A COMPARATIVE STUDY OF EFFICACY OF INTRA-ARTICULAR DEXMEDETOMIDINE VERSUS BUPRENORPHINE FOR POSTOPERATIVE ANALGESIA FOLLOWING ARTHROSCOPIC KNEE SURGERIES"

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TABLE OF CONTENTS

List of Figures

List Of Tables

List of Graphs

List of Abbreviation

IA - Intra -articular
VAS - Visual analogue scale
ACL - Anterior cruciate ligament
GABA - Gamma-aminobutyric acid
PAG - Periaqueductal Gray matter
DRG - Dorsal root ganglion
FMRI - Functional magnetic resonance imaging
RVM - Rostral ventromedial medulla
CNS - Central nervous system
NAS - Neonatal abstinence syndrome
MAT - Medication-assisted treatment
OTPS - Opioid treatment programs
SAMHSA Substance abuse and mental health service administration
HAART - Highly active antiretroviral therapy
DEA - Drug Enforcement Administration
FDA - Food and Drug Administration
OUD - Opioid use disorder
Mcg - microgram
Kg - kilogram
Ng - nanogram
Mg - milligram
ROS - Reactive oxygen species
ALI - Acute liver injury
ECG - Electro cardiogram
NPOBC - Negative postoperative behavioural changes
ERAS - Enhanced recovery after surgery
PONV - Post-operative nausea and vomiting
ASA - American Society of Anaesthesiologists
NIBP - Non-invasive blood pressure
SPO2 - Oxygen saturation
RBS - Random Blood sugar levels
RR - Respiratory Rate
RS - Respiratory system
CVS - Cardiovascular system
P/A - Per-abdomen
SBP - Systolic blood pressure
DBP - Diastolic blood pressure
MAP - Mean arterial blood pressure

"A **comparative study of the efficacy of intra-articular dexmedetomidine versus buprenorphine for postoperative analgesia following arthroscopic knee surgeries.''**

Abstract

Introduction

Arthroscopy for knee surgery is the most often used minimally invasive orthopaedic surgical technique. The aim of our study is to compare the efficacy of intra-articular Dexmedetomidine versus buprenorphine for postoperative analgesia following arthroscopic knee surgeries.

Material and Methods

This is a comparative study carried out for a period of one and a half years. Around 80 patients of both genders of ASA grade 1 and 2 who are undergoing arthroscopic knee surgeries were randomly divided into two groups of 40 each. Group B – Buprenorphine group (40 patients). Group D- Dexmedetomidine group (40 patients). Time to first rescue analgesia, the number of patients requiring rescue analgesia within the next 24hr, the visual analogue scale at rest and on mobilization at 1^{st},2^{nd},4^{th},8^{th},$12^{th,}$ and 24^{th}hr were measured. Side effects like sedation, pruritis, nausea, vomiting, respiratory depression, and hypotension were also monitored.

Results

The mean age of the study participants was 38.38±11.30 years amthe ong Buprenorphine group and 36.40±12.07 among the Dexmedetomidine group. Among the Buprenorphine group 52.5% were females and 47.5% were males. There was a statistically significant difference in VAS score at rest between the groups. There was a statistical significance difference in VAS score at mobilization between the groups. Among the Buprenorphine group bradycardia was about 5%. Among the Dexmedetomidine group bradycardia was about 2.5%. There was no statistical significance

between the groups. The mean time for first rescue analgesia was longer for the buprenorphine group 1016.22±137.54 min and the for the Dexmedetomidine group was 523.67±117.47 min.

Conclusion

In comparison to dexmedetomidine, buprenorphine produces analgesia for a longer period of time and reduces the amount of postoperative rescue analgesic that is required.

Keywords

Buprenorphine, Dexmedetomidine, rescue analgesia, knee surgery, arthroscopy

AIM and Objectives of the study

To compare the efficacy of intra-articular Dexmedetomidine versus buprenorphine for postoperative analgesia following arthroscopic knee surgeries

Primary objectives

1. To observe the time to first rescue analgesia (defined as the time elapsed from intra-articular injection to time of first analgesic request).

2. To observe the number of patients requiring rescue analgesia within the next 24 hours.

3. To observe visual analog scale(vas) score at rest and on mobilization at 1st,2nd,4th,8th,12th, and 24th hour.

Secondary objectives

4. To study changes in respiratory and hemodynamic parameters and adverse effects.

Introduction

Arthroscopy is the minimally invasive orthopaedic surgical technique that is utilised for knee surgery more frequently than any other method. The irritation of free synovial tissue nerve terminals, the anterior fat pad, and the joint capsule that occurs during surgical excision and resection is what causes the discomfort that patients experience after surgery. [1] Medication to relieve pain after surgery is essential in order to facilitate early patient mobility, which in turn reduces patient morbidity and speeds up postoperative recovery. In an effort to reduce the amount of postoperative pain that patients experience, researchers have been looking into multimodal approaches for analgesia. These treatments include intra-articular (IA) injections, peripheral nerve blocks, systemic analgesia, and neuraxial analgesia.

Buprenorphine is a type of opioid that acts as both an agonist and an antagonist, and its potency is approximately thirty times that of morphine. It is a superior option for use as a postoperative analgesic due to its high affinity for opioid receptors, high lipid solubility, and prolonged duration of action. [2] Dexmedetomidine is a highly selective Alpha- 2 adrenoceptor agonist that has sympatholytic, sedative-hypnotic, anxiolytic, and analgesic properties. It binds to Alpha 2 receptors eight times more strongly than clonidine does. [3] Dexmedetomidine is also used to treat pain

Review of Literature

History

Stein [4] presented the findings of the first clinical research investigating the treatment of intraarticular pain. At the conclusion of the procedure, 52 patients received injections of

morphine, saline, and naloxone directly into their affected joints. Following knee surgery involving intraarticular arthroscopy, a relatively low dose of morphine, one mg, provided complete pain relief that lasted for up to 18 hours. After naloxone was administered locally within the joint, the analgesic effects of morphine administered intravenously were no longer effective in reducing the patient's level of discomfort or its duration. Although analgesic, morphine 0.5 mg was not as effective as morphine 1 mg in treating the patient's pain.

Khouri[5] investigated the effects of morphine, bupivacaine, or a combination of the two following a surgical arthroscopy. He found that the combination was superior to any component alone when delivered promptly after the procedure.

Allen[6] did additional study on surgical arthroscopy and determined that a mixture of bupivacaine (0.125 percent), morphine, and epinephrine was the most effective way to control pain for practically the whole duration of the procedure, which lasted up to 24 hours.

Postoperative intraarticular injections of bupivacaine or morphine-induced analgesia that was comparable to that of a femoral nerve block, as was demonstrated by **De Andres**[7]. After non-arthroscopic ACL surgery, intraarticular morphine that was administered by a syringe away from the area of the joint, after the joint was sealed and the drain stopped, was found to be significantly more effective than saline. [8,9] It has been demonstrated that intraarticular injections of local anaesthetics alone can have an analgesic effect following surgical procedures. **Gyrn**[10] reported an improvement in the level of pain control after increasing the doses of bupivacaine and epinephrine that were administered as the only anaesthetic during diagnostic arthroscopy. Bupivacaine has a favourable effect, but prilocaine coupled with

epinephrine is also more successful than saline when it comes to relieving pain following surgical arthroscopy than saline by itself. [11]

After performing a complete knee replacement, **Badner**[12] administered bupivacaine at a concentration of 0.5 percent into the knee joint. This provided analgesia, reduced the patient's need for opioids and resulted in a minor improvement in early joint mobility. [12] In addition, Badner demonstrated analgesia after total knee replacement and matched epinephrine with intraarticular bupivacaine; however, the analgesia did not improve after the inclusion of morphine in the treatment. [13] Even while there was some indication that intraarticular bupivacaine with no epinephrine provided pain relief, intraarticular morphine was significantly more effective. It has been demonstrated that administering lidocaine directly into the joint can have the same beneficial effects as blocking the femoral nerve.

Pain Pathway

In order to provide the body with an early warning of prospective or actual harm, the nervous system is responsible for one of its most important functions: pain. It is an experience that involves the senses as well as emotions, and it is influenced by psychological elements such as previous experiences, and ideas about pain, fear, or worry.

General introduction to the physiological principles that underlie pain as well as the significant pain pathways and the pain receptors, the pathways that pain takes inside the spinal cord, and the transmission of pain signals to the spinal cord, various levels at which the sensation of pain can be altered, various kinds of pain, including visceral pain and neuropathic pain. [14]

Nociceptors

Nociceptors are specialised sensory receptors that are responsible for the detection of noxious, or painful, stimuli. They are also responsible for translating these stimuli into electrical signals, which are then transmitted to the central nervous system. It is the free nerve ends of primary afferent A and C fibers that make up these structures. They are found all throughout the body (skin, viscera, muscles, joints, and meninges), and they respond to mechanical, thermal, and chemical stimulation.

Damaged tissue causes the release of inflammatory mediators such as bradykinin, serotonin, prostaglandins, cytokines, and hydrogen ions, all of which have the ability to directly trigger nociceptors. They are also capable of lowering the threshold at which nociceptors become activated, hence reducing the amount of stimulation that is necessary to bring about this state. The first stage of sensitization is referred to by its acronym, PS1.

Primary afferent fibers

There are primary afferent A fibers that carry non-noxious inputs in addition to primary afferent C fibers, which are responsible for carrying noxious sensory information. Each of these types of fibers possesses unique features that enable the transmission of various kinds of sensory information. Type A fibers are highly myelinated and have a wide diameter, which enables them to transmit signals quickly. They have a low activation threshold; thus, they often react to a little touch and only transmit non-noxious stimuli. C fibers are minimally myelinated and have a smaller diameter than A fibers, so they conduct more slowly. They are sensitive to both mechanical and thermal stimuli and react accordingly. They cause pain that is both sudden and intense and are responsible for the first reflex response that is triggered by acute pain.

C fibers are the tiniest and least myelinated form of primary afferent fibers. Since this is the case, their conduction is the slowest. C fibers are polymodal, meaning that they respond to a

variety of stimuli including chemical, mechanical, and thermal. When the C fibers are activated, the pain is dull and achy.

The dorsal horn located in the spinal cord

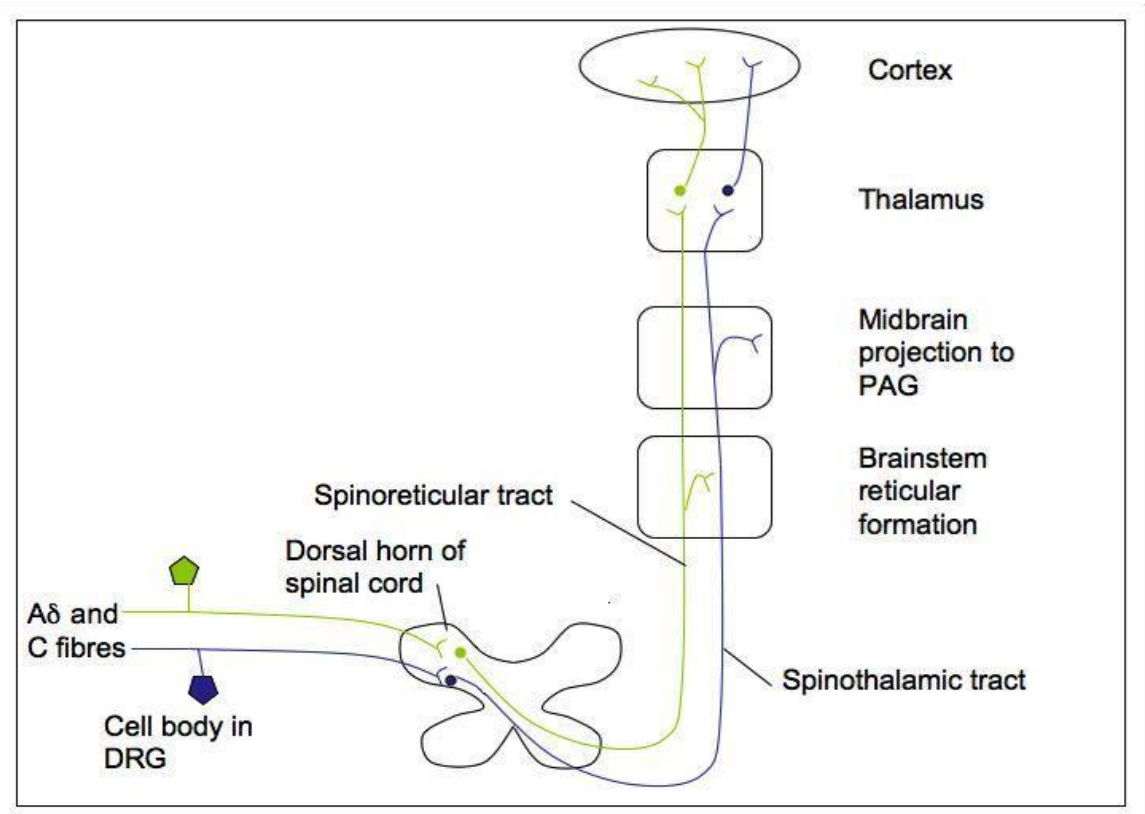
The dorsal horn of the spinal cord is where the A and C fibers make their synaptic connections with the secondary afferent neurons. It is possible to histologically separate the dorsal horn into 10 different layers that are referred to as Rexed laminae. In addition to making projections to other laminae, A and C fibers carry information to neurons in Rexed lamina I and II that are specifically responsible for nociceptive processing. Primary afferent terminals are responsible for the release of a variety of excitatory neurotransmitters, such as glutamate and substance P. Afferent neurons, interneurons, and descending modulatory pathways are all involved in the intricate interactions that take place in the dorsal horn. The activity of the secondary afferent neurons is determined as a result of these interactions. Important neurotransmitters that act at inhibitory interneurons include glycine and gamma-aminobutyric acid (GABA).

Ascending tracts in the spinal cord

There are two primary neural routes that are responsible for transporting nociceptive signals to higher areas in the brain.

The spinothalamic tract: secondary afferent neurons decussate within a few segments of the level of entry into the spinal cord and ascend in the contralateral spinothalamic tract to nuclei within the thalamus. This process takes place within a few segments of the level of entry into the spinal cord. After then, third-order neurons ascend until they reach their destination in the somatosensory cortex. There are also projections of the grey matter surrounding the periaqueductal region (PAG). The spinothalamic tract is responsible for the transmission of signals that are critical for the localization of pain.

The spinoreticular tract: fibers also decussate and ascend the contralateral cord in order to reach the brainstem reticular formation, after which they project to the thalamus and the hypothalamus. There are a great number of other projections that go to the cortex. The mental and emotional components of pain are mediated by this route.



Ascending pain pathways. DRG dorsal root ganglion, PAG periaqueductal grey matter

Pain processing in the brain

The sensation of pain is multifaceted and highly individual; it is influenced by a variety of factors, including cognition (for example, being distracted or exaggerating a problem), emotions, beliefs, and even heredity. It is essential for the somatosensory cortex to be involved in the localization of pain. Imaging techniques such as functional magnetic resonance imaging (fMRI), on the other hand, have shown that an extensive brain network is active during the feeling of acute pain. This is what is commonly referred to as the "pain matrix." The primary

and secondary somatosensory (S1 and S2), insular, anterior cingulate cortex, and prefrontal cortex, as well as the thalamus, are the regions of the brain that are most frequently activated, which demonstrates that all of these regions play a crucial role in the sense of pain.

Inhibition of pain transmission

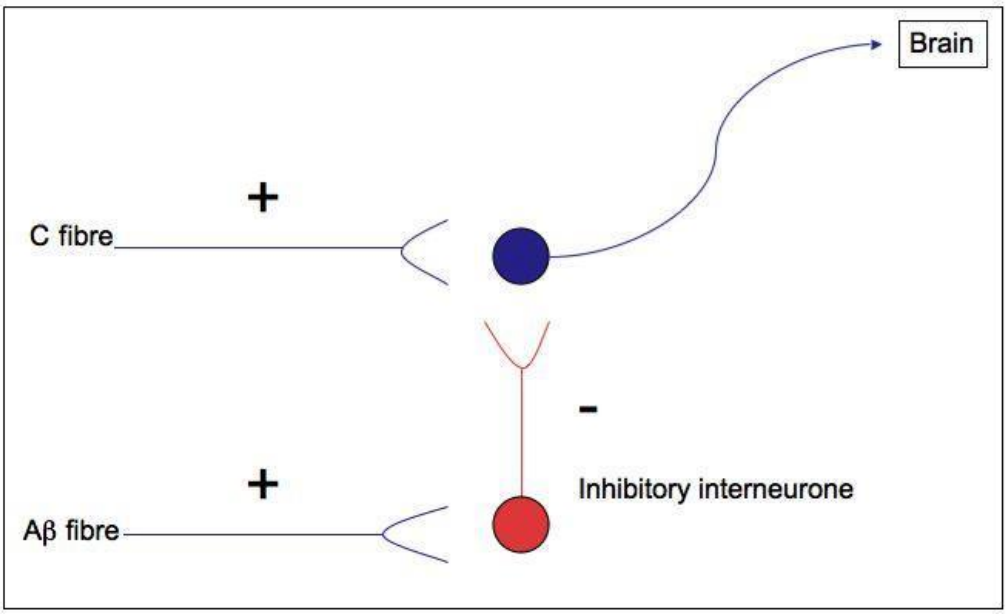
At the level of the spinal cord itself, as well as via descending inhibition from higher centres, there are mechanisms that can limit the transmission of pain signals.

Gate control theory of pain

Melzack and Wall came up with the idea for the gate control theory of pain in 1965 in order to describe a process of inhibitory pain modulation that occurs at the level of the spinal cord. This helps to explain why rubbing our heads after hitting them makes the pain go away more quickly. When tactile, non-noxious stimuli are used to stimulate Aβ fibers, inhibitory interneurons in the dorsal horn are also engaged, which ultimately leads to a suppression of pain signals that are sent via C fibers.

Descending inhibition

Two significant regions of the brain are engaged in the process of descending inhibitory regulation. These regions include the periaqueductal grey (PAG) in the midbrain and the rostral ventromedial medulla (RVM). The fact that both of these centres have significant numbers of opioid receptors, as well as endogenous opioids, helps to explain why opioids have analgesic properties. Descending pathways, which terminate in the dorsal horn, limit the transmission of pain signals. These are monoaminergic pathways, which mean that noradrenaline and serotonin are utilised as neurotransmitters.[14]



Neuropathic pain

Pain that is caused by damage to nerves in either the central nervous system or the peripheral nervous system is called neuropathic pain. Damage can be caused by a variety of factors, such as traumatic events or surgical procedures, diabetes mellitus, chemotherapy, radiotherapy, ischemia, infection, or cancer.

