using 20 ml of isobaric bupivacaine hydrochloride 0.25%+4mg dexamethasone; and high-dose dexamethasone group (Group DB8) that received TAP block using 20 ml of isobaric

bupivacaine hydrochloride 0.25%+8 mg dexamethasone. Results Postoperatively, pain scores were significantly lower in Group BD4 and Group BD8 compared with Group BC at rest and on movement at 6, 8, 12 and 24 h. There was a significant difference with respect to the duration of analgesia (P = 0.0001), 24 h consumption of paracetamol (P = 0.0001), 24 h consumption of meperidine hydrochloride (P = 0.001), the number of patients who needed meperidine hydrochloride rescue analgesic (P = 0.008), time to ambulation (P = 0.0001) and incidence of postoperative nausea and/or vomiting (P = 0.03) among groups. Conclusion Adding dexamethasone (4 or 8 mg) to isobaric bupivacaine TAP block reduces postoperative pain, reduces analgesic requirement and promotes early ambulation in bariatric patients undergoing laparoscopic vertical banded gastroplasty in comparison with isobaric bupivacaine TAP block alone. [111]

# MATERIALS AND METHODS

This study was conducted in the Department of Anaesthesiology, Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijayapur. After obtaining approval of the Institutional Ethical Committee and written informed patient consent 70 adult patients of ASA I and II scheduled to undergo laparoscopic surgeries under general anaesthesia were taken in the study and administered TAP block.

**STUDY DESIGN**: Prospective Randomized Single Blinded Control Trial.

**SOURCE OF DATA:**

This study will be carried out in the Department of Anaesthesiology, B.L.D.E (Deemed to be university) Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapur.

**METHOD OF COLLECTION OF DATA:**

**Study Design:** one and half year prospective randomized clinical trial.

**Study Period:** one and half year (December 2016 to August 2018).

**Sample Size:** 70 patients of both genders randomly divided into two groups of 35 each. (by computer generated random numbers).

**STATISTICAL DATA:**

In a previous study proportion of first attempt was found 83% in control group and 100% in study group (based on literature review). Using proportions of previous study at 95% confidence level and at 90% power in the study. Sample size will be 35 patients in each group. Age, sex and weight are comparable in each group.

**Formula used:-**

$$\frac{n = (Z\alpha + Z\beta)^2 x 2 x SD^2}{Md^2}$$

Z =Z statistics at a level of significance.

Md= anticipated mean difference.

SD= anticipated standard devience

**Statistical tests used**

**Chi squire test**

**ANOVA test**

**Mean+- SD**

**INCLUSION CRITERIA:**

1. Patients between 18-60 years of age
2. ASA 1 & 2
3. Either male or female
4. BMI<30kg/m2

**EXCLUSION CRITERIA:**

1. Patient refusal.
2. H/o allergy and contraindication to studied medication or anaesthetic agents.
3. Infection at local site
4. Patient's inability to describe postoperative pain to investigator (dementia, delirium, psychiatric and neurological disorder.
5. BMI > 30.
6. Pregnancy

Patients between age 18-60 years were randomly allocated into two groups of 35 patients each. Patients were randomized by sealed envelopes to undergo TAP block. Group 1 & 2 patients both underwent laparoscopic surgeries under general anaesthesia. Pre-operative anaesthesia assessment was made after requisite hematological, biochemical tests along with ECG and chest X-ray and through physical examination. At the pre-operative visit on the evening of or before surgery, the VAS scale scoring system was explained to all patients. Written informed consent was obtained from all patients to be included in the study. Pre-medication was given as Inj. Midazolam 0.02-0.03 mg/kg IV in the operation theatre. All the patients received a standardized general anaesthesia as per institute protocol. Anaesthesia was induced with propofol 2-4 mg/kg, fentanyl 2 mcg/kg and atracurium 0.5 mg/kg intravenous (IV) and anaesthesia was maintained with isoflurane and 40% oxygen in nitrous oxide. The study drug was administered according to the group allocated. Patients were reversed with neostigmine and glycopyrollate. Standard monitoring including non-invasive blood pressure monitoring, arterial oxygen saturation, electrocardiogram and end tidal carbon dioxide monitoring was done.

**Group 1 -** TAP block (after induction of General Anaesthesia) by 15 ml 0.25% Bupivacaine with Dexamethasone 8mg on both sides if surgical incision involved both sides of rectus sheath and unilateral if incision involved only one side of rectus sheath.

**Group 2 -** TAP block (after induction of General Anaesthesia) by 15 ml 0.25% Bupivacaine with normal saline 5ml.

Patients of both groups were followed in post-operative period for pain and adverse events if any. Pain was assessed by Visual analogue scale (0-10). If patient

experienced pain he/she was asked to grade the pain at rest and on movement. The time was noted calculating from the end of the surgery. Patients were followed for 24 hours and the results of 2 groups were compared. For TAP block the skin was prepared with 10% Betadine solution and a high-frequency (5 – 10 MHz) ultrasound probe (SonoSite M-Turbo. SonoSite, Inc, Bothwell, MO, USA). The probe was placed horizontally across the abdomen. The muscle layers in the antero-lateral part of the abdomen was traced by scanning from the midline towards the area between the iliac crest and the costal margin in the mid-axillary line.

The rectus abdominis muscle was identified, just off the midline, as an oval / elliptical structure. The ultrasound transducer was moved to scan laterally where the 3 muscle layers could be seen running parallel to one another. With an adequate ultrasound image, the regional block needle was inserted anterior to the transducer. The needle was placed in the Transversus abdominis plane and 2ml of 0.9% normal saline was given and splitting of plane was confirmed before injecting 15 ml of 0.25% bupivacaine (with Dexamethasone or normal saline) slowly. After injection, the fascial plane was seen to separate and form a well-defined hypoechoic elliptical shape between the internal oblique and transversus abdominis muscles.

