“A RANDOMISED CLINICAL TRIAL TO COMPARE THE EFFICACY AND SAFETY OF DEXMEDETOMIDINE-ROPIVACAINE VERSUS FENTANYL-ROPIVACAINE FOR EPIDURAL LABOR ANALGESIA”

BY

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IN

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Under the Guidance of

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DR.RESHMA R.S.

ABBREVIATIONS

BP - Blood Pressure

HR – Heart Rate

SpO2 – Saturation of Peripheral Oxygen

ASA – American Society of Anesthesiology

IP No. - Inpatient Number

CVS - Cardiovascular System

RS - Respiratory System

PA- Per Abdomen

SD - Standard Deviation

VAS - Visual Analog Scale

RSS - Ramsay Sedation Scale

FTVD – Full Term Vaginal Delivery

NST –Non Stress Test

PCEA- Patient Controlled Epidural Analgesia

APGAR - Appearance, Pulse, Grimace, Activity and Respiration

NBNA- Neonatal Behavioural Neurological Assessment

α – Alpha

μ - micro

mcg - Microgram

kg - Kilogram

mg - Milligram

ml – Millimeter

cm –centimeter

min -minutes

BMI – Body Mass Index

C – Cervical

T – Thoracic

L - Lumbar

S - Sacral

SBP –Systolic Blood Pressure

DBP –Diastolic Blood Pressure

MAP- Mean Arterial Pressure

P value - Probability value

S.No. – Serial Number

vs – versus

MD - mean difference

RR – risk ratio

ABSTRACT

Majority of women go through the most painful moments for human beings while giving birth. An epidural block is a superior potent approach of labor analgesia, which promotes painless delivery and is customised for each woman. Anesthesiologists have been looking for strategies to improve the effects of analgesia and to avoid the side effects associated with labor analgesia.

Ropivacaine combined with fentanyl has been successfully used to provide epidural analgesia. Opioids may produce adverse effects, such as pruritus, nausea, vomiting, respiratory depression and urinary retention. The non-opioid Dexmedetomidine is characterized by its high selectivity and more significant analgesic effects without causing respiratory depression. The safety and benefits of Dexmedetomidine as an adjuvant to ropivacaine as a novel form of epidural labor analgesia must be researched more. The results of our study gives insight in the epidural block and come up with a pioneering approach for labor analgesia.

OBJECTIVES OF THE STUDY: To compare the efficacy and safety of Dexmedetomidine- Ropivacaine versus Fentanyl- Ropivacaine for epidural labor analgesia.

METHODS: Total 68 primigravida (34 in each group) at term gestation, with cephalic presentation between the age group of 19-35, with no known comorbidities or obstetric complications in the active phase of labor, willing for epidural analgesia were assigned with two groups using Computer Generated Randomisation Table.

1) Group RD : 34 were given 0.1% Ropivacaine + 0.5 mcg/ml Dexmedetomidine

2) Group RF : 34 were given 0.1% Ropivacaine + 2 mcg/ml Fentanyl

After insertion of epidural catheter and administering a test dose of 3 ml 2% lignocaine with adrenaline, parturients received 10 ml of 0.5 mcg/ml Dexmedetomidine (Group RD) or 2 mcg/ml Fentanyl (Group RF) along with 0.1% Ropivacaine given as loading dose. After the loading dose

was given, maintenance of epidural analgesia was done using a Patient Controlled Analgesia (PCA) pump. The PCA pump was adjusted at a pace of 7 ml/hr with a rescue dose of 7ml (with lockout period of 25 min and total limit of 25 ml/hr). A rescue bolus was administered when visual analog scale (VAS) score is ≥ 5 (0 = no pain, 10 = maximum pain) by a PCA pump.

The primary objectives were to compare Dexmedetomidine and Fentanyl as adjuvants in epidural analgesia in terms of the time of onset of epidural analgesia, duration between epidural and delivery of baby, rescue analgesic dose requirement, Visual Analog Scale (VAS) score and maternal vitals. The secondary objectives were to observe Ramsay Sedation Scale (RSS) score, APGAR score of the baby and maternal side effects.

RESULTS: Dexmedetomidine group displayed better analgesic effect compared to fentanyl group. Group RD showed shorter mean onset time of analgesia (RD – 12.50±1.31 min vs. RF - 15.26±1.46 min), less local anaesthetics requirement (RD –47.54±5.37 ml vs RF –59.05±6.62 ml), less number of bolus doses (RD– 0.15±0.36 vs RF– 1.21±0.95) and shorter duration from the administration of epidural to the delivery of baby (RD –312.97±42.40 min vs. RF-345.94±14.67 min) than group RF which was statistically significant and with $p<0.001$.VAS scores in group RD was significantly less than that of group RF at most time points after epidural administration. Maternal systolic blood pressure was high in group RF than group RD and it showed statistical significance at 4 hours. Diastolic blood pressure was high in group RF than group RD after epidural administration and did not show any statistical significance. Maternal heart rate was significantly low in group RD at 90 minute from baseline. There was no fall in room air oxygen saturation in both groups at any time. The study showed side effects in both the groups, which was not statistically significant. Maternal hypotension, nausea, vomiting, bradycardia and shivering was observed in group RD while pruritus, hypotension, nausea, vomiting and shivering was seen in group RF. Ramsay Sedation Scale score was comparably low

in both groups and excessive sedation was not seen in both groups. Newborn Apgar scores were comparably high in both the groups.

CONCLUSION: The results of the study indicate that with 0.1% Ropivacaine, 0.5 mcg/ml Dexmedetomidine shows more effectiveness than 2 mcg/ml Fentanyl during epidural labor and is a safe alternative for labor pain.

KEY WORDS: Fentanyl, Dexmedetomidine, Adjuvant, Ropivacaine, Epidural, Labor analgesia

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INTRODUCTION

"The delivery of the infant into the arms of a conscious and pain-free mother is one of the most exciting and rewarding moments in medicine" – Donald D.Moir (Father of Labor Analgesia)

Some women breeze through giving birth while most women must go through the most painful moments during child birth. Labor pain causes anxiety, strain, pressure on the back, perineum and uneasiness. It influences the progress of labor and the fetal outcome. The sympathetic stimulation causes maternal hyperventilation, which causes respiratory alkalosis. Respiratory alkalosis, in turn, causes excessive catecholamine and cortisol release, which causes uterine vasoconstriction, which reduces placental blood flow and as a result, reduces oxygen transfer to the fetus, resulting in fetal metabolic acidosis. Therefore, reducing pain during labor will help to enhance perinatal and mother outcomes.[1,2]

During labor and delivery, pain always emanates from various locations. Contractions cause pain during the first stage of childbirth. It typically has a visceral or cramp-like quality, develops in the uterus and cervix and is caused by uterine ischemia and cervix dilatation. Distension of the vagina, perineum and pelvic floor is what causes the discomfort in the second stage of labor. The second stage of pain is characterized by a blend of somatic pain from the distension of vaginal and perineal tissues and visceral discomfort from uterine contractions. The woman also feels rectal pressure and an impulse to bear down in addition to the aforementioned.[3]

Labor pain, which is thought to increase minute ventilation and utilization of oxygen, typically results in respiratory alkalosis and shift to the left in the maternal oxyhaemoglobin dissociation curve, which reduces oxygen transfer to fetus.[4] We can infer that compensatory hypoventilation during the intervals between contractions results in momentary maternal and perhaps even fetal hypoxia.[4]

In 1847, Dr.James Young Simpson gave ether to a lady who was giving birth, marking the beginning of the modern era of labor analgesia. After a few years, Queen Victoria gave birth to her eighth child and John Snow was able to effectively administer her chloroform. Between 1900 and 1930, literature was published describing spinal, lumbar and caudal epidural, paravertebral and pudendal nerve blockade for obstetrics. The field of continuous neuraxial analgesia came up in the middle of the 20th century with the publication of the initial report on continuous caudal analgesia for delivery in 1943 by Hingson and Edwards.[7]

An ideal labor analgesic will typically have the following characteristics: administration simplicity, consistent, predictable, rapid onset, maternal calm demeanor and high level of regulation during the first and second stages of labor analgesia. It should throughout all stages of labor cause no motor block, enable movement and different positions for childbirth, retain the stimuli for expulsive attempts needed for the second stage of labor and facilitate the opportunity for delivery. Sadly, none of the methods that are currently in use have all of these characteristics.[5]

In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor. Gynecologists and anesthesiologists have to be aware of and jointly assess the choices available for administering analgesia in order to select the most customised plan and provide the highest level of satisfaction for women.

Both non-pharmacological and pharmacological therapies are used to relieve pain during childbirth. Hypnosis, biofeedback, intramuscular or subcutaneous sterile water injection, aromatherapy, relaxation techniques (yoga, music, audio), acupuncture or acupressure, manual techniques (massage, reflexology) and transcutaneous electrical nerve stimulation(TENS) are among the non-pharmacological interventions that are typically used.[8] Systemic opioids, patient controlled analgesia using opioids, inhalational techniques, Nonsteroidal Anti-Inflammatory

Drugs are examples of pharmacological therapies.[9] Currently a neuraxial blockade like a spinal, epidural or a combined spinal-epidural method is considered to be the gold standard.[10] The benefits of epidural analgesia is that effective pain reduction is achieved without appreciable motor block with lowering maternal catecholamines.[11]

For labor analgesia, an ideal local anaesthetic should provide a dependable sensory block, without causing a motor block or tachyphylaxis, and with a high safety profile to prevent overdosing or unintentional intravenous injection. Compared to racemic mixtures of two stereoisomers, such as bupivacaine, which has a low safety profile in terms of cardiovascular and central nervous system toxicity, single-enantiomer molecules, such as ropivacaine and levobupivacaine, have clear advantages.[12] Propyl homologues of bupivacaine, ropivacaine and L-bupivacaine, exhibit similar levels of protein binding, shorter elimination half-lives, increased plasma clearance and decreased lipid solubility.[12]

Synthetic opioids like lipid-soluble sufentanil and fentanyl can increase the potency of local amide anaesthetics by altering the minimum potency. Some adjuvant drugs which is utilised along with local anaesthetics are alpha-2 agonists like dexmedetomidine and clonidine, cholinesterase inhibitors like neostigmine and vasoconstrictors like epinephrine.

However, opioids like fentanyl can produce adverse effects including pruritus, nausea, vomiting, respiratory depression, urinary retention and decreased variability in fetal heart rate. At the same time alpha-2 agonist dexmedetomidine possesses anxiolytic, sedative and analgesic properties without causing respiratory depression. Studies regarding the benefits and safety of Dexmedetomidine as an adjuvant to Ropivacaine as a new method of labor analgesia with epidural block is limited.

This study compares alpha-2 agonist, dexmedetomidine as adjuvant to local anaesthetic ropivacaine in labor analgesics in terms of efficacy and safety when compared to an opioid, fentanyl as adjuvant in vaginal delivery in primigravida. There is not enough information available currently about the effectiveness and safety of dexmedetomidine in reducing labor pain.

The aim of our study was to compare the efficacy and safety of dexmedetomidine versus fentanyl when used with ropivacaine during epidural labor analgesia. The results of our study lay out insight into the epidural block and provide a pioneering approach to labor analgesia.

AIMS AND OBJECTIVES OF THE STUDY

AIM: TO COMPARE THE EFFICACY AND SAFETY OF DEXMEDETOMIDINE-ROPIVACAINE VERSUS FENTANYL-ROPIVACAINE FOR EPIDURAL LABOR ANALGESIA.

OBJECTIVES

PRIMARY OBJECTIVES: To compare Dexmedetomidine and Fentanyl as adjuvants in epidural analgesia in terms of :

- The onset of epidural analgesia, duration of analgesia and rescue analgesic dose requirement
- Visual Analog Scale (VAS) scores
- Maternal Vitals – Heart rate, Blood pressure, Oxygen saturation.

SECONDARY OBJECTIVES :

- Ramsay Sedation Scale (RSS) scores
- Apgar score of the baby
- Maternal Side Effects – bradycardia, hypotension, nausea, vomiting, respiratory depression, shivering, pruritus

REVIEW OF LITERATURE

Gehui Li et al[55] (2020) conducted a randomised controlled trial with combination of sufentanil, dexmedetomidine and ropivacaine to find its effects on epidural labor analgesia. Three groups were randomly selected from among 108 parturient women undergoing labor epidural analgesia: 0.1% Ropivacaine + 0.5 µg/ml Dexmedetomidine was given to Group RD; 0.1% Ropivacaine + 0.5 µg/ml Sufentanil was given to Group RS and 0.1% Ropivacaine + 0.25 µg/ml Dexmedetomidine + 0.25 µg/ml Sufentanil was given to Group RDS. After receiving a loading dose of 10 ml patients received patient-controlled epidural analgesia for maintenance. They observed that when compared to sufentanil, the combined adjuvant group RDS showed a better analgesic effect (VAS score at 20 min: RS -2.99 ±1.44 vs RD -2.87 ±1.53 vs RDS –1.84±1.15) , a quicker onset time (RS – 15.50± 2.67 min vs RD – 12.97± 3.13 min vs RDS – 9.68± 1.26 min), a decreased demand for local anaesthetics (RS - 65.44± 5.64 ml vs RD – 42.65± 6.44 ml vs RDS -50.34± 6.56 ml) and a decreased rate of pruritus(RS – 14.3% vs RD – 0% vs RDS - 0%). The study findings suggested that using sufentanil and dexmetomidine together improved the local anaesthetics efficacy during epidural labor.

Mei Fan et al[56] (2022) aimed a randomised controlled trial on the efficacy and safety of dexmedetomidine-ropivacaine versus sufentanil-ropivacaine for epidural labor analgesia. All 160 included parturient women were randomised into 2 groups of 80 to receive 0.1% ropivacaine combined with 10 ml 0.5 µg/ml dexmedetomidine (group RD) or 10 ml 0.5 µg/ml sufentanil (group RS).[56] They observed that Visual Analog Scale scores were lesser in both the two groups after the analgesic injection (at 120 min; RD: 2.6±1.0 vs. RS: 2.5±0.8).[56] The newborn Neonatal Behavioural Neurological Assessment (NBNA) (RD: 39.9±0.4 vs. RS: 39.8±0.5) and Apgar scores (RD:9.8±0.7 vs RS: 9.7±0.8) were high in both groups.No differences was seen in vital signs, Ramsay Sedation Scale (RSS) values, blood loss, duration of labor stages, onset time of analgesia and dose of analgesics between the 2 groups. The incidence of adverse reactions in parturient women like hypotension, shivering, nausea and vomiting and newborn like bradycardia and respiratory depression were low in both groups. They concluded that Dexmedetomidine or sufentanil combined with ropivacaine had similar analgesic effects for epidural labor analgesia.

Zhao et al [57] (2021) performed a meta-analysis and systemic review to evaluate ropivacaine combined with dexmedetomidine (RD) versus ropivacaine (R) alone for epidural anaesthesia. Eleven randomised controlled trials were involved with 336 patients in the RD group and 337 patients in the R group. According to the study, they found group RD to have shorter time to onset of sensory block (mean difference [MD]: 3.97 min) and motor block (MD: 2.43 min) and a longer duration of anaesthesia (MD: -164.17) than the R group. The R group showed stable hemodynamics than the RD group in heart rate (MD at 10 min: 8.73 beats/min) and blood pressure (MAP at 10 min: MD: 7.77 mm Hg). Compared to the RD group, the R group experienced more shivering (risk ratio RR: 2.82) and less bradycardia (RR: 0.29). The study findings led them to the conclusion that RD could be a better option for epidural anaesthesia than R alone, with superior anaesthetic results.[57]

Zhang et al [58] (2024) did a systematic review and meta-analysis on randomised controlled trials to find the application of dexmedetomidine in epidural labor analgesia. 8 studies comprising 846 parturients were considered for observations. All articles were published between 2017-2022. Five articles compared the effects of ropivacaine plus dexmedetomidine versus ropivacaine plus sufentanil (RD vs. RS), two articles compared the effects of ropivacaine plus dexmedetomidine versus ropivacaine alone (RD vs. R) and one article compared the effects of bupivacaine plus dexmedetomidine versus bupivacaine plus nalbuphine (BD vs. BN). The study inferred that dexmedetomidine used as an adjuvant along with local anaesthetics for labor analgesia with epidural can improve the VAS score of parturients (at 15 min, MD: -1.41) , not cause motor block and is safe for both the parturient and fetus. The incidence of pruritus in group dexmedetomidine was lower than that in the control group （MD 0.28) while incidence of maternal bradycardia was higher (MD 6.41) in dexmedetomidine group.

Tao Zhang et al [59] (2019) enrolled a randomised controlled trial to compare dexmedetomidine and sufentanil as adjuvants to local anaesthetic for epidural labor analgesia. In this double-blind trial, eighty nulliparous women were randomly assigned to two groups. Group D was given 0.5 µg/ml dexmedetomidine with 0.1% ropivacaine, while group S was given 0.5 µg/ml sufentanil with 0.1% ropivacaine. Group D experienced shorter first-stage labor time (D - 378.5± 52.6 min vs S - 406.5± 58.2 min) and lower visual analog scale readings following cervical dilation >3 cm in comparison to the control group. Total analgesic consumption was reduced in group D than group S (D- 71.5±12.2 ml vs S- 78.1±10.5ml). Ramsay Sedation Scale scores were higher in group D than those of the control group (D -2.8±0.6 vs S -2.4±0.5). They concluded that Dexmedetomidine was superior to sufentanil regarding analgesic effect with shorter duration in first-stage labor with epidural analgesia and reduced local anaesthetic requirement.[59]

Lifeng Ni et al [60](2024) did a randomised study to find whether epidural dexmedetomidine or esketamine is better than fentanyl to decrease ropivacaine use for labor analgesia. Total of 120 laboring nulliparous patients who needed labor analgesia were enrolled and assigned into 3 groups. Subjects were given either 0.075% ropivacaine + 0.4 μg/ml fentanyl or 0.4 μg/ml dexmedetomidine or 1.0 mg/ml esketamine as adjuvants. It was observed that the participants in the fentanyl group consumed 12.4 ml per hour of ropivacaine on an average, while the subjects in the dexmedetomidine and esketamine groups consumed 11.9 and 14.3 ml per hour on average, respectively. The fentanyl group saw the highest incidence of pruritus (F -9, E-0, D-0) whereas the esketamine group experienced the highest incidence of mild dizziness (F-0, E-16, D-0). It was derived that combined with ropivacaine, epidural fentanyl and dexmedetomidine was found to be equally effective for patient controlled epidural analgesia during labor. However, they were unable to prove that epidural esketamine was not inferior to epidural fentanyl when combined with ropivacaine.