In comparison to nociceptive pain, neuropathic pain manifests in a few distinctively different ways. Burning or 'like an electric shock' are two common ways that people describe the sensation of pain that comes on suddenly. Pain might be felt in response to a stimulus that does not normally induce pain (a condition known as allodynia), or there can be an exaggerated response to a stimulus that would normally cause pain (hyperalgesia). [14]

Arthroscopic Anatomy of the Knee Joint

The patellofemoral joint, the proximal tibiofibular joint, and the knee joint themselves, as well as the soft tissues that surround these joints, are all considered to be part of the knee when discussing its anatomy. The femur and the tibia form an angle of 174 degrees with one another in the frontal plane, which results in the knee being in a physiological valgus position. Women have a slightly higher incidence of valgus and recurvatum than men do. A circle with its centre 2–3 cm above the base of the patella on the buttock and a line that runs immediately beneath the tibial tubercle on the lower leg are the two elements that characterise the joint. [15]

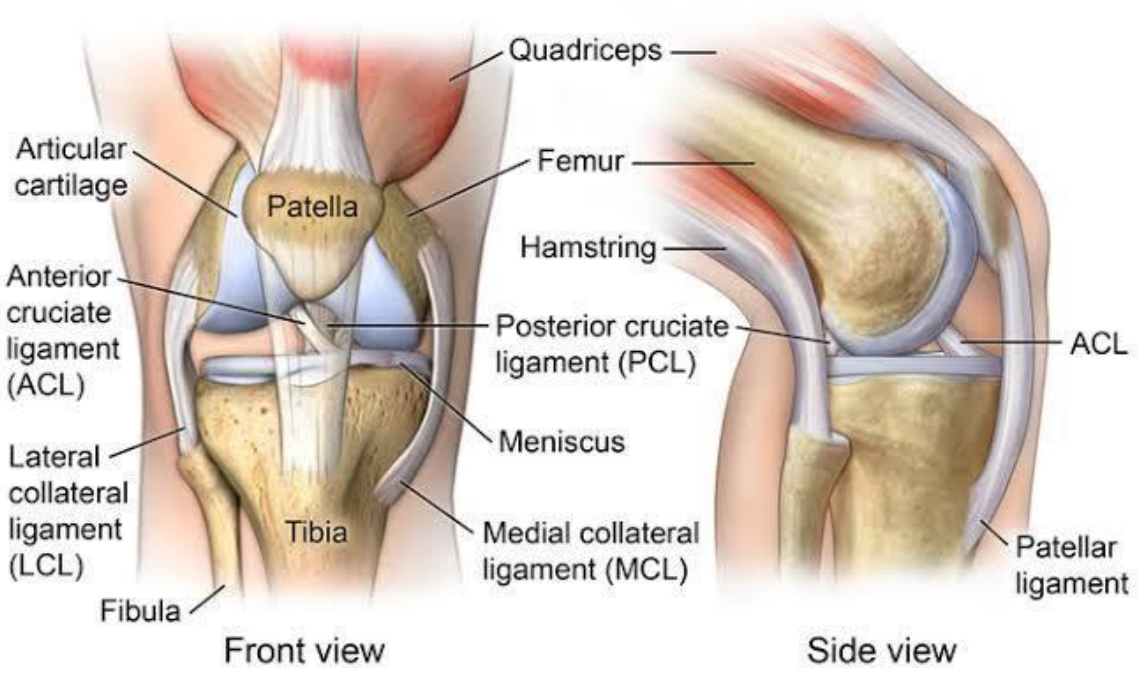


Figure 1: Knee Anatomy

The bone and soft tissues that go into making up this joint are responsible for the knee's four distinct topographic zones that may be found there. It has been demonstrated that the medial

area of the knee, which consists of the medial femoral condyle, the medial tibial plateau, the medial meniscus, and the medial portion of the capsule and ligaments, is a particularly valuable division in clinical knee arthroscopy. The lateral aspect of the knee contains the lateral arch complex, the lateral meniscus, the lateral ligaments, and the lateral tibial plateau in addition to the lateral femoral condyle and the lateral tibial plateau (lig. arcuatum). The centre section, also known as the pivot, is comprised of the intercondylar notch, which is home to crossed ligaments; the anterior and posterior intercondylar fields of the tibia (the lower part of the attachment of crossed ligaments of the knee); the intercondylar eminences; and the intercondylar tubercles. The femoropatellar portion is made up of a femoropatellar joint, infrapatellar adipose tissue, a patellar ligament, and a quadriceps tendon. It usually displays medial and lateral patellar plicas in addition to a suprapatellar depression. In addition to this, the suprapatellar recess can frequently be seen in this area of the kneecap. [16,17]

Intra-articular Pain Regulation via Cellular Mechanisms

Elucidation has also been done regarding the analgesic effects that drugs have when they are administered into the intraarticular region prior to the injury. The recording of activity from tiny afferent nerve fibers within an articular space has the potential to expose a wealth of information. The activation of receptors is preserved throughout the entirety of the usual range of motion of the knee joint in a cat. The activation of receptors can rise by as much as 400% to 500% when an inflammatory condition is produced. [18] In a subsequent study[19] researchers established that damaged tissues activate receptors that had been inactive during the course of normal movement. The researchers came to the conclusion that intraarticular space receptors are multi-modal and have the ability to produce nociceptive responses in response to tissue destruction or chemical mediators of injury (i.e., prostaglandins or substance P). Spinal hypersensitivity is a condition that only manifests itself after inflammation has taken place; the

spinal cord does not play a part in its development. [20] There is evidence to suggest that local anaesthetics play a role in intraarticular analgesia due to their capacity to suppress the release of substance P and restrict the migration of calcium within the cell in response to nociceptive signals. [21]

Importance of Intra-Articular Injection in Clinical Practice for Postoperative Pain Management

The data that is now available suggests that local anaesthetics, opioids, adrenergic agents, and other drugs that are administered intraarticularly following intraarticular surgery are successful at relieving pain. When administered parenterally, these drugs do have some impact; however, the superior efficacy and sustained relief from pain that they provide more than makes up for this drawback. It is likely that the inhibition of the inflammatory response to surgical insult and the reduction or avoidance of hypersensitivity are both related to this effect.

When the potential for unfavorable impacts is factored in, these benefits become much more significant. Analgesia does not have any of the typical adverse consequences that are associated with opioids, and it does not have any such effects on the body as a whole either. Even though a substantial quantity of the local anaesthetic is administered in certain circumstances, only trace amounts of the drug are found in the plasma. The single known case of local anaesthetic toxicity was caused by injecting bupivacaine into an intraarticular fracture. This led to the development of the condition. [21]

In spite of the fact that the majority of the published research has concentrated on intraarticular injections into the knee, there is some evidence that shows additional intraarticular regions may have the same potential. After surgery on the shoulder, either open or arthroscopic, an intraarticular injection may be able to assist ease some of the discomforts. [22,23] Following joint surgery, intra-articular injections can be used to give analgesia and pain relief with a reduced risk of adverse consequences. This adverse reaction is a potential risk with a wide range of medications, including opioids and local anaesthetics, among others. Intraarticular analgesia is most likely caused by a change in the pain receptors that are found within the joint itself or by a stoppage in the transmission of nociceptive signals.

Buprenorphine

Buprenorphine is a synthetic opioid that is employed in the treatment of both chronic pain and addiction to opioids. The second half of the 1960s was the time period in which its inception took place. Thebaine is a man-made analogue of an alkaloid that is naturally found in poppy flowers. As a drug that falls under category III, it has the potential to produce mild to severe physical dependence as well as mild to severe psychological reliance. Fundamentals of how buprenorphine works, the adverse effects it produces, how hazardous it is, how much of the medication to provide to a patient, how the medicine affects them, how it is monitored, and other related topics. The members of the interdisciplinary team who provide care for patients struggling with issues linked to pain management or opioid addiction should be well-versed in the aforementioned ideas.

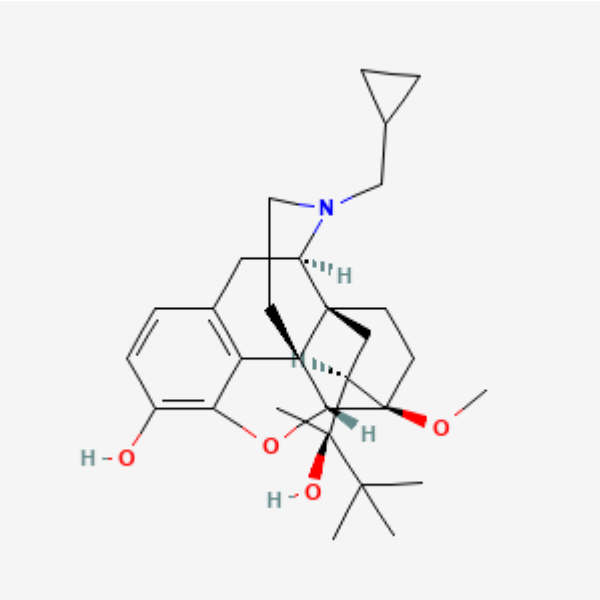


Figure 2: Buprenorphine

Indications

- To treat people with opioid dependence who cannot take methadone
- There is a lengthy waiting of more than three months to join a methadone clinic, or there are no suitable methadone facilities or healthcare practitioners.
- For patients with opioid dependence who are tolerant to or have not responded to methadone treatment.
- People who have a recent history of opioid dependence or who require opioid agonists less frequently may also profit from buprenorphine.

Cause and effect

Because it is just a partial agonist at the mu receptor, buprenorphine only exerts a modest influence on the opiate receptors. In addition, it has a dual role at the delta receptor, functioning both as a mild agonist and an antagonist. Because of its action on the brain as well as the spinal cord, it is an efficient analgesic (CNS). Particularly, the partial agonism that buprenorphine exhibits at the mu receptor sets it apart from other opioids. This property is responsible for several of the characteristics that set it apart from other substances, including the fact that its

analgesic effects reach a plateau at greater doses before they start to have the opposite effect. When administered in agonist substitution therapy for the treatment of opioid addiction, buprenorphine is a more secure choice than methadone due to the ceiling effects it has on respiratory depression.

On mu-opioid receptors, buprenorphine produces an action that is gradual in onset and of modest efficacy. The patient goes through withdrawal with fewer and milder symptoms, which distinguishes it as a different option from conventional full-agonist opioid medications like morphine and fentanyl.

When buprenorphine is administered orally, its bioavailability drastically decreases because of an effect known as the first-pass effect. The majority of the medication is metabolised by the liver and the small intestine. These organs are responsible for the process. Ingestion of drugs by the sublingual route has been shown to be the most efficient way. Using this strategy allows one to avoid the first-pass effect while simultaneously accelerating the absorption process. The tablet doesn't start working until about a minute or two after placing it under the tongue, and the full effect doesn't come in for about three to four hours after that.

The cytochrome CYP 34A enzymes in your body convert buprenorphine into a metabolite called norbuprenorphine, which is an active metabolite with just a little amount of intrinsic action. After being administered sublingually, the half-life of buprenorphine is approximately 38 hours (ranging from 25 to 70 hours). Buprenorphine levels may rise when taking medications that have a potent inhibitory impact on the CYP3A4 enzyme, such as ketoconazole or protease inhibitors, but they may fall when taking medications that activate this enzyme, such as carbamazepine, topiramate, phenytoin, or barbiturates. Buprenorphine

levels may rise when taking medications that have a potent inhibitory impact on the CYP3A4 enzyme, such as ketoconazole

The kidneys are responsible for excreting less than twenty percent of the medicine and its metabolite, while the balance of the drug is removed in the urine and the faeces, respectively. This medicine is beneficial for treating opioid dependence since it has a gradual onset of action and a long duration of activity. If the patient has reached a constant dose, the doctor may decide to prescribe it every other day instead.

Negative Consequences

In addition to its potential effects as a CNS depressive, hypotensive, QT interval extender, and seizure-lowering agent, buprenorphine possesses several activities that are similar to anticholinergic activity. Some of the other adverse effects of buprenorphine include urinary retention, sweating, dry mouth, miosis, headache, nausea, vomiting, disorientation, and memory loss.

The Potential for Abuse of Buprenorphine

Buprenorphine is only a partial opioid agonist; yet, despite the fact that it has a moderate risk for addiction, it is still abused by some individuals. An individual who abuses buprenorphine would first crush the pill into powder, then either inject it or dilute the powder in water before snorting it. People in the United States, where buprenorphine may also be obtained in a sublingual formulation, are understandably concerned about the possibility of the medication being misused and sold illegally. Because of this, naloxone is incorporated into the sublingual version to prevent the drug from being injected. To reduce the risk of abuse and diversion even further, the majority of patients receive their daily doses of medication while being monitored

for the first two months of their treatment. Additionally, pharmacists maintain a close check on patient compliance in order to limit the number of cases of things like lost or stolen "carries" and multiple instances of double prescriptions. When opioid-naive individuals are given buprenorphine that has been diverted and mixed with benzodiazepines, alcohol or other drugs that act on the central nervous system, an overdose is always a risk.

Contra indications

The only real reason you shouldn't use buprenorphine is if you have a hypersensitivity to it. When used on individuals who have respiratory depression or gastrointestinal obstruction, extreme caution is required in order to avoid adverse effects.

In addition, people who are addicted to full opioid agonists like heroin or morphine should avoid taking buprenorphine because taking both substances at the same time could hasten the onset of withdrawal symptoms.

Buprenorphine does not need to be administered in a different manner to patients who have renal impairment. In patients with hepatic impairment, it is possible to prevent toxicity by adjusting the dosage administered. [24-26]

Use of Buprenorphine in Pregnant Patients in Special Populations

Neonatal abstinence syndrome (NAS) is a condition that can affect infants who were exposed to opioids while they were still in the womb. These infants may develop withdrawal symptoms shortly after delivery (NAS). The use of buprenorphine during pregnancy has been given a Category C status, which indicates that there is a possibility that the drug could have negative

effects on the developing foetus. Because buprenorphine is able to cross the placental barrier, this risk is increased. Convulsions, agitation, apnea, increased tone, tremor, and depression of respiration are some of the signs that can be seen in a newborn who has this disease. Babies born to mothers who used buprenorphine during pregnancy may exhibit withdrawal symptoms anywhere from the first day of life up until the eighth day of life, depending on the severity of the drug's exposure to the mother.

Medicine-assisted treatment, sometimes known as MAT, is a kind of treatment for substance use disorders that combines behavioural therapy and medication in order to get better results (OTPs). Methadone maintenance treatment during pregnancy has been found to improve outcomes for both the mother and the infant in opioid-dependent women who are expecting children. In trials that are similar to this one, maintenance therapy with buprenorphine has been associated with improved results for both the mother and the unborn child. It's possible that the subsequent NAS will be less severe than what's seen with methadone. In patients who are pregnant, methadone is now considered to be a drug that belongs in category B, while buprenorphine is considered to be a substance that belongs in category C. The use of buprenorphine during pregnancy has been given a Category C status, which indicates that there is a possibility that it will have negative effects on the developing foetus. If an opioid was used during pregnancy, there is a risk that the newborn would have withdrawal symptoms shortly after birth. Because buprenorphine is able to cross the placental barrier, this risk is increased. It can present itself in a new born in any one of the following ways

- Tremors (trembling)
- Fever
- Irritability
- Sleep problems
- Tachypnea
- Excessive and/or high-pitched crying
- Increased muscle tone
- Hyperreflexia
- Seizures
- Yawning, stuffy nose, and sneezing
- Poor feeding and suck, slow weight gain
- Vomiting
- Diarrhea
- Dehydration
- Sweating

Babies born to mothers who used buprenorphine during pregnancy may exhibit withdrawal symptoms anywhere from the first day of life up until the eighth day of life, depending on the severity of the drug's exposure to the mother. The Substance Misuse and Mental Health Services Administration (SAMHSA) suggests the following as a means of combating substance abuse and mental health issues:

There is a lack of consensus between experts as to whether or not methadone, buprenorphine, or buprenorphine/naloxone use during pregnancy has an effect on the capacity of the baby to develop normally; as a result, the mother should be made aware

of this fact. In addition to this, the doctor should reassure her that the advantages of treatment with medication for opioid use disorder exceed the potential drawbacks.

There is currently no evidence that opioid pain relievers like buprenorphine and methadone contribute to an increase in the number of birth abnormalities, and the impact that these medications have, even in the short term, on neurological development is, at most, minor.

It is only under very specific conditions and with the woman's informed consent that the woman can be moved from the combination treatment to the buprenorphine-alone treatment. Opioid-dependent women who are early in their pregnancies or who announce their plans to become pregnant are contentious topics in the medical community. There are differing opinions on whether or not these women should be shifted from a buprenorphine/naloxone combination to buprenorphine alone. Opioid-dependent men who are early in their pregnancies or who announce their plans to become pregnant are also contentious topics.

There is mounting evidence that the combination product does not have a detrimental effect on the outcomes for newborns; the decision should be taken by the practitioner and the patient after carefully examining the benefits and the risks associated with either option.

Breast-Feeding Women

Recent research has shown that the opioid painkiller buprenorphine does enter breast milk. Due to the fact that it has a low bioavailability, it is currently unknown how much of it is absorbed

by the circulatory system of a breastfed infant. Some case studies assert that NAS does not present itself once the mother stops nursing, while others say that buprenorphine does not prevent the condition. However, the scant evidence that has suggests that it might not be necessary to stop using buprenorphine in nursing mothers, despite the fact that the drug's manufacturers advise against its use in such women.

Elderly

There is currently a paucity of information regarding the effects that buprenorphine has on those who are 65 and older. It is important to proceed with caution while administering buprenorphine to older patients because this demographic has a decreased overall rate of absorption, distribution, and metabolism of the medication. There is also a potential for unfavorable reactions to the medication.

Patients who have been diagnosed with HIV

Opioid addiction is a common secondary disease that occurs in persons living with HIV. Even though highly active antiretroviral therapy (HAART) has the potential to improve both life expectancy and quality of life, it is nevertheless imperative that the issue of opiate addiction be addressed. Patients who took buprenorphine had a greater likelihood of taking their medication exactly as it was recommended, despite the fact that it did not affect the effectiveness of the HAART treatment.

As a result of the fact that many HAART medications also affect the microsomal enzymes in the liver, medical professionals are advised to carefully monitor the liver function and drug

levels of patients who are taking buprenorphine at the same time. Some patients may require a different buprenorphine dosage.

Hepatitis

Patients who are battling an addiction to opiates may additionally be suffering from hepatitis B or C. Because the liver is in charge of breaking down buprenorphine, these individuals require constant monitoring of both their liver function and their medication levels. It is critical for medical professionals to make individuals diagnosed with hepatitis aware that buprenorphine injections include a risk of causing harm to the liver.

The Agony of Suffering

Because of its high affinity for the mu-opioid receptor, buprenorphine's ability to relieve pain is restricted, despite the fact that it functions as an opioid. Because it is only a partial agonist and because it has a ceiling effect, buprenorphine is not very effective as a pain reliever. Because of the strong binding that this chemical has with the mu receptors, it is able to block the attachment of complete agonists to those receptors. People whose pain is being treated with buprenorphine have the option of also taking non-steroidal anti-inflammatory medicines (NSAIDs) if they so wish. The initial dosage of buprenorphine, which is usually between 2mg and 8 mg, can be increased to a maximum of 24 mg per day. There are also additional treatments available, including medication that treats seizures, regional anesthesia, and nerve blocks.