**Fig 21 A: The ultrasound machine used at our hospital. ((SonoSite M-Turbo, SonoSite, Inc, Bothwell, MO, USA)**

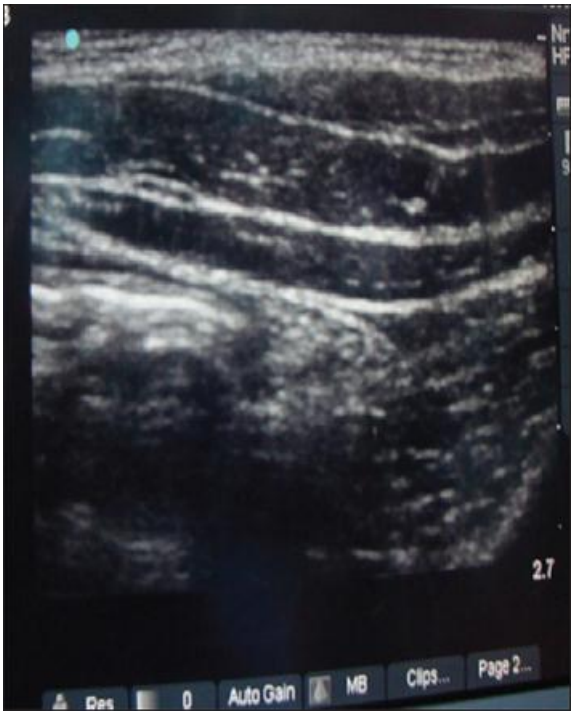



**Fig:21 B: Sono-anatomical depiction of the different plane.**

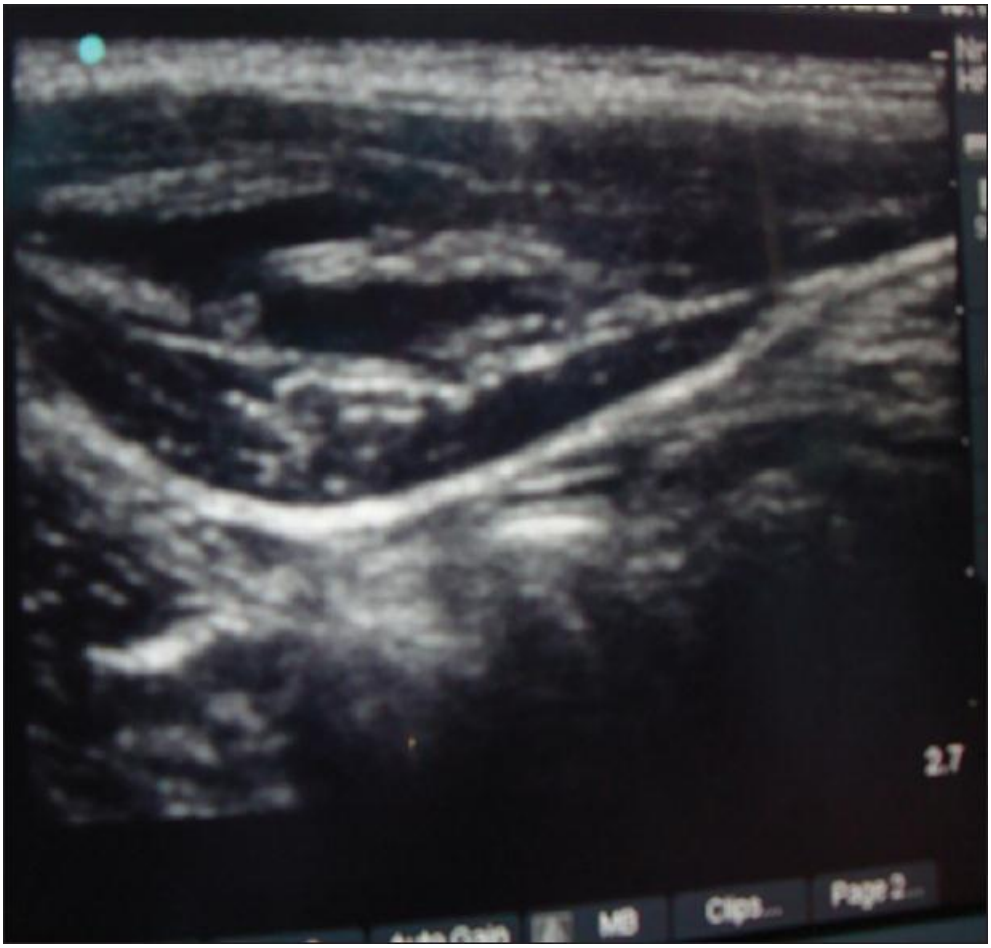



**Fig:22 Widening of slit by LA injected between internal oblique and transversus abdominis**

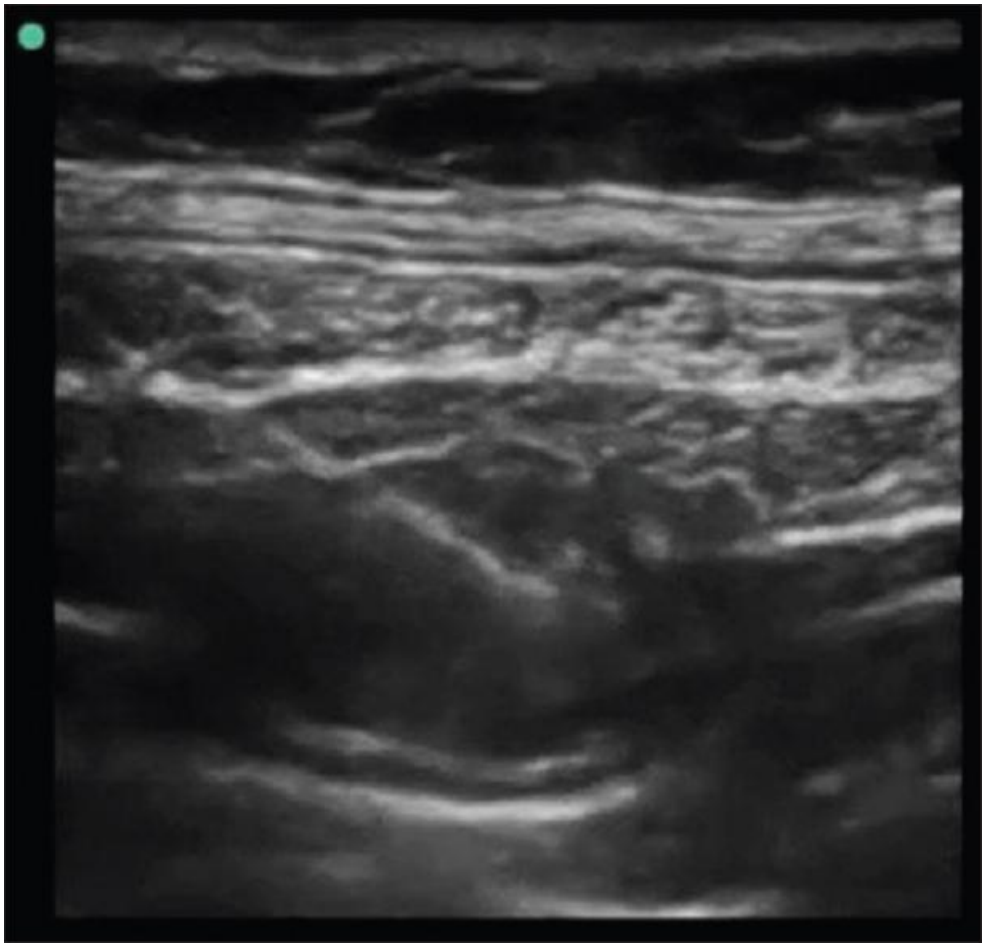


**Fig:23 Spread of drug in transversus abdominis plane**

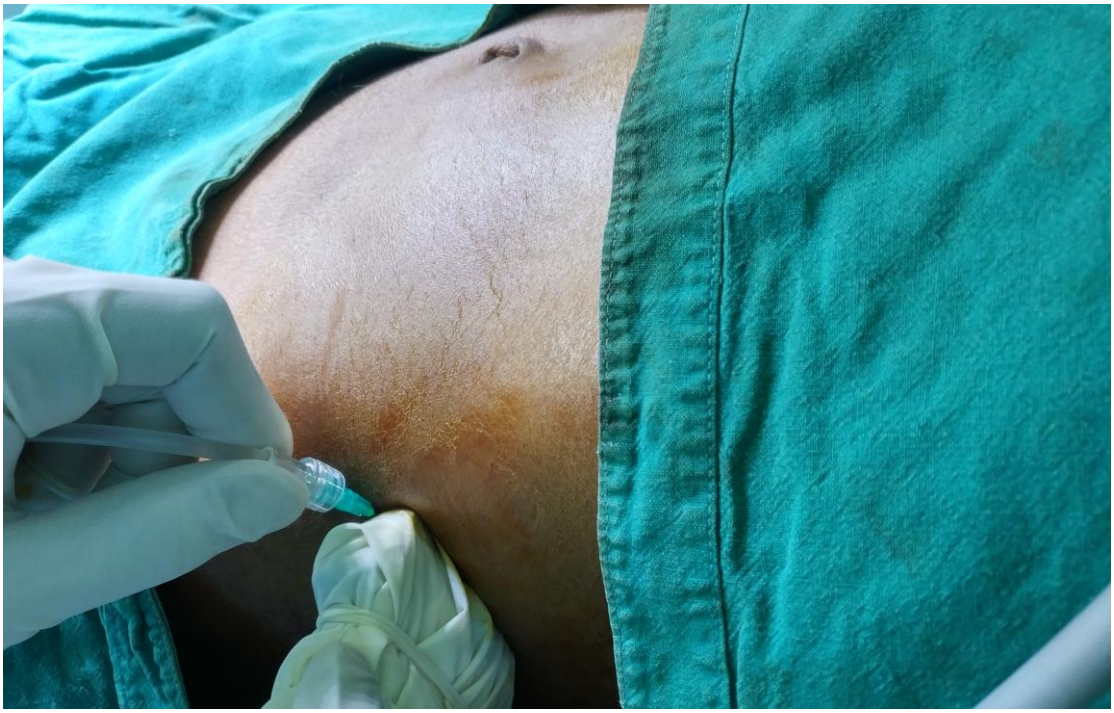


**Fig:24 Illustration of TAP block in a intubated patient after induction of anaesthesia. After depositing the drug the spread of local anaesthetic was ensured in the plane. If a patchy opacity appeared within the muscle either superficial or deep to the transversus abdominis plane, then the needle was repositioned until local anaesthetic was seen to spread within the plane, separating the fascia between the muscle.**

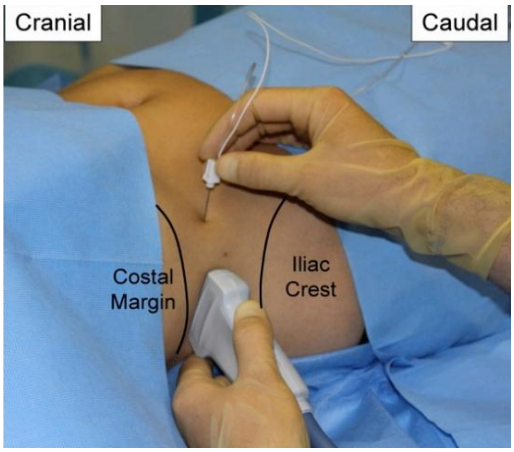



**Fig:25: Image showing surface landmarks for the TAP block.**

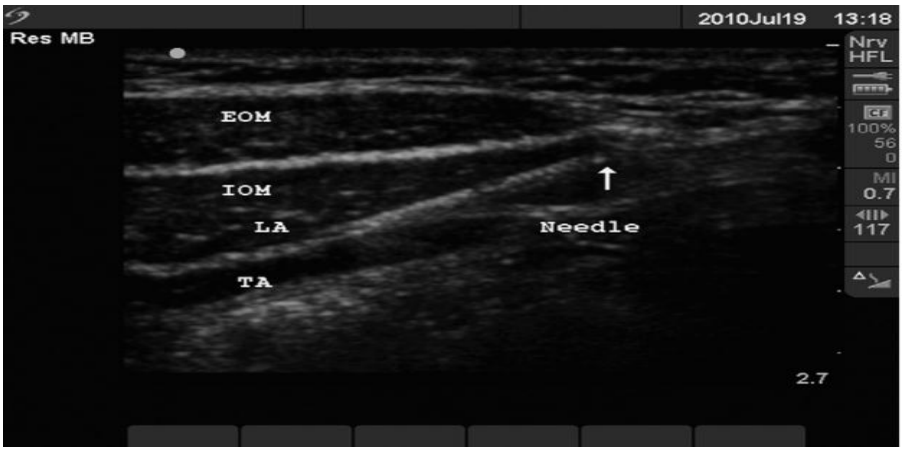



**Fig:26: Sono-anatomical structures with needle in-situ.**

Patient's baseline vitals heart rate, blood pressure, oxygen saturation were noted during surgery, every fifteen minutes for the first hour and later third hourly after surgery for 24 hours. The findings were noted by a blinded observer. After completion of the surgical procedure and emergence from anaesthesia, patients were transferred to the postoperative recovery room for further monitoring of post-operative pain.

In postoperative recovery room, all patients were monitored for heart rate, blood pressure, oxygen saturation, pain (VAS) and PONV. Rescue analgesia was given as Inj. Paracetamol (1gm) intravenously every 8hrs and Inj. Pentazocine (30

mg) intramuscularly in case of visual analogue scale (VAS)≥ 4. Time at which patient demanded rescue analgesia was noted and the VAS score at that time was also noted. All recordings were done by a blinded observer. Pain was assessed by visual analogue scale (VAS).

**VISUAL ANALOGUE SCALE**

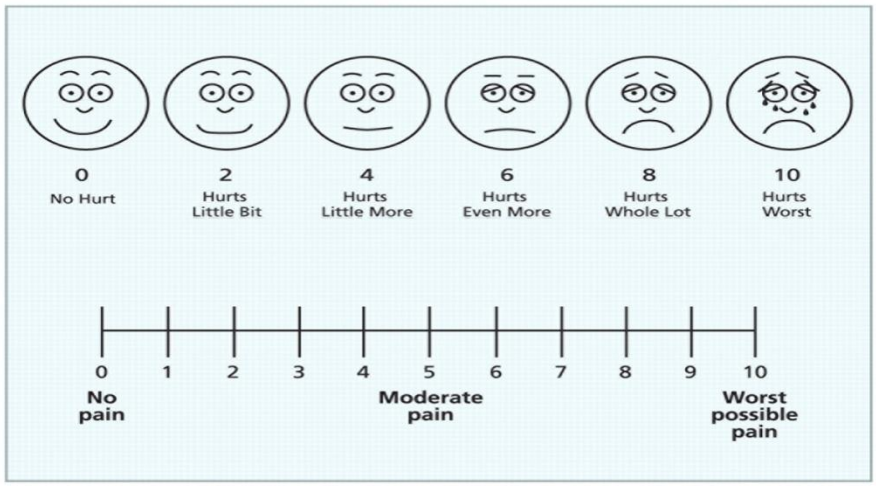



**fig:27**

**PONV SCORE:**

0 = no nausea/vomiting.