Ru-Ying Pang et al [61](2022) conducted a randomised controlled study of the epidural dexmedetomidine to fentanyl in decreasing ropivacaine dose in Programmed Intermittent Epidural Bolus with Patient Controlled Epidural Analgesia in labor. In this research, a total of 128 patients were divided into four groups and given epidural fentanyl at a dose of 2 μg/ml or dexmedetomidine at a dose of 0.3, 0.4, or 0.5 μg/ml to relieve labor pain. A significant difference was observed in the average amount of epidural ropivacaine consumed per hour between the groups. The 2 μg/ml fentanyl group and the 0.3, 0.4 and 0.5 μg/ml dexmedetomidine group received an average of 16.2±3.3, 14.0±3.1, 13.1±3.7 and 12.1±2.5 ml/hr of epidural ropivacaine, respectively. Compared to the three dexmedetomidine groups, the fentanyl group had a much greater frequency of PCEA. Of the patients in the 2 μg/ml fentanyl, 0.3, 0.4, and 0.5 μg/ml dexmedetomidine group, 82.5%, 44.6%, 44.4% and 22.0% needed additional PCEA. In the fentanyl group, pruritus was seen in 17.5% of patients and none reported pruritus in all of the groups with dexmedetomidine. The research indicated that epidural dexmedetomidine (0.3 and

0.4 μg/ml) outperformed standard dose epidural fentanyl in lowering the average hourly dosage of ropivacaine provided and minimising side effects related to opioids.[61]

Warda Ali et al [62] (2021) conducted a randomised control study to assess the efficacy of fentanyl against dexmedetomidine in addition to low-dose ropivacaine-dexamethasone for intrathecal labor analgesia in primigravida women. The trial had 60 participants with each group consisting of 30 patients. Group I got 2.5 mg of 0.1% ropivacaine injected intrathecal (diluted to 2.5 ml with normal saline) plus 4 mg dexamethasone plus 5 μg dexmedetomidine. Group II was given 25 μg of fentanyl instead of 5 μg of dexmedetomidine.[62] The study derived that compared to intrathecal ropivacaine-dexamethasone coupled with fentanyl, the combination of dexmedetomidine and ropivacaine-dexamethasone produced a more effective selective sensory block with a longer duration of analgesia, a delayed S1 regression time and less adverse effects on the mother and fetus. The study also suggested that for primigravida, dexmedetomidine or fentanyl offers a safe and effective adjuvant to intrathecal ropivacaine-dexamethasone with a fast onset, deep analgesia and hemodynamic stability during the labor.[62]

Yun Wang et al [63] (2022) put forward a retrospective, multicentre study on different doses of ropivacaine either with sufentanil or with dexmedetomidine for epidural anaesthesia regarding labor pain management. In this study, for epidural anaesthesia during vaginal delivery or cesarean section, 115 patients received 0.125% ropivacaine with 0.5-μg/ml sufentanil (SR1),109 patients received 0.08% ropivacaine with 0.5-μg/ml sufentanil (SR2) or 124 patients received 0.125% ropivacaine with 0.5-μg/ml dexmedetomidine (DR1) or 135 patients received 0.08% ropivacaine with 0.5-μg/ml dexmedetomidine (DR2). They came to conclusion that for hypertensive mothers and newborns, epidural analgesia with 0.08% ropivacaine plus 0.5-µg/ml dexmedetomidine is an efficient and safe anaesthetics combination.

ANATOMY

VERTEBRAL COLUMN[14]

Because it is evident that proper delivery of the therapeutic solutions to the neural structures is essential, anatomy plays a major role in regional anaesthesia.

The vertebral column, which is made up of a group of bones known as vertebrae, is a flexible and flexuous column.

The spine consists of 33 vertebrae.

- 7 cervical (C1-C7)
- 12 thoracic (T1-T12)
- 5 lumbar (L1-L5)
- 5 sacral (S1-5 fused into one)
- 4 coccygeal (often fused into one)

The upper 3 sections which are distinct for life are called true or movable vertebrae while those of the sacral and coccygeal are referred to as fixed or false vertebrae. While there are differences in the vertebral architecture at various levels of vertebral column, it is possible to determine common elements.[14]

There are specific characteristics that set apart the cervical, thoracic and lumbar vertebrae. The foramina in the transverse processes of the cervical vertebrae set them apart from the thoracic and lumbar vertebrae. The articular facets for the ribs on the thoracic vertebral body set it apart from the lumbar and cervical vertebrae.[14]

A typical lumbar vertebra has the following parts:

1. Body, for weight bearing

2. Vertebral arch, to protect neural structures

3. Spinous process

4. Transverse process

5. Superior and inferior articular processes

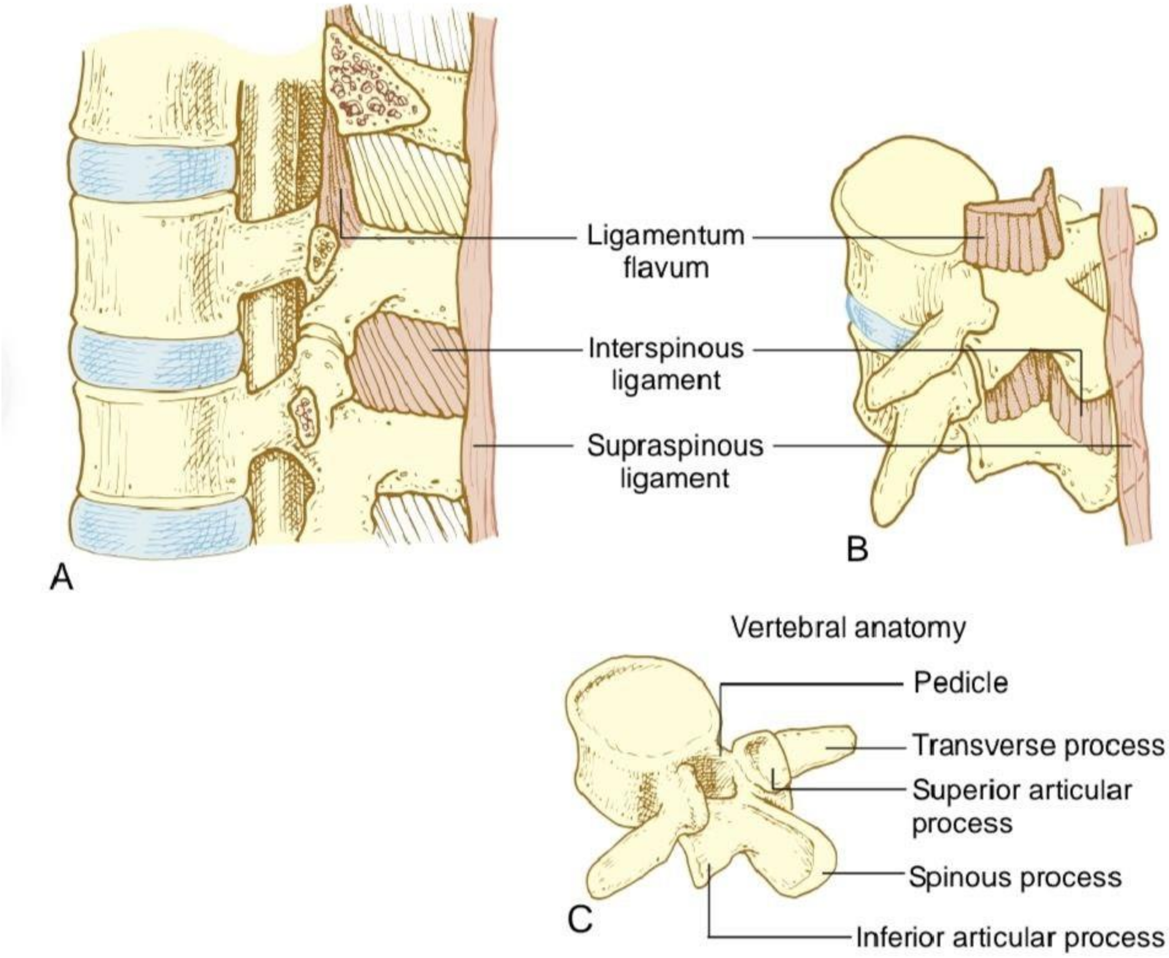

Ligamentum flavum
Interspinous ligament
Supraspinous ligament
A
B
Vertebral anatomy
Pedicle
Transverse process
Superior articular process
Spinous process
Inferior articular process
C

Figure 1. VERTEBRAL ANATOMY (A) Sagittal view (B) Oblique view showing ligamentum flavum (C) Oblique view of a single lumbar vertebra.[34]

BODY

It has a kidney-like form. They can support weight. Hyaline cartilage covers the flat articular surfaces and is securely attached to the fibrocartilagenous intervertebral discs (nucleus pulposus and annulus fibrosus). The connection of the bodies is strengthened by the anterior and posterior longitudinal ligaments. The broad anterior longitudinal ligaments are loosely linked to bodies and firmly attached to the intervertebral discs. Though it is joined similarly, the posterior longitudinal ligament is narrower.[14]

VERTEBRAL ARCH

It is made up of laminae and pedicles, which encircle and shield the spinal cord and its coverings. The vertebral arch two halves are separated into two sections by the root of transverse process. The strong, rounded pedicle that forms the arch anterior surface transfers stress. The lamina, which is flat and mostly defensive in nature, completes it posteriorly. Four articular processes extend from the vertebral arches, two of which project up and two down to articulate with related processes on neighbouring vertebrae.[14]

TRANSVERSE PROCESSES

They are two in number as well as being thin and long. They serve as levers for ligaments and muscles that are especially involved in lateral flexion and rotation.

SPINOUS PROCESS

It has a quadrangular shape, is nearly horizontal and thickened along its posterior and inferior borders. They serve as levers for the muscles that regulate the vertebral column active motions and posture. Spinous processes of the cervical, the first two thoracic, and the last four lumbar vertebrae are particularly horizontal and are opposite the bodies of their respective vertebrae. The tips of the other spinous processes are angled down and face away from the bodies of the vertebrae below.The first lumbar spinous process tip, which is located across from the intervertebral disc, is an exception.

SUPERIOR AND INFERIOR ARTICULAR PROCESS

The pedicles and laminae connections give rise to the superior articular processes. They rise upward behind the pedicles and settle to a position slightly above the articular facets and transverse processes.

The posterior surfaces are oriented medially and backwards. The inferolateral portions of the laminae are the source of the inferior articular processes, which extend downward.

The superior articular processes of the vertebra below have facets that they articulate with and they are situated below the level of the transverse process.

INTERVERTEBRAL FORAMINA

The spinal nerves and related vessels flow through a network of intervertebral foramina on the lateral surface of the vertebral column. It facilitates movement between the spinal canal and the paravertebral area.

The anaesthetic solution and catheter may also flow through one of these foramina since the areolar tissue around them is lax and soft in the young person. Because of this, older people require less local anaesthetic solution to create an epidural block than younger people do.

During puberty, the sacral and coccygeal vertebrae unite. A meticulously precise network of ligaments, intervening cartilages and muscles works in a synergistic and antagonistic manner to maintain the stability of these vertebrae and spinal column from giving way.

The thoracic and sacral regions are principal and concave anteriorly, whereas the cervical and lumbar regions are secondary and convex anteriorly, making up the four anatomical curvatures of the vertebral column. The distribution of local anaesthetic in the subarachnoid and epidural spaces is greatly influenced by these curves.

LIGAMENTS

Multiple ligaments that bind the spinal column together provide it flexibility and stability.

1. Supraspinous ligament
2. Interspinous ligament
3. Ligamentum flavum
4. Anterior longitudinal ligament
5. Posterior longitudinal ligament

SUPRASPINOUS LIGAMENT

Connecting the apices of the spines from the 7th cervical vertebra of the sacrum is a strong, thick band of fibrous tissue. It is broad and thick in the lumbar area. It extends from the C7 vertebra to the occipital protuberance and merges into the neck ligaments in the cervical region, where it is specialized as the ligamentum nuchae.

INTERSPINOUS LIGAMENT

It is a thin, fibrous structure that connects adjacent spines. Stretching from the apex and upper surface of the lower spine to the root and inferior surface of the corresponding higher vertebrae, the fibers are almost membraneous. They usually join the ligamentum flavum in front and the supraspinous ligament in the back.

LIGAMENTUM FLAVUM

It is made up of elastic yellow tissues. The direction of the fibers is perpendicular. They stretch from the upper lamina anterior inferior surface to the lower lamina anterior superior surface. Both a right and a left portion of the ligament exist. The vertex of the internal surface of the left and right ligamentum flavum makes contact with the interspinous ligament, forming an acute angle.The dorsomedian connective tissue band extends from the ligamentum flavum apex, periosteum into the extradural compartment and into the spinal dura matter.

POSTERIOR LONGITUDINAL LIGAMENT

It is divided by the basivertebral veins approximately between the posterior surfaces of the vertebral bodies and the vertebral canal.

ANTERIOR LONGITUDINAL LIGAMENT

It adheres to the discs between the vertebral bodies as well as extending down from its front.

SPINAL MENINGES

The spinal cord is ensheathed from within:

DURA MATER: the inner meningeal layers of the cerebral dura mater are represented by it; the extradural space represents the outer, endosteal layers. Fibrous slips connect it to the posterior longitudinal ligament, particularly in the vicinity of the lower part of the spinal canal. A robust fibrous layer creates a tubular sheath that is connected to the foramen of magnum borders above and ends at the lower border of the second sacral vertebra below.

ARACHNOID MATER: The cranial and spinal nerves are encircled by the thin, transparent arachnoid mater, which is tightly adhered to the dura and extends to the point where the nerves escape the skull and vertebral canal.

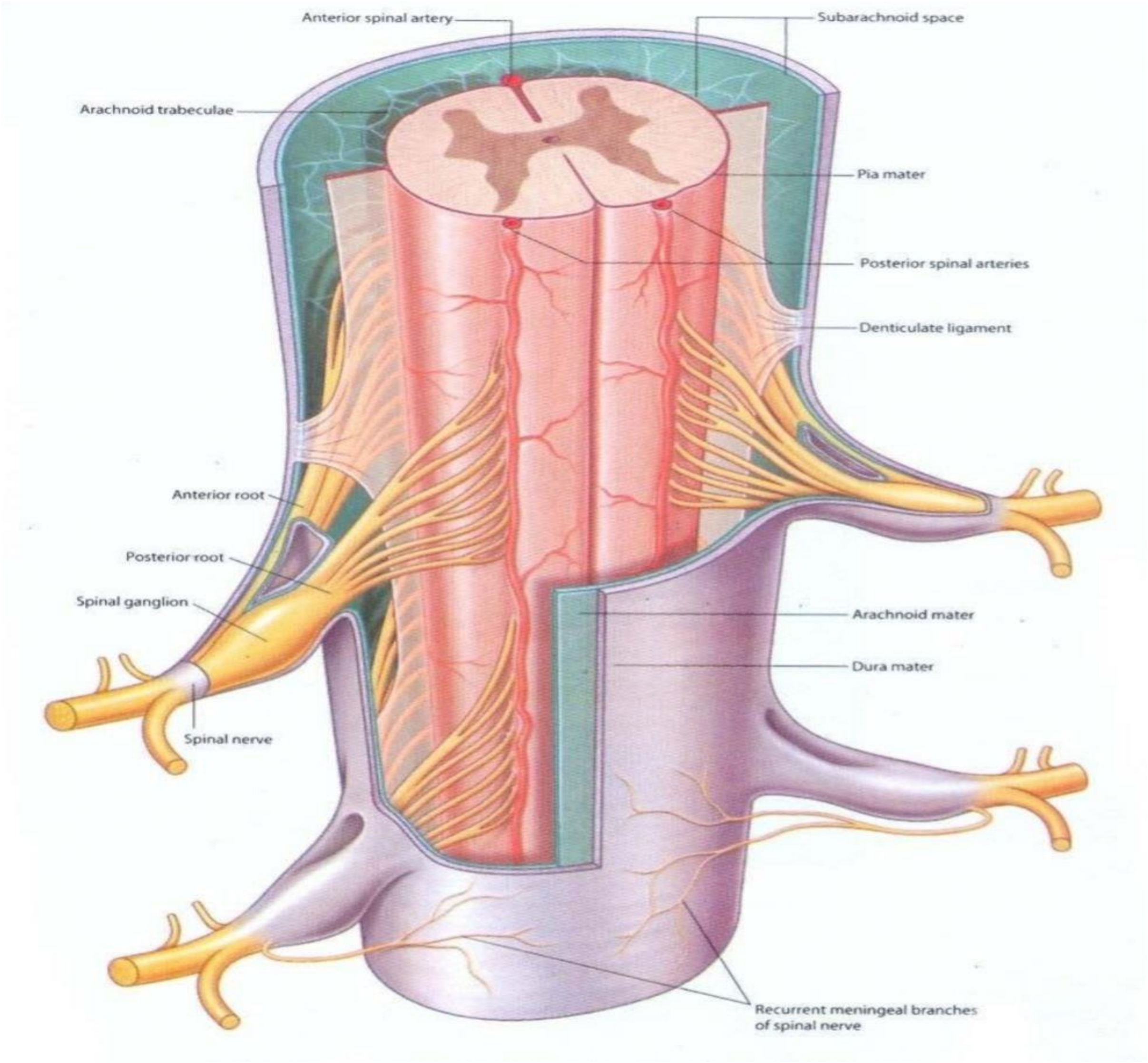

Anterior spinal artery
Subarachnoid space
Arachnoid trabeculae
Pia mater
Posterior spinal arteries
Denticulate ligament
Anterior root
Posterior root
Spinal ganglion
Arachnoid mater
Dura mater
Spinal nerve
Recurrent meningeal branches of spinal nerve

Figure 2.MENINGES COVERING THE SPINAL CORD

PIA MATER : The subarachnoid space, which is filled with CSF, divides this from the arachnoid. The pia mater inserts delicate septa into its composition and carefully invests the cord. A fibrous band called the denticulate ligament extends from each lateral border of the pia mater into the subarachnoid space. It is connected to the dura as far down as the first lumbar nerve by a number of pointed processes. Pia mater terminates as an extension and the filum terminate is connected to the coccyx periosteum and pierces the distal end of the dural sac.

DENTICULATE LIGAMENTS: Denticulate ligaments are folds of the pia mater that fuse with the arachnoid and dura mater after extending laterally along the anterior and posterior root attachment lines. In terms of structure, they serve as a suspension system for the spinal cord inside the dural area. These ligaments have an elastic mechanical property with a stress- stress modulus of 3-5 grams.

NERVE SUPPLY OF MENINGES

There are no nerve fibers in the posterior side of the dura and arachnoid, so a dural puncture causes no pain. Spinovertebral nerves supply the anterior portion. These all pass through the intervertebral foramen and goes downward for two segments and upward for one.

SPINAL NERVES:

These are 31 pairs in number:

1. 8 cervical
2. 12 thoracic
3. 5 lumbar
4. 5 sacral
5. 1 coccygeal

Anterior root is efferent and motor. Sympathetic pre ganglionic axons arise from cells in the intermediolateral horn of the spinal cord from T1 to L2.

Posterior root: is larger than anterior. All the afferent impulses from whole body including viscera pass into the posterior roots.

Each posterior roots has a ganglion and conveys fibers of (1)Pain (2)Tactile (3)Thermal

(4)Deep or muscle sensation from bones, joints, tendons (5)Afferent from the viscera and (6)Vasodilator fibres.