Buprenorphine for Chronic Pain Management

People who suffer from chronic pain or pain that is made worse by opioid use disorder may find that buprenorphine, which is an effective analgesic, offers them additional benefits. Legally prescribing buprenorphine for pain patients does not require a waiver for any physician, nurse, physician assistant, nurse practitioner, midwife, or clinical pharmacist who holds a valid DEA registration. According to statements made by the Drug Enforcement Administration (DEA), "Restrictions and requirements [related to addiction treatment] do not in any way limit a practitioner's competence to utilise opioids for the treatment of pain while functioning in the ordinary course of medical practice." Because of this, there are no limitations placed on the kind of medications that can be utilised to assist a patient in tapering down or weaning off of opioid analgesic therapy. In the context of drug addiction therapy, this does not constitute detoxification. [27] In order to get the desired effect of pain reduction, it is possible to achieve so with low doses of buprenorphine delivered via buccal or patch form, or with buprenorphine that has been synthesised by a compounding pharmacy. Giving a patient one month's worth of the buprenorphine patch at dosages that are decreasing in magnitude from 20 mcg/hour to 15 mcg/hour to 10 mcg/hour to 7.5 mcg/hour and, finally, 5 mcg/hour is an efficient approach for gradually weaning a patient off of buprenorphine. Due to regulations imposed by the FDA, addicts who have not been medically diagnosed with pain are not permitted to lawfully utilise pain medications that contain buprenorphine.

Buprenorphine's Benefits in Treating Chronic Pain

Buprenorphine is a very powerful medication that can alleviate pain. Due to the fact that it has a ceiling effect on respiratory suppression, it possesses an outstanding safety profile (meaning higher doses will not stop breathing and only rarely cause overdose). Unless the patch

formulation is utilised, buprenorphine is often administered in divided doses because its onset of action can take anywhere from 30 minutes to an hour, and its average duration of pain relief can last for up to eight hours.

As with any other opioid, buprenorphine should only be used with extreme caution and only in situations when the potential advantages outweigh the potential risks. It is possible that buprenorphine, in comparison to other opioids, is a safer analgesic alternative for patients who suffer from severe acute pain and substance use disorders. This is especially true in emergency rooms and hospitals, where patient histories are not always easily accessible.

people who are suffering the adverse effects of long-term opioid use or who are consuming potentially deadly amounts of opioids for pain management. patients who are experiencing the bad effects of long-term opioid use.

Buprenorphine, in contrast to other long-acting opioids, does not accumulate in patients with renal impairment and has a relatively low risk of adverse medication interactions. Buprenorphine is a safer alternative to other long-acting opioids because it has a longer half-life, partial agonist activity at the mu receptor, and antagonistic activity at the kappa receptor. These three characteristics combine to make it an effective painkiller. [28] Sleep apnea, low testosterone levels, impotence, osteopenia, opioid-induced hyperalgesia, mood disorders (anxiety and depression), and dysregulation of the hypothalamic-pituitary-adrenal axis are a few examples of conditions that can be caused by an imbalance in this axis. When compared to other long-acting opioids, the data suggest that buprenorphine offers superior pain treatment. This body of research is continuing to grow. [29]

The promise of relieving the common side effects of full agonist opioids that were discussed above can be enticing, despite the fact that some patients are reluctant to convert to a prescription that is utilised in the treatment of addiction. The fact that buprenorphine is classified as a Schedule III drug rather than a Schedule II drug (refills can be requested over the phone) serves to encourage other patients.

People of Advanced Age who Suffer from Chronic Pain

When elderly individuals who have been using opiates for an extended period of time make the switch to buprenorphine, there is a potential reduction in the risk of medical problems and accidental overdose (e.g., sleep apnea and hypogonadism). As a result, Buprenorphine might be a better choice than the daily opioid medication that is now being administered to older patients.

In-Hospital and Emergency Room Pain Management

When provided by medical professionals in emergency rooms or hospitals, buprenorphine can be used for effective pain treatment even in the absence of a waiver from the DEA. Buprenorphine has the potential benefit of reducing the risk of addiction, sedation, and respiratory depression. It also has the potential benefit of providing longer-lasting pain relief, and it may reduce the risk of inciting a return to use when opioids are essential for patients who have an opioid use disorder. As with other opioid analgesics, buprenorphine should only be used in severe situations when all other pain management options have been tried and found to be ineffective.

Buprenorphine Use in the Hospital and During Surgery

Patients who suddenly stop using methadone or buprenorphine are at a greater risk of experiencing pain flare-ups, returning to their previous drug-using ways, and having to remain in the hospital for longer than necessary. When treatment with buprenorphine is resumed after a pause of any length, there are also many logistical obstacles to overcome. [30] The maintenance dose of buprenorphine is currently recommended by SAMHSA for use during the postoperative period. [31] Recent studies have indicated that maintaining patients on buprenorphine, in conjunction with other analgesics as required, is an effective strategy to treat inpatient and perioperative pain, and it may also minimise the length of time patients need to spend in the hospital. If the patient is not obtaining adequate pain relief from the maintenance doses, further doses of buprenorphine or another opioid may be given in addition to those.

It is not necessary to get a waiver from the DEA in order to administer or dispense buprenorphine or methadone to hospitalised patients who have been admitted for severe medical conditions other than opiate dependence.

DEXMEDETOMIDINE

pharmacology and pharmacodynamics

Dexmedetomidine is a potent, flexible, and highly selective short-acting alpha-2 agonist. It possesses properties that make it effective as a sedative, anxiolytic, perioperative sympatholytic, and hypnotic. [32] It has a function very similar to that of clonidine, that of a highly selective alpha-2 agonist. Compared to dexmedetomidine, clonidine has a selectivity for alpha2: alpha1 receptors that are 220:1, while dexmedetomidine's selectivity is 1620:1. In 2008, the Food and Drug Administration gave its approval for the use of dexmedetomidine as a procedural sedative and for patients who did not require intubation. In addition, it has qualities that relieve pain, calm inflammation, and reduce the need for anaesthesia. [33] Dexmedetomidine is a sedative that provides continuous sedation, maintains stable hemodynamics, and is simple to titrate. These qualities make it an excellent choice for usage in intensive care units. [32,34]

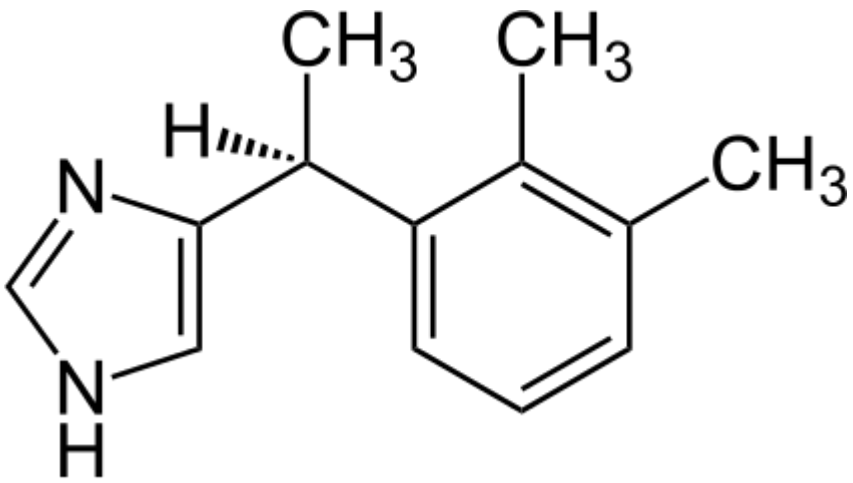


Figure 3: Chemical formula of Dexmedetomidine (https://upload.wikimedia.org/wikipedia/commons/thumb/0/0b/Dexmedetomidine_Structural_Formula_V.1.svg/430px-Dexmedetomidine_Structural_Formula_V.1.svg.png)

- **Formulation and Dosing**

Dexmedetomidine hydrochloride, 100mcg/ml, is the form in which it is sold in the USA. A maintenance dose of 0.2 to 0.7mcg/h, calibrated to the appropriate level of sedation and avoiding any hypotensive effects, is given after a loading dose of 1 mcg/ml over 10 min for ICU sedation.

- For procedural sedation, a similar dosing regimen of 1 mcg/ml over 10 min is injected, followed by a maintenance dose of 0.6 mcg/h. [32]

Figure 4: Dexmedetomidine (https://www.wgcriticalcare.com/wp-content/uploads/2016/10/2-Dex-Vials.png)

With a selectivity ratio of 1620:1, dexmedetomidine has a very high degree of sensitivity. In spite of the fact that it is a powerful agonist of the alpha-2 adrenergic receptor, the chemical mechanism behind its effects is yet unknown. Because, most likely, the activation of inhibitory G proteins as well as the nitric oxide, cGMP pathway was responsible for this effect. By binding to each of the three distinct types of G protein-coupled receptors, dexmedetomidine is able to produce an agonistic effect (alpha-2A, alpha-2B, and alpha-2C). The central nervous system (CNS) and the smooth arteries of the cardiovascular system have a high concentration of alpha-2A, alpha-2C, and alpha-2B receptors, respectively.

By binding specifically to alpha-2A receptors in all three subtypes of alpha-2A receptors, dexmedetomidine is able to cause hyperpolarization of noradrenergic neurons. This is accomplished by blocking adenyl cyclase and lowering levels of adenosine monophosphate. This prevents the input of calcium which is necessary for the fusion of neurotransmitter vesicles, which in turn slows neuronal conduction. Both blood pressure and heart rate are lowered as a result of this negative feedback loop, which works by inhibiting the sympathetic response. [34] Through its action on the alpha-2 receptor, dexmedetomidine is able to prevent the release of norepinephrine from presynaptic neurons. It does this via acting on alpha-2 receptors in the dorsal horn, which cause sleepiness, and by stimulating the locus ceruleus, which is responsible for pain perception.

Pharmacokinetics

Due to the fact that dexmedetomidine has high lipophilicity, it is rapidly dispersed across two different compartments. The patient's body mass index (BMI), liver function, plasma albumin binding, and cardiac output are all factors that have the potential to influence clearance and distribution volumes. In the past, the only route of administration that was approved was intravenously, but today oral and intranasal formulations are available. Both the intranasal and buccal routes of administration of dexmedetomidine have been shown to be effective in treating children and adults who are difficult to work with.

After being given intravenously, dexmedetomidine has a quick rate of distribution, with a t1/2 of only six minutes for distribution and two hours for the terminal half-life. In the majority of instances, the active influence of an IV loading dosage begins to present itself anywhere between 5 and 10 minutes after administration, and it reaches its peak anywhere between 15 and 30 minutes after that. Intranasal administration begins to be effective after forty-five minutes, and after ninety to one hundred minutes, it has reached its maximum potency. There is no variation between the pharmacokinetic profiles of males and females, nor is there a difference in the protein binding that occurs in either gender. Oral administration of dexmedetomidine is inefficient because of the high levels of first-pass metabolism that occur, which results in just 16 percent bioavailability.

Distribution

Proteins have strong connections to dexmedetomidine. It is well known to easily break through the blood-brain barrier as well as the placental barrier. This is due to the fact that 94% of it is coupled to albumin and alpha-1-glycoprotein, both of which have a broad volume distribution. The distribution volume of the typical adult falls somewhere in the range of 1.3 to 2.4 lit/kg. Patients who have low albumin levels, as well as newborns and young toddlers under the age of two, have a bigger volume of distribution. This is also true for adults. [32]

Metabolism

Because of biotransformation, less than one percent of dexmedetomidine is eliminated in its unaltered state in the urine (of which 95 percent is excreted through kidneys and 5 percent via stool). A ratio of 0.7 indicates that dexmedetomidine is extracted from the liver.

Dexmedetomidine is metabolised by the enzymes uridine 5'-diphosphate-glucuronosyltransferases (UGT2B10) and uridine glucuronosyltransferase UGT1A4. In liver microsomes, the enzyme CYP2A6 is responsible for up to 5% of the hydroxylation reaction that occurs during metabolic processing. Patients with hepatic impairment had a higher unbound percentage, which resulted in a larger volume of distribution and a longer elimination half-life. Patients with renal impairment had a smaller unbound percentage. Patients whose liver function is deteriorating should have a reduction in the dosage of dexmedetomidine that they take. However, even when given the same amount, patients who have renal impairment may be more susceptible to the sedative effects of dexmedetomidine over a longer period of time. It's possible that this is due to an increase in the amount of medication that has been unbound. [32]

Elimination

The clearance of dexmedetomidine in healthy individuals ranges from 0.6 to 0.7 liters per minute. Low albumin levels can be a barrier to clearance, particularly in patients who are being treated in intensive care units. However, the impact of low albumin levels may be minimal for substances that have large extraction ratios. This is because the clearance of medicines is determined more by blood flow than by plasma protein levels. Dexmedetomidine clearance is decreased when cardiac output is decreased. However,

the pharmacokinetics of dexmedetomidine in a patient who is being treated in an intensive care unit might be affected by a number of circumstances, including low albumin levels, end-organ failure, and hemodynamic abnormalities. Two more factors that can have an impact on the way medicine is metabolised are the patient's ethnicity and the polymorphisms found in their alpha-2 receptors. [32]

Pharmacodynamics

Dexmedetomidine's interaction with central presynaptic and postsynaptic alpha-2 receptors is responsible for both its sedative and hypnotic actions. The results are different depending on the concentration, which ranges from 0.2 to 0.3 ng/ml. Sedation and relief from pain are brought on by the binding of alpha-2 receptors in the postsynaptic space of the spinal cord and the locus cereus. Its strong affinity for the alpha-2 receptor is the cause of all of these vagolytic effects, including bradycardia and vasodilation. It is possible to employ dexmedetomidine to mimic the physiological effects of sleep and wakefulness in a manner that is comparable to those of natural sleep. If the patient is kept awake, there is a lower chance that they would develop delirium. At doses between 0.2 and 0.7mcg/kg/hr, respiratory depression is quite uncommon. Dexmedetomidine reduces the transmission of pain, most likely by influencing the actions of neurotransmitters like substance P.

There is a 24-hour limit on how long dexmedetomidine can be used in the intensive care unit before medication loses its approval. Another advantage of dexmedetomidine is that it reduces the amount of time spent in the intensive care unit (ICU) as well as the amount of time spent on mechanical ventilation by 22 and 14 percent, respectively. [32]

The Downside

The majority of people who have adverse consequences from postsynaptic alpha-2 receptor activation suffer from hemodynamic abnormalities such as hypertension, bradycardia, and hypotension. Bradycardia, dry mouth, and nausea are additional potential adverse reactions that could occur. Fever, muscle weakness, bronchospasm, respiratory depression, conduction abnormalities, arrhythmia, A-V block, tachycardia, syncope, neuropathy, paresthesia, potassium abnormality with EKG alterations, lactic acidosis, and high glucose levels are further symptoms that have been observed. [33] In a similar manner, tachyphylaxis may manifest itself if an intravenous infusion is maintained for more than twenty-four hours.

Effects on the Heart

The effects of dexmedetomidine on the cardiovascular system occur in two stages. Dexmedetomidine boluses given in high doses can cause tachycardia and an increase in blood pressure, whereas dexmedetomidine boluses given in moderate doses can lower blood pressure and cardiac output while maintaining the same level of stroke output. This is due to the fact that the vasoconstriction caused by alpha-2 causes baroreceptors to produce bradycardia, which in turn leads to increased vagal activity, both of which contribute to hypotension. Because of its sympatholytic properties, dexmedetomidine causes a decrease in the amount of catecholamines found in the blood. [32]

When dexmedetomidine is administered as a bolus by fast infusion, its ability to antagonise alpha-2 receptors is lost. As a consequence, there is a momentary increase in blood pressure and a fall in heart rate, but both of these effects disappear within about 15 minutes. This impact is mediated, in great part, by alpha-2A receptors located in the central nervous system. Activation of alpha-2B receptors has been linked to the development of hypertension. When administering dexmedetomidine, considerable caution should be exercised with patients who are already suffering from heart conditions and whose volume reserves are low. Because of the possibility of developing pulmonary hypertension at high doses, the use of dexmedetomidine is limited to patients who already have some form of heart disease.

Influence on respiration

Both the respiratory drive and the ventilatory response to CO2 are maintained at plasma concentrations as low as 2.4 ng/ml. As the dosage is increased, there is a little decrease in the tidal volume. There is no influence on the respiratory drive even at a concentration of 14.9 ng/ml, which is substantially outside of the therapeutic range. Although the hypercapnic ventilatory response to the use of dexmedetomidine decreases with age, it can still lead to respiratory depression, especially in the elderly when taken with other hypnotics or opioids that decrease respiratory drive. This is especially true in situations where the elderly are given a combination of these

medications. Because of this, it is only allowed to be used in the critical care unit, and only if the patient is under constant monitoring for their cardiac and respiratory function. One of the dexmedetomidine's key advantages is that, when used with other anaesthetic medicines, it has relatively less of an impact on the respiratory system. Dexmedetomidine is protective because, in addition to its antioxidant capabilities, it inhibits the generation of reactive oxygen species (ROS), which is a typical side effect of acute lung injury (reactive oxidative species).

This is due in part to the fact that it stimulates alpha-2 adrenoreceptor activity, which in turn increases lung alveolar epithelial cell survival and proliferation in situations when there has been acute damage to the lung (ALI). As a consequence of this, dexmedetomidine is the medication of choice for the sedation of ALI patients at this time. [35]

Elderly

It's possible that some of the negative effects, including those on blood pressure and how well the heart works, will be more prominent in older people. If a loading dose that is greater than 0.7 micrograms per kilogram is delivered, hypotension may result. It is important to use extreme caution while administering dexmedetomidine to senior patients because of the higher risk of hypotension and bradycardia associated with this medication, as well as the fact that older patients frequently have comorbid illnesses. [32] Patients who are receiving continuous infusions should have continuous monitoring of their pulse oximetry and electrocardiogram (ECG), and this is especially important for

patients whose cardiac ejection fractions are less than 30% or who have other cardiac comorbidities.

Obese

When dealing with obese patients, it is of the utmost importance to monitor their breathing as closely as possible. It is possible that when they take dexmedetomidine in conjunction with other opioids, their susceptibility to developing obstructive sleep apnea would be worsened. Dexmedetomidine provides a multitude of benefits, some of which include improved pain management, lower utilisation of opioids, and reduced requirement for antiemetic medication.

There is a possibility that the effects of dexmedetomidine when combined with other anaesthetics, sedatives, or opioids, will be additive or additively amplified. The use of vasodilators or medicines with a negative chronotropic effect should be addressed carefully, much as the use of dexmedetomidine may exacerbate the harmful effects of cardio depressants. Both of these types of medications should be used with extreme care. Patients whose heart rates have dropped by more than 30 percent from baseline should be continuously monitored because they are at an increased risk of developing severe bradycardia, which can lead to the complete cessation of electrical activity in the heart and potentially death. [36] A fast bolus has the potential to be lethal for anyone, including people who are otherwise healthy yet have increased vagal tones. It has been discovered that the use of neuromuscular blocking medications in conjunction with dexmedetomidine does not result in any significant side effects.

There is evidence that tolerance and tachyphylaxis develop in patients who receive dexmedetomidine for longer than 24 hours.