1 = nausea/retching.

2 = Vomiting.

3 = severe vomiting/projectile.

**Statistical analysis**

The statistical analysis was done using SPSS for Windows version 16.0 software. For non-continuous data Chi-square test was used. The mean and standard deviation of the parameters studied during observation period were calculated for two treatment groups and compared using Student 't' test. The critical value of ‘p’ indicating the probability of significant difference was taken as <0.05 for comparisons.

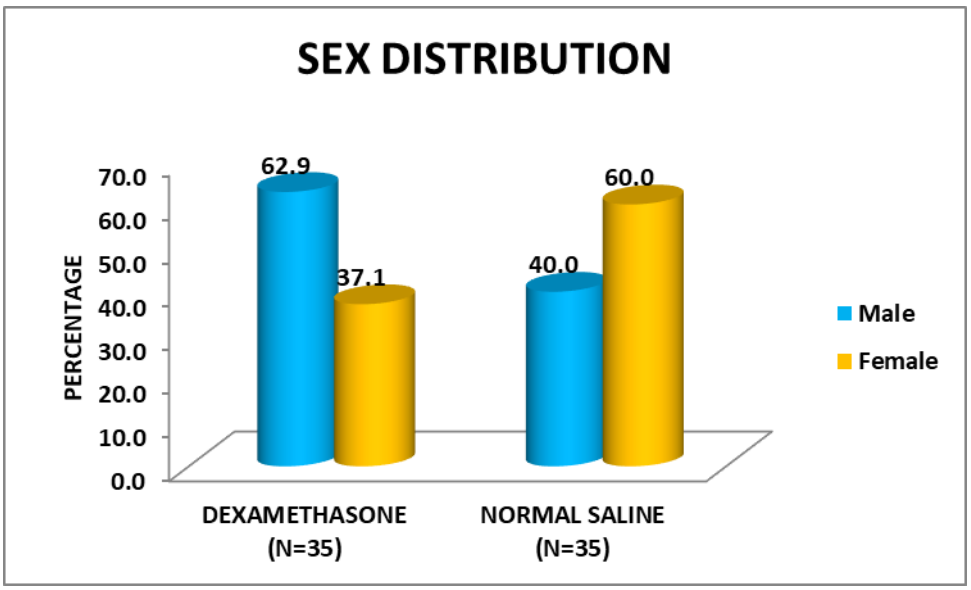
All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square ($\chi^2$)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test. If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office.

# OBSERVATIONS AND RESULTS

**TABLE 1: DISTRIBUTION OF CASES ACCORDING TO SEX BETWEEN STUDY GROUPS**

| SEX | STUDY (N=35) | | CONTROL (N=35) | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Male | 22 | 62.9 | 14 | 40.0 | 0.056 |
| Female | 13 | 37.1 | 21 | 60.0 | |
| Total | 35 | 100.0 | 35 | 100.0 | |

**GRAPH 1: DISTRIBUTION OF CASES ACCORDING TO SEX BETWEEN STUDY GROUPS**

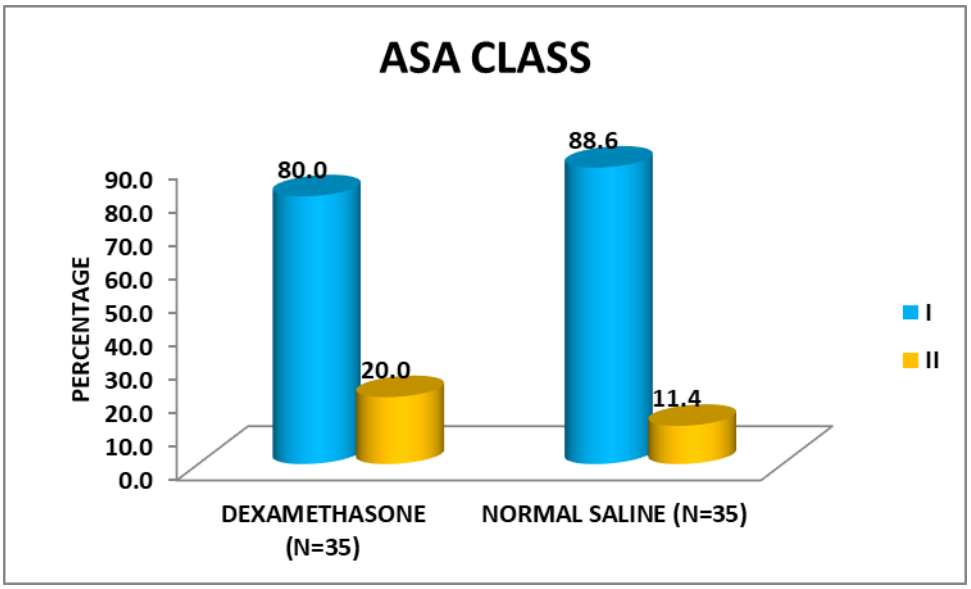



Out of 36 males and 34 females studied in both comparative groups No statistical significance noted thus duration of post analgesia with TAP block is not influenced by sex of the subject/patient.

**TABLE 2: DISTRIBUTION OF CASES ACCORDING TO ASA CLASS BETWEEN STUDY GROUPS**

| ASA_Class | STUDY (N=35) | | CONTROL (N=35) | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| I | 28 | 80.0 | 31 | 88.6 | 0.324 |
| II | 7 | 20.0 | 4 | 11.4 | |
| Total | 35 | 100.0 | 35 | 100.0 | |

**GRAPH 2: DISTRIBUTION OF CASES ACCORDING TO ASA CLASS BETWEEN STUDY GROUPS**

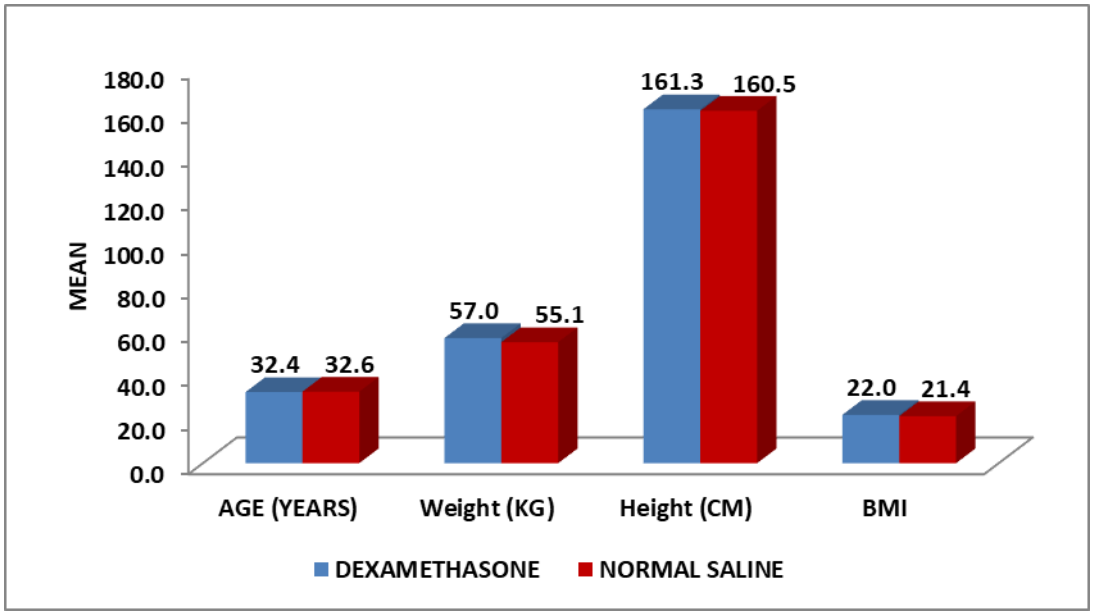



Total of 70 ASA class I and II subjects were studied. No statistical significance noted in any group. TAP block with dexamethasone or normal saline is not influenced by ASA class of the patient undergoing the Block/procedure.

**TABLE 3: COMPARISION OF MEAN DEMOGRAPHIC PARAMETERS BETWEEN STUDY GROUPS**

| DEMOGRAPHIC PARAMETERS | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| AGE (YEARS) | 32.4 | 12.1 | 32.6 | 11.7 | 0.952 |
| Weight (KG) | 57.0 | 5.7 | 55.1 | 9.6 | 0.322 |
| Height (CM) | 161.3 | 6.6 | 160.5 | 7.7 | 0.68 |
| BMI | 22.0 | 2.7 | 21.4 | 3.2 | 0.416 |

**GRAPH 3: COMPARISION OF MEAN DEMOGRAPHIC PARAMETERS BETWEEN STUDY GROUPS**

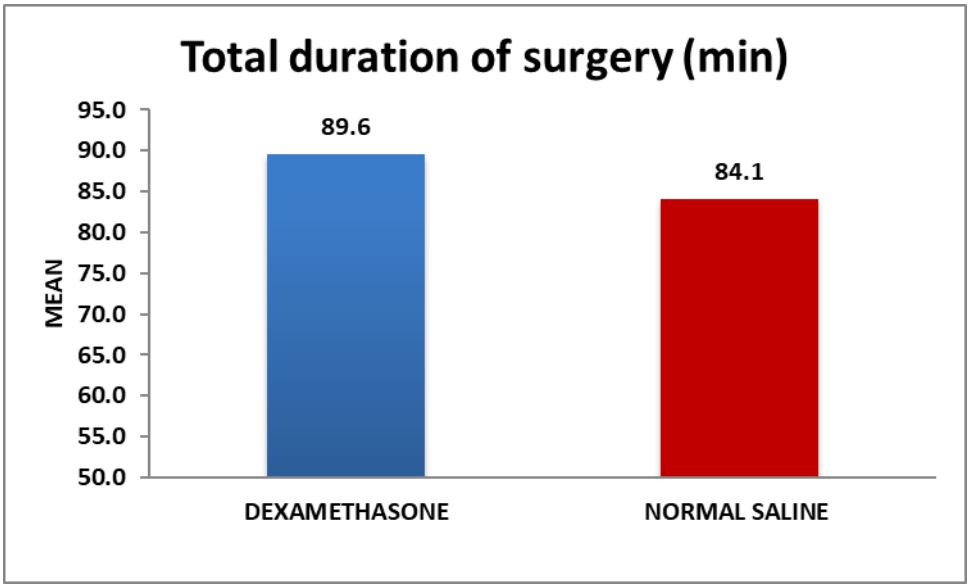



Parameters like AGE/WEIGHT/HEIGHT/BMI were assessed for influencing the duration of post op analgesia with TAP block in both groups. No statistical P value determined.