The principal spinal nerve trunks are formed by the anterior and posterior roots, each of which has a covering of dura, arachnoid and pia. These roots then traverse the extra dural space and combine in the intervertebral foramina to generate the anterior and posterior mixed nerves.

EPIDURAL SPACE[14,15,16,17,18]

DEFINITION

The elliptical epidural space encircles the dural sac, which runs from the foramen magnum to the coccyx. It connects laterally to the paravertebral space via the intervertebral disc foraminae.

BOUNDARIES

Periosteal and spinal layer of dura join at the foremen magnum, which borders the epidural space superiorly. The sacrococcygeal membrane borders the epidural space inferiorly and the posterior longitudinal ligament borders it anteriorly encompassing the ligamentum flavum and the anterior surface of the vertebral laminae posteriorly, the pedicle of the vertebrae and the intervertebral foramina laterally and the posterior side of the vertebral bodies and the intervertebral discs.

EPIDURAL SPACE ANATOMY

The dura adheres tightly to the periosteum of the vertebral bodies in the anterior aspect, although this area is more expansive and distensible posteriorly. The paravertebral space and the epidural space interact laterally through the foramina between vertebrae. The increase in connective tissue elements that comes with age may obstruct this communication.

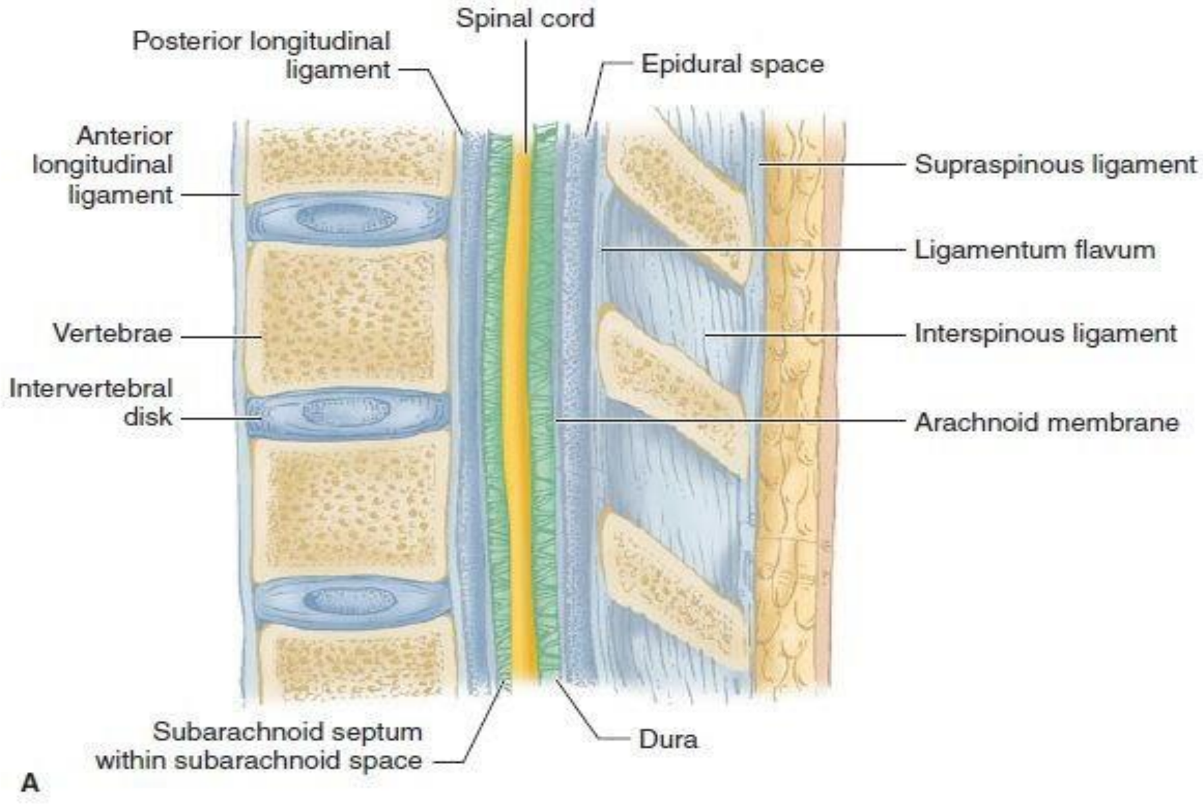

Spinal cord
Posterior longitudinal ligament
Epidural space
Anterior longitudinal ligament
Supraspinous ligament
Ligamentum flavum
Vertebrae
Interspinous ligament
Intervertebral disk
Arachnoid membrane
Subarachnoid septum within subarachnoid space
Dura
A

Figure 3.BOUNDARIES OF EPIDURAL SPACE

Under the midline sagittal plane, the following tissues must be pierced in order to reach the epidural space:

- Skin
- Subcutaneous tissue
- Supraspinous ligament
- Interspinous ligament
- Ligamentum flavum

A crucial landmark for the technical identification of the epidural space during induction is the ligamentum flavum. The advancing needle encounters minimal resistance in the first three tissues, but eventually encounters resistance when reaching the ligamentum flavum. The resistance suddenly gives up as the needle goes through this structure. It is critical to understand this point while administering epidural analgesia because any additional advancement could cause subarachnoid penetration.

CONTENTS OF EPIDURAL SPACES

The spinal nerve roots travel across the epidural space to reach their corresponding intervertebral foramina, accompanied by their dural cuffs. These move nearly horizontally in the cervical region, but as they descend, they become progressively inclined until the lower lumbar and sacral roots are nearly vertical, due to the difference in length between the spinal cord and the spinal canal.

The thickness and size of the roots vary substantially. The cervical and lumbosacral roots that supply the limbs are thicker than the thoracic roots. There is a correlation between the size variation and neural populations in the roots. Strong resistance to epidural blocking is linked to the enormous diameter and dense neural population of the dorsal and ventral roots of the first sacral segments. Inadequate local anaesthetic penetration is the cause of prolonged latency and inadequate S1 segment analgesia. This is noteworthy because it plays a crucial part in the epidural anaesthesia mechanism of action.

Invaginating the epidural veins in dural cuff area, arachnoid villi and granulations drain CSF from vessels into epidural fat, in which lymphatics remove the fluid.

EPIDURAL VESSELS

In the vicinity of the dural cuffs, the branches of the iliac, aortic and subclavian arteries cross the epidural space and enter the subarachnoid area. Blood is supplied by these branches all the way to the spinal roots. All of the blood flow to the spinal cord, with the exception of the cervical region, travels through the epidural space.

On either side of the line, the epidural veins are grouped into longitudinal plexuses. They are devoid of valves. Despite being separated into anatomical sections, these veins all connect to one another to form a network of segmental anastomosis that is horizontal. They communicate with the vertebral, ascending cervical, deep cervical, intercostal, iliolumbar and lateral sacral veins in addition to connecting with intervertebral foramina. The epidural veins provide a link between the cerebral veins above and the pelvic veins below because they lack valves.

Large abdominal tumors or late pregnancy can obstruct the inferior vena cava, causing the epidural veins to swell while coughing or straining. The dilation of the epidural veins reduces the effective epidural space volume. In these situations, a small amount of drug tends to disperse over a large area in the epidural space, thus reducing the need for the local anaesthetics.

FAT

A sack of semifluid, lobulated fat cushions the contents of the spinal canal. Injectable solutions go up and down between the fatty areolar tissues of the epidural region. One of the three contenders for the drug portion, the epidural fat serves as a crucial pharmacological area and depot for injected local anaesthetics and medications. The neural tissue of the spinal roots and cords and the blood vessels inside the spinal canal are the other two rivals.

Drugs with high lipoprotein binding and lipid solubility tend to go into the fat and stay there for a period of time, depending on their pharmacodynamics and how quickly the local blood flow is going to compete with them for uptake. The degree of compliance of the epidural fat changes with age and individuals. Young adults and children show relatively little resistance to it.

LYMPHATICS

Lympatics travel anteriorly from each intervertebral foramen, encircling and draining the dural sac before emptying into the longitudinal channels in front of the vertebral column. Significant volumes of connective tissue are seen ventrally, where it forms a strong bond with the anterior longitudinal ligaments in the spinal canal and the dura mater. The plica mediana dorsalis of the duramater is a unique midline fold of connective tissue that connects the dura to the ligamentum flavum in the midline. It stretches longitudinally in the midline. The epidural space is narrowed in the midline and divided into the right and left sides by these midline bands.

During epidural anaesthesia, certain outcomes can be explained by the dorsomedial link between the ligamentum flavum and the dura. The dorsomedian fold needs to be separated by the epidural needle during insertion. A catheter inserted may cause it to tilt slightly to either side of the midline. An individual may experience a unilateral block or a patchy condition when there is a genuine dorsomedian band or membrane. The challenge and effort required to move the epidural catheter freely into the epidural area are further explained by the dorsomedian connections.

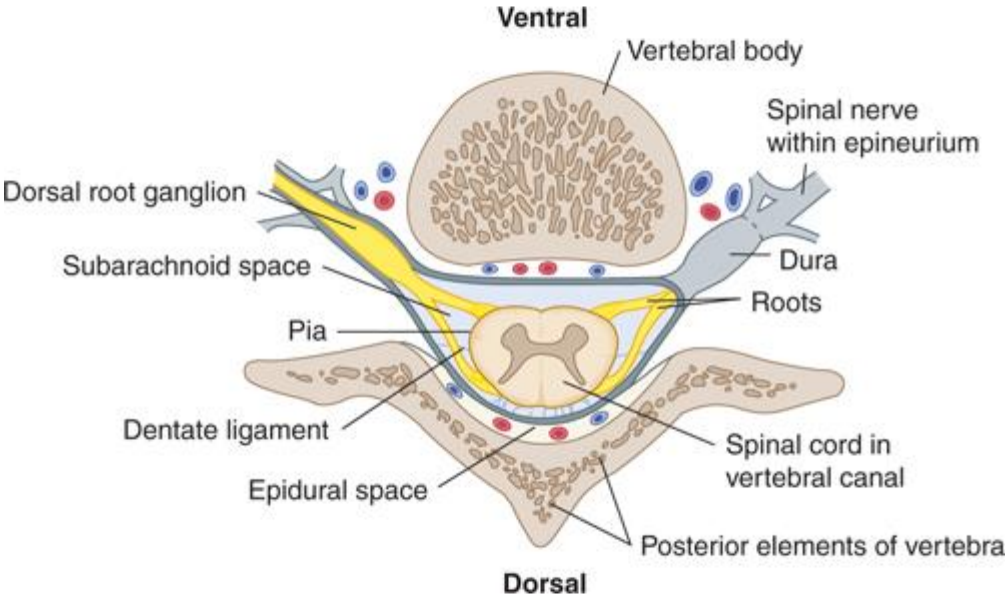

Ventral
Vertebral body
Spinal nerve within epineurium
Dorsal root ganglion
Subarachnoid space
Dura
Roots
Pia
Dentate ligament
Epidural space
Spinal cord in vertebral canal
Posterior elements of vertebra
Dorsal

Figure 4 . CROSS SECTION OF EPIDURAL SPACE

IDENTIFICATION OF EPIDURAL SPACE

a) Negative pressure methods:

· Hanging drop technique of Guterrietz

· Capillary tube technique of Odom

· Manometer technique

b) Loss of resistance methods

· Syringe technique

· Spring loaded syringe technique

· Macintosh Balloon technique

· Brooks device technique

· Vertical tube of Dawkins technique

c) Other techniques:

· Ultrasonic localization

· And the oxford- epidural space indicator.

RECENT TECHNIQUES

- Doppler guiding
- Utilising auditory amplification of the sound produced by the epidural needle as it passes through the ligamentum flavum and interspinous ligament.
- The guided pressure transducer approach.

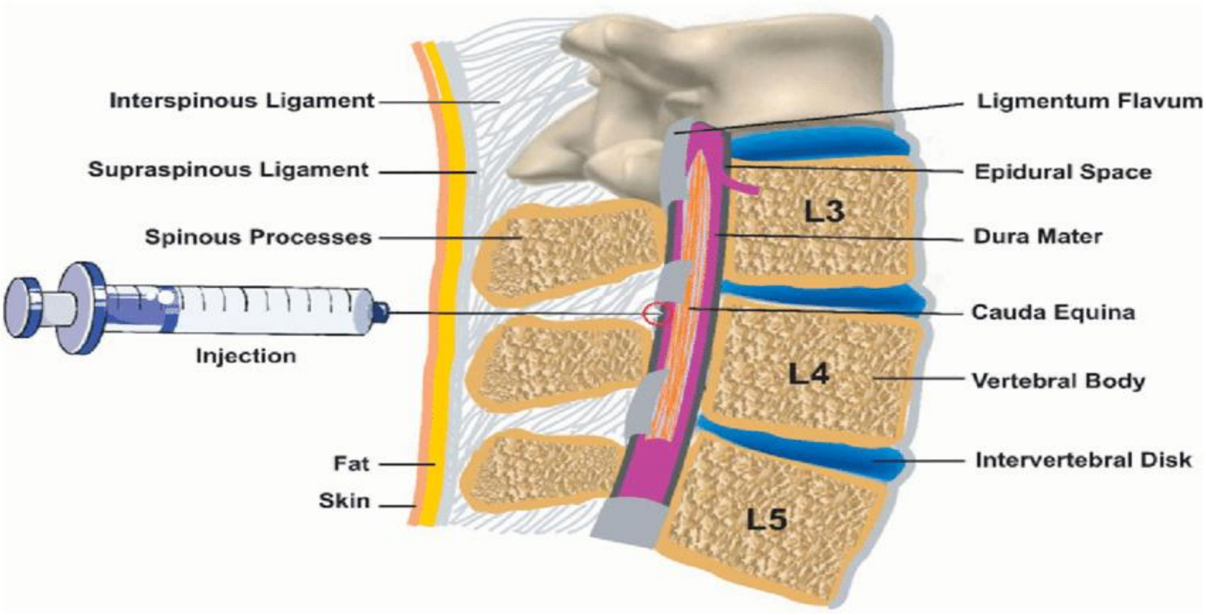

Interspinous Ligament
Supraspinous Ligament
Spinous Processes
Injection
Fat
Skin
L3
L4
L5
Ligmentum Flavum
Epidural Space
Dura Mater
Cauda Equina
Vertebral Body
Intervertebral Disk

Figure 5. TECHNIQUE OF EPIDURAL ADMINISTRATION

The syringe technique was employed in our investigation to measure the loss of resistance with air upon ligamentum flavum penetration.

An overview of fate of injected solution in epidural space:

The possible ways that a local anaesthetics or other agent injected into the epidural space could spread: superior and inferior spread is mainly in posterior portion of epidural space between dura and ligamentaum flavum.

The spread is superiorly to magnum. Diffusion may occur from the base of the dura to the cerebral CSF, potentially resulting in the blockage of vital centres such as the vasomotor, respiratory and cranial nerves.

Inferiorly spread is through the sacral hiatus, caudal canal and through anterior sacral foramina. Paravertebral neural blockage is produced by passing lateral through paravertebral space and intervertebral foramina. Spinal nerve root blockage is produced by quick access to CSF at the dura cuff region and the spinal cord is subsequently accessed.

The thin epidural space between the posterior longitudinal ligament and the dura is located anteriorly. Moreover, injection solutions can reach the CSF through the subarachnoid space through slow diffusion. Drugs may be absorbed directly into the brain through vascular absorption via epidural veins and drugs are also absorbed by epidural fat.

PHARMACOLOGY

Local anaesthetics are chemical compounds which have the ability to reversibly block the transmission of nerve cell impulses.

CLASSIFICATION

Two classes of clinically important drugs can be distinguished based on the link between the aromatic part and the intermediate chain. Procaine, chloroprocaine and methocaine are among the amino ester group that have an ester link. The amino amides, which include lignocaine, bupivacaine, mepivacaine, prilocaine and ropivacaine, have an amide bond between the aromatic head and the intermediate chain.

PHARMACOLOGY OF ROPIVACAINE

C17H26N2o.Hcl

S-(-)-1-propyl-2’,6’-pipecoloxylidide hydrochloride monohydrate

STRUCTURAL FORMULA

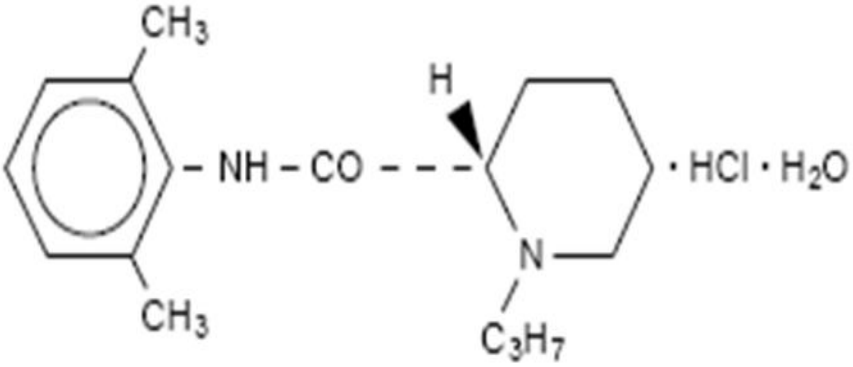


Figure 6. STRUCTURAL FORMULA OF ROPIVACAINE HYDROCHLORIDE

PHYSICOCHEMICAL PROPERTIES

PRESENTATION

20ml ampules containing a colorless, transparent solution of 0.2%, 0.5%, and 0.75% ropivacaine hydrochloride.

MECHANISM OF ACTION

By reversibly inhibiting sodium ion influx, ropivacaine prevents impulse conduction in nerve fibers.[19] Potassium channel blockage that is dosage dependent amplifies this effect.[20] Compared to bupivacaine, ropivacaine is less lipophilic and has a lower propensity to penetrate large myelinated motor fibers. As a result, it acts only on the A-beta and C neurons that transmit pain, not on the A-beta fibers that are involved in motor function. .

PHARMACOKINETICS OF ROPIVACAINE

1. ABSORPTION

The total dose given, routes of administration, the hemodynamics of patient, circulatory state and vascularity of the site can affect the degree to which ropivacaine is absorbed. Up to 80mg, pharmacokinetics are dose proportionate and linear. Complete and biphasic absorption of 150mg of ropivacaine from the epidural space has occurred. The mean t1/2 of initial phase is 14 min, afterwards by a slower phase with a mean absorption t ½ of 4.2 hours.[23]

2. DISTRIBUTION

Ropivacaine has a 94% binding to plasma proteins, primarily to alpha-1 acid glycoprotein. An increase in the degree of protein binding and a corresponding decrease in ropivacaine clearance are the reasons for the increase in total plasma concentration during continuous epidural infusion.[23] During epidural administration during caesarean section, ropivacaine rapidly crosses the placenta, resulting in nearly full equilibrium of the free fraction of ropivacaine in the maternal and fetal circulation.

3. METABOLISM AND EXCRETION

Ropivacaine undergoes significant metabolism in the liver, mostly by aromatic hydroxylation to 3’-hydroxy-ropivacaine by cytochrome P450 1A2 and N-dealkylation to 2’,6’pipecoloxylidide by CYP3A4.[24]

86% of the drug excretion in urine following intravenous dose delivery is done by the kidney, which serves as the primary excretory organ for ropivacaine.