Toxicity

When administered to diabetic rats for the purpose of local nerve blocks, dexmedetomidine has the potential to induce substantial nerve damage. [37] However, it is also recommended that caution be exercised when using precedes in combination with local anaesthetics in patients who have peripheral neuropathy. This is because the combination has the potential to induce severe motor and sensory impairment. In a separate study that had comparable findings, it was discovered that the addition of dexmedetomidine to a nerve block as an adjuvant not only exacerbated the severity of the systemic adverse effects, but it also made the block continue for a substantially longer period of time. [38] An overdose of dexmedetomidine almost always results in cardio depressive effects, some of which may call for supportive therapy.

Delirium of Emergence

When a person's capacity to think clearly and concentrate their attention is briefly hampered, this can lead to acute confusion, also known as delirium. After the anaesthetic medicines have been removed at the conclusion of a surgical procedure, the majority of patients have a relatively painless return to their regular level of consciousness. Emergent delirium only affects a very small number of people, and those who are most likely to experience it are the old and the very young. There is an increased likelihood of postoperative respiratory depression as well as airway blockage,

and the estimated incidence may reach as high as 80 percent in patients who are of paediatric age. [39] Dexmedetomidine is beneficial in lowering the incidence of postoperative delirium as well as negative alterations in behaviour when it is given at a dose of 0.5 micrograms per kilogram (NPOBC). After induction of anaesthesia, the patient's heart and lungs need to be carefully monitored while dexmedetomidine is being administered to them. Negative postoperative behavioural changes in children can include inconsolable sobbing, irritability, feeding and sleeping troubles, temper tantrums, and nightmares. Children who have undergone general anaesthesia for surgical operations can also experience negative postoperative behavioural changes. It's possible that these signs and symptoms won't start showing up for a few days, a week, or even longer after the procedure.

Use of Dexmedetomidine Before Surgery to Reduce Postoperative Pain

The effectiveness of dexmedetomidine in reducing postoperative pain has been validated by a number of randomised controlled trials and systematic reviews. [40-44]

According to the findings of a meta-analysis that was carried out in 2012 on 1792 patients, dexmedetomidine was able to cut patients' intake of opioids by 30 percent 24 hours after surgery. Acetaminophen, clonidine, ketamine, and nonsteroidal anti-inflammatory medications are not as effective as dexmedetomidine when it comes to relieving pain. Dexmedetomidine is the best option. [40] Dexmedetomidine is intriguing for the treatment of ERAS as well as for people who suffer from persistent pain for this reason. In spite of its effectiveness in reducing postoperative pain, opioid consumption, and nausea and vomiting, a meta-analysis conducted in 2015 found that

dexmedetomidine had little impact on recovery time (PONV). [41,45] For instance, the findings of a Cochrane review indicated that there was an insufficient similarity between the studies regarding the use of dexmedetomidine in abdominal surgery in order to conduct a meta-analysis. [42,43,46] Dexmedetomidine, in addition to being an efficient painkiller, has the added benefit of soothing young patients and preventing the development of increasing agitation. This is an additional advantage of the medication.

According to the findings of a number of clinical tests, dexmedetomidine offers superior postoperative analgesia with fewer unintended side effects than its intraoperative counterpart, remifentanil.

Dosage and Administration Schedules for Medications [47,48]

The majority of the literature on postoperative pain management includes reference to the intravenous administration of dexmedetomidine; nevertheless, the amounts that are utilised vary, and the ideal dose is unknown. It should be emphasized that a loading dose of intravenous dexmedetomidine may not be required in some cases. [49]

Review of clinical study

In 2019, **Pulin Bihari Das** and **Somya Samal** conducted a study to determine whether or not intra-articular Dexmedetomidine and buprenorphine were effective following

arthroscopic knee surgery. At a tertiary care centre, a clinical research study that was based on randomization was carried out. There were going to be two groups of thirty people each, for a total of sixty people who were going to have elective arthroscopic knee procedures. The intra-articular dose of buprenorphine given to Group B was 100 micrograms, while the intra-articular dose of dexmedetomidine given to Group D was 100 micrograms. They kept track of how long it took before patients needed their first rescue analgesia, how many patients needed it over the next 24 hours, how patients felt on a visual analogue scale (VAS) while they were at rest, and how often patients were able to move around in the first, second, fourth, eighth, and twelve hours of the study. People in treatment group B were reported to have considerably longer wait periods before receiving their first dosage of rescue analgesia. This was one of the observed differences between the two treatment groups. After the first, second, fourth, and eighth hours, resting VAS scores were comparable across the two groups. However, after twelve and twenty-four hours, VAS values with intra-articular buprenorphine were significantly lower than those with intra-articular dexmedetomidine. Throughout the first three hours of ambulation, the VAS values for both medicines were comparable; however, dexmedetomidine proved to be significantly more beneficial during the eighth, twelfth, and twenty-fourth hours. It was demonstrated that the analgesia provided by intra-articular buprenorphine lasted significantly longer than that provided by intra-articular dexmedetomidine, which resulted in a reduced need for postoperative rescue analgesics. [50]

A comparative study of intra-articular injections of clonidine and dexmedetomidine was carried out in 2016 by **Basavaraj Patil**, **D.G. Talikoti**, and **Shivanand Karigar** in order to assess the duration of postoperative analgesia and the stability of the patient's

hemodynamic status following arthroscopic knee surgeries. According to the findings, dexmedetomidine provided postoperative analgesia that lasted significantly longer than that produced by clonidine. After providing the dose that was recommended by the clinical research, neither group had any major adverse effects. [51]

Research conducted by **S.A.L.W.A. M.S. Hayes et al**.[52] in 2012 found that patients who received intra-articular injections of midazolam and bupivacaine for postoperative analgesia after arthroscopic knee surgeries had significantly lower visual analogue scores, both at rest and during movement, and a longer time before making their first postoperative analgesic request.

According to the findings of research carried out in 2011 by **Hirano Guara Sobrinho et al.**, patients who underwent total knee arthroplasty and received an intra-articular injection of s (+)-ketamine reported much less pain than those who got a placebo. The complete sample can be partitioned into the following three classes: According to the findings of the study, intraarticular s (+)-ketamine did not give any greater pain alleviation after surgery when compared to a saline solution. This was the conclusion reached by the researchers. A 0.9% saline solution was used to provide 0.25mg/kg of ketamine to Group A, 0.5mg/kg of ketamine to Group B, and 20 ml of saline to Group C. The administration of the ketamine was done intra-articularly. [53]

The effects of intra-articular dexmedetomidine on postoperative analgesia following arthroscopic knee surgery were investigated by **R.R. Al-Metwalli** and colleagues. Peripherally acting as an analgesic, dexmedetomidine is a drug that acts as an agonist

for the alpha-2 adrenergic receptor. The authors of this study came to the conclusion, based on their findings, that the intra-articular administration of dexmedetomidine to patients who were undergoing arthroscopic knee surgeries resulted in an improvement in postoperative analgesia, a prolongation of the time before the first analgesic request was made, and a reduction in the overall need for postoperative analgesia. [54]

When comparing intravenous (IV) dexmedetomidine and intravenous (IV) buprenorphine, **Samal et al**. discovered that the latter significantly reduced the amount of time required for the initial rescue analgesia. [50] In addition, it was discovered by **Varrassi et al**.[55] that administering 100 mcg of buprenorphine improved postoperative pain relief and decreased the requirement for further analgesics. The number of patients in the dexmedetomidine group who required rescue analgesia within 24 hours was considerably higher than the number of patients in the buprenorphine group who required such treatment. Similar studies have found that people who take injectable buprenorphine have a reduction in their consumption of narcotic pain medications. [56]

In comparison, the analgesic effects of 100 mcg of intravenous buprenorphine to 100 mcg of intravenous dexmedetomidine have a longer duration of action and a lower necessity for postoperative rescue analgesics.

In 2008, Al-Metwalli and colleagues conducted a study in which they compared three groups using intra-articular dexmedetomidine, intravenous dexmedetomidine, and a placebo. They came to the conclusion that intra-articular dexmedetomidine in a dose of 1 mcg/kg enhanced postoperative pain relief, decreased the need for postoperative analgesia, and prolonged the time until the first analgesic request was made. [57]

Patients were randomly assigned to one of three groups: bupivacaine, bupivacaine with 1 mcg/kg dexmedetomidine, or bupivacaine with 1 mcg/kg fentanyl. The study was conducted in 2009 by **El-Hamamsy et al**. in a volume of 30 ml. They came to the conclusion that the addition of dexmedetomidine and fentanyl to bupivacaine led to a reduction in postoperative pain scores, an increase in the amount of time that passed before the first request for analgesia was made, a reduction in the amount of postoperative analgesia that was required, and an increase in the duration of pain relief when compared with bupivacaine used on its own. [58]

In 2014, **Alipour** et al. conducted an investigation into the effectiveness of intra-articular dexmedetomidine. They came to the conclusion that intra-articular dexmedetomidine in a dose of 1 mcg/kg alleviates postoperative pain, decreasing the need for narcotics as analgesics and increasing the amount of time that passes before the patient requests their first analgesic.[59]

MATERIALS AND METHODS.

SOURCE OF DATA:

This study is 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, Vijayapura.

METHOD OF COLLECTION OF DATA:

Study Design: Comparative study.

Study Period: One and a half years.

Sample Size:80 patients of both genders of ASA grade 1 and 2 who are undergoing arthroscopic knee surgeries were randomly divided into two groups of 40 each.

STATISTICAL DATA

With the Anticipated Proportion of requirement of rescue analgesia in group B and group D with arthroscopic knee surgery patients 20 % and 50% ([ref]), the study would require a sample size of 40 per group. (i.e., a total sample size of 80 assuming equal group sizes), to attain a power of 80% for detecting a difference in proportions between two groups at a two-sided p-value of 0.05.

Formula used

- $$n= \frac{(z_{\alpha}+z_{\beta})^2\ 2\ p*q}{MD^2}$$

Where Z= Z statistic at a level of significance

MD= Anticipated difference between two proportions

P=Common Proportion

q= 100-p

Statistical Analysis

- The data obtained were entered in a Microsoft Excel sheet, and statistical analysis will be done using a statistical package for the social sciences (Version 20).
- Results were presented as Mean±SD, counts and percentages, and diagrams.
- For normally distributed continuous variables in between two groups will be compared using an independent t-test and for not normally distributed variables Mann Whitney U test was used. Categorical variables between the two groups were compared using the Chi-square test/Fisher\s Exact test.

$p<0.05$ was considered statistically remarkable. All statistical tests as performed in two-tailed.

INCLUSION CRITERIA

➢ Patients aged between 18-60 years.

➢ Patients of either sex.

➢ Patients with ASA Grade I & II.

➢ Patients selected for elective arthroscopic knee surgeries (meniscectomy, ligament repair, removal of loose bodies, and arthroscopic debridement)

➢ **EXCLUSION CRITERIA**

➢ Patient refusal

➢ Pregnant women.

➢ Patients with H/o Cardio-Respiratory disorders

➢ Patients with Hepatic and Renal diseases.

➢ Patients with H/o convulsions & neurological deficits.

➢ Patients with Spinal deformities & Psychiatric diseases.

➢ Patients having known allergy to buprenorphine, dexmedetomidine, and local anesthetics.

METHODOLOGY:

Pre-anesthetic evaluation: Patients were included in the study through a pre-operative thorough assessment, which consists of the following:

- **History:**

  History of underlying medical illness, previous history of surgery, previous anesthetic exposure, and hospitalization were taken.

  Physical examination:

- The general condition of the patient.
- Vital signs- heart rate, blood pressure, respiratory rate.
- Height and weight
- Systemic examination of the cardiovascular system, respiratory system, central nervous system, and vertebral system.

Airway assessment by Mallampati grading.

PROCEDURE:

The study was conducted in our institute on 80 patients who were undergoing arthroscopic knee surgeries

- Patients were randomly divided into two equal groups by computerized randomisation

Group B – Buprenorphine group (40 patients)

Group D- Dexmedetomidine group (40 patients)

- All patients of both groups were premedicated with inj. Glycopyrrolate 0.2mg IV and inj. midazolam 1mg IV after placement of all routine monitors (NIBP, SP02, ECG), all vitals were recorded before and after premedication.
- Patients in both groups were induced under spinal anaesthesia with inj. Bupivacaine heavy 0.5%,3ml, under all aseptic and antiseptic precautions.
- Temperature, pulse, BP, and SP02 were monitored throughout the intraoperative period.
- After completing the surgery, the patients were given the following drugs intra-articular through an arthroscopic port depending on the group.
- Group D received Inj.Dexmedetomidine 100mcg +Inj Bupivacaine 0.25%, 20ml.Group B received Inj.Buprenorphine 100mcg +Inj Bupivacaine 0.25%,20ml.
- All vitals like temperature, pulse, BP., and VAS score for pain were monitored and recorded postoperatively at 1^{st},2^{nd},4^{th},8^{th},12^{th}, and 24^{th} hr.
- Adverse events including nausea, vomiting, hypotension, bradycardia, depression of respiration, pruritis, and urinary retention, were recorded.
- All patients were instructed preoperatively in the use of the 10cm Visual Analogue Scale of pain,0= no pain to 10 = the worst imaginable pain
- Visual analog scale (VAS) consists of a 10cm line, marked at 1cm each on which the patient marks a line that represents the intensity of pain he/she is experiencing. Mark '0' means no pain, and mark '10' represents the worst possible pain. The numbers marked by the patient are taken as units of pain intensity.
- Inj. Tramadol 100mg was given intravenously as rescue analgesic if patients complained of pain.

VAS Score Intensity of pain

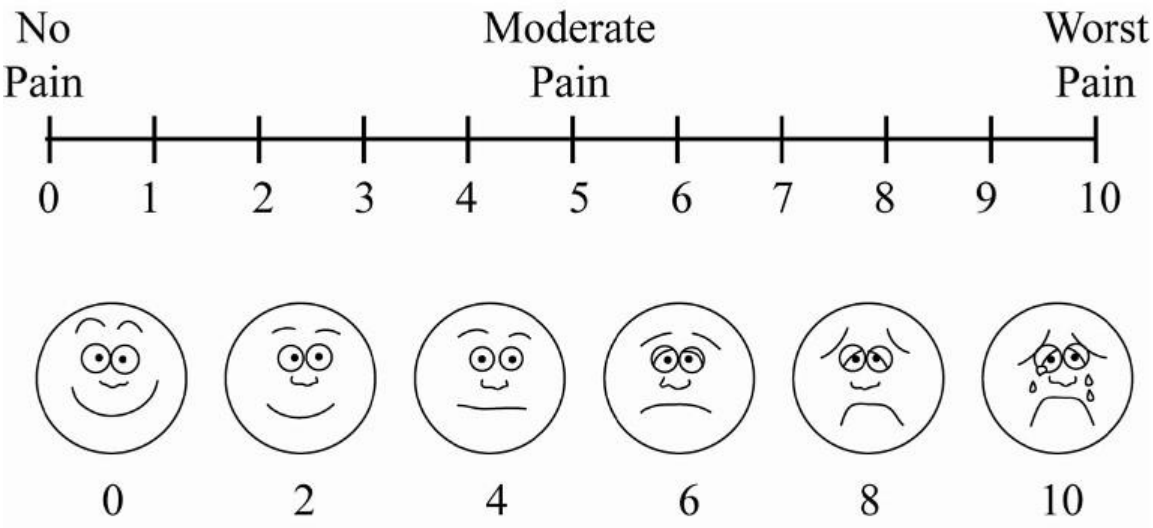
0 – No pain

1-3 Mild pain.

4-6 Moderate pain.

7-9 Severe pain.

10- Worst possible pain.



- Following observations were recorded:

1.Time to first rescue analgesia.

2.The number of patients requiring rescue analgesia within the next 24h.

3.Visual analog scale at rest and on mobilization at 1st,2nd,4th,8th, 12th, and 24h.

4. Side effects like sedation, pruritis, nausea, vomiting, respiratory depression, and hypotension.

Duration of analgesia: is the time interval between the onset of analgesia (VAS score <3), till

Patient complaints of pain (VAS score ≥ 3) when rescue analgesia is given.

Quality of analgesia: were assessed the duration of analgesia using pain score and we compared in both the groups.

Hypotension – is defined as a fall of systolic B.P. by 20% from basal systolic B.P.

Respiratory depression – Bradypnea appears to be a more reliable clinical sign of early respiratory depression and a respiratory rate of less than ten breaths/ min will be recorded as respiratory depression.

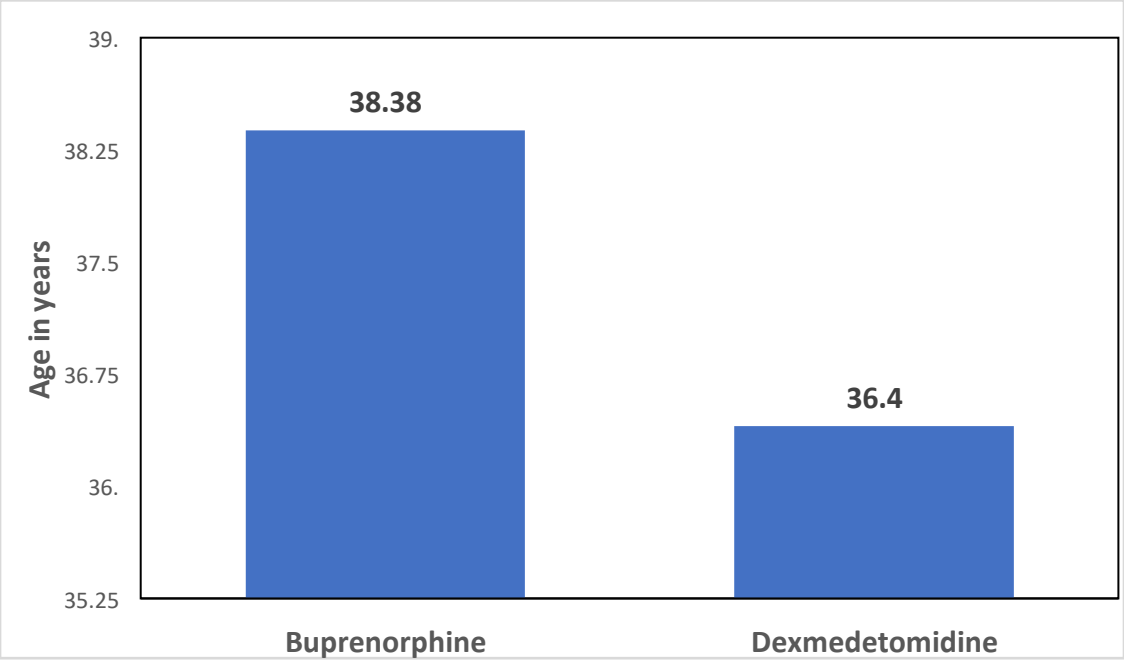
Bradycardia – A fall of heart rate by 20% from the basal heart rate. All the observations and particulars of each patient were recorded in a proforma, a copy of which is enclosed.