**TABLE 4: COMPARISION OF MEAN DURATION BETWEEN STUDY GROUPS**

| DURATION | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Total duration surgery | 89.6 | 17.6 | 84.1 | 7.0 | 0.094 |

**GRAPH 4: COMPARISION OF MEAN DURATION BETWEEN STUDY GROUPS**

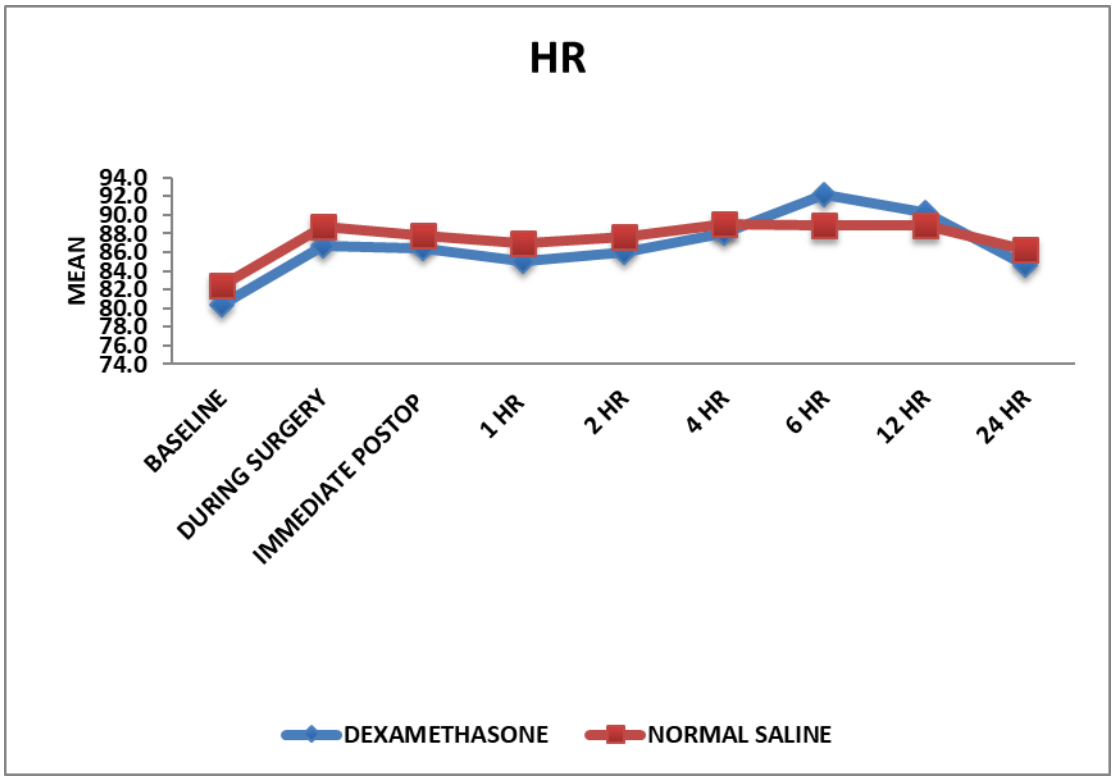



Total duration of surgery was assessed for influencing the duration of post op analgesia with TAP block in both groups. No statistical P value determined.

**TABLE 5: COMPARISION OF MEAN HR ACCORDING TO TIME**

| HR | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| BASELINE | 80.3 | 9.2 | 82.4 | 9.8 | 0.356 |
| DURING SURGERY | 86.7 | 9.3 | 88.7 | 9.9 | 0.393 |
| IMMEDIATE POSTOP | 86.3 | 10.1 | 87.8 | 10.7 | 0.553 |
| 1 HR | 85.1 | 9.7 | 86.9 | 10.4 | 0.449 |
| 2 HR | 85.9 | 9.0 | 87.6 | 9.5 | 0.456 |
| 4 HR | 88.1 | 7.6 | 89.0 | 8.5 | 0.638 |
| 6 HR | 92.2 | 8.4 | 88.9 | 8.3 | 0.106 |
| 12 HR | 90.2 | 6.9 | 88.9 | 7.5 | 0.428 |
| 24 HR | 84.7 | 6.6 | 86.3 | 6.5 | 0.311 |

**GRAPH 5: COMPARISION OF MEAN HR ACCORDING TO TIME**

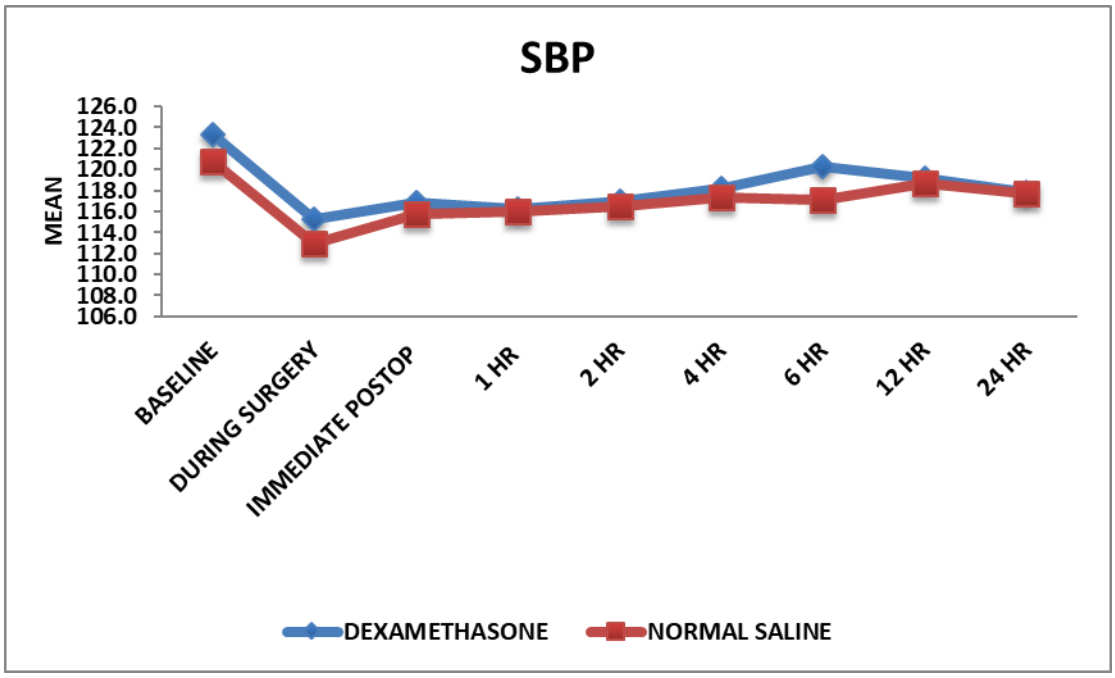



Heart rate was assessed among all subjects for influencing the duration of post op analgesia with TAP block in both groups. No statistical P value determined.

**TABLE 6: COMPARISION OF MEAN SBP ACCORDING TO TIME**

| SBP | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| BASELINE | 123.4 | 9.5 | 120.8 | 8.4 | 0.237 |
| DURING SURGERY | 115.3 | 9.2 | 113.0 | 7.3 | 0.254 |
| IMMEDIATE POSTOP | 116.9 | 10.0 | 115.8 | 6.6 | 0.592 |
| 1 HR | 116.3 | 7.7 | 116.0 | 6.6 | 0.868 |
| 2 HR | 116.9 | 8.7 | 116.5 | 7.7 | 0.817 |
| 4 HR | 118.2 | 8.1 | 117.4 | 7.5 | 0.648 |
| 6 HR | 120.2 | 8.3 | 117.1 | 7.2 | 0.1 |
| 12 HR | 119.2 | 7.7 | 118.7 | 7.8 | 0.783 |
| 24 HR | 117.9 | 6.2 | 117.7 | 7.3 | 0.888 |

**GRAPH 6: COMPARISION OF MEAN SBP ACCORDING TO TIME**

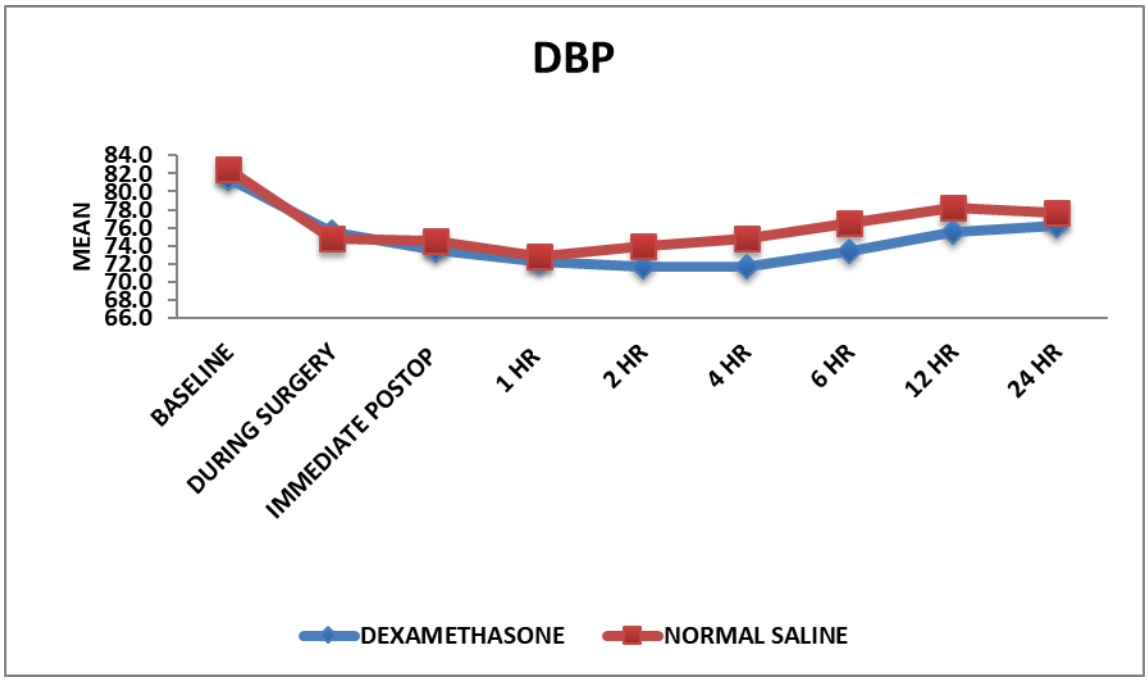



Systolic blood pressure was assessed for influencing the duration of post op analgesia with TAP block in both groups. No statistical P value determined.