TOXICITY OF ROPIVACAINE

If used at the recommended dosage, it has very few adverse effects. Compared to bupivacaine, it is less neurotoxic and cardiotoxic.

CENTRAL NERVOUS SYSTEM

The risk of central nervous system toxicity from an accidental intravascular ropivacaine injection is minimal.[21] Objective symptoms are often excitatory in character and include tremors, shivering and twitching of the muscles; initially, the muscles of the face (perioral numbness) and part of the extremities are affected. The threshold for convulsive episodes following an unintentional intravascular injection is higher with ropivacaine.

CARDIOVASCULAR SYSTEM

Intravascular ropivacaine injections can have considerable cardiovascular effects, such as alterations to contractility, conduction time and QRS width, although these effects are considerably less pronounced than those of bupivacaine.[22]

AUTONOMIC NERVOUS SYSTEM

Preganglionic beta fibers which are myelinated have a quicker conduction time and are more susceptible to the effects of local anaesthetics, such as ropivacaine. Preganglionic sympathetic fibers are involved in epidural anaesthesia, which results in extensive vasodilation and subsequent hypotension.

PHARMACOLOGY OF FENTANYL

Fentanyl is a synthetic opioid that is derived from phenylpiperidine. It is 75–125 times more potent than morphine and shares structural similarities with pethidine.[25]

STRUCTURAL FORMULA

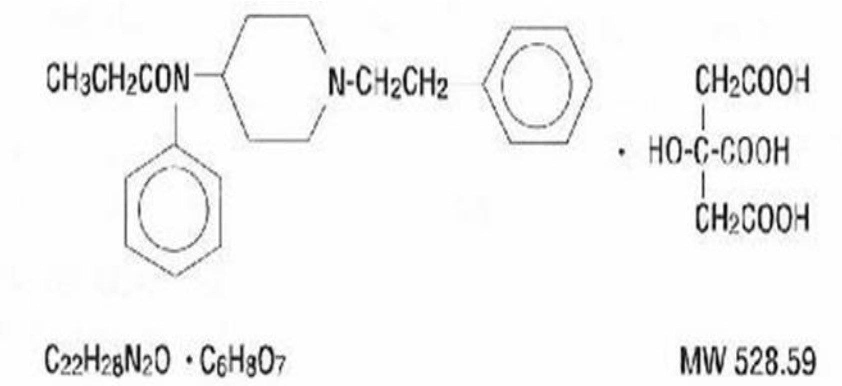


Figure 7 . STRUCTURAL FORMULA OF FENTANYL

PHYSICOCHEMICAL PROPERTIES

It is a crystalline powder that is white in color and soluble in both methyl alcohol and water. Only 8.5% is unionised at the physiological pH of 7.4 and the molecular weight - 528.59. pKa - 8.43 . Slow redistribution t1/2 is 13-28 minutes and elimination t1/2 is 3.1-7.9 hours.[26]

POTENCY

Fentanyl is 1000 times more potent than Meperidine.At the same time 50 -100 times more potent than Morphine.[26]

100 mcg of Fentanyl equals to 10 mg of Morphine and 75 mg of Meperidine[26]

MODE OF ACTION

Analgesic effects of fentanyl are primarily due to its strong selectivity as a µ receptor agonist. It works by raising the concentration of calcium within cells, which raises K+ conductance and causes cell membrane hyperpolarization. Both the pre and postsynaptic responses are diminished by this reduced membrane conductance. The primary mechanism of analgesia is the interaction with µ receptors located at supraspinal locations. Additionally, fentanyl binds to kappa receptors to produce drowsiness, anaesthesia and spinal analgesia.

METABOLISM

Cytochrome P-4503A4 plays a major role in Fentanyl metabolism[27]

It is metabolised to norfentanyl, hydroxypropionyl-fentanyl and hydroxypropionyl-norfentanyl in the liver by the process of N-demethylation. Lesser than 10% is excreted through urine unchanged.

PHARMACOKINETICS

About 40% of the fentanyl is absorbed by red blood cells and 80% of fentanyl is bound to plasma proteins. Because of its extensive distribution with volume of distribution of 3.2–5.9L/kg in tissues of the body, fentanyl has a comparatively long half-life.

Compared to morphine, fentanyl has a quicker onset of action and greater potency because it is a highly lipophilic substance. Fentanyl rapidly redistributes, resulting in a short duration of action. With 75% of the initial injected fentanyl dose getting first-pass pulmonary uptake, the lungs function as a major, inactive storage site, limiting the initial amount of drug that enters the systemic circulation.

ELIMINATION HALF-LIFE

Despite the clinical perception that fentanyl is a short-acting drug, the elimination t1/2 of 3.1-7.9 hours of fentanyl is longer than that of morphine. This can be accounted for by the fact that fentanyl has larger volume of distribution and the rapid re-distribution. Patients with cirrhosis do not experience a significant prolongation of the half-time, but it is prolonged in the elderly.[28]

USES

Fentanyl can be used in a wide range of dosages. It has been given by transdermal, transmucosal (oral, intranasal), neuraxial (epidural, intrathecal), intramuscular, intravenous (bolus, infusion, PCA) and inhalational methods.

Studies indicate that moderate to good analgesia is associated with a steady-state plasma concentration (Cp) of 0.6-3ng/ml. However, clinically significant respiratory depression is linked to plasma concentrations greater than 2 ng/ml. Therefore, a plasma concentration Cp of 0.6–2 ng/ml is the therapeutic window. For balanced anaesthetic technique in short surgical procedures, fentanyl is used in the dose of 2 mcg/kg.

Fentanyl anaesthesia at high doses (50–100 mg/kg) combined with oxygen or nitrous oxide alone has been used for prolonged surgical operations and cardiac procedures. Routine use of postoperative ventilation is recommended when high doses are given. A loading dosage of 50 to 150 mg and a continuous infusion of 0.5 to 1.5 mg/kg/hour are used to treat postoperative pain.

EPIDURAL ADMINISTRATION

It can be given as a bolus, bolus plus continuous infusion, continuous infusion plus bolus, PCEA and PCEA with a continuous fixed/variable background infusion. 50–200 μg (1-3 μg/kg) is the average single dose, which produces analgesia in 15 minutes and lasts for up to 2-4 hours. Moreover, an infusion can be administered at a rate of 0.5 to 2.5 μg/kg/hr. The standard PCEA form bolus doses are 20–25 μg, with a 6–10 minute lockout interval (with a 0.5–1 μg/kg/hr background infusion).[25]

While at rest, analgesia is very effective; while moving or coughing, pain scores rise. This contrasts with the effective analgesia that intrathecal fentanyl injection provides for both ambulation, coughing and also at rest.[25]

EFFECTS

CARDIOVASCULAR SYSTEM

- The mechanics of the papillary muscles are not significantly affected by the dosage of l mcg/kg.
- Heart rate is lowered with doses of 7 mcg/kg during induction, while mean arterial pressure remains same.
- Myocardial contractility is 50% lower at 10 mcg/kg.
- In individuals with coronary artery disease, 20 to 25 mcg/kg reduces heart rate, MAP, systemic and pulmonary vascular resistance, and PCWP by l5%.
- There is hemodynamic stability at 75 mcg/kg. Clinical studies supporting the hemodynamic

stability of high-dose fentanyl in cardiac and non-cardiac surgery have been published.

- The release of histamine is rare.

RESPIRATORY SYSTEM

- Tidal volume increases and respiratory rate falls at 1 to 2 mcg/kg of fentanyl.
- It reduces the ventilatory response to hypoxia and hypercarbia, as well as the respiratory rate and tidal volume, at dosages higher than 3 mcg/kg.
- It possesses antitussive effects.

- Early muscle relaxant administration can control the "Wooden-chest" syndrome, or rigidity in the chest wall caused by an action on GABAnergic interneurons' μ receptors.

CENTRAL NERVOUS SYSTEM

Fentanyl causes CNS depressant. It has no hypnotic or sedative effects at low dosages (1-2 microgram/kg). The Edinger Westphal nucleus is stimulated, wherefore miosis is observed. After an epidural injection, the central effects are noticeably fewer than those following an IV.

GASTROINTESTINAL SYSTEM

It causes the sphincter of Oddi to spasm, which raises the pressure in the common bile duct. It lowers GI motility and produces nausea and vomiting.

GENITOURINARY SYSTEM

Urine retention results from increased tone in the ureters, bladder detrusor muscle and vesicle sphincter.

SIDE EFFECTS

A significant post-operative concern with fentanyl is persistent and recurred ventilatory depression. The reason for the secondary spike in fentanyl levels could be either washout from the lungs during the post-operative period or reabsorption from the gastrointestinal tract.[28] Even at high dosages, fentanyl does not cause the release of histamine contrary to morphine. Hypotension is therefore not likely. Nonetheless, fentanyl causes a substantial depression of the carotid sinus baroreceptor reflex (10μg/kg IV), which results in bradycardia.[28]

It can result in changes in somatosensory evoked potentials, skeletal muscle rigidity, and a mild increase in intracranial pressure (6–9 mmHg), usually accompanied by a drop in cerebral perfusion pressure and mean arterial pressure.[25]

PHARMACOLOGY OF DEXMEDETOMIDINE [28,29]

The pharmacologically active dextroisomer of medetomidine, dexmedetomidine, is an imidazole molecule that exhibits selective and specific alpha 2-adrenoceptor agonism.

Dexmedetomidine is (+)-4-(2, 3-dimethyle phenyl) ethyl-1 H-imidazole monohydrochlorid with empirical formula C13H16HCl.

STRUCTURAL FORMULA

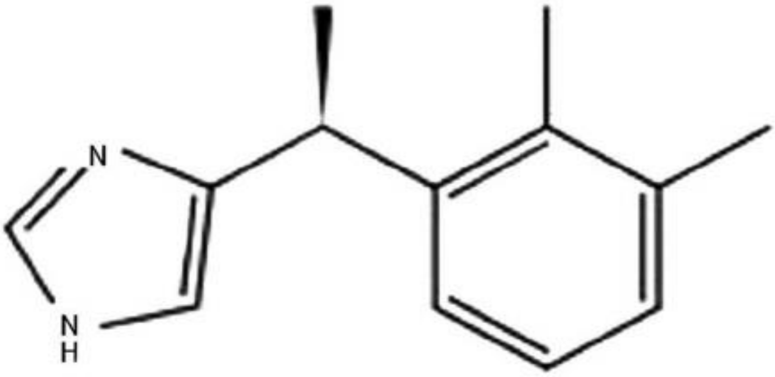


Figure 8.STRUCTURAL FORMULA OF DEXMEDETOMIDINE

MECHANISMS OF ACTION

After binding to G-Protein-coupled α2-AR, which has three subtypes (α2A, α2B, and α2C) with varying physiological functions and pharmacological activity, alpha2-AR agonists produce clinical effects.[29] These receptor subtypes are widely distributed in blood vessels, vital organs, and the peripheral, central, and autonomic nervous systems. The pontine locus ceruleus, a vital nucleus governing sympathetic nervous system function, alertness, memory, analgesia, and arousal, has one of the highest densities of alpha-2 receptors.

It produces sedation and analgesia via binding to the α2 receptors in the spinal cord and locus ceruleus, respectively. Increased affinity for the α2 receptor specifically causes vasodilatation and vagomimetic action on the heart (bradycardia).

PHARMACODYNAMICS

Compared to clonidine, dexmedetomidine is eight to ten times more selective for α2-AR .

After a steady intravenous infusion of low and medium dosages (10-300 mcg/kg), alpha-2 selectivity is found. Both α1 and α2 activities are seen after slow intravenous infusion of high doses (>1000mcg/kg) or with rapid intravenous in animals.

PHARMACOKINETICS

Dexmedetomidine exhibits a rapid distribution phase after intravenous administration, with a distribution half life of six minutes and a terminal elimination half life (t1/2) of roughly two hours.[28] When administered intravenously (IV) for up to 24 hours, dexmedetomidine displays linear kinetics in the range of 0.2–0.7 micrograms (mcg)/kg/hr.[29] The volume of distribution is roughly 118 liters in its steady state. 94% is bound to proteins.

Because first pass metabolism is extensive, oral bioavailability is low. Nevertheless, bioavailability is high (84%) following sublingual and intranasal administration, suggesting a possible use in premedication and pediatric sedation.

Excreted in urine (95%) and feces (4%), it undergoes almost complete biotransformation with very little unaltered dexmedetomidine . Direct glucuronidization is the primary mechanism in biotransformation, however cytochrome P450-mediated metabolism is also involved.

ADVERSE EFFECTS

The side effects that are most commonly reported include bradycardia, dry mouth, nausea, hypertension, and hypotension. Other side effects that have been documented include cyanosis, fever, rigors, and muscle weakness. Syncope, neuropathy, paresthesia, paresis, hyperkalaemia, lactic acidosis, angina pectoris, AV Block, cardiac arrest, T-wave inversion, tachycardia, pulmonary edema, bronchospasm, respiratory depression and hyperglycemia are among the possible outcomes.

Dexmedetomidine hydrochloride was shown to be tolerable in healthy individuals whose plasma concentrations ranged from 1.8 to 13 times the upper limit of the therapeutic range. The most noteworthy side effect seen in individuals with the greatest plasma concentration was an AV block, which went away on its own in less than a minute.[28]

Adverse effects can be minimized by lowering or eliminating the loading dose. It is possible to reverse dexmedetomidine with the specific antagonist Atipamezole.

ROUTES AND DOSES

INTRAVENOUS: Loading dose of 1 mcg/kg over 10-20 minutes after which a maintenance infusion in the dose of 0.2 to 0.7mcg/kg/hr. The rate of infusion can be increased in increments of 0.1mcg/kg/hr or higher.

INTRAMUSCULAR : 2.5 mcg/kg has been used for premedication.

SPINAL: 0.1 to 0.2 mcg/kg

EPIDURAL: 1 to 2mcg/kg

PERIPHERAL NERVE BLOCK: 1mcg/kg

BUCCAL: 1 to 2 mcg/kg

INTRANASAL: 1 to 2mcg/kg

Dexmedetomidine Hydrochloride injections are available as 50mcg/0.5ml, 100mcg/ml and 200mcg/2ml.

CLINICAL APPLICATIONS

PREMEDICATION

Dexmedetomidine is widely used in premedication because it is a sedative, anxiolytic, analgesic, sympatholytic, and has stable hemodynamics.[28] It decreases the consumption of oxygen during surgery by upto 8% and after surgery by upto 17%. The premedication dosage is 0.33–0.67 mcg/kg intravenously or 2.5 μg/kg intramuscularly, administered 15 minutes before to surgery.[29]

INTENSIVE CARE UNIT SEDATION

Although numerous studies have shown that dexmedetomidine can be safely used for longer periods of time, the FDA has now approved its usage in intensive care units for a maximum of

24 hours . Dexmedetomidine reduces the need for opioids (>50%) and produces high PaO2/FIO2 with minimal respiratory depression, making it an advantageous sedative for postoperative patients on mechanical ventilation.

PROCEDURAL SEDATION

Dexmedetomidine is administered as a 1 mcg/kg dosage for procedural sedation, with a 0.2 mcg/kg/h infusion afterward. Onset of action is within five minutes, and within fifteen minutes, its peak effect happens. Transesophageal echocardiography, colonoscopy, awake carotid endarterectomy, shockwave lithotripsy, vitreoretinal surgery, tonsillectomy in pediatric patients and other procedures have all been safely performed using it.

AS AN ADJUVANT IN LOCAL & REGIONAL TECHNIQUES

Because dexmedetomidine is highly lipophilic, it may rapidly penetrate the cerebrospinal fluid and bind to the spinal cord α2-AR to produce analgesic effects.[28] It increases the duration that local anaesthetics cause both motor and sensory blockage, regardless of the method.

It has been effectively applied to intravenous regional anaesthesia (IVRA) and improves both peripheral and central neural blockade by local anaesthetics. When added to lidocaine for IVRA, 0.5 μg/kg dexmedetomidine enhances intraoperative-postoperative analgesia and anaesthetic quality without producing adverse effects.

ATTENUATION OF RESPONSE TO TRACHEAL INTUBATION AND EXTUBATION

When administered intravenously (15 minutes before to surgery), doses of 0.33 to 0.67 μg/kg of dexmedetomidine reduce the hemodynamic response to endotracheal intubation by its sympatholytic property.

USE IN MRI AND CT SCAN

Children receiving MRIs have responded well to the use of high dosage dexmedetomidine (3 mcg/kg IV load over 10 minutes with an infusion of 1 mcg/kg/hour) for sedation.

AWAKE INTUBATION

Dexmedetomidine used for securing the airway with a fibreoptic intubation

OBSTETRIC USE

Due to its high lipophilicity, dexmedetomedine crosses the placenta but rapidly disappears .[30]

Mahdy et al. discovered that patients in the fentanyl and control groups experienced much shorter sensory and motor block durations following intrathecal dexmedetomidine injection and that no group mothers or infants experienced any negative side effects.[36]

Following intrathecal delivery of dexmedetomidine, Fyneface-Ogan et al. observed negligible changes in maternal blood pressure, baseline fetal heart rate, pH of umbilical venous blood, and APGAR score.[37]

MECHANISM OF LABOR PAIN

Labor pain is a crescendo-type pain that comes and goes. When labor proceeds, the duration, frequency and intensity of the pain all increase and the time between painful episodes gets shorter. There are two types of pain related to the reproductive system: visceral and somatic.[32]

Skin and underlying tissue stimulation elicits somatic sensations and dermatomes characterize the superficial nerves involved. The internal organs are the source of the visceral component, which solely experiences pain.

Dilation of the cervix and the lower uterine segments, together with the uterine contractions, are the causes of labor pains during the first stage of childbirth. The term "visceral pain" refers to Thoracic T10, 11, 12, and Lumbar L1 dermatomes, which are part of the Lamina V of the dorsal horn synapse. These cells receive afferents from skin regions that are supplied by the same spinal cord segments.Opioids inhibit these. Compression of adjacent viscera, such as the bladder and the rectum, increases the pain as the presenting part descends. When the cervix is fully dilated, less painful sensations originate in this structure; however, uterine contractions continue, and the pelvis and perineum experience significant pressure effects.[38]

As the fetal presenting part descends, the distention of the pelvic floor, perineum, and vagina causes pain during the second stage of labor. Through the pudendal nerve-Sacral S2,3,4 route, thin myelinated, rapidly conducting A-delta fibers transmit pain. Somatic pain is Sharp and precisely localized to the vagina and perineum. Dense somatic analgesia is provided by local anaesthetics.[38]

CENTRAL PATHWAY

A delta fibers and C fibers carry the nociceptive information to the dorsal horn. In the thalamus and cortex, synapses and fibers cross to convey information. This activity is both centrally and peripherally modulated. Bradykinin, 5-hydroxytryptamine and prostaglandins can all be released locally in the uterus peripherally to increase peripheral nerve activity.