Results

Table 1: Distribution of age among the study participants (N=80)

Sl no	Group	Mean±SD	P
1	Buprenorphine(B)	38.38±11.30	0.45
2	Dexmedetomidine(D)	36.40±12.07	

Figure 1: Distribution of age among the study participants (N=80)

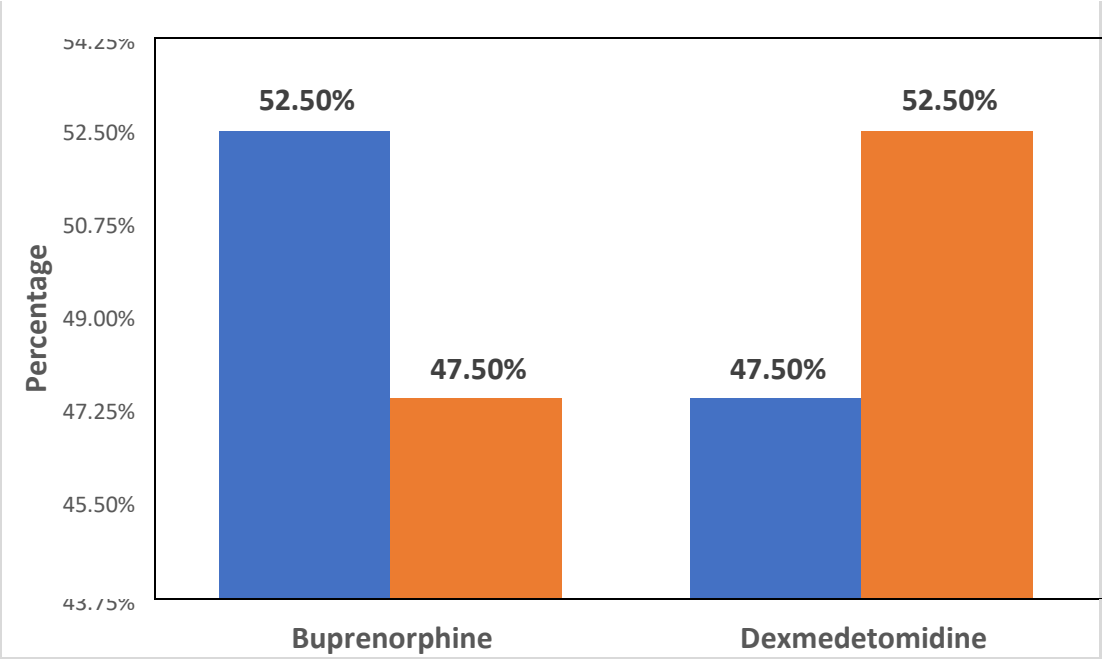


The mean age of the study participants was 38.38±11.30 years among the Buprenorphine group and 36.40±12.07 among the Dexmedetomidine group. There was no statistical significance between the groups.

Table 2: Distribution of gender among the study participants (N=80)

Slno	Gender	Buprenorphine (B)	Dexmedetomidine (D)	X^2, (Df), p
1	Female	21 (52.5)	19 (47.5)	0.200 (1) 0.65
2	Male	19 (47.5)	21 (52.5)	

Figure 2: Distribution of gender among the study participants (N=80)

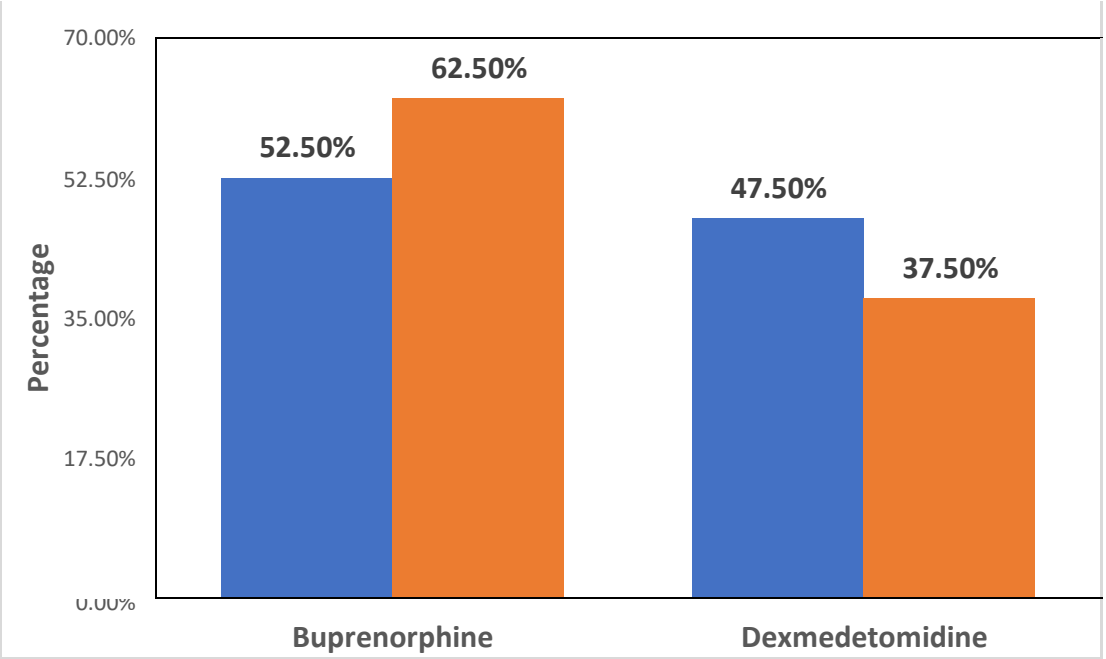


Among the Buprenorphine group, 52.5% were females and 47.5% were males. Among the Dexmedetomidine group, 47.5% were females and 52.5% were males. There was no statistical significance between the groups.

Table 3: Distribution of ASA grade among the study participants (N=80)

Slno	ASA grade	Buprenorphine (B)	Dexmedetomidine (D)	X^2, (Df), p
1	I	21 (52.5)	25 (62.5)	0.82 (1) 0.36
2	II	19 (47.5)	15 (37.5)	

Figure 3: Distribution of ASA grade among the study participants (N=80)

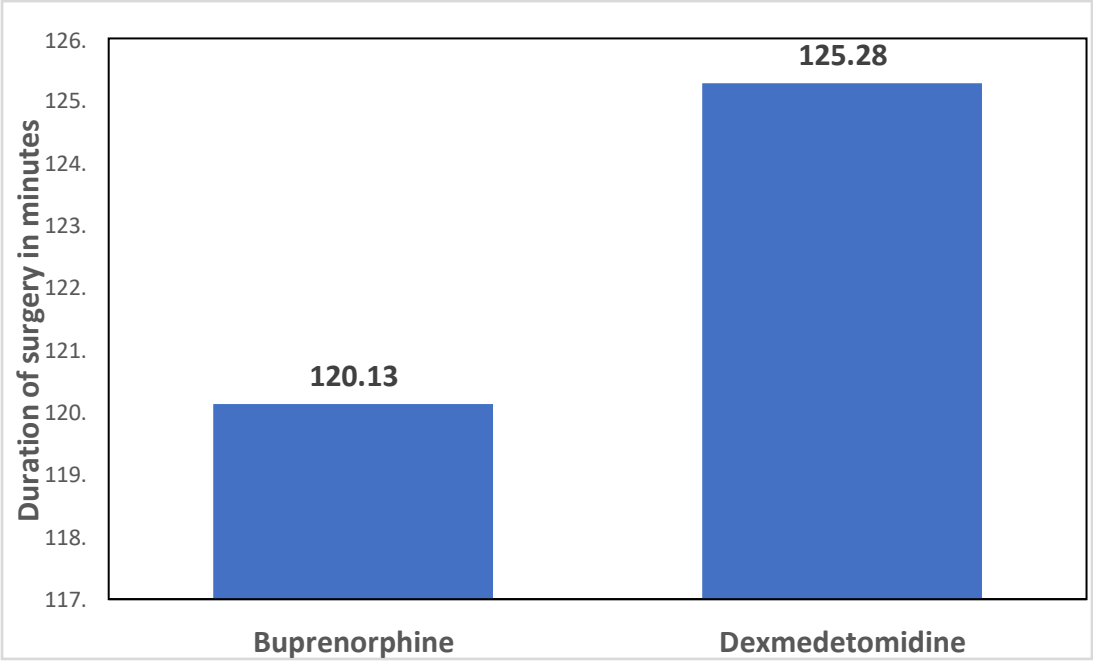


Among the Buprenorphine group ASA I were about 52.5% and ASA II were about 47.5%. Among the Dexmedetomidine group ASA I were about 62.5% and ASA II were 37.5%. There was no statistical significance between the groups.

Table 4: Distribution of duration of surgery among the study participants (N=80)

Slno	Group	Mean±SD	P
1	Buprenorphine(B)	120.13±2.19	0.67
2	Dexmedetomidine(D)	125.28±1.05	

Figure 4: Distribution of duration of surgery among the study participants (N=80)

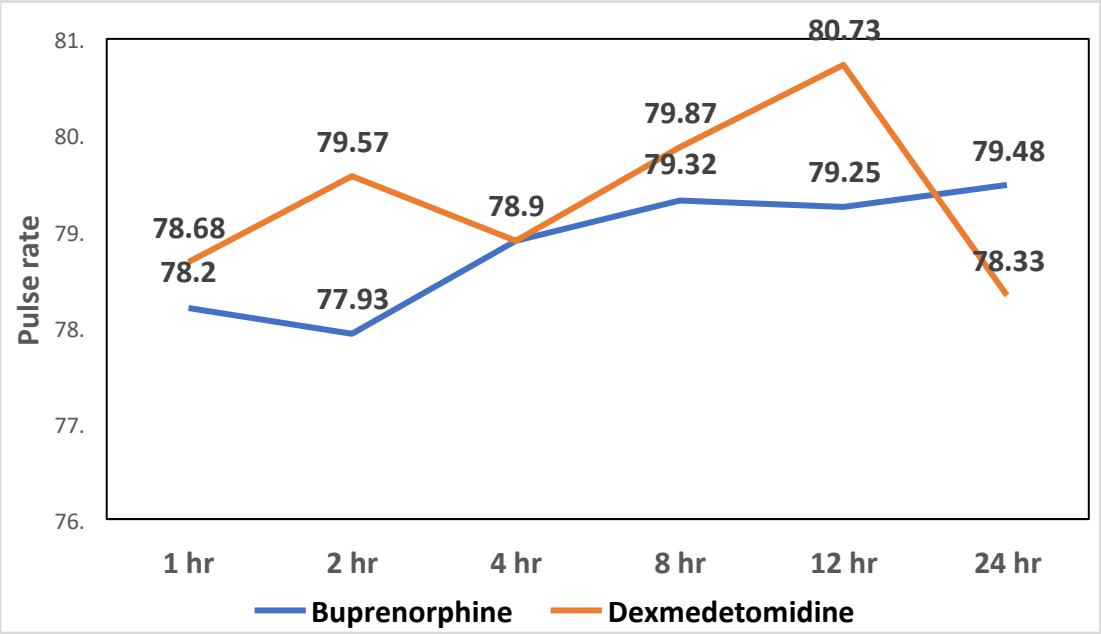


The mean surgery duration of the study participants was 120.13±2.19 minutes among the Buprenorphine group and 125.28±1.05 minutes among the Dexmedetomidine group. There was no statistical significance between the groups.

Table 5: Distribution of pulse rate among the study participants (N=80)

Slno	Pulse rate	Buprenorphine (B)	Dexmedetomidine (D)	P
1	1 hr.	78.20±8.39	78.68±7.27	0.78
2	2 hr.	77.93±7.37	79.57±6.01	0.29
3	4 hr.	78.90±7.48	78.90±6.22	1.00
4	8 hr.	79.32±7.93	79.87±7.08	0.74
5	12 hr.	79.25±7.97	80.73±6.06	0.35
6	24 hr.	79.48±8.70	78.33±5.83	0.49

Figure 5: Distribution of pulse rate among the study participants (N=80)



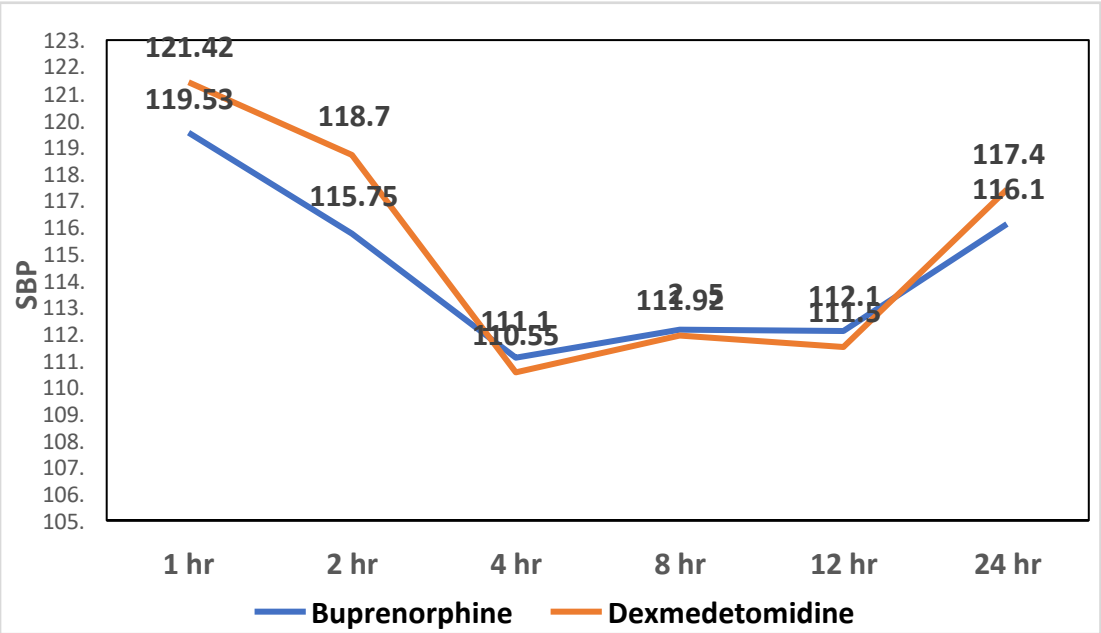
Among buprenorphine group Pulse rate at 1 hr. 78.20±8.39/min, at 2 hr 77.93±7.37/min, at 4 hr 78.90±7.48/min, at 8 hr 79.32±7.93/min, at 12 hr 79.25±7.97 and at 24 hr. 79.48±8.70/min. Among the dexmedetomidine group at 1 hr 78.68±7.27/min, at 2 hr 79.57±6.01/min, at 4 hr

78.90±6.22/min, at 8 hr 79.87±7.08/min, at 12 hr 80.73±6.06/min and at 24 hr. 78.33±5.83/min. There was no statistically significant difference in pulse rate between the groups.

Table 6: Distribution of SBP among the study participants (N=80)

Slno	SBP	Buprenorphine (B)		Dexmedetomidine (D)		P
		Mean	SD	Mean	SD	
1	1 hr.	119.53	11.19	121.42	9.66	0.42
2	2 hr.	115.75	11.03	118.70	8.82	0.19
3	4 hr.	111.10	7.80	110.55	10.36	0.24
4	8 hr.	112.15	7.61	111.92	9.80	0.91
5	12 hr.	112.10	7.61	111.50	7.03	0.56
6	24 hr.	116.10	4.17	117.40	6.71	0.61

Figure 6: Distribution of SBP among the study participants (N=80)

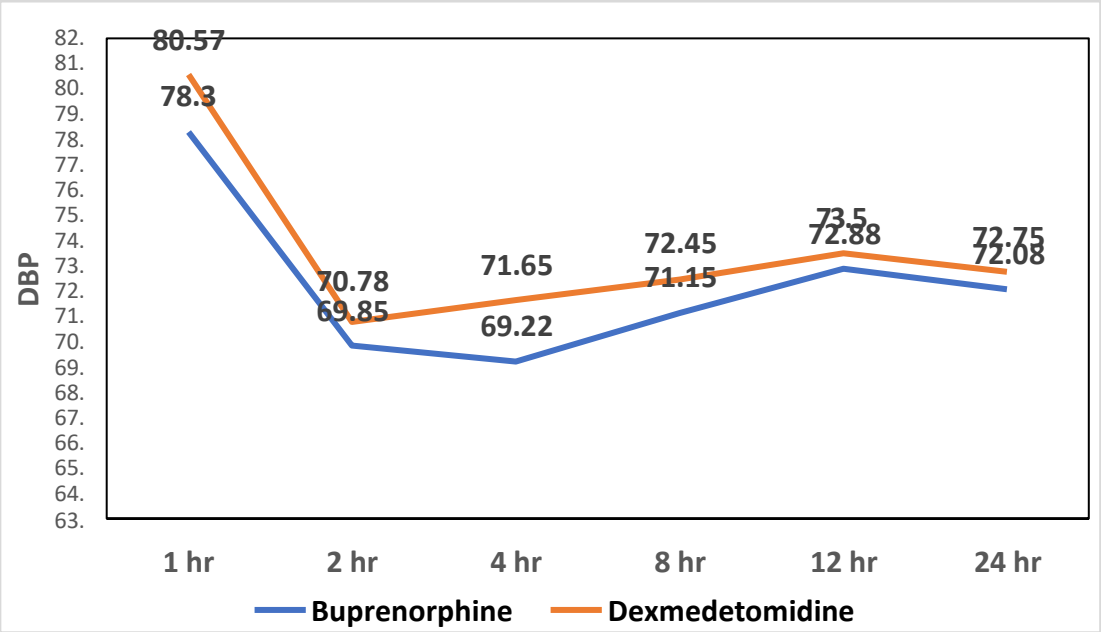


Among the buprenorphine group SBP at 1 hr was 119.53± 11.19 mm of Hg, at 2 hr 115.75± 11.03 mm of Hg, at 4 hr 111.10± 7.80 mm of Hg, at 8 hr 112.15±. 7.61 mm of Hg, at 12 hr 112.10± 7.61 mm of Hg, and at 24 hr 116.10± 4.17 mm of Hg. Among the dexmedetomidine group at 1hr 121.41± 9.66 mm of Hg, at 2 hr 118.70± 8.82 mm of Hg, at 4 hr 110.55± 10.36 mm of Hg, at 8 hr 111.92 ± 9.80 mm of Hg, at 12 hr 111.50 ± 7.03 mm of Hg and at 24 hr 117.40± 6.71 mm of Hg. There was no statistical significance in SBP between both groups.