**TABLE 7: COMPARISION OF MEAN DBP ACCORDING TO TIME**

| DBP | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| BASELINE | 81.5 | 10.9 | 82.5 | 8.1 | 0.655 |
| DURING SURGERY | 75.5 | 8.8 | 74.9 | 8.1 | 0.779 |
| IMMEDIATE POSTOP | 73.6 | 7.6 | 74.6 | 7.6 | 0.595 |
| 1 HR | 72.2 | 6.3 | 72.9 | 7.8 | 0.698 |
| 2 HR | 71.7 | 7.0 | 73.9 | 7.3 | 0.186 |
| 4 HR | 71.7 | 7.0 | 74.9 | 6.7 | 0.056 |
| 6 HR | 73.3 | 6.7 | 76.5 | 5.9 | 0.041 |
| 12 HR | 75.5 | 9.0 | 78.3 | 6.3 | 0.136 |
| 24 HR | 76.2 | 9.3 | 77.7 | 7.3 | 0.458 |

**GRAPH 7: COMPARISION OF MEAN DBP ACCORDING TO TIME**

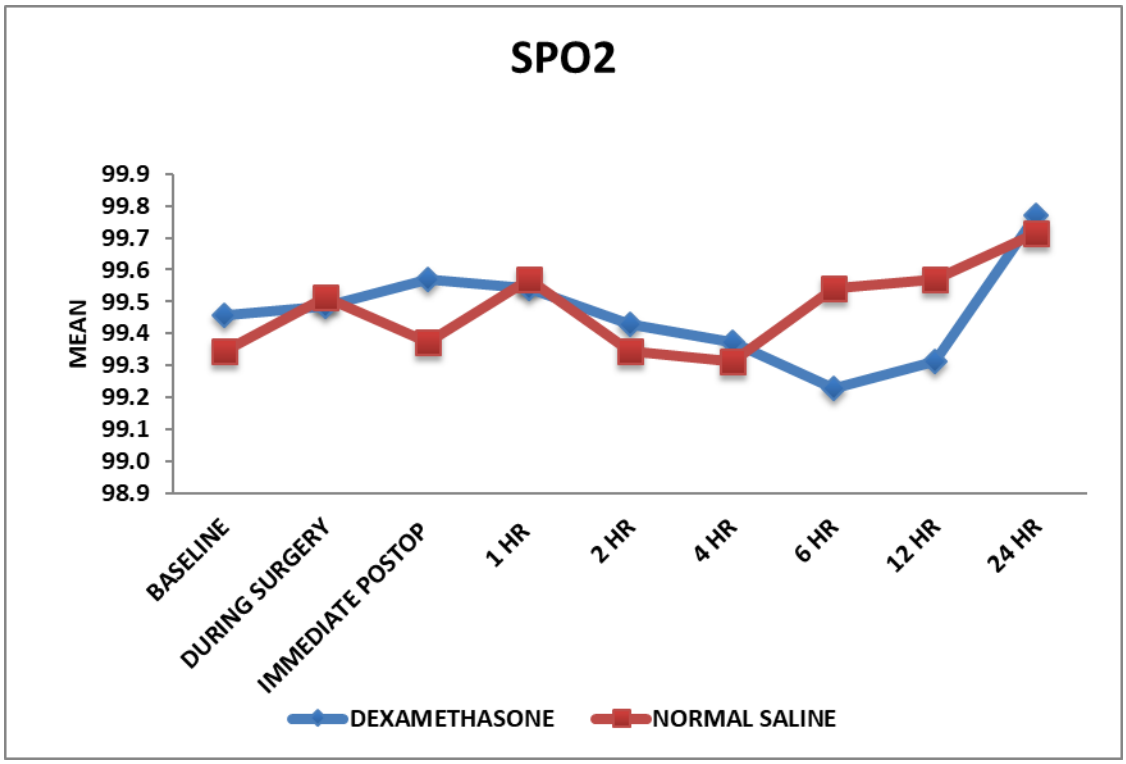



Diastolic blood pressure was assessed for influencing the duration of post op analgesia with TAP block in both groups. No statistical P value determined.

**TABLE 8: COMPARISION OF MEAN SPO2 ACCORDING TO TIME**

| SPO2 | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| BASELINE | 99.5 | 0.6 | 99.3 | 0.5 | 0.364 |
| DURING SURGERY | 99.5 | 0.5 | 99.5 | 0.5 | 0.814 |
| IMMEDIATE POSTOP | 99.6 | 0.5 | 99.4 | 0.5 | 0.096 |
| 1 HR | 99.5 | 0.8 | 99.6 | 0.5 | 0.856 |
| 2 HR | 99.4 | 0.8 | 99.3 | 0.8 | 0.651 |
| 4 HR | 99.4 | 0.8 | 99.3 | 0.9 | 0.781 |
| 6 HR | 99.2 | 0.6 | 99.5 | 0.6 | 0.033 |
| 12 HR | 99.3 | 0.6 | 99.6 | 0.6 | 0.075 |
| 24 HR | 99.8 | 0.4 | 99.7 | 0.5 | 0.591 |

**GRAPH 8: COMPARISION OF MEAN SPO2 ACCORDING TO TIME**



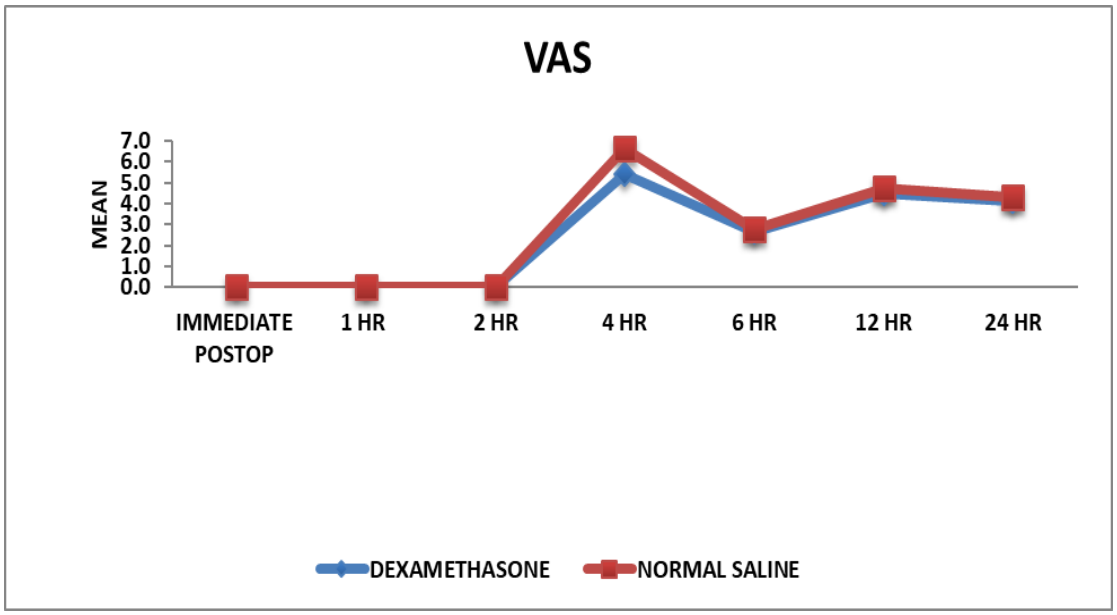

Standard oxygen saturation parameters were assessed for influencing the duration of post op analgesia with TAP block in both groups. No statistical P value determined.

**TABLE 9: COMPARISION OF MEAN VAS ACCORDING TO TIME**

| VAS | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| IMMEDIATE POSTOP | 0.0 | 0.0 | 0.0 | 0.0 | - |
| 1 HR | 0.0 | 0.0 | 0.0 | 0.0 | - |
| 2 HR | 0.0 | 0.0 | 0.0 | 0.0 | - |
| 4 HR | 5.4 | 2.3 | 6.6 | 1.7 | 0.014* |
| 6 HR | 2.6 | 0.9 | 2.8 | 1.0 | 0.462 |
| 12 HR | 4.5 | 1.4 | 4.7 | 1.0 | 0.321 |
| 24 HR | 4.1 | 1.4 | 4.3 | 1.2 | 0.579 |

Note: * significant at 5% level of significance ($p<0.05$)