Information from visceral and somatic structures converges in the spinal cord at the same spinal segment.[39] This is one of the mechanisms for the referred pain to dermatomes of body wall from viscera. The sensation generated is diffuse because the laminae triggered by visceral nociceptive fibers also receive input from several other spinal cord segments. As a result, dull, central pain is felt in the area of the body wall that T11 innervates. This is located anteriorly, just below the umbilicus. The T11 dermatome innervates the skin across the lumbo-sacral junction posteriorly.

Anterior horn is the recipient of nociceptive visceral routes from the dorsal horn. Additionally, they travel through numerous interconnected pathways, including the dorsal column, solitary nucleus, spinoreticular tract, and spinothalamic tract, as they move cephalad. The emotional reactions to pain are mediated by the spinothalamic tract (fast impulse conduction) and the spinoreticular tract (slower impulse conduction). These tracts also contribute to the analgesia that is brought on by descending control system activity.

Opioid-sensitive midbrain areas known as periaqueductal grey matter send either adrenergic or serotonergic neurons to the spinal cord dorsal horn. In the spinal cord, enkephalinergic interneurons directly block nociceptive transmission, which modulates pain. Opioid-mediated analgesia is induced by pregnancy itself. To reduce discomfort is the goal of pain management. Once a portion of the dorsal column pathway is anesthetized, regional nerve blocks work well.

PATTERNS OF PAIN STIMULATION

The first stage of labor pain is referred to the dermatome supplied by the same segments of spinal cord that receive nociceptive input from the cervix and the uterus.[33] Only the Thoracic T11 and T12 dermatomes experience dull aching pain throughout the first stage latent phase.[33]Pain increases in the T11 and T12 dermatomes and extends to the T10 and L1 dermatomes when labor advances to the active phase of the first stage.[33] The anus, lower part of the sacrum, the perineum, and frequently the thighs are the areas with the sharpest pain in the late first and early second stages.[33] Sharp and well-localized, this pain is similar to that produced by stimulation of superficial somatic structures and is mostly felt in the area supplied by the pudendal nerves.[33] Additionally, parturients experience cramping and burning in their thighs and legs during this stage.[33]

This is most likely the outcome of activation of different pain-sensitive pelvic tissues, including:

1. Traction on the parietal peritoneum of the pelvis

2. Tension and stretching in the rectum, urethra, and bladder
3. Tension and stretching of the pelvic muscles, fascia and ligaments.
4. Improper pressure applied to one or more lumbosacral plexus roots.[33]

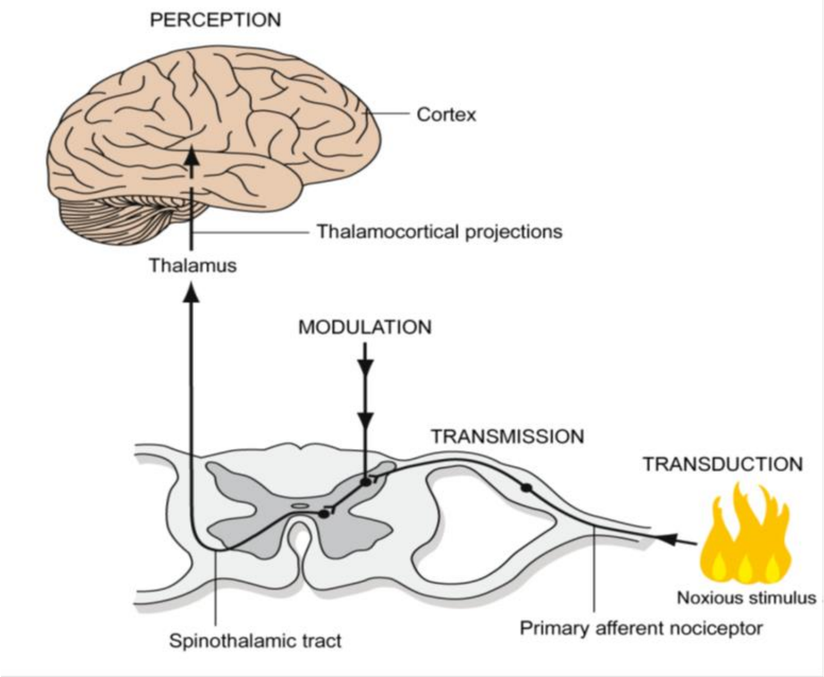

PERCEPTION
Cortex
Thalamocortical projections
Thalamus
MODULATION
TRANSMISSION
TRANSDUCTION
Noxious stimulus
Primary afferent nociceptor
Spinothalamic tract

Figure 9. PERCEPTION OF PAIN IN LABOR

BENEFICIAL EFFECTS OF EPIDURAL ANALGESIA

1. Epidural analgesia decreases the release of cortisol and catecholamines via inhibiting sympathetic efferent and nociceptive inputs. This lessens the myocardium workload.[33]

2. Opioids reduce hyperventilation when they produce analgesia, but the depressive impact may still result in hypoventilation and hypoxia.[33] When total pain is relieved by epidural analgesia, there is no longer a brief period of hyperventilation during a contraction, which in turn prevents hypoventilation during uterine relaxation. As a result, the PaO2 rises to 100 mm Hg and the PaCO2 stays in the 28–32 mm Hg range.[33]

3. The rise in blood pressure and cardiac output brought on by pain is eliminated by epidural analgesia. Therefore, it is advantageous for expectant mothers, given that maternal hypotension is avoided.[33]

4. Continuous lumbar epidural analgesia reduces maternal metabolism, oxygen consumption, and the overall work of labor by relieving pain and anxiety. As a result, it considerably lowers acidosis in both mothers and fetus. In this regard, epidural analgesia is far superior to the analgesia provided by systemic opioids.[33]

5. When epidural analgesia is administered appropriately, the majority of pain will be relieved, which will prevent many of the previously described psychological and emotional reactions to severe pain.[33]

6. The reflex inhibition of gastric motility is blocked by epidural analgesia. it does not prolong the gastric emptying . As a result, it benefits the entire gastrointestinal system.[33]

7. By lowering sympathetic hyperactivity, effective analgesia can minimize or eradicate uterine hyperactivity or hypoactivity and convert uncoordinated contractions into a regular labor pattern. Furthermore, it enhances any hypoperfusion of the placenta and any decline in the flow of blood through the uterus.[33]

8. Research has demonstrated that epidural analgesia enhances intervillous blood flow in parturients through its vasomotor blocking action. All fetus benefit from this, but is important to those at risk—such as those born to women who have diabetes, heart disease, or hypertension.To attain these benefits, maternal hypotension must be firmly prevented by suitable preventive measures (e.g., intravenous infusion of fluids, leftward displacement of the uterus).[33]

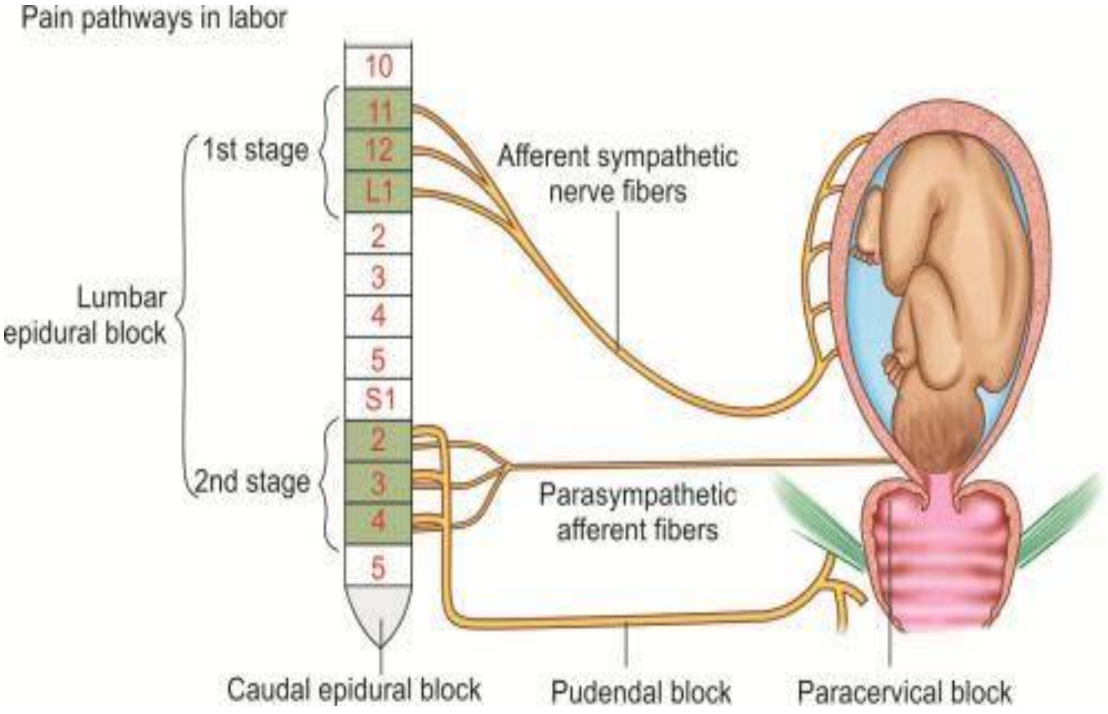

Pain pathways in labor
10
11
12
L1
2
3
4
5
S1
2
3
4
5
1st stage
Lumbar epidural block
2nd stage
Afferent sympathetic nerve fibers
Parasympathetic afferent fibers
Caudal epidural block
Pudendal block
Paracervical block

Figure 10. PAIN PATHWAY IN LABOR

METHODS OF PAIN RELIEF IN LABOR

There are several methods for labor analgesia, such as psychoprophylaxis, transcutaneous electrical nerve stimulation (TENS), systemic medication, inhalational techniques and neuraxial blocks. Furthermore, other regional methods such as caudal and paracervical blocks are used infrequently.[8]

PSYCHOPROPHYLAXIS

Grantley Dick-Read coined the term "natural childbirth" in 1933 because he thought childbirth was a painless process that didn't require medical attention.[34] For parturients natural childbirth became an option after Fernand Lamaze publicised it.[34]

Other techniques include acupuncture, which doesn't seem to be helpful during delivery and hypnosis, which works for just a few percent of parturients but is not generally helpful.[35]

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

This is assumed to lower pain by limiting central transmission at a presynaptic level and so inhibiting nociceptive transmission at the dorsal horn.[34] It is also believed that TENS increases the central release of dynorphins and endorphins. Reports, however, have not been able to support its efficacy in labor analgesia.[34]

PARENTERAL TECHNIQUES

SYSTEMIC MEDICATION

Although they cause a variety of side effects, including respiratory depression, nausea and vomiting, as well as severe drowsiness, opioids are the most often used class of drugs.[34] They may induce respiratory depression in the baby and freely cross the placenta.[34] Opioids that are frequently utilized include remifentanil, butorphanol, fentanyl and pethidine.[31]Ketamine and sedative-tranquilizers are two other systemic drugs used to relieve labor pain.[34]

INHALATIONAL ANALGESIA

In order to reduce discomfort during childbirth, inhalational analgesia involves the use of inhaled anaesthetics at subanaesthetic concentrations.[34] It relieves pain to a limited extent. For many years, Entonox (a 50:50 N2O/O2 mixture) has been employed as an adjuvant to systemic and regional labor techniques as well as an independent analgesic.[31]There have also been effective uses of isoflurane (0.2–0.25%), enflurane (0.2%) and desflurane (0.2%).[34]

REGIONAL ANALGESIA TECHNIQUES

In labor analgesia, a range of regional approaches are employed to achieve the best possible analgesia with a minimum of depressive effects.[34]

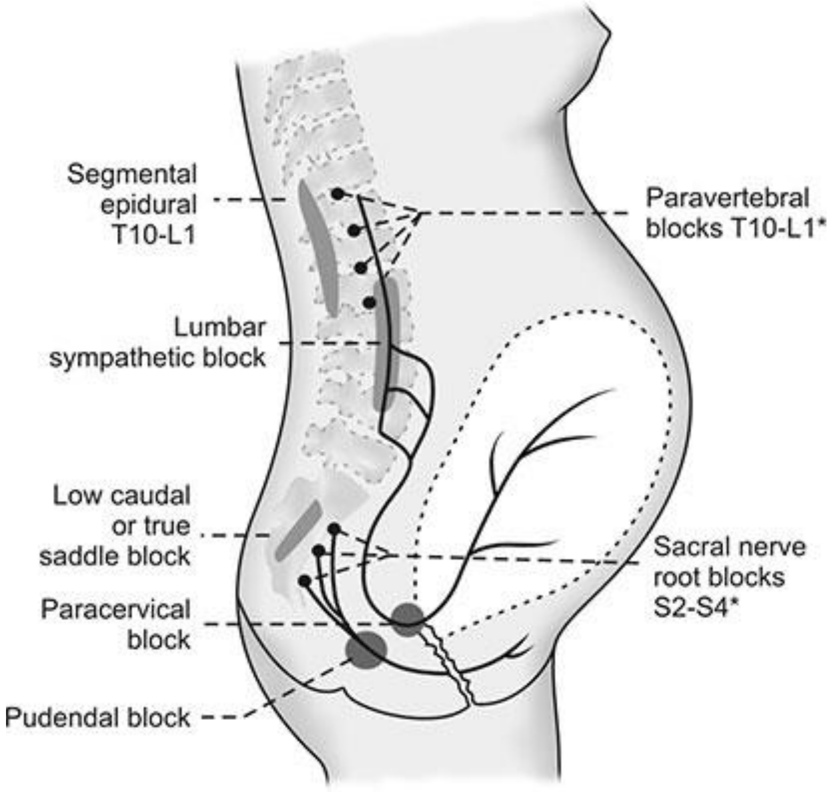

Segmental epidural T10-L1
Paravertebral blocks T10-L1*
Lumbar sympathetic block
Low caudal or true saddle block
Sacral nerve root blocks S2-S4*
Paracervical block
Pudendal block

Figure 11. REGIONAL ANALGESIA TECHNIQUES

EPIDURAL ANALGESIA

During labor, lumbar epidural analgesia provides a secure and efficient method for pain management. To provide a T10-L1 sensory block, low dosages of opioid combinations and local anaesthetics are used. Effective pain relief without significant motor block and a decrease in maternal catecholamines are two advantages of epidural analgesia.[34]

SPINAL ANALGESIA

A single subarachnoid injection of an opioid or local anaesthetic causes rapid onset of labor analgesia which is effective as well.[34]

COMBINED SPINAL EPIDURAL ANALGESIA

In obstetrics, the combined spinal-epidural (CSE) method is frequently employed because it provides efficient, rapid onset of analgesia with a low risk of toxicity or motor block. Furthermore, it offers the capacity to provide analgesia for as long as necessary.[34]

PATIENT-CONTROLLED ANALGESIA [40,41,42,43]

Since 1971, patient-controlled analgesia (PCA) has been used to maximize pain treatment; the first PCA pump to be sold commercially debuted in 1976. By enabling patients to instantly administer a predefined bolus dosage of medication at the touch of a button, PCA aims to effectively provide pain relief at the patient's selected dose and schedule.

Every bolus can be given either by itself or in coupled with a continuous drug infusion. It gives the patient more control over how much pain relief they receive, uses less local anaesthetic, has fewer side effects (including motor block), increases patient satisfaction and lessens the need for clinicians to supplement analgesia.

PCEA is a dependable and efficient way to keep epidural labor analgesia maintained. Many other drug combinations and settings have been utilized successfully, as long as appropriate drug volumes are permitted. Excellent analgesia can be achieved by combining opioids with low quantities of ropivacaine or bupivacaine. Dilute local anaesthetic solutions (up to 0.125% bupivacaine or 0.2% ropivacaine) can be used to reduce motor block.

For the majority of patients, a background infusion seems appropriate because it lessens the need for unforeseen medical interventions from the clinician and might even improve analgesia when it is used. It has been possible to employ background infusion rates of 2 to 10 ml/h with success. For labor PCEA, there is still no perfect lockout interval or bolus dosage.

INDICATIONS

PCA can be helpful in the acute pain when there is insufficient pain management after the initial opioid delivery in the emergency room.[41]Burns, trauma, pancreatitis and vaso-occlusive pain crisis are typical examples.

In order to manage the pain until the underlying cause is identified and addressed, PCA would be utilized as an adjuvant treatment.

PCA might also be appropriate for patients with chronic diseases who have lower levels of ongoing chronic pain. The most prevalent examples include complicated regional pain syndrome, phantom limb syndrome and metastatic disease.

Patients recovering from surgery are also excellent candidates for PCA, particularly if they have an epidural or indwelling nerve catheter.

Individuals experiencing labor pain are also considered reliable candidates for epidural PCA. The patient can effectively lessen and regulate the discomfort brought on by contractions, particularly if it is exacerbated by induction drugs like oxytocin.

CONTRAINDICATIONS[40]

Absolute contraindications :

- ‘The patient is not able to understand the concept behind PCA
- Systemic infection or diseases at the site of PCA placement preference
- Reactions allergic to the prescribed drug
- Trauma or burns in the PCA placement area
- Neurological deficiencies that existed prior to the anticipated placement of an indwelling nerve catheter
- Elevated ICP during the insertion of an epidural catheter

Relative contraindications include:

- Chronic renal failure
- antithrombotic therapy

- Bleeding disorder
- Sleep apnea

While there are many different types of PCA pumps available, they all have the same basic features: a patient button, programming screen, medication chamber, and locking device. A medical professional will insert a syringe with medication into the pump and set its parameters, including the PCA dose, lockout interval, continuous infusion rate, initial loading dose and limits. The drug line is then attached to a fluid infusion line for intravenous PCA.

COMPLICATIONS

Complications associated are “run-away” pumps, failure to use anti-reflux valves, incorrect syringe placement, PCA by proxy and machine tampering.[40]

It has been demonstrated that PCA treatment increases patient satisfaction and is more successful at controlling pain than non-patient controlled opioid injections.

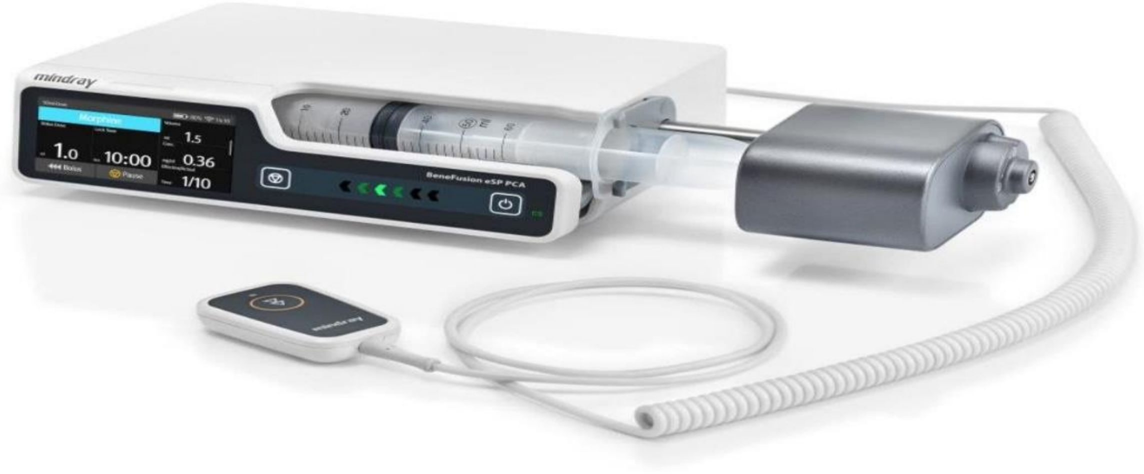


Figure 12. PATIENT CONTROLLED ANALGESIA PUMP

THE APGAR SCORE [44,45,46,47,48,]

The standard method for assessing neonates is the Apgar score, which is a standardized evaluation of a newborn condition right after birth and how they react to resuscitation measures.