Table 7: Distribution of DBP among the study participants (N=80)

Slno	DBP	Buprenorphine (B)		Dexmedetomidine (D)		P
		Mean	SD	Mean	SD	
1	1 hr.	78.30	9.73	80.57	8.60	0.27
2	2 hr.	69.85	3.70	70.78	6.65	0.44
3	4 hr.	69.22	6.62	71.65	4.99	0.25
4	8 hr.	71.15	6.30	72.45	6.23	0.38
5	12 hr.	72.88	4.68	73.50	4.86	0.67
6	24 hr.	72.08	5.10	72.75	3.92	0.65

Figure 7: Distribution of DBP among the study participants (N=80)

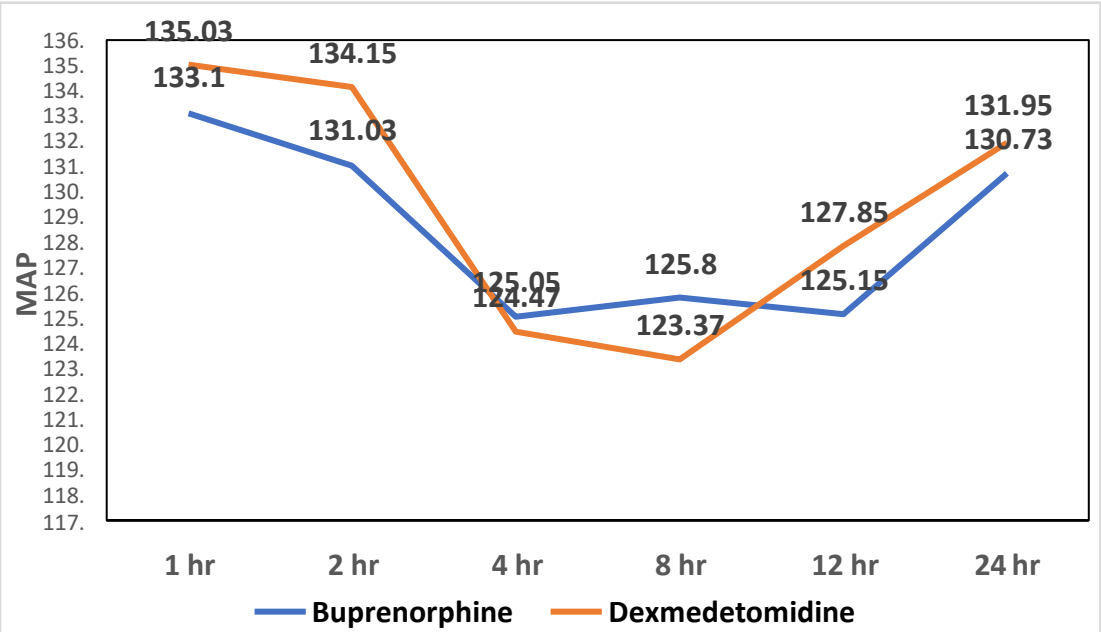


. Among buprenorphine group DBP at 1 hr was 78.30± 9.73 mm of Hg, at 2 hr 69.85± 3.70 mm of Hg, at 4 hr 69.22± 6.62 mm of Hg, at 8 hr 71.15±. 6.30 mm of Hg, at 12 hr 72.88± 4.6,8 mm of Hg and at 24 hr 72.08± 5.10 mm of Hg. Among the dexmedetomidine group at 1hr 80.57± 8.60 mm of Hg, at 2 hr 70.78± 6.65 mm of Hg, at 4 hr 71.65± 4.99 mm of Hg, at 8 hr 72.45 ± 6.23 mm of Hg, at 12 hr 73.50 ± 4.86 mm of Hg and at 24 hr 72.75± 3.92 mm of Hg. There was no statistical significance in DBP between both groups.

Table 8: Distribution of MAP among the study participants (N=80)

Slno	MAP	Buprenorphine (B)		Dexmedetomidine (D)		P
		Mean	SD	Mean	SD	
1	1 hr.	133.10	13.14	135.03	13.45	0.52
2	2 hr.	131.03	14.89	134.15	12.60	0.31
3	4 hr.	125.05	10.07	124.47	13.31	0.71
4	8 hr.	125.80	9.50	123.37	12.68	0.45
5	12 hr.	125.15	9.66	127.85	8.92	0.46
6	24 hr.	130.73	5.32	131.95	8.57	0.71

Figure 8: Distribution of MAP among the study participants (N=80)

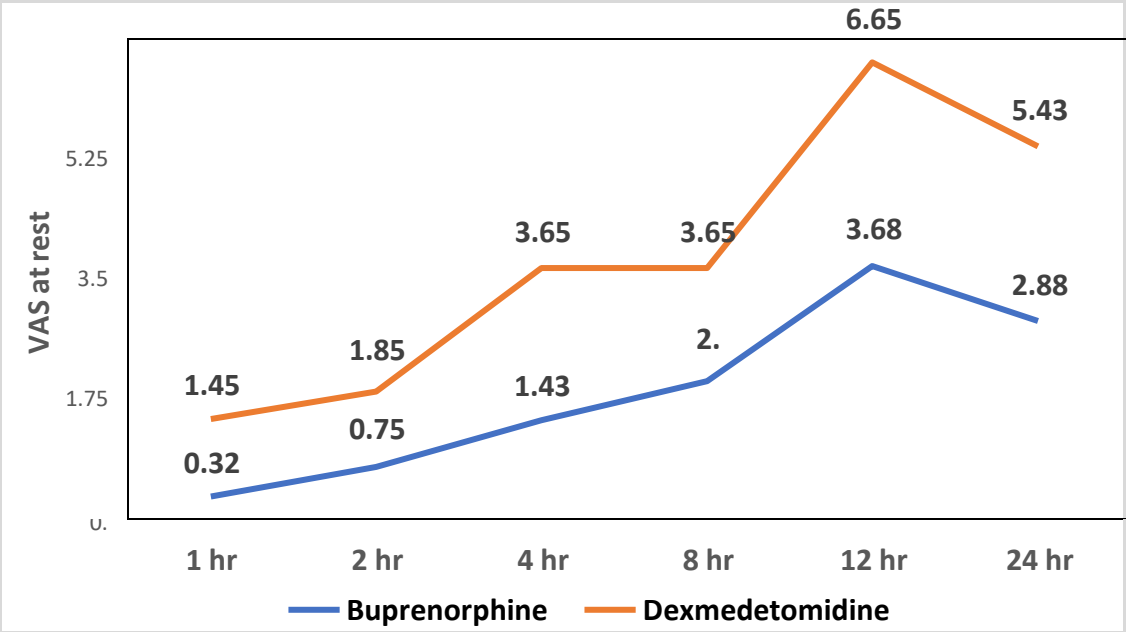


Among the buprenorphine group MAP at 1 hr was 133.10± 13.14 mm of Hg, at 2 hr 131.03± 14.89 mm of Hg, at 4 hr 125.05± 10.07 mm of Hg, at 8 hr 125.80±. 9.50 mm of Hg, at 12 hr 125.15± 9.66 mm of Hg, and at 24 hr 130.73± 5.32 mm of Hg. Among the dexmedetomidine group at 1hr was 135.03± 13.45 mm of Hg, at 2 hr 134.15± 12.60 mm of Hg, at 4 hr 127.47± 13.31 mm of Hg, at 8 hr 123.37 ± 12.68 mm of Hg, at 12 hr 127.85 ± 8.92 mm of Hg and at 24 hr 131.95± 8.57 mm of Hg. There was no statistical significance in MAP between both groups

Table 9: Distribution of VAS at rest among the study participants (N=80)

Slno	**VAS at rest**	**Buprenorphine (B)**	**Dexmedetomidine (D)**	**P**
1	1 hr.	0.32±0.47	1.45±0.50	<0.001
2	2 hr.	0.75±0.74	1.85±0.80	<0.001
3	4 hr.	1.43±0.50	3.65±1.23	<0.001
4	8 hr.	2.00±0.85	3.65±1.47	<0.001
5	12 hr.	3.68±0.99	6.65±1.16	<0.001
6	24 hr.	2.88±0.88	5.43±1.13	<0.001

Figure 9: Distribution of VAS at rest among the study participants (N=80)

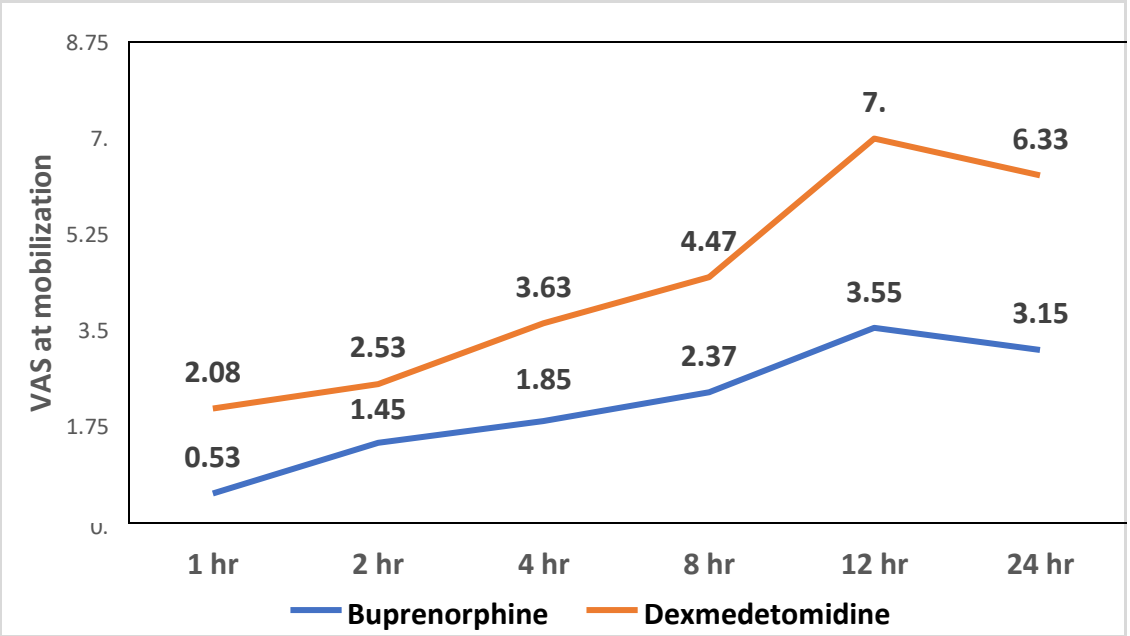


Among buprenorphine group VAS at rest at 1 hr 0.32±0.47, at 2 hr 0.75±0.74, at 4 hr 1.43±0.50, at 8 hr 2.00±0.85, at 12 hr 3.68±0.99 and at 24 hr 2.88±0.88. Among dexmedetomidine group at 1 hr 1.45±0.50, at 2 hr 1.85±0.80, at 4 hr 3.65±1.23, at 8 hr 3.65±1.47, at 12 hr 6.65±1.16 and at 24 hr 5.43±1.13. There was a statistically significant difference in VAS score at rest between the groups.

Table 10: Distribution of VAS at mobilization among the study participants (N=80)

Slno	VAS at mobilization	Buprenorphine (B)	Dexmedetomidine (D)	P
1	1 hr	0.53±0.51	2.08±0.86	<0.001
2	2 hr	1.45±0.50	2.53±0.50	<0.001
3	4 hr	1.85±0.80	3.63±1.00	<0.001
4	8 hr	2.37±0.49	4.47±1.08	<0.001
5	12 hr	3.55±1.19	7.00±1.37	<0.001
6	24 hr	3.15±0.77	6.33±1.18	<0.001

Figure 10: Distribution of VAS at mobilization among the study participants (N=80)

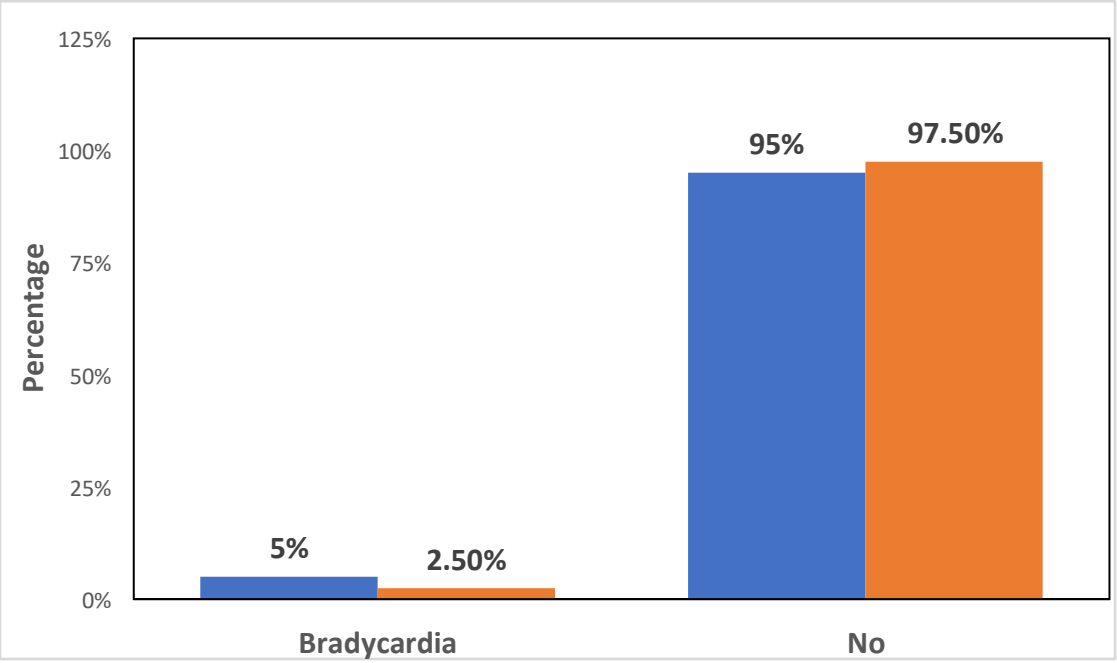


Among the buprenorphine group VAS at mobilization at 1 hr 0.53±0.51, at 2 hr 1.45±0.50, at 4 hr 1.85±0.80, at 8 hr 2.37±0.49, at 12 hr 3.55±1.19 and at 24 hr 3.15±0.77. Among dexmedetomidine group at 1 hr 2.08±0.86, at 2 hr 2.53±0.50, at 4 hr 3.63±1.00, at 8 hr 4.47±1.08, at 12 hr 7.00±1.37and at 24 hr 6.33±1.18. There was statistical significance difference in VAS score at mobilization between the groups.

Table 11: Distribution of adverse events among the study participants (N=80)

Slno	**Adverse events**	**Buprenorphine (B)**	**Dexmedetomidine (D)**	**X^2, (Df), p**
1	Bradycardia	2 (5.0)	1 (2.5)	0.346 (1) 0.56
2	No	38 (95.0)	39 (97.5)	

Figure 11: Distribution of adverse events among the study participants (N=80)

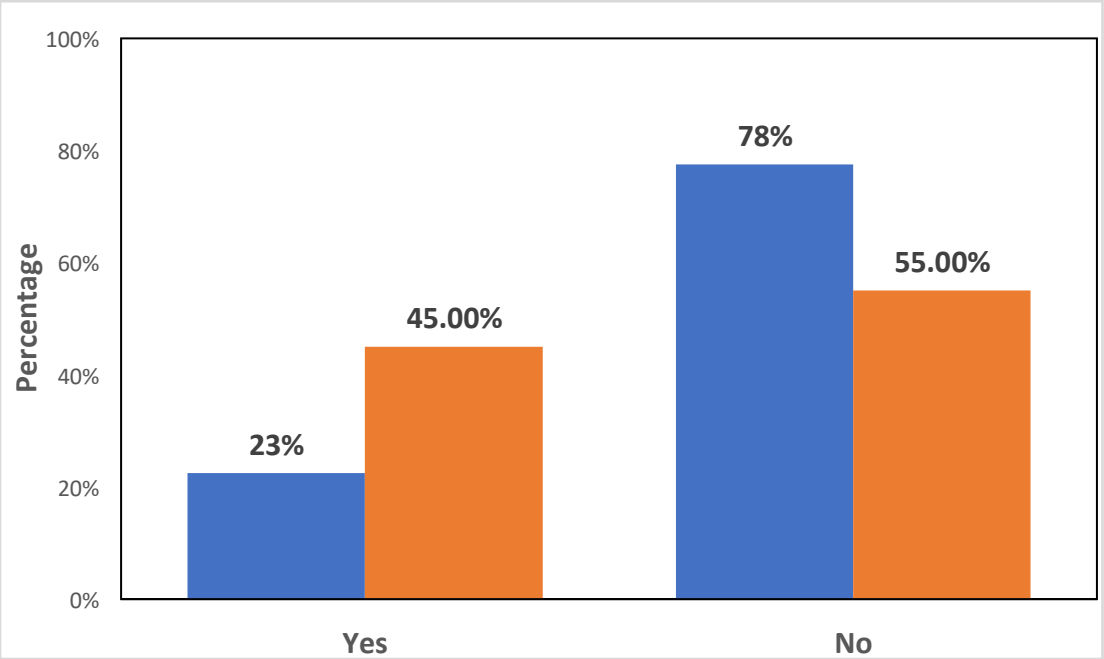


Among Buprenorphine group bradycardia were about 5%. Among Dexmedetomidine group bradycardia were about 2.5%. There was no statistical significance between the groups.

Table 12: Distribution of rescue analgesia among the study participants (N=80)

Slno	Rescue analgesia	Buprenorphine (B)	Dexmedetomidine (D)	X^2, (Df), p
1	Yes	9 (22.5)	18 (45.0)	4.53 (1) 0.03
2	No	31 (77.5)	22 (55.0)	

Figure 12: Distribution of rescue analgesia among the study participants (N=80)

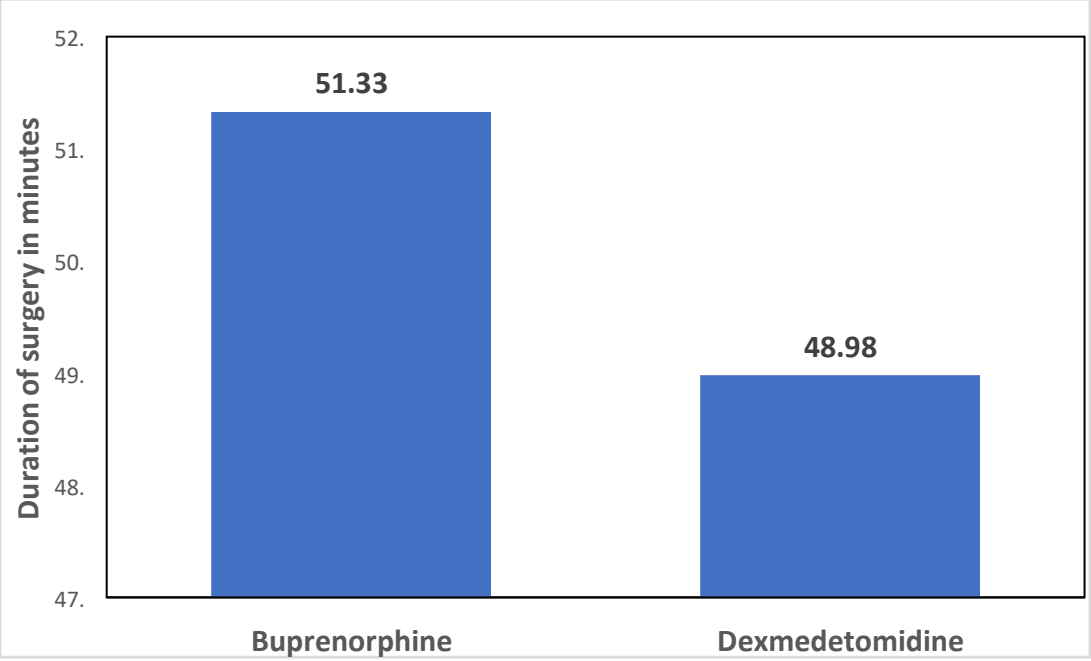


Among Buprenorphine group rescue analgesia were given for 22.50%. Among Dexmedetomidine group rescue analgesia were given for 45.0%. There was statistical significance between the groups.