**GRAPH 9: COMPARISION OF MEAN VAS ACCORDING TO TIME**



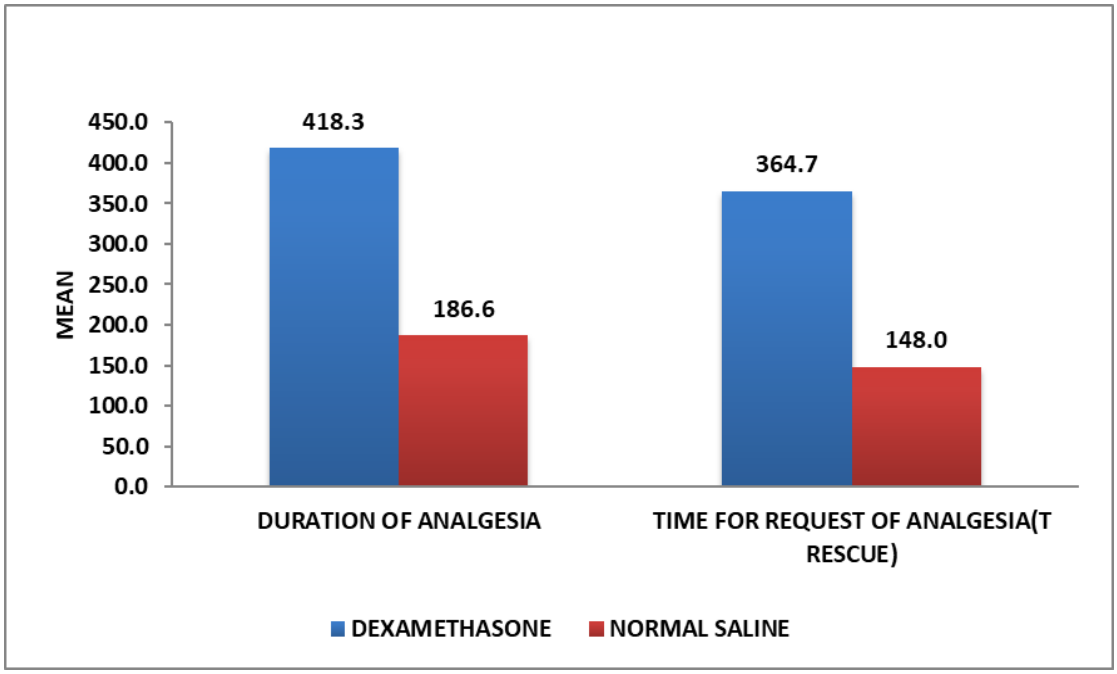

On calculation of mean VAS score in both comparative groups statistical significance noted on 4$^{th}$ and 12$^{th}$ hour post-operative period in a group with dexamethasone as adjuvant in TAP block, indicating increased duration of post-op analgesia in dexamethasone group.

**TABLE 10: COMPARISION OF MEAN PARAMETERS ACCORDING TO TIME**

| PARAMETERS | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Duration Analgesia | 418.3 | 94.9 | 186.6 | 67.6 | <0.001* |
| TIME FOR REQUEST OF ANALGESIA (T RESCUE) | 364.7 | 19.8 | 148.0 | 14.2 | <0.001* |

Note: * significant at 5% level of significance (p<0.05)

**GRAPH 10: COMPARISION OF MEAN PARAMETERS ACCORDING TO TIME**



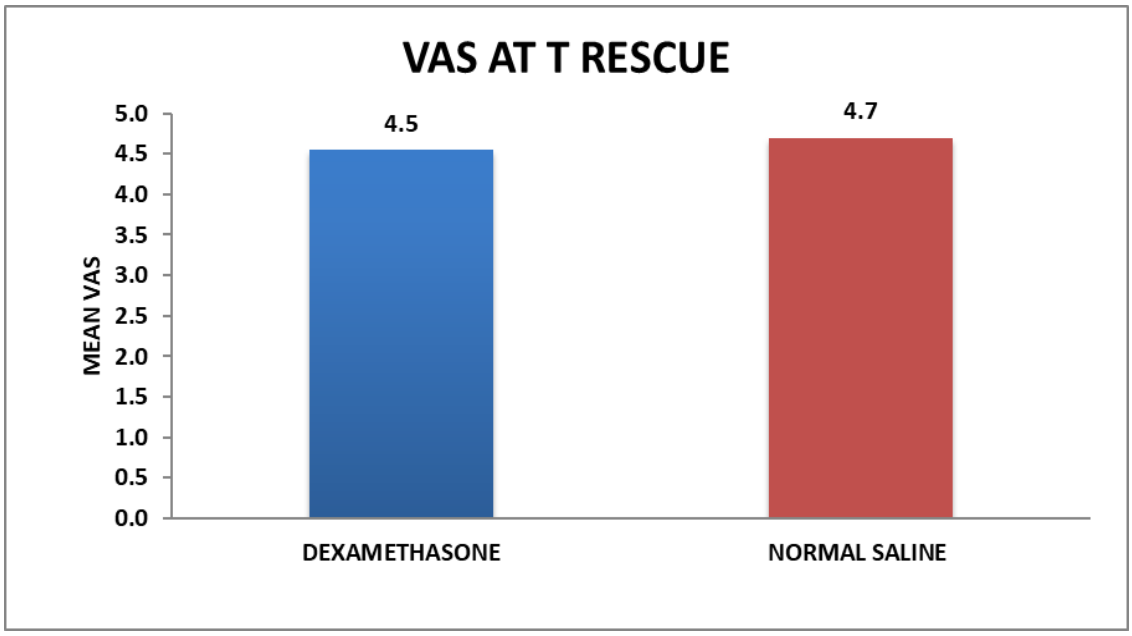

Total duration of analgesia and time request of analgesia was assessed with TAP block in both groups. The duration of analgesia increased considerably in study group. The time for request of analgesia was increased (364.7 min) in study group when compared to control group (148.0 min).

**TABLE 11: COMPARISION OF MEAN VAS AT T RESCUE ACCORDING TO TIME**

| VAS AT T RESCUE | STUDY | | CONTROL | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| | 4.5 | 1.0 | 4.7 | 1.06 | 0.423 |

Note: * significant at 5% level of significance ($p<0.05$)

**GRAPH 11: COMPARISION OF MEAN VAS AT T RESCUE ACCORDING TO TIME**



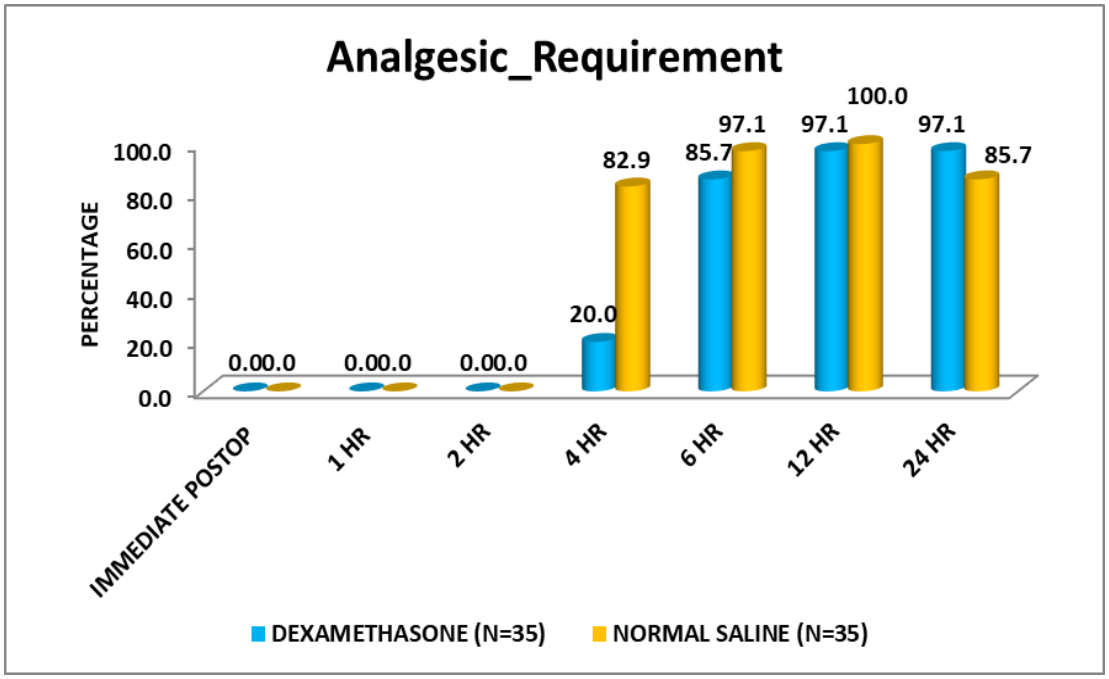

On calculation of mean VAS at T rescue score in both comparative groups no statistical significance noted in post-operative period in the group with dexamethasone as adjuvant in TAP block, indicating increased duration of post-op analgesia in dexamethasone group.

**TABLE 12: ANALGESIC REQUIREMENT BETWEEN STUDY GROUPS**

| Analgesic Requirement | STUDY(N=35) | | NORMAL SALINE (N=35) | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| IMMEDIATE POSTOP | 0 | 0.0 | 0 | 0.0 | - |
| 1 HR | 0 | 0.0 | 0 | 0.0 | - |
| 2 HR | 0 | 0.0 | 0 | 0.0 | - |
| 4 HR | 7 | 20.0 | 29 | 82.9 | <0.001* |
| 6 HR | 30 | 85.7 | 34 | 97.1 | 0.088 |
| 12 HR | 34 | 97.1 | 35 | 100.0 | 0.314 |
| 24 HR | 34 | 97.1 | 30 | 85.7 | 0.088 |

Note: * significant at 5% level of significance (p<0.05)

**GRAPH 12: ANALGESIC REQUIREMENT BETWEEN STUDY GROUPS**



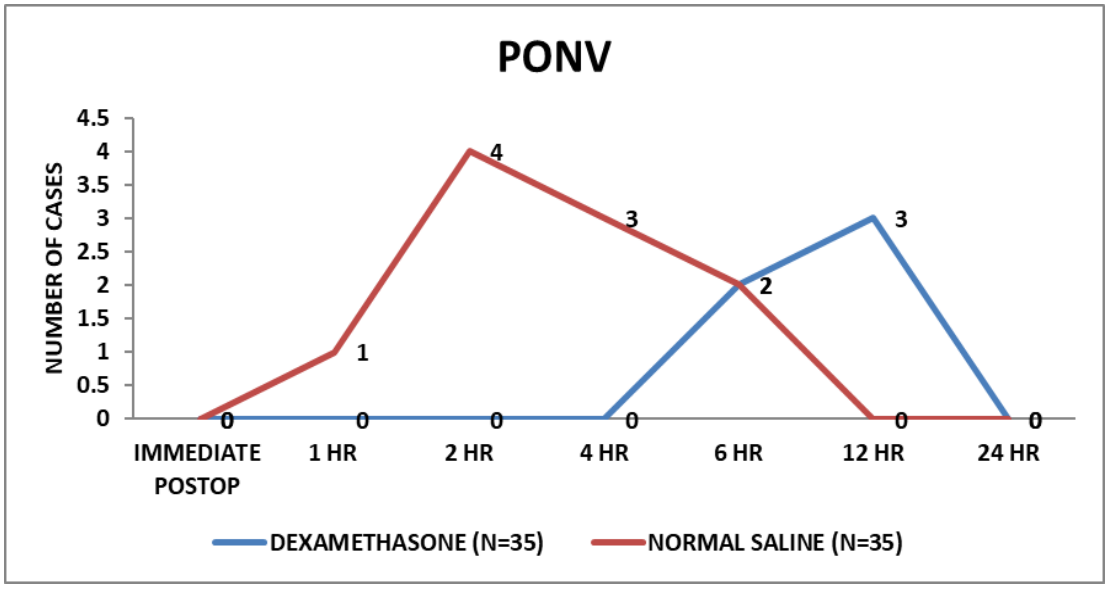

Statistical significance noted in need for post-operative analgesic at 4th hour where seven subjects needed analgesics (20%) in dexamethasone group compared to twenty -nine subjects required analgesics (82%) in normal saline group. Similar difference noted in 6th and 12th hour. Hence TAP with adjuvant dexamethasone is efficacious and superior in postoperative analgesic management