INTRODUCTION

In order to rapidly assess the clinical condition of a newborn infant at one minute of age and the necessity of immediate care for establishing breathing, Dr.Virginia Apgar developed a scoring system in 1952. After that, Dr. Apgar released a second study with more patients in it. For newborns, this scoring method offered a uniform evaluation following birth.

The five components of the Apgar score are color, heart rate, reflexes, muscle tone and respiration.[45] A score of 0, 1, or 2 is assigned to each of these components. The clinical indicators of newborn depression, such as cyanosis or pallor, bradycardia, hypotonia, apnea or gasping respirations and a reduced reflex reaction to stimulus, are thus measured by the Apgar score. All newborns have their score reported at 1 and 5 minutes after birth; infants with a score below 7 have their score reported at 5-minute intervals until 20 minutes after birth.

INDICATIONS

All newborns should have their Apgar scores recorded in the clinical record at one and five minutes. The American College of Obstetrics and Gynecology and the American Academy of Pediatrics recommend expanded Apgar score recording in infants scoring less than seven in order to track their response to resuscitation.[46]

CONTRAINDICATIONS

There are no known contraindications to using Apgar score when evaluating neonates. Under specific circumstances (such as a newborn who requires immediate surgery or paralysis), the score might not accurately represent the underlying physiology.

The following evaluation is used to determine the score:

BREATHING EFFORT

The respiratory score is zero if the newborn is not breathing.

The respiratory score is 1 if breathing is weak, irregular or gasping.

The newborn respiratory score is two if they are crying uncontrollably. [45]

HEART RATE

The most important factor in evaluating if resuscitation is necessary is heart rate, which is assessed using an ECG or stethoscope.

The heart rate score is 0 in the absence of a heartbeat.

Heart rate score is 1 if heart rate is less than 100 beats per minute.

When the heart rate exceeds 100 beats per minute, the heart rate score is 2.[45]

MUSCLE TONE

The muscle tone score is 0 in inactive neonates with loose and floppy muscle tone.

Muscle tone in newborns with some flexion and tone is scored at 1.

The muscle tone score is 2 in newborns moving actively and having flexed muscles that are resistant to extension.[45]

GRIMACE RESPONSE OR REFLEX IRRITABILITY IN RESPONSE TO STIMULATION

The reflex irritability reaction score is 0 in a newborn who is not responding to stimulus. [45]

A newborn with a reflex irritability response score of 1 will grimace in reaction to stimulus.

The reflex irritability reaction of a newborn that sneezes, coughs, or screams in response to stimulation is 2.

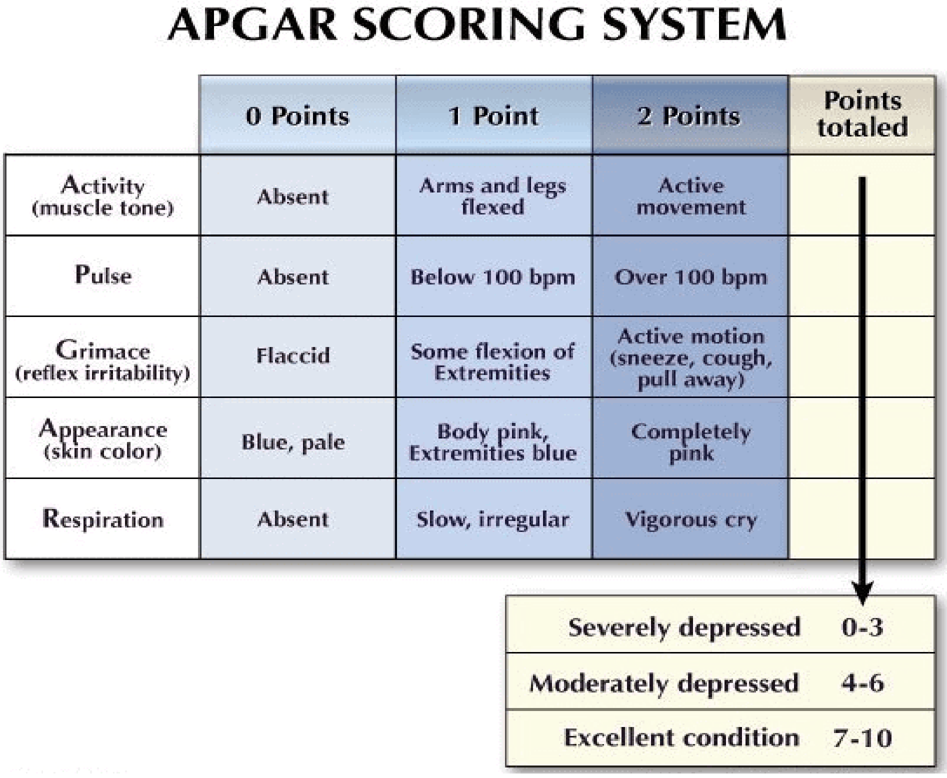
COLOR

Even at the 5-minute mark, the majority of newborns will receive a 1 for color since peripheral cyanosis is typical for healthy newborns.

The neonate receives a zero for color if they are blue or pale.

The infant receives a score of 1 for color if their extremities are blue but they are pink.

The neonate receives a 2 for color if they are completely pink.



APGAR SCORING SYSTEM

	0 Points	1 Point	2 Points	Points totaled
Activity (muscle tone)	Absent	Arms and legs flexed	Active movement	
Pulse	Absent	Below 100 bpm	Over 100 bpm	
Grimace (reflex irritability)	Flaccid	Some flexion of Extremities	Active motion (sneeze, cough, pull away)	
Appearance (skin color)	Blue, pale	Body pink, Extremities blue	Completely pink	
Respiration	Absent	Slow, irregular	Vigorous cry	

Severely depressed	0-3
Moderately depressed	4-6
Excellent condition	7-10

Figure 13. APGAR SCORING SYSTEM

CLINICAL SIGNIFICANCE

Rather than being used as an outcome measure, Apgar scores were intended to assist in identifying newborns who need breathing support or other resuscitation techniques. In population studies, low 5-minute Apgar scores are associated with a higher risk of cerebral palsy and mortality, although they are not always linked to specific neurologic disabilities.

LIMITATIONS

It is a subjective representation of the infant's physiological state at a particular moment in time. Maternal sedation or anaesthesia, congenital abnormalities, gestational age, trauma, and inter-observer variability are just a few of the variables that can affect the Apgar score.[45] Tone, color and reflex irritability are examples of subjective score elements that partially dependent on the infant's physiologic maturity.

VISUAL ANALOG SCALE SCORE[71]

In 1921, Hayes and Patterson developed the visual analog scale (VAS) to measure pain. In clinical and epidemiologic research, it is commonly used to measure the prevalence or severity of specific symptoms. The VAS is a one-dimensional measure of pain intensity that may be used to compare the amount of pain felt by patients with similar conditions or to monitor a patient's pain progression. A wide range of adult populations, such as those with cancer, rheumatoid arthritis, chronic pain and allergic rhinitis, have made substantial use of VAS. In addition to mood, hunger, asthma, dyspepsia and ambulation, it has also been used to rate pain. It is an easy-to-use, trustworthy and beneficial tool for assessing the management of illness.[71]

In order to depict a continuum between the two extremes of the scale, a single handwritten mark is placed at one position along a 10-cm line: "no pain" is on the left end (0 cm) and "worst pain" is on the right (10 cm). Based on self-reported measurements of symptoms, the scores are calculated. The patient's discomfort is measured from the left end of the scale to their markers, and the results are expressed in millimeters.[71]

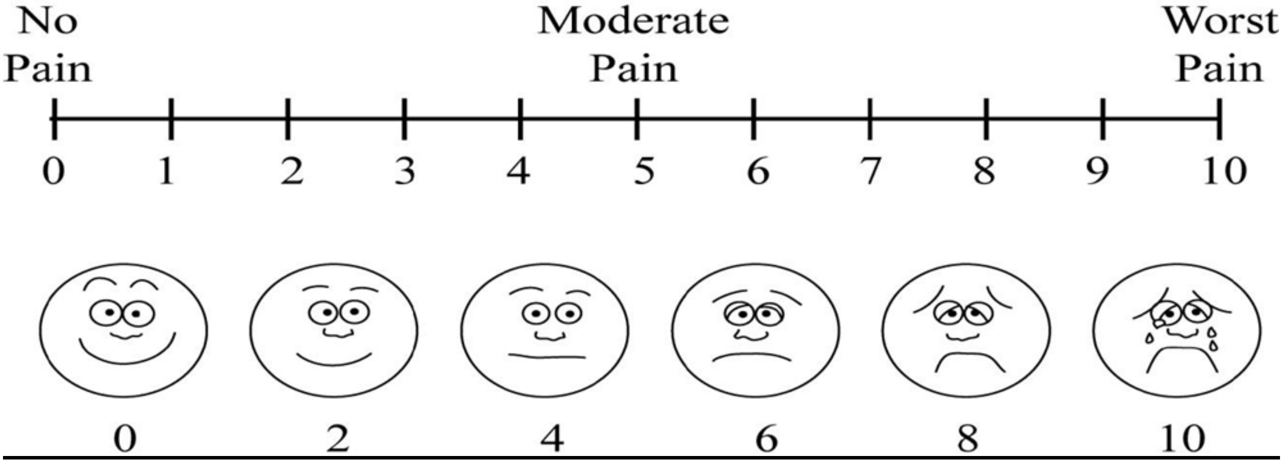


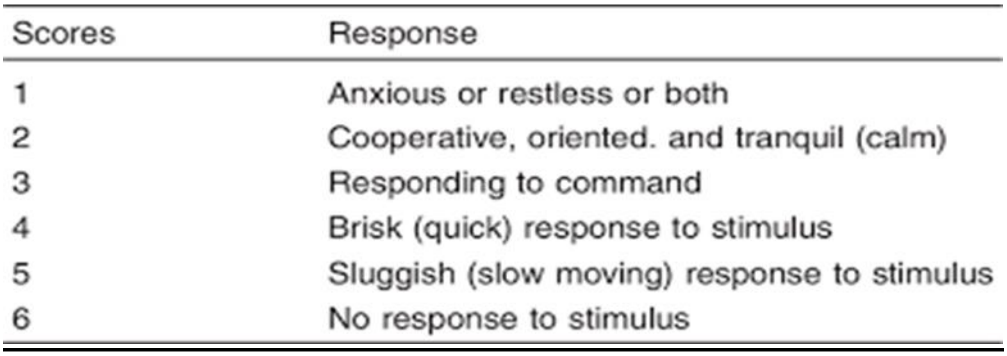
Figure 14. VISUAL ANALOG SCALE (VAS) SCORE

RAMSAY SEDATION SCALE SCORE [72]

One of the most used sedation measures is the Ramsay Sedation Scale.Six categories are used to classify a patient's state of sedation, ranging from no response to stimuli to severe agitation.

Using a sedation evaluation tool can increase the accuracy of administering drugs causing sedation. This may result in fewer instances of over-sedation and more instances of adequate sedation, as well as lower dosages of sedatives and analgesics, shorter periods of mechanical breathing and maybe even lower usage of vasopressor drugs.[72]

Ramsay Sedation Scale scores are assessed in the following order: behavior observation (scores 1 or 2), speech response assessment (score 3), loud auditory stimulus assessment (scoring 4 to 6) and if necessary, evaluation of reaction to light glabellar tap.



Scores	Response
1	Anxious or restless or both
2	Cooperative, oriented. and tranquil (calm)
3	Responding to command
4	Brisk (quick) response to stimulus
5	Sluggish (slow moving) response to stimulus
6	No response to stimulus

Figure 15. RAMSAY SEDATION SCALE SCORES

FETAL EFFECT OF LOCAL ANAESTHETICS

All the local anaesthetics pass through the placenta to a certain extent. Placental transfer is dependent on the fetal and maternal protein binding, flow of placental blood and drug permeability.[50]The extent of maternal protein binding is the determining factor for amount of free drug for transfer. Free unionised base is essential for penetration of membrane and is dependant on pKa of the drug at a given pH. The fetal effects of local anaesthetics are because of the amount of free cation present in the plasma of fetus which is dependant on pka of drugs and fetal protein binding.[51]

The combination of local anaesthetic with epidural opioids help to reduce the concentration of local anaesthetic requirement and behave as synergistic with local anaesthetics because the two drugs act on different sites.[51]

The gold standard at delivery for understanding uteroplacental function and fetal acid-base status is cord blood gas analysis. The pH, base excess and pCO2 of the umbilical artery specify the fetal status and the early neonatal time, the measurements of the umbilical vein indicate the placental and maternal acid-base balance.[49]

A meta-analysis comparing epidural and systemic opioid analgesia was completed by Reynolds et al. [52] in order to investigate the impact of these anaesthetic procedures on the acid-base status at delivery. They came to the conclusion that an improvement in base excess was linked to epidural analgesia, indicating that placental exchange is successfully protected using this method.

Prior to placental transfer, local anaesthetic drugs given epidurally must be absorbed into the systemic circulation in order to have an effect on the fetus. Because they are weak bases, local anaesthetics ionize to relatively modest degrees at physiological pH. Although they have a high degree of protein binding, both ropivacaine and buprivacaine are extremely lipid soluble. Large epidural venous plexuses allow for some systemic absorption, which is then transferred via simple diffusion over the placenta.[53]

All opioids cross the placenta in significant quantities. Fentanyl is very lipid soluble and can rapidly cross the placenta. Venkata HG et al suggested that the baby may not be significantly affected by the fentanyl dosage that was given during pregnancy. They are able to lower the incidence of episodes of hypotension and poor newborn result by lowering the dosages of bupivacaine and adding fentanyl.[54] Following intrathecal delivery of dexmedetomidine, Fyneface-Ogan et al. observed negligible changes in baseline fetal heart rate, pH of umbilical venous blood and APGAR score.[37]

Studies have shown negligible effects of local anaesthetics on fetal outcome even though placental transfer of drugs is found.

MATERIALS AND METHODS

SOURCE OF DATA

This study was carried out in the Labor Room Complex, B.L.D.E (DU) Shri. B.M. Patil Medical College, Hospital and Research centre, Vijayapura

METHOD OF COLLECTION OF DATA

STUDY DESIGN: A Randomised Clinical Trial

STUDY PERIOD: From September 2022 to April 2024

STUDY SIZE: 68 (GROUP RD -34, GROUP RS-34)

SAMPLE SIZE CALCULATION

Using G*Power ver. 3.1.9.4 software for sample size calculation, The Gestational age(weeks) for Group RF (Mean=37.41,SD=3.94), Group RD (Mean=39.10,SD=0.91),this study required a total sample size of 68 (for each group 34 with equal group sizes).So to achieve a power of 80% for detecting a difference means(t-tests - Means: Difference between two independent means (two groups) with a 5% level of significance.

STATISTICAL ANALYSIS

The data obtained is entered in a Microsoft Excel sheet and statistical analyses are performed using a statistical package for the social sciences (SPSS) (Version 20).Results are presented as Mean, SD, counts and percentages and diagrams. For normally distributed continuous variables between the two groups were compared using an independent sample t-test. For not normally distributed variables, the Mann-Whitney U test was used. For Categorical variables between the two groups are compared using the Chi-square test/Fisher's exact test. If $p<0.05$ was considered statistically significant.

RANDOMISATION

Done using Computer Generated Randomisation Table into two groups

1) Group RD: receive 0.1% Ropivacaine +0.5 mcg/ml Dexmedetomidine
2) Group RF: receive 0.1% Ropivacaine + 2 mcg/ml Fentanyl

Results was recorded using a preset performance

STUDY POPULATION

Primigravida at term gestation, with cephalic presentation between the age group of 19-35, with no known comorbidities or obstetric complications in the active phase of labor, willing for epidural analgesia.

INCLUSION CRITERIA:

- Primigravida with cephalic presentation
- A.S.A. grades I and II
- Maternal age 19 to 35 years

- Term gestation more than or equal to 35 weeks
- Single fetus
- Cervical dilatation >/= 4 cm

EXCLUSION CRITERIA

- Hypotension /Hypertension
- Obesity
- Endocrine diseases
- Fetal compromise
- Preterm gestation
- Coagulopathies
- Allergy to study agents
- Contraindications to epidural analgesia

The patient was excluded from the study if epidural anaesthesia fails or the epidural catheter got dislodged or an inadvertent epidural puncture occurred.

METHODOLOGY

Institutional review board approval was sought for the study. CTRI registration was done (CTRI registration number: CTRI/2023/06/053707). Informed consent was obtained from all patients before the procedure.

PREANAESTHETIC EVALUATION

Pre anaesthetic evaluation consists of:

HISTORY

History of underlying medical condition, previous history of surgery, anaesthetic exposure and hospitalization elicited.

PHYSICAL EXAMINATION

- General condition of a patient
- Vital parameters -heart rate, blood pressure, respiratory rate, oxygen saturation
- Height, weight and BMI
- Examination of Spine, respiratory system, cardiovascular system and central nervous system.
- Airway assessment by Mallampati grading

Procedure was explained to the patients and patient attenders.

INVESTIGATIONS

Routine investigations included complete blood count including platelet count, bleeding time, clotting time, urine routine, HIV, HBsAg, random blood sugar, blood grouping and typing.

PROCEDURE

- All primigravida undergoing vaginal delivery and willing for epidural labor analgesia in B M Patil Medical College and Hospital were considered. The patient was evaluated whether she fits into the inclusion criteria.

- Written informed consent was obtained from all the included parturient women.

- Participants were assigned to 2 groups using computer generated randomisation table:

1. Group RD receiving 10 ml 0.1% Ropivacaine +0.5 mcg/ml Dexmedetomidine
2. Group RF receiving 10 ml 0.1% Ropivacaine + 2 mcg/ml Fentanyl

- The same anaesthesiologist group performed all procedures to eliminate any possible effects of the anaesthetic technique.

PREPARATION OF THE PARTURIENT

- The parturient was prepared in accordance with the standard delivery protocols.

- The back was prepared in order to perform the epidural block. Prior to initiating the epidural block, the attending obstetrician evaluated the pelvic adequacy for vaginal birth and the degree of cervical dilatation.

- After the parturient was examined, the baseline blood pressure, heart rate and room air saturation were recorded.

- The non-dominant hand was used to secure an 18G cannula to an intravenous line and 500 ml of Ringer lactate solution was preloaded into the parturient.