Table 13: Distribution of time for first rescue analgesia among the study participants (N=80)

Slno	Group	Mean±SD	P
1	Buprenorphine(B)	1016.22±137.54	<0.001
2	Dexmedetomidine(D)	523.67±117.47	

Figure 13: Distribution of time for first rescue analgesia among the study participants (N=80)



Mean time for first rescue analgesia was longer for buprenorphine group 1016.22±137.54 min and for Dexmedetomidine group it was 523.67±117.47 min.

Discussion

There is a trend toward arthroscopic reconstruction of the knee joint for patients who have sustained knee joint damage. This trend is being driven by a number of causes, including the growing demand for hospital beds, the prevalence of infections acquired in hospitals, and the financial repercussions. In spite of the rise in the number of outpatient surgical procedures, one

of the factors that prevents their widespread use is a lack of a proper understanding of approach to postoperative pain management.

For patients who have undergone knee arthroscopy, a variety of postoperative analgesic techniques have been utilised. Because systemic opioids can cause unpleasant side effects such nausea and vomiting, as well as respiratory depression, sleepiness, and pruritis, it may be preferable to administer analgesia locally. After arthroscopic knee surgeries, one of the most effective and straightforward strategies for pain management is intra-articular medication injection, which also facilitates early ambulation for the patient.

Ropivacaine is structurally comparable to bupivacaine, but due to the fact that it is less lipid soluble, it poses a lower risk of toxicity to the central nervous system and the heart. Dexmedetomidine produces drowsiness, analgesia, and sympatholysis when it is administered intravenously; however, when it is administered intramuscularly in conjunction with local anaesthetics, it reduces postoperative pain without producing any notable side effects. Analgesia that is both strong and long-lasting can be attributed to buprenorphine's status as a partial agonist with a higher receptor affinity than that of morphine.

Age

In our study the mean age of the study participants 38.38±11.30 years among Buprenorphine group and 36.40±12.07years among Dexmedetomidine group. There was no statistical significance between the groups. In Das et al[60] study mean age in years was 34.16±9.55 for buprenorphine group and 35.18±9.2 among dexmedetomidine group. In a study by Manula devi et al[61] mean age in years was 37.22±13.36 for buprenorphine group and 32.78±11.9 among dexmedetomidine group.

Gender

In our study among Buprenorphine group 52.5% were females and 47.5% males and among Dexmedetomidine group 47.5% were females and 52.5% were males. There was no statistical significance between the groups. In Das et al[60] 26 males and 4 females among buprenorphine group; 25 males and 5 females among dexmedetomidine group. In a study by Manula devi et al[61] 8 females and 10 males were in buprenorphine group ; 2 females and 16 males in dexmedetomidine group.

ASA

In our study among Buprenorphine group ASA I were about 52.5% and ASA II were about 47.5% and among Dexmedetomidine group ASA I were about 62.5% and ASA II were 37.5%. There was no statistical significance between the groups. In a study by Manula devi et al[61] among buprenorphine group 13 in ASA 1 and 5 in ASA II. Among dexmedetomidine group 14 in ASA I and 4 in ASA II.

Duration of Surgery

The mean surgery duration of the study participants 120.13±2.19 minutes among Buprenorphine group and 125.28±1.05 minutes among Dexmedetomidine group. There was no statistical significance between the groups. In Das et al[60] study mean surgery duration of the study participants was 49.2±10.4 min for buprenorphine group and 50.9±10.5 min among dexmedetomidine group. In a study by Manula devi et al[61] mean surgery duration of the study participants was 2.5±10.4 hrs for buprenorphine group and 2.39±7.5 hrs among

dexmedetomidine group. In Bansal et al[62] mean duration of surgery 187.58± 9.14min among buprenorphine group and 186. 92±9.67min among dexmedetomidine group.

Pulse rate

In our study among buprenorphine group Pulse rate at 1 hr 78.20±8.39/min, at 2 hr 77.93±7.37/min, at 4 hr 78.90±7.48/min, at 8 hr 79.32±7.93/min, at 12 hr 79.25±7.97 and at 24 hr 79.48±8.70/min. Among dexmedetomidine group at 1 hr 78.68±7.27/min, at 2 hr 79.57±6.01/min, at 4 hr 78.90±6.22/min, at 8 hr 79.87±7.08/min, at 12 hr 80.73±6.06/min and at 24 hr 78.33±5.83/min. There was no statistical significance difference in pulse rate between the groups. In Das et al[60] study there was no significant change in hemodynamic parameters among the two groups. In a study by Manula devi et al[61] mean pulse rate of 70.31 ranging from 66.13 and74.5 among buprenorphine group. Mean pulse rate of 69.76 ranging from 65.3 and 74.22 among dexmedetomidine group.

SBP

In our study among buprenorphine group SBP at 1 hr was 119.53± 11.19 mm of Hg, at 2 hr 115.75± 11.03 mm of Hg, at 4 hr 111.10± 7.80 mm of Hg, at 8 hr 112.15±. 7.61 mm of Hg, at 12 hr 112.10± 7.61 mm of Hg and at 24 hr 116.10± 4.17 mm of Hg. Among the dexmedetomidine group at 1hr 121.41± 9.66 mm of Hg, at 2 hr 118.70± 8.82 mm of Hg, at 4 hr 110.55± 10.36 mm of Hg, at 8 hr 111.92 ± 9.80 mm of Hg, at 12 hr 111.50 ± 7.03 mm of Hg and at 24 hr 117.40± 6.71 mm of Hg, there is no any statistical significance between the groups. In Das et al[60] study there was no significant change in hemodynamic parameters among

the two groups. In a study by Manual Devi et al[61] hemodynamic parameters were comparable between the groups and did not show any statistical significance.

DBP

In our study among buprenorphine group DBP at 1 hr was 78.30± 9.73 mm of Hg, at 2 hr 69.85± 3.70 mm of Hg, at 4 hr 69.22± 6.62 mm of Hg, at 8 hr 71.15±. 6.30 mm of Hg, at 12 hr 72.88± 4.6,8 mm of Hg and at 24 hr 72.08± 5.10 mm of Hg. Among the dexmedetomidine group at 1hr 80.57± 8.60 mm of Hg, at 2 hr 70.78± 6.65 mm of Hg, at 4 hr 71.65± 4.99 mm of Hg, at 8 hr 72.45 ± 6.23 mm of Hg, at 12 hr 73.50 ± 4.86 mm of Hg and at 24 hr 72.75± 3.92 mm of Hg, there is no statistical significance between both groups. In Das et al[60] study there was no significant change in hemodynamic parameters among the two groups. In a study by Manual Devi et al[61] hemodynamic parameters were comparable between the groups and did not show any statistical significance.

MAP

In our study among the buprenorphine group MAP at 1 hr was 133.10± 13.14 mm of Hg, at 2 hr 131.03± 14.89 mm of Hg, at 4 hr 125.05± 10.07 mm of Hg, at 8 hr 125.80±. 9.50 mm of Hg, at 12 hr 125.15± 9.66 mm of Hg and at 24 hr 130.73± 5.32 mm of Hg. Among the dexmedetomidine group at 1hr was 135.03± 13.45 mm of Hg, at 2 hr 134.15± 12.60 mm of Hg, at 4 hr 127.47± 13.31 mm of Hg, at 8 hr 123.37 ± 12.68 mm of Hg, at 12 hr 127.85 ± 8.92 mm of Hg and at 24 hr 131.95± 8.57 mm of Hg, there is no statistical significance in MAP between both groups, In Das et al[60] study there was no significant change in hemodynamic parameters among the two groups. In a study by Manual Devi et al[61] hemodynamic parameters were comparable between the groups and did not show any statistical significance.

VAS at rest

In our study among the buprenorphine group VAS at rest at 1 hr 0.32±0.47, at 2 hr 0.75±0.74, at 4 hr 1.43±0.50, at 8 hr 2.00±0.85, at 12 hr 3.68±0.99 and at 24 hr 2.88±0.88. Among the dexmedetomidine group at 1 hr 1.45±0.50, at 2 hr 1.85±0.80, at 4 hr 3.65±1.23, at 8 hr 3.65±1.47, at 12 hr 6.65±1.16 and at 24 hr 5.43±1.13. There was a statistical significant difference in VAS score at rest between the groups. However, from the 8th hr VAS score was significantly high in the IA Dexmedetomidine group at rest. In Das et al[60] found no significant difference in pain intensity at rest as assessed by VAS at 1, 2, 4, and 8 hr between the buprenorphine and dexmedetomidine group. However, at the 12th and 24th hr, the VAS score was significantly high in the IA dexmedetomidine group at rest. In a study by Manual Devi et al[61] pain scores at rest relatively less (analysis showing $P < 0.001$ for VAS-R and $P < 0.05$ for VAS-M) in IA dexmedetomidine group.

VAS at mobilization

In our study Among buprenorphine group VAS at mobilization at 1 hr 0.53±0.51, at 2 hr 1.45±0.50, at 4 hr 1.85±0.80, at 8 hr 2.37±0.49, at 12 hr 3.55±1.19 and at 24 hr 3.15±0.77. Among dexmedetomidine group at 1 hr 2.08±0.86, at 2 hr 2.53±0.50, at 4 hr 3.63±1.00, at 8 hr 4.47±1.08, at 12 hr 7.00±1.37and at 24 hr 6.33±1.18. There was statistical significance difference in VAS score at mobilization between the groups, but significantly high in IA Dexmedetomidine from the 8th hr. In Das et al[60] study VAS scores on ambulation were comparable at 1st, 2nd, and 4th hr, but significantly higher in the dexmedetomidine group as compared to buprenorphine at 8th, 12th, and 24th hr.

Buprenorphine provides a longer duration of analgesia with less pain scores. This could be because it only acts as a partial agonist, has a high receptor affinity, and dissociates slowly from the local peripheral opioid receptor. [63] In a study by Manual Devi et al[61] pain scores at movement were relatively less (post hoc analysis showing $P < 0.001$ for VAS-R and $P < 0.05$ for VAS-M) in the IA dexmedetomidine group. In a study by Bansal et al[62] on comparing the visual analogue scale in both groups, there was not much of a significant difference in the VAS Score. Both groups showed a decrease in the intensity of pain as compared to preoperative and immediate post-operative

Adverse events

In our study among the Buprenorphine group bradycardia was about 5% i.e., 2 patients had bradycardia and among the Dexmedetomidine group bradycardia was about 2.5% i.e. only one patient had bradycardia. In Das et al[60] study, only two patients in the buprenorphine group had hypotension as compared to one in the dexmedetomidine group, though statistically not significant. In a study by Manula devi et al[61] no adverse effects were reported with dexmedetomidine group. In a study by Bansal et al[62] dexmedetomidine group showed much fewer complications and side-effects as compared to buprenorphine group.

Rescue analgesia

Among the Buprenorphine group rescue analgesia was given to 22.50% i.e., 9 patients received rescue analgesia. Among the Dexmedetomidine group, rescue analgesia was given to 45.0% i.e.,18 patients received rescue analgesia when VAS is ≥3 ,There was statistical significance between the groups. In the study conducted by Das et al[60], only six patients in the buprenorphine group and fifteen patients in the dexmedetomidine group required rescue

analgesia within the first twenty-four hours (P = 0.03). In a study by Manula Devi et al[61], rescue analgesia was given at 2.00±0.8 among the buprenorphine group and 0.94±0.8 among the dexmedetomidine group.

Time for first rescue analgesia

In our study meantime for the first rescue analgesia was longer for the buprenorphine group 1016.22±137.54 min and for the Dexmedetomidine group it was 523.67±117.47 min. In our study, the time to first rescue analgesia was significantly higher in the buprenorphine than the dexmedetomidine group. In the study conducted by Das et al[60], the time it took for patients receiving IA buprenorphine (954.2 96.4 min) to experience their first rescue analgesia was significantly longer than it was for patients receiving IA dexmedetomidine (628 85.4 min). Varrassi et al [64] came to the same conclusion, stating that 100 micrograms of buprenorphine provided better postoperative pain and reduced the need for postoperative analgesics. The number of patients in the dexmedetomidine group who required rescue analgesia within 24 hours was significantly higher when compared to the number of patients in the buprenorphine group who required such treatment. This is comparable to a study in which patients who received intravenous buprenorphine required a lower total number of rescue analgesics. [65]

Summary

The most popular minimally invasive orthopaedic surgical method is arthroscopy for knee surgery. After surgery, postoperative pain is most typical. Early mobilisation, pain reduction that reduces patient morbidity, and postoperative recovery are all enhanced by postoperative pain medication. In an effort to reduce the amount of postoperative pain that patients experience, researchers have been looking into multimodal approaches for analgesia. These

treatments include intra-articular (IA) injections, peripheral nerve blocks, systemic analgesia, and neuraxial analgesia.

A comparison of the effectiveness of BUPRENORPHINE AND INTRA-ARTICULAR DEXMEDETOMIDINE FOR POST-OPERATIVE ANALGESIA FOLLOWING ARTHROSCOPIC KNEE SURGERIES performed over the course of 1.5 years on 80 patients who were undergoing arthroscopic knee procedures in the department of anaesthesia at Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura. After meeting the inclusion and exclusion criteria, patients were randomly split into two equal groups: B - Buprenorphine group (40 patients), and D - Dexmedetomidine group (40 patients). Both groups' participants received premedication injections as a preventative measure. After inserting all standard monitors (NIBP, SP02, ECG.), glycopyrrolate 0.2 mg IV and midazolam 1 mg IV, all vitals were recorded before and after premedication. Patients in both groups were induced with injections of Bupivacaine heavy 0.5%, under spinal anaesthesia while being subjected to strict aseptic and antiseptic measures. Throughout the intraoperative time, temperature, pulse, B.P., and SP02 were measured. Depending on the group, the medications were administered intraarticularly to the patients after the surgery.

Visual analogue scale at rest and on mobilisation at 1st, 2nd, 4th, 8th, 12th, and 24 hours were measured, along with the time until the first rescue analgesia was administered.

Sedation, pruritis, nausea, vomiting, respiratory depression, and hypotension were all kept an eye on, as side effects. Participants in the study had an average age of 38.38 ±11.30 years for the buprenorphine group and 36.40 ±12.07 years for the dexmedetomidine group. 52.5% of the Buprenorphine group members were women, while 47.5% were men. In terms of the VAS score at rest, there was a statistically significant difference between the groups. At mobilisation, there was a statistically significant difference in VAS scores between the groups. About 5% of the buprenorphine group experienced bradycardia. About 2.5% of the

Dexmedetomidine group had bradycardia. Between the groups, there was no statistically significant difference. The Buprenorphine group meantime for first rescue analgesia was 1016.22137.54 min, while the dexmedetomidine group meantime for first rescue analgesia was 523.67117.47 min.

Conclusion

In our study, we have observed that compared to IA dexmedetomidine, IA buprenorphine produces postoperative analgesia for a longer period of time and reduces the amount of postoperative rescue analgesic that is required, with a mean duration of analgesia being 1016.22±137.54min when compared to IA dexmedetomidine which is 523.67±11.47min without any significant adverse effects.

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SCHEME OF CASE TAKING

PROFORMA

STUDY: "TO COMPARE THE EFFICACY OF INTRA-ARTICULAR BUPRENORPHINE VERSUS DEXMEDETOMIDINE FOR POSTOPERATIVE ANALGESIA FOLLOWING ARTHROSCOPIC KNEE SURGERIES"

PATIENT DETAILS: **DATE: -**

Name:

Age/ Sex:

I.P No:

Group allotted by randomization: GroupB / GroupD

1. Type of surgery:

2. Indication:

Significant History:

General Physical Examination:

Pallor: Icterus: Cyanosis:

Clubbing: Koilonychia: Lymphadenopathy:

Edema: Teeth: Dentures:

Vital Parameters

Pulse: Blood Pressure:

Respiratory Rate: Temperature:

Systemic Examination

1. CVS 2.RS:

3. C.N.S. 4.Per Abdomen:

Airway Assessment:

Mallampati Grade: Cervical Spine:

Mouth opening: Neck Movement:

A.S.A. Grade:

Investigation

Haemoglobin: T.L.C.: S. Urea: S. Creatinine:

R.B.S: Platelet count: Urine Routine:

Chest Xray: ECG.:

Anaesthesia start time:

Surgery start time:

Surgery end time:

Time of the first complaint of pain in postoperative period:

Time to first rescue analgesia

VAS SCORE: postoperatively at rest at 1^{st}, 2^{nd}, 4^{th}, 8^{th}, 12^{th}, and 24^{th} h

VAS SCORE postoperatively on mobilisation at 1^{st}, 2^{nd}, 4^{th}, 8^{th}, 12^{th}, and 24^{th} h

Side effects:

Demographic data and duration of surgery

Parameters	GroupB(n=40)	Group D (n =40)	P
Age(male/female)			
Gender(male/female)			
Body weight(kg)			
Duration of surgery			

Analgesia requirement during next 24h

Parameters	Group B (n= 40)	Group D(n=40)	P
Time to first rescue analgesia			
Number of Patients requiring rescue analgesia			

The Visual analog scale at rest

VAS at rest(h)	GroupB	Group D	P
1			
2			
4			
8			
12			
24			

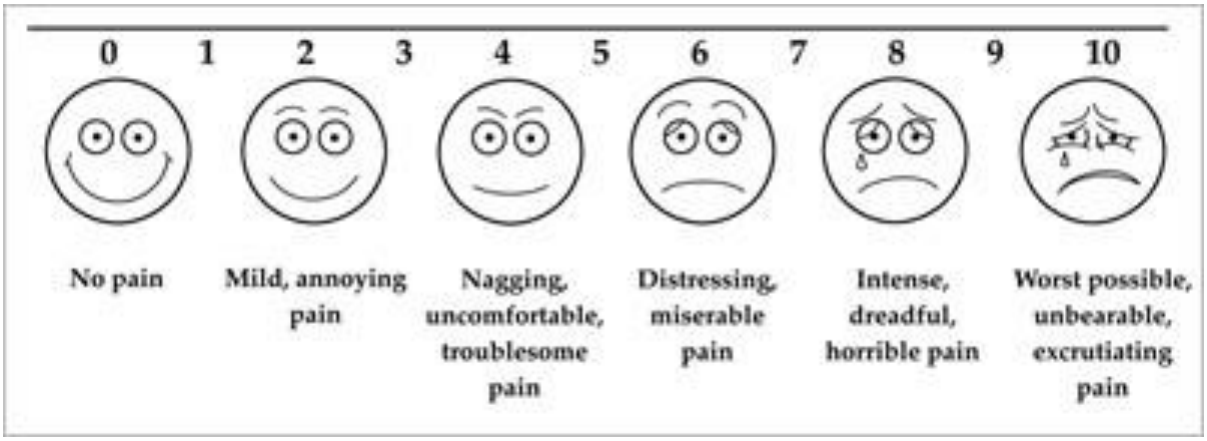
The visual analogue scale on mobilization

VAS on mobilization(h)	Group(B)	Group(D)	P
1			
2			
4			
8			
12			
24			

Adverse effects

Adverse effects	Group B	Group D	P
Bradycardia			
Hypotension			
Nausea			
Vomiting			
Pruritis			
Urinary retention			
Hematoma			