**TABLE 13: PONV BETWEEN STUDY GROUPS**

| PONV( > 1) | STUDY (N=35) | | CONTROL (N=35) | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| IMMEDIATE POSTOP | 0 | 0.0 | 0 | 0.0 | - |
| 1 HR | 0 | 0.0 | 1 | 2.9 | 0.314 |
| 2 HR | 0 | 0.0 | 4 | 11.4 | 0.040* |
| 4 HR | 0 | 0.0 | 3 | 8.6 | 0.077 |
| 6 HR | 2 | 5.7 | 2 | 5.7 | - |
| 12 HR | 3 | 8.6 | 0 | 0.0 | 0.077 |
| 24 HR | 0 | 0.0 | 0 | 0.0 | - |

Note: * significant at 5% level of significance (p<0.05)

**GRAPH 13: PONV( > 1) BETWEEN STUDY GROUPS**




On calculation of PONV score in both comparative groups statistical significance noted on 1st/ 2nd /4th and 6th hour post-operative period, with highest incidence in 2nd hour with four patients experiencing PONV in the group with normal saline as adjuvant in TAP block, indicating less incidence of post-op nausea and vomiting in dexamethasone group.

# DISCUSSION

This randomized clinical trial demonstrated that the TAP block with dexamethasone as an adjuvant added to bupivacaine when used as a part of multimodal analgesia provides effective analgesia for patients undergoing laparoscopic surgeries. It reduced the intensity of break through pain and requirement of opioids postoperatively. All blocks were done under ultrasound guidance which ensured the exact location. There was no block related complication.

The standard regimen of paracetamol, opioid and NSAID at our institution didn't provide good postoperative pain relief in all patients following laparoscopic surgeries. Substantial component of pain experienced by the patient is from abdominal wall incision in abdominal surgeries any interventions that block pain from abdominal wall will provide good post-operative pain relief so a multimodal analgesia regimen is needed for providing effective postoperative pain relief,. Transversus Abdominis Plane Block is a type of abdominal field block that anaesthetizes the nerve supplying the abdominal wall is being used for providing post-operative pain relief after abdominal surgeries both in adults and children. Adding dexamethasone to the block increases the duration of the block thereby providing increased duration of analgesia and reduced the incidence of PONV also.

In the postoperative period the intensity of postoperative pain was assessed by VAS scoring for pain. On the first complaint of pain by the patient or a VAS score of more than 4 a rescue analgesic was administered and the time was noted. The time elapsed between the administration of the block and the first rescue analgesic was recorded as the duration of post-block analgesia. The VAS scores were recorded every second hour from the time of drug administration. The VAS scores in the

dexamethasone group (V6 h = 3.70 ± 0.68) were comparable with the VAS scores noted with the studies done by Ra *et al*. [107] (V6 h = 3.1 ± 1.55) and Aveline *et al*. [98] who employed the same concentration in their studies. The intensity of pain as experienced by the patient in the postoperative period was lesser in the dexamethasone group than in the normal saline group. In a qualitative study by Nurçin Gülhaş *et al*. [108] in 2015 demonstrated that the addition of dexamethasone to ultrasound guided TAP block had decreased postoperative pain scores, increased the time to first analgesic requirement, reduced postoperative narcotic requirements and adverse events related to it. The rate of nausea or vomiting were also reduced with shorter length of hospital stay in patients undergoing total abdominal hysterectomy. TAP Block with dexamethasone group had reduced VAS Scores throughout the 24hr postoperative period. The patients in TAP Group had significantly decreased VAS scores ($p<0.05$) for 24hr period except at 0,1hr postoperative period with a mean VAS Score of 2. Similarly decreased VAS Scores was also observed by Mc Donnell *et al*. [83] G. Niraj *et al*. [17]

The duration of post-block analgesia was defined as the time from the injection of the LA to the first complaint of pain by the patient, at which point he received Injection Pentazocine 30 mg IM. In the normal saline group this duration was found to be 186.6 ± 67.6 min and in dexamethasone group it was found to be 418.3 ± 94.9 min. The difference in the duration of analgesia provided by the two groups was found to be statistically significant ($P < 0.05$). In our study, the patients who received the TAP block had a significant reduction in the post-operative rescue analgesics consumption ($p < 0.03$) at 2, 4 and 6 hrs. The duration of TAP block is still limited by the efficacy of LA administered and the dose used, which is again dependent on the maximum permitted dose for that agent. This has led to the use of

adjuvants such as clonidine, dexmedetomidine to prolong the effect of LA in TAP block. In a randomized control study, $MgSO_4$ (150 mg) was added as an adjuvant to bupivacaine in USG-guided TAP block proved that it reduces post-operative pain scores, prolongs the duration of analgesia and decreases demands for rescue analgesics. [6] In another randomized controlled trial which demonstrated that addition of clonidine to bupivacaine in single-shot TAP block for cesarean section under SA prolongs analgesia by 10–12 hour and reduces overall postoperative analgesic requirements by more than 75 mg compared to bupivacaine alone. [25] In another study by Almarakbi *et al.* the addition of dexmedetomidine to bupivacaine in TAP block achieves better local anaesthesia and provides better pain control post-operatively without any major side-effects. [26] The effects when fentanyl was added as an adjuvant suggested that the addition of 2.5 µg/ml fentanyl to the TAP block procedure (0.375% ropivacaine) was unable to improve the duration and quality of analgesia following caesarean delivery. In addition, as the cumulative fentanyl consumption was significantly lower in both the groups postoperatively. [27]

The opioids sparing effect has been documented by Niraj *et al*. in their study with TAP block which had the similar result of reduced opioids consumption as that which had been observed in our retrospective analysis of the data of TAP block in laparoscopic surgery. [75] Indicating the reduced incidence of the opioids-related side effects.

Time to rescue analgesia was prolonged in our study in all the subcategories of laparoscopic surgeries where TAP block was administered which was in accordance with the study of McDonnell *et al*. [63] and Carney *et al*. [62]

This shows the effectiveness of TAP block as a part of multimodal analgesia regimen and its ability of reducing opioid requirement and opioid related adverse

effects. In our study we found that addition of dexamethasone to TAP Block, showed reduced analgesics requirement for 24 hour period in comparison to TAP block with normal saline. The TAP block reduced the pain scores with its ability to block transmission of nociceptive impulse from abdominal wall. This shows that adding dexamethasone to TAP Block can increase duration of the block by providing good pain relief for a period of 24hrs. This is in accordance with study by El Sharnouby *et al.* [111]

TAP block also reduced the incidence of PONV. As for post-operative pain management the use of opioids results in PONV. Pain and postoperative nausea vomiting top the list of causes of dissatisfaction. Our analysis shows that not only analgesic requirements in TAP block are lower but also the pain scores and the PONV incidence is also significantly smaller. Many direct and indirect factors could have contributed toward this desirable outcome for PONV. Other than direct relation of opioids consumed, higher pain scores are known to directly increase PONV as well. Supporting this studies included in our analysis by Soltani Mohammadi *et al.* [113] and Parikh *et al.* [112] demonstrated that overall numeric rating scale (NRS) for pain had significantly lower values with the use of TAP block because it provided analgesia for quite longer duration. Thereby limiting the use of opioid for postoperative pain ultimately reducing the incidence of PONV. The addition of dexamethasone a potent anti-emetic was also a contributing factor. In calculating the incidence of PONV, any score of above zero at any time point was taken as indicator that the patient had PONV. Many clinical studies also observed similar reduction in PONV incidence McDonnell *et al.* [63]

Although analgesic requirements in the study (dexamethasone) group increased in comparison to the control (normal saline) group during the 24 hr period

because less amount of analgesics were used in the study group. Indicating a prolonged duration of the block.

Limitations of our study, first we restricted our study period to 24 hours however many studies have already shown that TAP Block alone with normal saline provides analgesia for around 48hrs so adding dexamethasone increased the block's duration. Secondly, blinding was not perfect as sensations were lost over the abdomen and is a single blinded study.

**Future recommendations:**

Further studies should be undertaken to evaluate the effectiveness of adding various drugs (opioid) with local anaesthetics in Transversus Abdominis Plane Block.

**Conclusion:**

TAP Block is easy to perform under ultrasound guidance without complication and it provides effective analgesia. Adding dexamethasone as an adjuvant to TAP block produces immense post-operative analgesia with concomitant increase in duration of analgesia which reduced VAS score and rescue analgesic dose requirements. It also reduced PONV considerably.

# SUMMARY & CONCLUSION

This randomized single blind controlled study was conducted in the Department of Anaesthesiology, B.L.D.E (deemed to be university) SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR. KARNATAKA. After obtaining approval by the Institutional Ethical Committee and written informed patient consent seventy adult patients of ASA I and II scheduled to undergo laparoscopic surgeries under general anaesthesia in the age group of 18-60 years were randomized into two groups comprising thirty-five each.

Group 1: TAP block (after induction of General Anaesthesia) by 15 ml 0.25% bupivacaine with Dexamethasone 8mg, on both sides.

Group 2: TAP block (after induction of General Anaesthesia) by 15 ml 0.25% bupivacaine with normal saline 5ml.