- Standard monitoring of hemodynamic parameters was ongoing.

PERFORMING THE BLOCK

- When cervical dilatation reached 4 cm or more, the parturient was positioned in a sitting posture. The back was cleaned with povidone iodine and skin contact was kept for 3 minutes.

- Epidural analgesia was performed at the L2/L3 or L3/L4 intervertebral space using an 18 G epidural needle to insert an epidural catheter 3-4 cm into the epidural space.

- A skin wheal was raised in midline over this space and the subcutaneous tissues were infiltrated with 5 ml of 2% lignocaine with a 23G hypodermic needle.

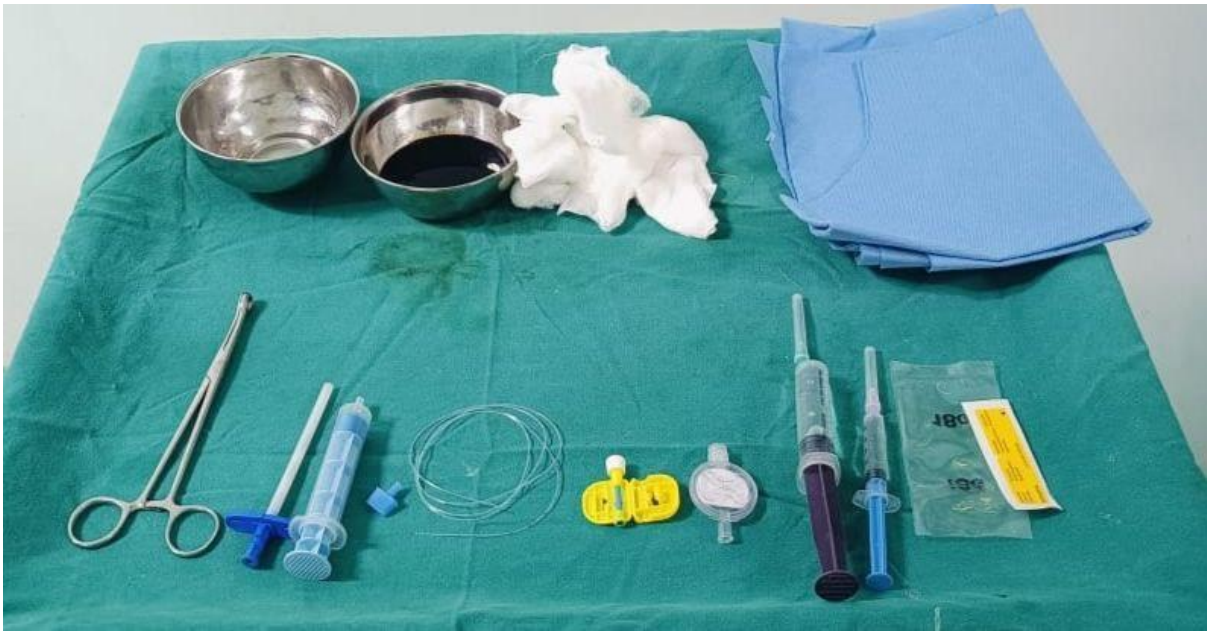


Figure 16. EPIDURAL TROLLEY

Figure 17. PERFORMING EPIDURAL BLOCK

- Epidural technique was done with18 G Tuohy epidural needle. Epidural needle placed in the space by loss of resistance technique. After the confirming the epidural space, catheter was placed with 3-4 cm inside the epidural space.

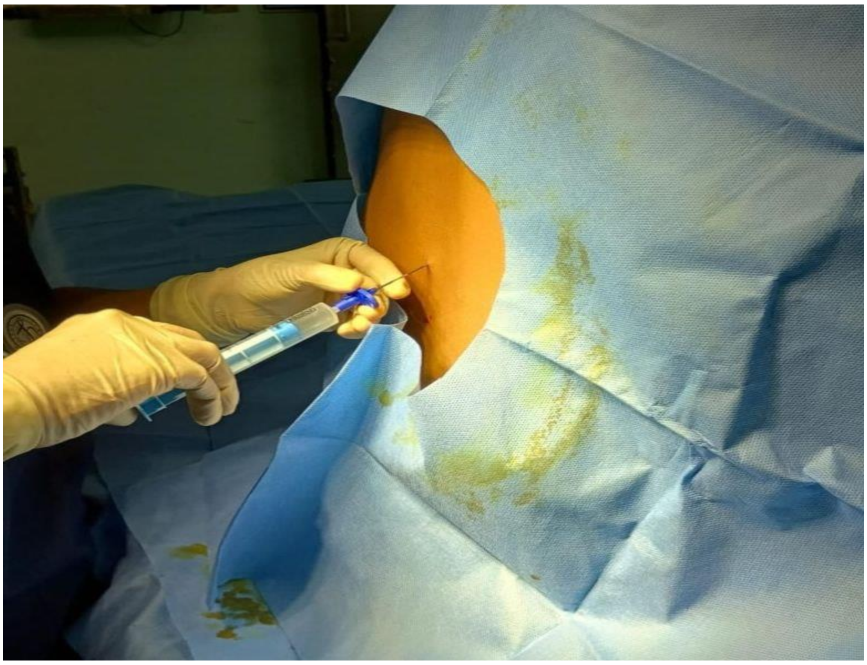


Figure 18.LOSS OF RESISTANCE TECHNIQUE

- After administering a test dose of 3 ml of 2% lignocaine with adrenaline for 5 min, parturients received 10 ml 0.5mcg/ml Dexmedetomidine (Group RD) or 2 mcg/ml Fentanyl (Group RF) together with 0.1% Ropivacaine as the loading dose.

- The parturient was turned to her back and instructed to lie down following the injection.

- The maintenance of patient-controlled epidural analgesia was administered after the loading dose using a Patient Controlled Analgesia (PCA) pump. The pump was adjusted at a pace of 7ml/h with a rescue dose of 7 ml with a set lockout interval of 25 min and limit of 25 ml/h. Patients experiencing insufficient pain relief was given an extra 5 ml bolus of the drug solution via epidural administration .

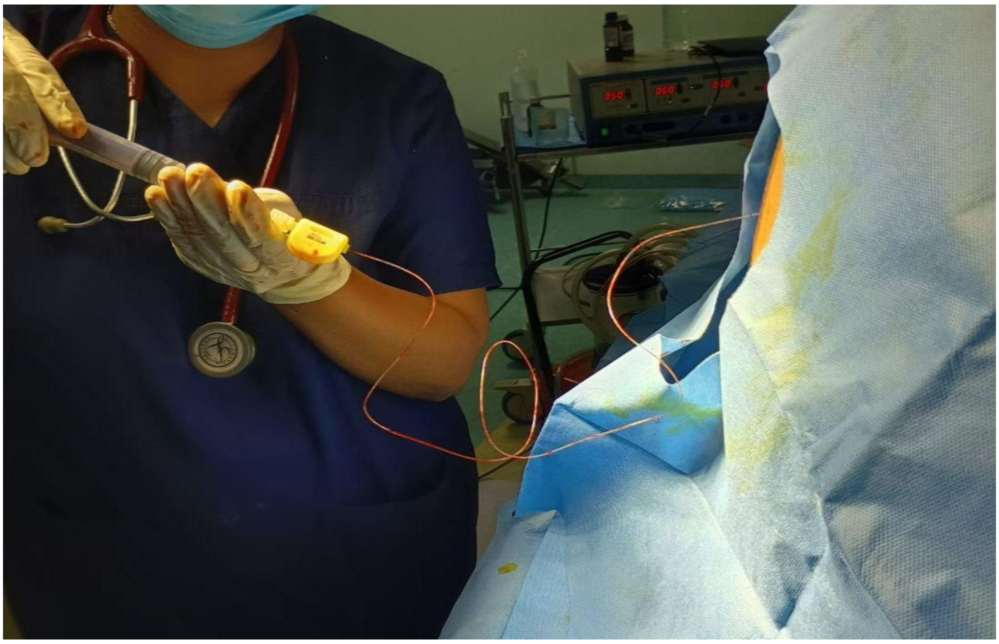


Figure 19. ADMINISTRATION OF BOLUS DOSE

- Maternal vitals such as systolic blood pressure, diastolic blood pressure, heart rate and oxygen saturation on room air was observed and noted. The labor pain was assessed using Visual Analog Scale (VAS) scores. The time of onset of action of analgesia, total local anaesthetics consumption, duration from epidural administration to delivery and Ramsay Sedation Scale (RSS) scores were noted.

- Side effects like maternal bradycardia, hypotension, nausea,vomiting, shivering, respiratory depression and pruritus were noted and managed.

- If hypotension was seen, the mother was put on a left-lateral posture or phenylephrine was given as an active vasoconstricting agent.

- The Visual Analog Scale score (0 shows no pain and 10 indicate the most unbearable pain) was evaluated before epidural insertion (taken as baseline VAS) and at 5, 10, 20, 30, 60, 90 and 120 min after the initial bolus drug combination was injected. The time of the initial bolus was taken as 0 min.

- The time of onset of analgesia was defined as the time between the end of the bolus dose administration and mother showing a VAS score< 3. Duration of the labor was defined as time from epidural administration to delivery of the baby. Rescue analgesia doses in each group were monitored.

- The adverse effects were defined as: respiratory depression when SpO2 falls <90% on room air; hypotension – reduction in systolic blood pressure >20% from baseline (before analgesia) or blood pressure below 90/60 mmHg; maternal bradycardia – heart rate reduction >20% from baseline (before analgesia) or below 60 beats per minute.

- The level of sedation was evaluated using the Ramsay Sedation Scale score.RSS values were recorded for each hour during labor. Excessive sedation was defined as a value of RSS value >4.

- The attending obstetrician assessed the labor progress in terms of cervical dilation, effacement, and station of head. Fetal monitoring was done continuously by Non Stress Test.

- After delivery, the epidural infusion using pump was discontinued and the epidural catheter was removed.

- The neonates were evaluated using the Apgar score. The total score of Apgar score is 10, which is depending on five signs of neonatal activity, pulse, grimace, appearance and respiration (10= normal newborn; <7= mild asphyxia; <4= severe asphyxia).[45]

RESULTS

- Data collected from the study was entered in Microsoft office excel sheet and was analysed by standard statistical software.
- The results were summarised by descriptive statistics like mean and standard deviation for numerical variables and counts and percentage for categorical variables. Numerical variables are compared between groups by Mann-Whitney U test. Chi square test was employed for intergroup comparison of categorical variables. Analysis was done and p value <0.05 was considered statistically significant.

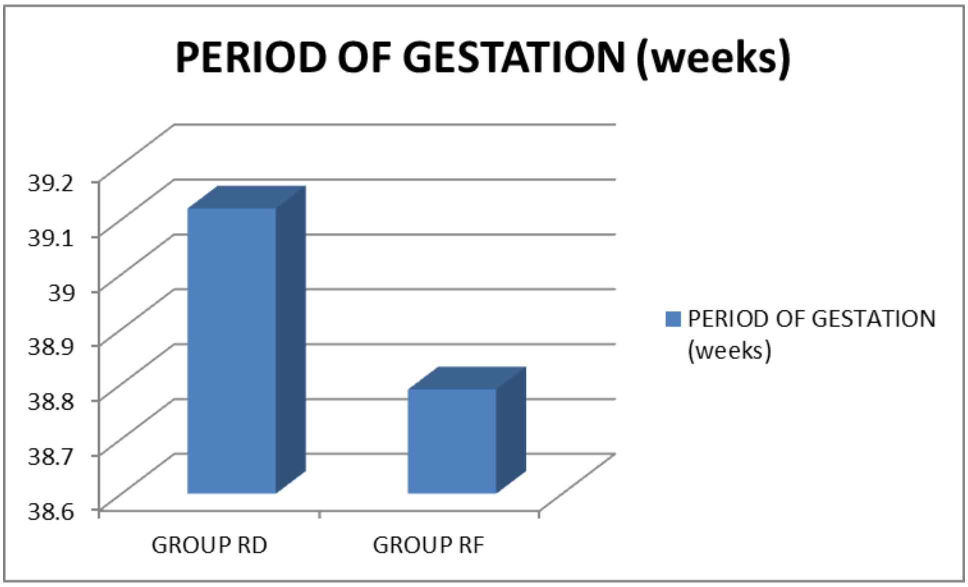
DEMOGRAPHIC BASELINE VARIABLES

The following table and bar diagrams describe the demographic variables among the patients in group RD and group RF.

Table 1. DEMOGRAPHIC VARIABLES AMONG BOTH GROUPS

DEMOGRAPHIC DATA	GROUP RD (n=34)		GROUP RF (n=34)		Mann-Whitney U test	p value
	Mean	Standard Deviation	Mean	Standard Deviation		
PERIOD OF GESTATION (weeks)	39.12	1.29	38.79	1.25	516.50	0.43
HEIGHT (cms)	152.44	3.39	151.24	3.47	457.00	0.14
WEIGHT (kgs)	64.44	6.51	61.59	5.96	451.50	0.12
BMI (kg/m2)	27.62	2.33	26.85	2.19	498.00	0.33

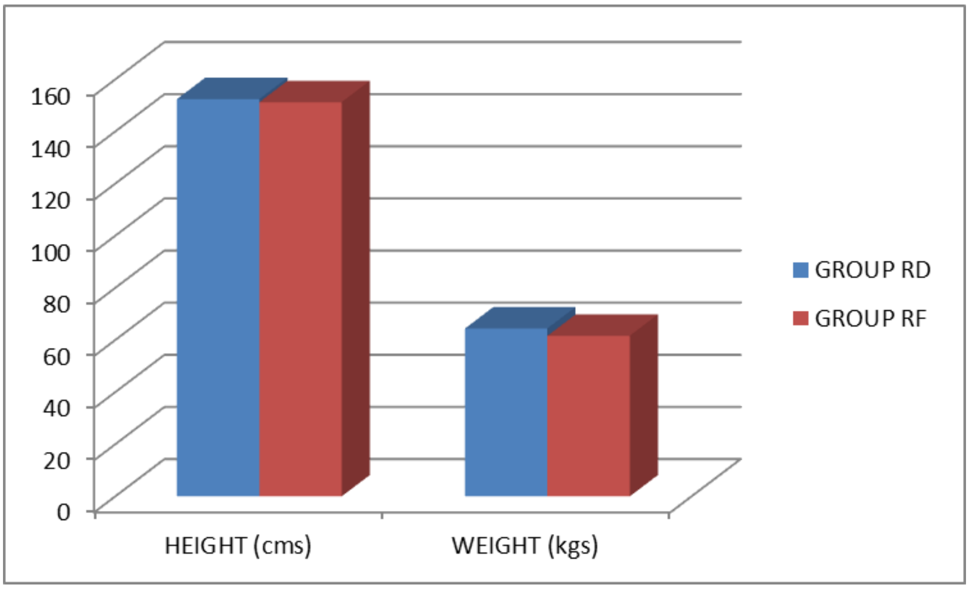
Graph 1. COMPARISON OF PERIOD OF GESTATION IN WEEKS



In group RD, the mean period of gestation is 39.12± 1.29 weeks and in group RF, the mean period of gestation is 38.79± 1.25 weeks.

The two groups are comparable in period of gestation with P value 0.434 which is **statistically insignificant.**

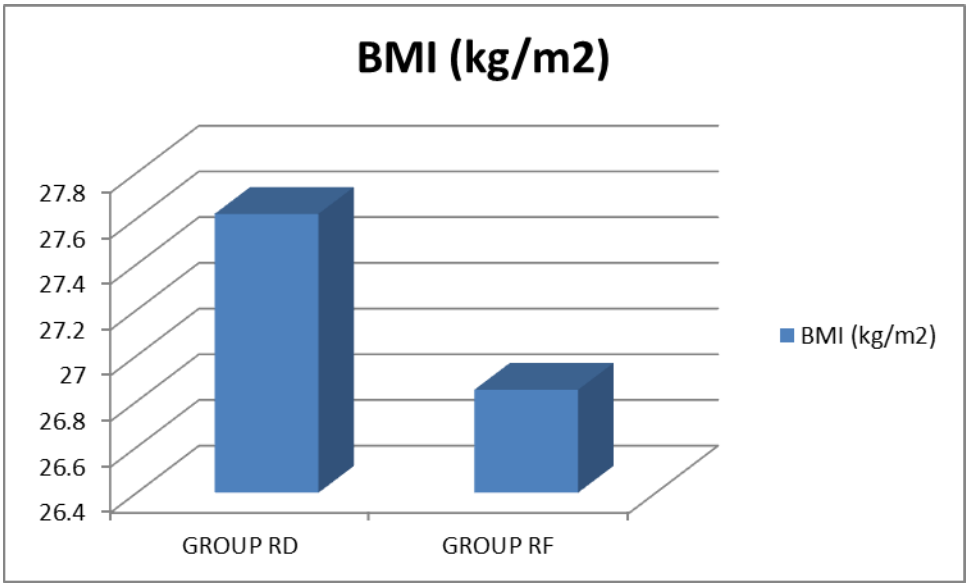
Graph 2. COMPARISON OF HEIGHT IN CENTIMETERS AND WEIGHT IN KILOGRAMS



In group RD, the mean height is 152.24 ± 3.39 cm and in group RF, the mean height is 151.24 ±3.47 cm. In group RD, the mean weight is 64.44 ± 6.51 kg and in group RF, the mean weight is 61.59 ±5.96 kg .

The two groups are comparable in height and weight with P value 0.14 for height and P value 0.12 for weight that are **statistically insignificant.**

Graph 3. COMPARISON OF BODY MASS INDEX IN KILOGRAM PER SQUARE METER



In group RD, the mean BMI is 27.62 ± 2.33 kg/m2 and in group RF, the mean BMI is 26.85 ± 2.19 kg/m2 .