VAS SCALE



COMMENTS:-

PRIMARY INVESTIGATOR SIGNATURE:-

GUIDE SIGNATURE

STUDY SUBJECT CONSENT STATEMENT

I confirm that **Dr. RAJESHWARI B V** has explained 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 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

A COMPARATIVE STUDY OF EFFICACY OF INTRA-ARTICULAR DEXMEDETOMIDINE VERSUS BUPRENORPHINE FOR POSTOPERATIVE ANALGESIA FOLLOWING ARTHROSCOPIC KNEE SURGERIES

ORIGINALITY REPORT

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Master chart

S NO	AGE	SEX	GROUP	ASA GRADE	DURATION OF SURGERY (Min)	Pulse (Hours)						SBP (Hours)						DBP (Hours)						MAP (Hours)						VAS AT REST (Hours)						VAS AT MOBILIZATION (Hours)						ADVERSE EVENTS	RESCUE ANALGESIA	TIME FOR RESCUE ANALGESIA
						1	2	4	8	12	24	1	2	4	8	12	24	1	2	4	8	12	24	1	2	4	8	12	24	1	2	4	8	12	24	1	2	4	8	12	24			
1	51	F	B	1	118	70	83	78	71	90	86	124	121	94	100	98	111	78	64	60	64	67	70	139	140	105	112	108	125	0	2	1	3	5	4	1	2	2	2	2	2	NO	YES	893
2	27	M	B	1	120	87	83	85	79	86	73	100	93	117	120	109	120	65	72	48	60	64	70	112	100	140	140	124	137	1	0	1	3	3	2	1	1	2	3	3	3	NO	NO	NIL
3	33	F	B	2	121	88	74	88	75	86	73	120	116	113	110	113	116	73	69	64	70	71	69	136	132	129	123	127	132	0	2	2	3	5	2	0	1	3	3	5	2	NO	YES	806
4	49	M	B	1	118	83	78	79	85	72	86	140	127	118	118	124	122	83	67	72	73	75	71	159	147	133	133	140	139	0	0	2	2	5	2	0	1	2	2	3	3	NO	YES	1019
5	19	F	B	1	120	86	71	88	72	87	74	138	126	114	119	117	121	113	73	72	83	81	76	146	144	128	131	129	136	1	1	1	1	4	4	1	2	2	2	5	4	NO	NO	NIL
6	34	F	B	2	124	86	82	82	90	77	72	127	126	106	98	106	111	87	73	74	75	70	68	140	144	117	106	118	125	0	0	1	1	4	2	0	1	2	2	5	4	NO	NO	NIL
7	28	F	B	1	121	59	59	62	51	63	54	126	121	111	111	116	112	77	67	72	62	68	72	142	139	124	127	132	125	0	1	2	1	5	4	1	1	3	3	5	4	BRADYCARDIA	YES	856
8	53	F	B	1	125	89	75	84	86	74	76	107	106	96	100	107	110	70	71	69	70	72	74	119	118	105	110	119	122	0	1	1	2	4	3	0	1	1	2	4	3	NO	NO	NIL
9	43	M	B	2	118	71	84	71	74	82	72	121	124	110	112	109	120	73	69	72	71	72	70	137	142	123	126	121	137	1	0	1	3	3	2	1	1	1	2	3	4	NO	NO	NIL
10	44	F	B	1	116	79	85	73	87	81	75	123	120	112	110	114	116	80	74	72	70	73	73	137	135	125	123	128	130	0	0	1	3	4	2	1	1	3	2	4	2	NO	NO	NIL
11	40	F	B	2	123	90	88	76	81	70	75	114	117	120	120	116	120	78	72	70	76	78	60	126	132	137	135	129	140	1	2	1	3	3	4	1	2	1	2	5	3	NO	NO	NIL
12	41	F	B	1	123	79	83	90	83	88	89	120	120	110	110	120	122	83	71	74	76	78	80	132	136	122	121	134	136	0	1	1	1	2	4	0	2	1	2	5	4	NO	NO	NIL
13	35	M	B	2	116	70	70	73	78	73	70	120	117	119	115	117	116	74	70	74	70	74	78	135	133	134	130	131	129	0	1	2	2	5	4	0	2	1	2	2	3	NO	YES	841
14	28	F	B	2	119	74	76	80	88	71	73	107	90	115	117	119	116	79	74	73	75	72	70	116	95	129	131	135	131	0	2	1	2	4	2	1	1	3	3	3	4	NO	NO	NIL
15	36	M	B	2	120	73	73	88	79	84	78	127	120	112	115	116	116	75	65	68	70	72	70	144	138	127	130	131	131	0	1	2	2	4	4	1	2	3	2	3	3	NO	NO	NIL
16	52	M	B	1	125	90	86	88	76	84	89	107	105	120	121	120	116	83	69	68	70	72	74	115	117	137	138	136	130	0	0	1	1	5	2	1	2	1	3	2	4	NO	YES	845
17	57	M	B	2	125	89	70	77	74	84	85	130	127	115	117	115	116	73	71	72	76	78	80	149	146	129	131	127	128	0	0	2	2	4	2	0	2	2	3	5	3	NO	NO	NIL
18	37	M	B	2	123	71	86	70	84	70	81	98	94	110	120	116	112	70	72	70	78	78	60	107	101	123	134	129	129	0	0	2	2	2	2	0	2	1	3	5	4	NO	NO	NIL
19	45	M	B	1	117	75	87	86	79	89	78	127	120	105	120	98	112	77	69	75	78	78	70	144	137	115	134	105	126	0	1	1	3	4	3	0	1	2	2	2	2	NO	NO	NIL
20	22	F	B	1	123	81	83	88	83	85	90	93	98	89	91	100	110	65	55	54	51	60	60	102	112	101	104	113	127	0	0	2	1	4	3	0	2	3	3	4	3	NO	NO	NIL
21	60	F	B	2	118	80	72	86	78	73	90	124	121	94	100	98	111	78	64	60	64	67	70	139	140	105	112	108	125	1	2	1	3	3	2	1	2	1	3	2	4	NO	NO	NIL
22	44	F	B	2	126	50	59	59	62	51	58	100	93	117	120	98	112	65	72	48	60	64	70	112	100	140	140	109	126	1	1	1	2	3	4	0	2	3	3	5	2	BRADYCARDIA	NO	NIL
23	51	M	B	1	125	79	84	73	81	70	79	120	116	113	110	113	116	73	69	64	70	71	69	136	132	129	123	127	132	1	1	2	3	2	4	1	1	1	3	3	3	NO	NO	NIL
24	45	F	B	2	118	71	73	80	83	83	82	140	127	118	118	124	122	83	67	72	73	75	71	159	147	133	133	140	139	0	0	2	1	4	2	0	2	2	2	3	2	NO	NO	NIL
25	28	M	B	2	118	74	86	82	86	79	70	138	126	114	119	117	121	113	73	72	83	81	76	146	144	128	131	129	136	0	1	2	1	3	2	1	2	2	2	2	3	NO	NO	NIL
26	26	F	B	1	123	76	86	73	76	78	70	127	126	106	98	106	111	87	73	74	75	70	68	140	144	117	106	118	125	0	0	1	1	2	3	1	1	2	2	2	3	NO	NO	NIL
27	42	M	B	1	125	77	72	81	73	81	85	126	121	111	111	116	112	77	67	72	62	68	72	142	139	124	127	132	125	1	1	1	3	4	2	0	2	1	2	4	2	NO	NO	NIL
28	23	M	B	1	116	81	71	80	88	79	88	107	106	96	100	107	110	70	71	69	70	72	74	119	118	105	110	119	122	1	0	1	3	3	2	1	1	1	2	4	4	NO	NO	NIL
29	22	M	B	2	120	77	83	73	87	73	89	121	124	110	112	109	120	73	69	72	71	72	70	137	142	123	126	121	137	0	1	1	2	4	3	1	1	1	2	5	3	NO	NO	NIL
30	57	M	B	1	126	86	72	70	88	85	75	123	120	112	110	114	116	80	74	72	70	73	73	137	135	125	123	128	130	0	0	2	1	4	3	0	2	3	2	5	4	NO	NO	NIL
31	40	F	B	1	117	75	89	75	81	84	89	114	117	120	120	100	112	78	72	70	76	78	78	126	132	137	135	107	123	1	0	2	1	5	3	1	1	1	3	3	2	NO	YES	904
32	27	F	B	1	118	75	76	71	88	72	87	120	120	110	110	120	122	83	71	74	76	78	80	132	136	122	121	134	136	0	0	2	3	2	4	1	1	2	2	3	3	NO	NO	NIL
33	23	M	B	2	124	83	73	79	80	79	90	120	117	119	115	117	121	74	70	74	70	74	78	135	133	134	130	131	135	0	2	2	2	2	3	0	1	3	2	3	3	NO	NO	NIL
34	44	F	B	2	122	88	71	84	70	79	75	107	90	115	117	119	116	79	74	73	75	72	70	116	95	129	131	135	131	0	1	2	1	3	4	0	1	2	2	2	3	NO	NO	NIL
35	40	F	B	2	122	87	73	83	70	84	88	127	120	112	115	116	116	75	65	68	70	72	70	144	138	127	130	131	131	0	0	2	2	3	2	1	2	1	2	3	4	NO	NO	NIL

38	30	M	B	1	120	78	87	73	72	82	78	114	117	120	120	100	112	78	72	70	76	78	78	126	132	137	135	107	123	0	2	1	3	5	3	0	1	2	3	2	4	NO	YES	182
39	58	M	B	2	118	76	88	72	85	82	85	120	120	110	110	120	122	83	71	74	76	78	80	132	136	122	121	134	136	1	1	1	3	4	4	1	1	1	3	5	4	NO	NO	NIL
40	36	F	B	1	117	80	70	80	78	84	78	120	117	119	115	117	121	74	70	74	70	74	78	135	133	134	130	131	135	1	1	1	1	3	2	0	1	2	2	4	4	NO	NO	NIL
41	43	M	D	1	120	84	78	84	71	76	84	124	121	94	100	98	111	78	64	60	64	67	70	139	140	105	112	108	125	1	3	3	4	6	7	3	3	5	4	8	6	NO	NO	NIL
42	39	M	D	1	126	89	79	81	76	79	83	100	93	117	120	109	120	65	72	48	60	64	70	112	100	140	140	124	137	2	1	3	2	5	4	3	3	3	3	7	8	NO	NO	NIL
43	40	M	D	1	126	77	80	78	79	84	86	120	116	113	110	113	116	73	69	64	70	71	69	136	132	129	123	127	132	2	1	5	4	5	6	1	3	3	6	8	7	NO	NO	NIL
44	52	F	D	1	120	87	84	81	89	82	87	140	127	118	118	124	122	83	67	72	73	75	71	159	147	133	133	140	139	2	3	3	5	6	5	3	3	3	4	9	5	NO	NO	NIL
45	28	F	D	2	125	70	73	84	78	78	76	138	126	114	119	117	121	113	73	72	83	81	76	146	144	128	131	129	136	2	3	4	4	7	6	2	2	5	4	6	8	NO	YES	306
46	57	M	D	1	126	80	77	90	84	76	87	127	126	106	98	106	111	87	73	74	75	70	68	140	144	117	106	118	125	2	2	5	2	7	7	3	3	5	5	9	7	NO	YES	325
47	27	F	D	2	120	79	84	76	71	81	75	126	121	111	111	116	112	77	67	72	62	68	72	142	139	124	127	132	125	2	2	4	3	8	7	1	2	5	6	9	5	NO	YES	435
48	23	M	D	1	126	71	76	81	78	79	80	107	106	96	100	107	110	70	71	69	70	72	74	119	118	105	110	119	122	1	3	4	5	8	4	2	3	3	4	7	7	NO	YES	614
49	18	F	D	2	126	80	77	85	76	71	71	121	124	110	112	109	120	73	69	72	71	72	70	137	142	123	126	121	137	1	2	2	6	6	7	3	2	5	4	9	6	NO	NO	NIL
50	30	F	D	2	122	71	90	87	79	76	71	123	120	112	110	114	116	80	74	72	70	73	73	137	135	125	123	128	130	1	2	4	4	5	4	3	2	3	3	7	7	NO	NO	NIL
51	54	F	D	1	122	87	75	72	90	80	79	114	117	120	120	116	120	78	72	70	76	78	60	126	132	137	135	129	140	2	1	5	6	6	5	2	2	3	6	7	5	NO	NO	NIL
52	20	M	D	1	119	85	80	83	86	76	74	120	120	110	110	120	122	83	71	74	76	78	80	132	136	122	121	134	136	1	1	4	3	8	6	1	3	4	5	7	5	NO	YES	646
53	53	M	D	1	117	81	78	78	70	84	72	120	117	119	115	117	116	74	70	74	70	74	78	135	133	134	130	131	129	2	1	4	3	8	7	2	2	2	6	5	6	NO	YES	638
54	26	F	D	1	126	87	72	80	84	80	77	107	90	115	117	119	116	79	74	73	75	72	70	116	95	129	131	135	131	1	2	3	3	8	5	3	2	4	5	8	8	NO	YES	358
55	29	F	D	2	117	74	74	73	82	72	88	127	120	112	115	116	116	75	65	68	70	72	70	144	138	127	130	131	131	1	3	5	3	5	7	3	2	4	4	7	6	NO	NO	NIL
56	58	F	D	1	121	84	81	74	76	78	73	107	105	120	121	120	116	83	69	68	70	72	74	115	117	137	138	136	130	2	1	2	6	8	5	1	2	4	3	5	7	NO	NO	NIL
57	35	M	D	1	122	73	84	74	74	76	76	130	127	115	117	115	116	73	71	72	76	78	80	149	146	129	131	127	128	1	1	2	2	7	5	3	3	3	5	7	5	NO	NO	NIL
58	48	F	D	1	120	85	84	78	90	87	71	98	94	110	120	116	112	70	72	70	78	78	60	107	101	123	134	129	129	1	1	5	6	8	4	3	3	4	6	6	5	NO	YES	541
59	45	M	D	2	125	70	75	89	75	90	87	127	120	105	120	98	112	77	69	75	78	78	70	144	137	115	134	105	126	1	2	5	6	7	4	1	3	4	3	8	6	NO	YES	627
60	43	M	D	1	122	88	84	79	78	89	79	93	98	89	91	100	110	65	55	54	51	60	60	102	112	101	104	113	127	1	2	5	3	8	5	2	3	4	6	9	5	NO	YES	488
61	56	F	D	2	118	52	59	65	56	62	65	124	121	94	100	98	111	78	64	60	64	67	70	139	140	105	112	108	125	1	1	4	6	8	6	1	2	4	5	6	7	BRADYCARDIA	YES	559
62	47	F	D	2	126	81	75	79	81	86	71	100	93	117	120	98	112	65	72	48	60	64	70	112	100	140	140	109	126	1	2	2	3	5	5	1	2	2	3	6	6	NO	NO	NIL
63	32	F	D	1	123	86	82	80	89	84	86	120	116	113	110	113	116	73	69	64	70	71	69	136	132	129	123	127	132	2	3	5	6	7	5	3	2	3	6	9	8	NO	YES	597
64	39	M	D	1	123	74	89	70	80	80	75	140	127	118	118	124	122	83	67	72	73	75	71	159	147	133	133	140	139	2	1	5	2	7	6	3	2	2	4	6	5	NO	YES	578
65	45	F	D	2	117	78	80	71	79	78	84	138	126	114	119	117	121	113	73	72	83	81	76	146	144	128	131	129	136	1	1	4	6	8	4	2	3	2	3	9	8	NO	YES	389
66	27	M	D	2	117	88	80	86	83	82	73	127	126	106	98	106	111	87	73	74	75	70	68	140	144	117	106	118	125	2	2	5	5	5	5	1	3	5	4	5	5	NO	NO	NIL
67	21	M	D	2	124	78	85	72	79	88	80	126	121	111	111	116	112	77	67	72	62	68	72	142	139	124	127	132	125	1	2	2	2	8	7	3	3	4	4	7	5	NO	NO	NIL
68	24	M	D	1	118	85	84	70	77	86	79	107	106	96	100	107	110	70	71	69	70	72	74	119	118	105	110	119	122	1	2	5	3	6	5	1	3	2	5	5	5	NO	NO	NIL
69	32	F	D	2	119	80	90	76	90	83	77	121	124	110	112	109	120	73	69	72	71	72	70	137	142	123	126	121	137	1	2	3	3	7	6	3	3	3	4	9	7	NO	YES	487
70	29	M	D	1	121	75	76	85	81	77	83	123	120	112	110	114	116	80	74	72	70	73	73	137	135	125	123	128	130	1	1	2	2	5	6	2	3	2	3	6	6	NO	NO	NIL
71	32	M	D	2	125	72	86	84	89	89	76	124	120	126	130	128	128	84	70	76	74	72	76	137	137	143	149	147	145	1	1	2	4	7	5	3	3	5	4	6	5	NO	NO	NIL
72	56	M	D	1	125	80	86	89	90	88	80	120	116	120	120	121	121	102	79	74	80	80	80	126	128	135	133	135	135	2	2	2	2	7	7	2	2	3	3	6	8	NO	NO	NIL
73	37	M	D	1	124	79	89	81	87	87	86	122	116	112	118	120	120	80	84	80	81	79	78	136	127	123	130	134	134	2	3	5	3	7	7	3	2	4	4	5	7	NO	YES	402
74	26	F	D	1	122	73	74	83	86	73	79	116	114	110	110	120	120	74	71	70	80	80	80	130	128	123	120	133	133	2	2	4	2	5	4	1	2	5	6	6	8	NO	NO	NIL
75	30	F	D	1	122	80	83	73	78	81	71	124	118	119	124	120	120	83	75	79	72	74	76	138	132	132	141	135	135	1	1	3	2	8	4	2	3	4	4	9	8	NO	YES	544
76	21	F	D	2	126	77	77	77	73	87	77	112	124	116	114	118	120	96	71	77	78	80	84	117	142	129	126	131	132	2	3	2	4	5	4	2	2	4	6	7	6	NO	NO	NIL
77	31	F	D	1	122	83	76	70	83	81	82	118	116	110	117	121	120	74	81	82	84	89	80	133	128	119	128	132	133	1	3	2	2	6	4	1	2	5	4	6	5	NO	NO	NIL
78	18	M	D	1	125	83	78	70	70	87	70	116	114	128	130	138	121	86	73	76	80	84	81	126	128	145	147	156	134	2	1	2	2	7	5	2	2	3	6	7	7	NO	NO	NIL
79	35	M	D	2	121	70	75	84	81	85	80	93	98	89	91	100	110	65	55	54	51	60	60	102	112	101	104	113	127	1	3	5	3	5	7	1	3	3	4	7	8	NO	NO	NIL

IEC/NO-09/2021
22-01-2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A comparative study of efficacy of intra-articular dexmedetomidine versus buprenorphine for postoperative analgesia following arthroscopic knee surgeries.

Name of PG student: Dr Rajeshwari B V Department of Anaesthesiology

Name of Guide/Co-investigator: Dr Basavaraj Patil, , Assistant Professor of Anaesthesiology

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

14