Pain was assessed in both the groups by VAS score postoperatively. Rescue analgesics (Inj. Paracetamol and Inj. Pentazocine) were given as per requirement for the management of pain.

All recordings were done by a blinded observer. All data were analyzed statistically by Students t test and Chi-Square test. Data were considered significant when $p < 0.05$. TAP Block group with dexamethasone had reduced VAS Score and reduced the incidence of PONV throughout the 24 hour postoperative period. From our study we drew the conclusion that TAP Block is easy to perform under ultrasound guidance and use of dexamethasone as an adjuvant to bupivacaine prolonged the duration of the block without drug complication and it provides effective analgesia. TAP Block holds good as part of a multimodal analgesia regimen for patients undergoing laparoscopic surgeries.

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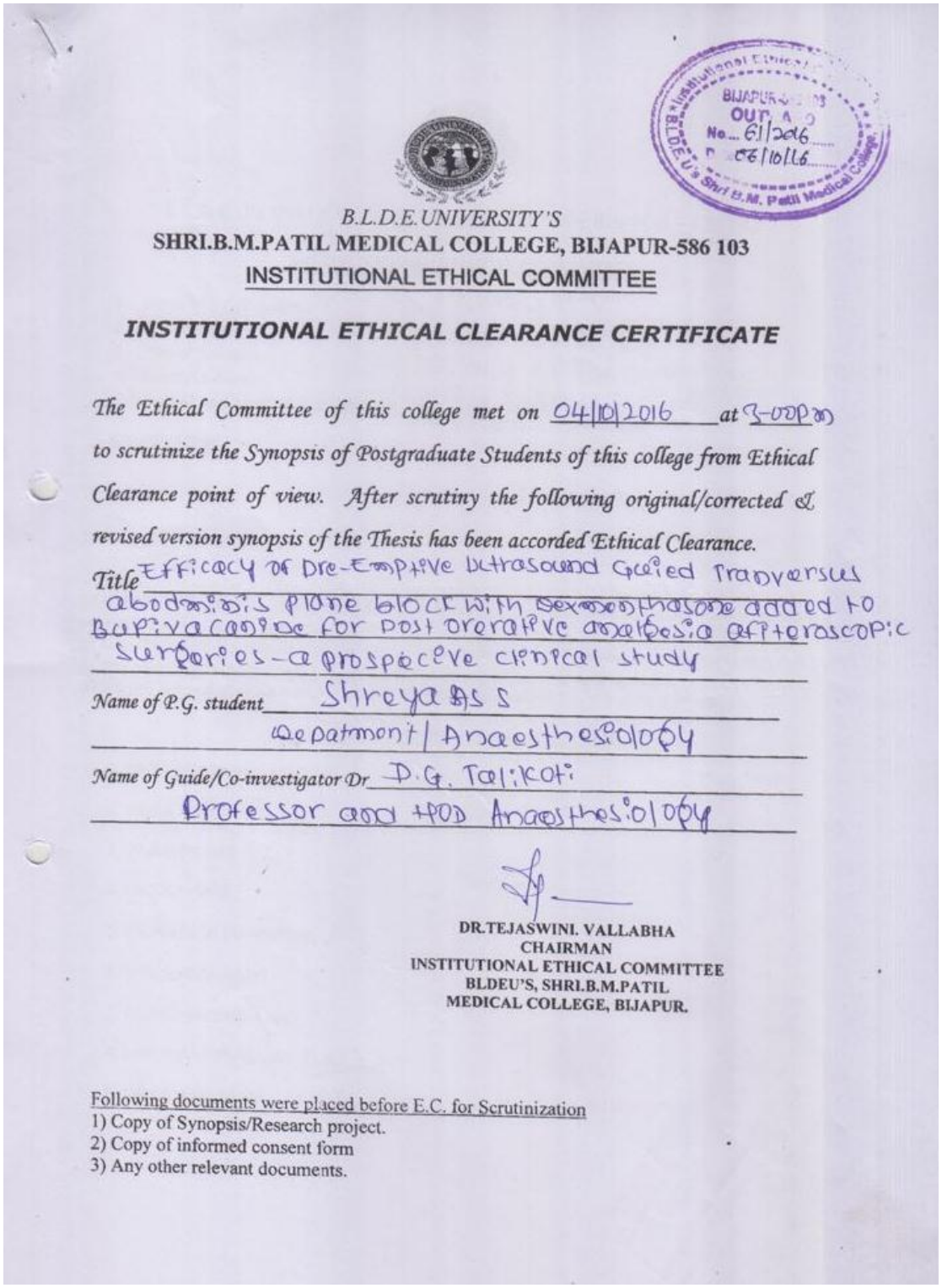
# ANNEXURES

## ETHICAL COMMITTEE CERTIFICATE



B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

**INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE**

*The Ethical Committee of this college met on* 04/10/2016 *at* 3-00 P.M. *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

*Title* Efficacy of Pre-Emptive Ultrasound Guided Transversus abdominis plane block with Dexamethasone added to Bupivacaine for Post operative analgesia after laparoscopic surgeries - a prospective clinical study

*Name of P.G. student* Shreya S S

Department / Anaesthesiology

*Name of Guide/Co-investigator Dr* D.G. Talikoti

Professor and HOD Anaesthesiology

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

# INFORMED CONSENT FORM

B.L.D.E. (Deemed to be University) SHRI B.M. PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR – 586103, KARNATAKA

**TITLE OF THE PROJECT : "EFFICACY OF PRE-EMPTIVE ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK WITH DEXAMETHASONE ADDED TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA AFTER LAPAROSCOPIC SURGERIES- A RANDOMISED CLINICAL STUDY"**

**PRINCIPAL INVESTIGATOR:** **Dr. Shreyas S**

Department of Anaesthesiology

BLDE (Deemed to be University)

Shri B.M. Patil Medical College Hospital & Research Centre, Sholapur Road, Vijayapur-586103.

Email: shreyaz90@gmail.com

**PG GUIDE : Dr.D.G.Talikoti**

Professor and HOD, Dept of Anaesthesiology

BLDE (Deemed to be University)

Shri B.M. Patil Medical College Hospital & Research Centre, Sholapur Road, Vijayapur-586103.

**PURPOSE OF RESEARCH:**

I have been informed that this study is: **"EFFICACY OF PRE-EMPTIVE ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK WITH DEXAMETHASONE ADDED TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA AFTER LAPAROSCOPIC SURGERIES- A RANDOMISED CLINICAL STUDY"**

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

**PROCEDURE:**

I understand that I will be participating in the study: **"EFFICACY OF PRE-EMPTIVE ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK WITH DEXAMETHASONE ADDED TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA AFTER LAPAROSCOPIC SURGERIES- A RANDOMISED CLINICAL STUDY"**

**RISKS AND DISCOMFORTS:**

I understand that my ward may experience some pain while intubating and I understand that necessary measures will be taken to reduce these complications as and when they arise.

**BENEFITS:**

I understand that my wards participation in this study will help in finding out: **"EFFICACY OF PRE-EMPTIVE ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK WITH DEXAMETHASONE ADDED TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA AFTER LAPAROSCOPIC SURGERIES- A RANDOMISED CLINICAL STUDY"**

**CONFIDENTIALITY:**

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

**REQUEST FOR MORE INFORMATION:**

I understand that I may ask more questions about the study at any time. **Dr. Shreyas S** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me for keep for careful reading.

**REFUSAL OR WITHDRAWL OF PARTICIPATION:**

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **Dr. Shreyas S** will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

**INJURY STATEMENT:**

I understand that in the unlikely event of injury to me/my ward, resulting directly due to my participation in this study, such injury will be reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: **Dr. Shreyas S**

(Investigator)

Patient's signature Witness to above signature

## STUDY SUBJECT CONSENT STATEMENT:

I confirm that **Dr. Shreyas S** has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

# PROFORMA

**STUDY: "EFFICACY OF PRE-EMPTIVE ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK WITH DEXAMETHASONE ADDED TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA AFTER LAPAROSCOPIC SURGERIES- A RANDOMISED CLINICAL STUDY"**

PATIENT DETAILS: DATE:

I. Name: Age/ Sex: I.P No:

Ward: Group allotted by randomization: Group 1 / Group 2

II. 1. Type of the surgery: Duration of surgery (min):

2. Indication:

III. Significant History:

IV. General Physical Examination:

Pallor Icterus Cyanosis Clubbing Koilonychia

Lymphadenopathy Ooedema

V. Vital Parameters

Pulse Blood Pressure Respiratory Rate Temperature

VI. Systemic Examination

1. CVS 2.RS 3. CNS

VII. Airway Assessment: MP Grade: ASA Grade:

VIII. Investigation

1. Routine

2. Special (if any)

## 1. Haemodynamic variables during intraoperative period:

| Observation | HR | SBP/DBP (MBP) | SaO2 | OPOID REQUIREMENT | OTHERS |
|---|---|---|---|---|---|
| BASELINE | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| DURING SURGERY | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

2. **Haemodynamic variables during postoperative period**

| **OBSERVATION** | **HR** | **SBP/DBP (MBP)** | **$SAO_2$** | **VAS (0-10)** | **TFA*** | **T RESCUE** | **VAS AT T RESCUE** | **PONV SCORE** |
|---|---|---|---|---|---|---|---|---|
| IMMEDIATE<br>POST-OP<br>PERIOD | | | | | | | | |
| 1 HRS | | | | | | | | |
| 2 HRS | | | | | | | | |
| 4 HRS | | | | | | | | |
| 6 HRS | | | | | | | | |
| 8 HRS | | | | | | | | |
| 12 HRS | | | | | | | | |
| 24 HRS | | | | | | | | |

## KEY TO MASTER CHART

| | |
|---|---|
| SL NO | : Serial number |
| DX | : Study group |
| NS | : Control group |
| ASA_Class | : American society of anaesthesiologists classification |
| BMI | : Body mass index |
| HR | : Heart rate |
| SBP | : Systolic blood pressure |
| DBP | : Diastolic blood pressure |
| SPO2 | : Oxygen saturation |
| VAS | : Visual analogue score |
| PONV | : Post operative nausea vomitting |
| T RESCUE | : Time for Request of Analgesia |
| VAS AT T RESCUE | : Visual analogue score at Time for request of analgesia |