Both groups are comparable in BMI with P value 0.33 which is **statistically insignificant.**

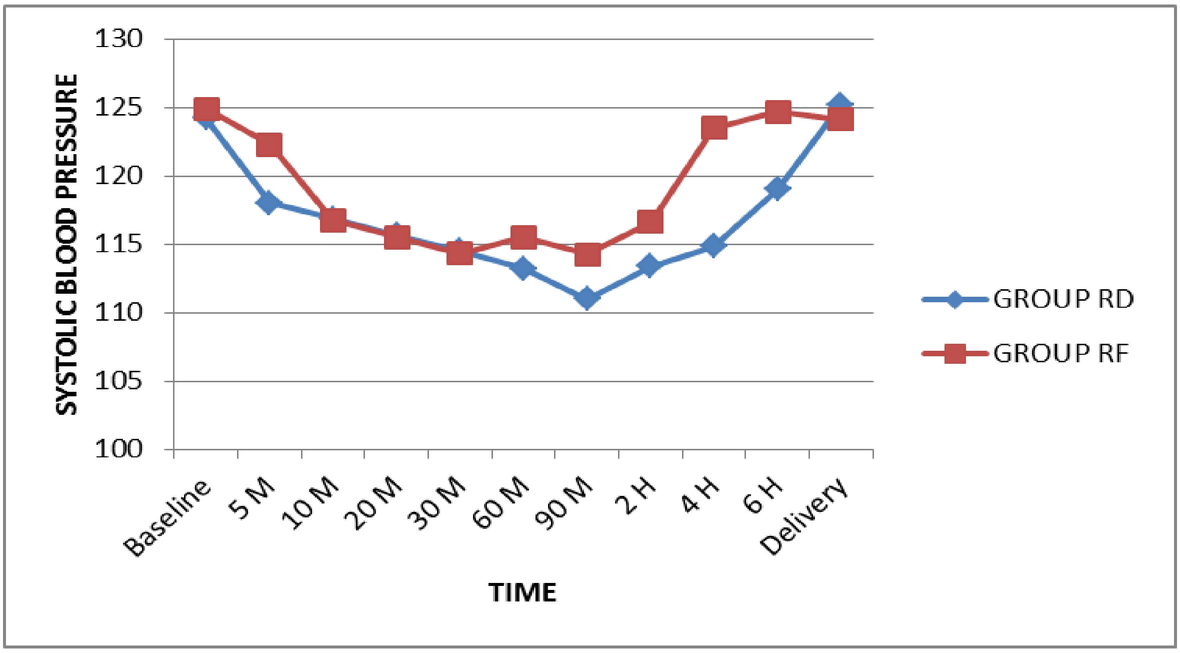
MATERNAL VITALS

The following tables and graphs compare the maternal vitals among patients in group RD and group RF.

Table 2. COMPARISON OF MATERNAL SYSTOLIC BLOOD PRESSURE

Maternal Systolic Blood Pressure	GROUP RD (n=34)		GROUP RF(n=34)		Mann-Whitney U test	p value
	Systolic BP (mmHg)	Standard Deviation	Systolic BP (mmHg)	Standard Deviation		
Baseline	124.18	8.70	124.88	8.82	569.00	0.912
5 Minutes	118	7.46	122.29	7.35	422.00	0.054
10 Minutes	116.88	6.51	116.76	6.15	564.00	0.863
20 Minutes	115.65	6.04	115.53	6.25	556.50	0.790
30 Minutes	114.53	7.81	114.29	6.41	514.00	0.438
60 Minutes	113.24	8.38	115.53	8.25	480.50	0.228
90 Minutes	111	9.50	114.24	10.01	461.00	0.149
2 Hours	113.35	7.35	116.59	7.09	453.50	0.122
4 Hours	114.81	6.60	123.47	5.86	174.00	0.001**
6 Hours	119	6.22	124.67	5.03	3.00	0.280
Delivery	125.18	8.35	124.12	6.69	532.00	0.571

Graph 4 . COMPARISON OF MATERNAL SYSTOLIC BLOOD PRESSURE(mmHg)



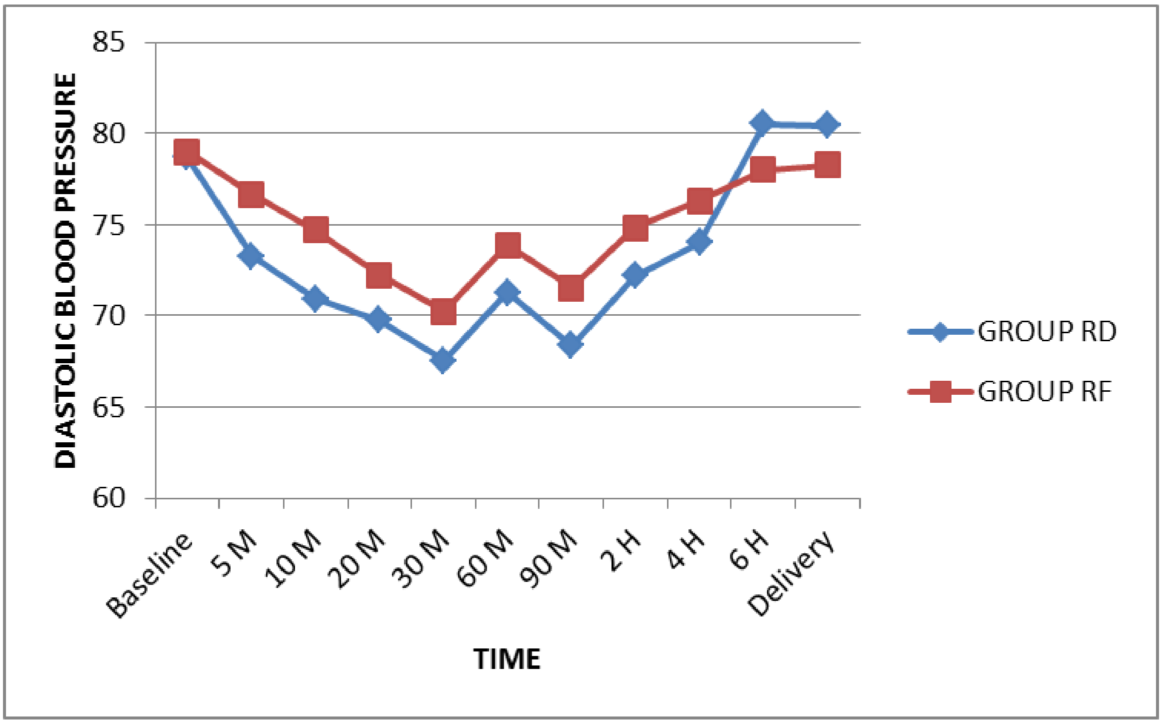
Maternal systolic blood pressure is significantly high in group RF than group RD at 4 hours ($p<0.05$) .The difference in maternal systolic blood pressure between group RD and group RF is **statistically significant at 4 hours.**

Both groups are comparable in maternal systolic blood pressure at baseline, 5 minutes, 10 minutes,20 minutes,30 minutes,60 minutes,90 minutes, 2 hours, 6 hours and at delivery and **statistical non-significant** at these time points.

Table 3. COMPARISON OF MATERNAL DIASTOLIC BLOOD PRESSURE(mmHg)

Maternal Diastolic Blood Pressure	GROUP RD (n=34)		GROUP RF(n=34)		Mann-Whitney U test	p value
	Diastolic BP (mmHg)	Standard Deviation	Diastolic BP (mmHg)	Standard Deviation		
Baseline	78.71	5.63	79	6.57	569.50	0.916
5 Minutes	73.29	5.82	76.65	6.34	419.50	0.050
10 Minutes	70.94	5.49	74.71	10.82	351.50	0.074
20 Minutes	69.76	5.18	72.24	6.14	343.50	0.076
30 Minutes	67.53	5.35	70.23	7.59	273.50	0.094
60 Minutes	71.29	6.61	73.88	6.89	369.00	0.118
90 Minutes	68.35	5.94	71.53	7.88	238.50	0.064
2 Hours	72.18	5.36	74.82	6.87	442.50	0.093
4 Hours	74	5.924	76.29	5.35	430.50	0.142
6 Hours	80.50	3.42	78	4.00	3.50	0.372
Delivery	80.41	6.69	78.24	6.13	379.50	0.167

Graph 5 . COMPARISON OF MATERNAL DIASTOLIC BLOOD PRESSURE(mmHg)

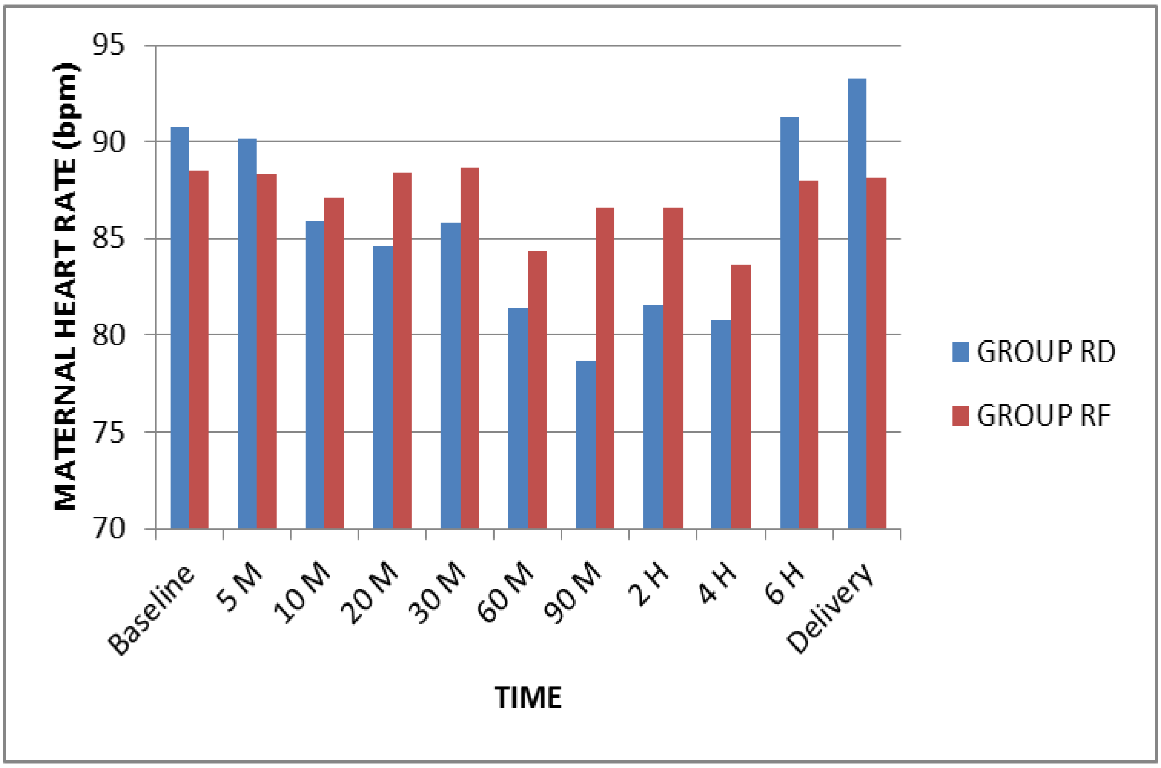


Both groups are comparable in maternal diastolic blood pressure at baseline, 5 minutes, 10 minutes,20 minutes,30 minutes,60 minutes,90 minutes, 2 hours,4 hours, 6 hours and at delivery and is **statistical non- significant** at these time points.

Table 4 . COMPARISON OF MATERNAL HEART RATE

Maternal Heart Rate	GROUP RD (n=34)		GROUP RF(n=34)		Mann-Whitney U test	p value
	Heart Rate (bpm)	Standard Deviation	Heart Rate (bpm)	Standard Deviation		
Baseline	90.79	4.63	88.53	11.12	501.50	0.347
5 Minutes	90.18	5.65	88.35	10.43	558.50	0.811
10 Minutes	85.91	7.21	87.15	10.44	541.50	0.654
20 Minutes	84.56	7.40	88.44	10.39	452.00	0.122
30 Minutes	85.79	8.01	88.65	10.51	498.00	0.326
60 Minutes	81.38	12.58	84.32	9.95	499.50	0.335
90 Minutes	78.68	11.35	86.56	10.65	363.00	0.008**
2 Hours	81.53	13.98	86.56	10.71	455.50	0.133
4 Hours	80.75	13.09	83.62	10.97	466.00	0.317
6 Hours	91.25	3.40	88	4.00	3.50	0.372
Delivery	93.29	10.19	88.15	8.81	416.00	0.057

Graph 6. COMPARISON OF MATERNAL HEART RATE (beats per minute)



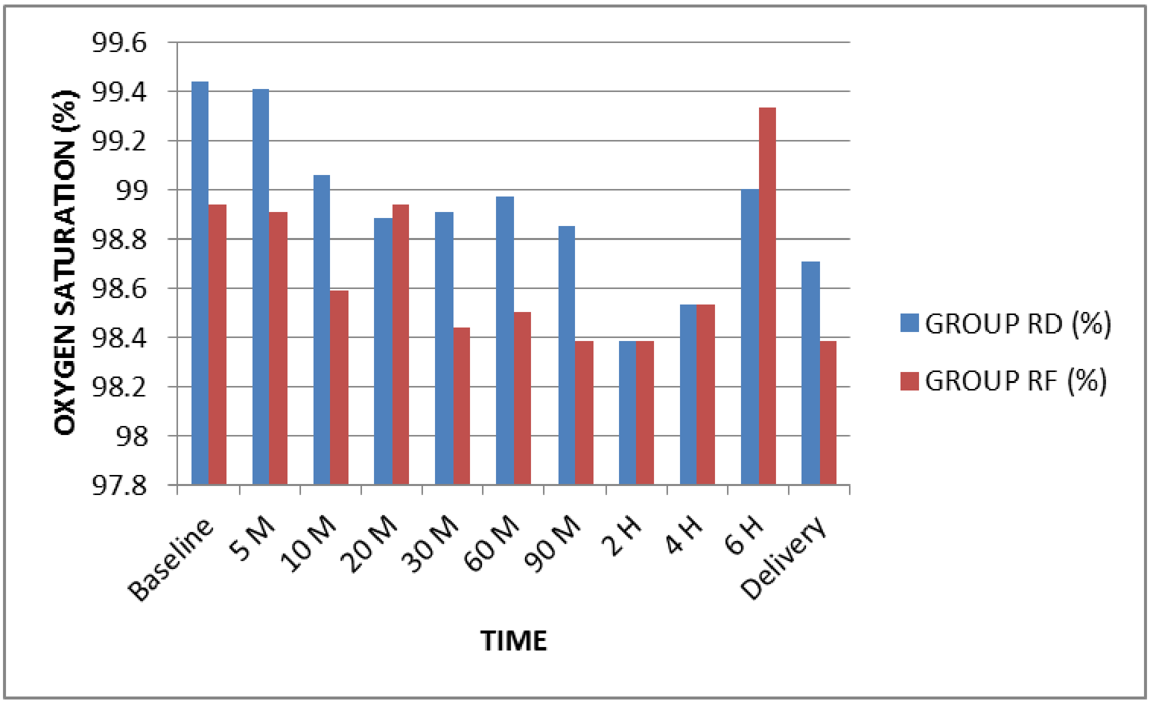
Maternal heart rate is significantly low in group RD than group RF at 90 minutes after epidural administration (p<0.05). The difference in maternal heart rate between group RD and group RF is **statistically significant** at 90 minutes.

Both groups are comparable in maternal heart rate at baseline, 5 minutes, 10 minutes,20 minutes,30 minutes,60 minutes, 2 hours,4 hours, 6 hours and at delivery and is **statistical non-significant** at these time points.

Table 5.COMPARISON OF MATERNAL OXYGEN SATURATON

Maternal SpO2	GROUP RD (n=34)		GROUP RF(n=34)		Mann-Whitney U test	p value
	SpO2 on Room Air (%)	Standard Deviation	SpO2 on Room Air (%)	Standard Deviation		
Baseline	99.44	0.71	98.94	0.81	383.00	0.070
5 Minutes	99.41	0.70	98.91	0.83	386.00	0.062
10 Minutes	99.06	0.81	98.59	1.10	441.00	0.080
20 Minutes	98.88	0.77	98.94	0.81	556.00	0.774
30 Minutes	98.91	0.83	98.44	1.13	438.50	0.075
60 Minutes	98.97	0.79	98.50	1.10	439.00	0.076
90 Minutes	98.85	0.85	98.38	1.11	432.00	0.063
2 Hours	98.38	1.18	98.38	1.12	455.50	0.990
4 Hours	98.53	0.92	98.53	1.08	466.00	0.995
6 Hours	99	0.82	99.33	0.58	4.50	0.554
Delivery	98.71	1.17	98.38	1.02	483.50	0.230

Graph 7. COMPARISON OF MATERNAL OXYGEN SATURATON (%)

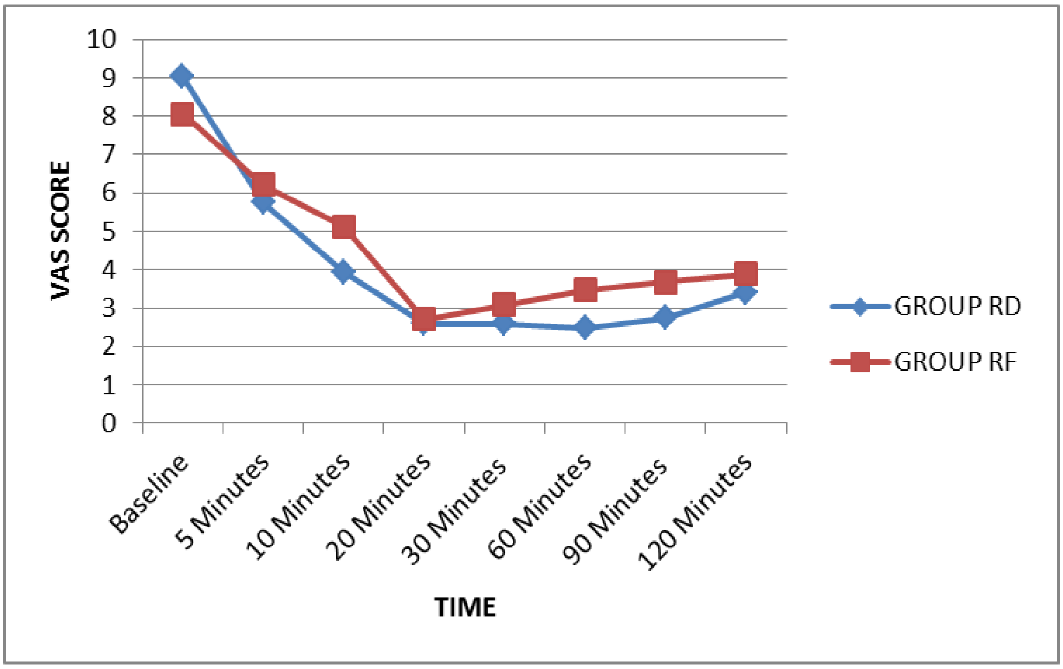


Both groups are comparable in maternal oxygen saturation at baseline, 5 minutes, 10 minutes,20 minutes,30 minutes,60 minutes,90 minutes, 2 hours,4 hours, 6 hours and at delivery and is **statistical non-significant** at these time points.

Table 6. COMPARISON OF VISUAL ANALOG SCALE SCORE

Visual Analog Scale	GROUP RD (n=34)		GROUP RF(n=34)		Mann-Whitney U test	p value
	Mean	Standard Deviation	Mean	Standard Deviation		
Baseline	9.03	5.87	8.06	0.74	527.00	0.937
5 Minutes	5.76	0.78	6.21	0.64	397.50	0.016**
10 Minutes	3.94	0.69	5.12	0.73	168.00	0.001**
20 Minutes	2.59	0.50	2.71	0.46	510.00	0.314
30 Minutes	2.59	0.50	3.09	0.45	324.00	0.001**
60 Minutes	2.47	1.02	3.47	0.56	191.00	0.001**
90 Minutes	2.74	0.86	3.68	0.68	240.00	0.001**
120 Minutes	3.41	0.82	3.88	0.84	410.00	0.027**

Graph 8. COMPARISON OF VISUAL ANALOG SCALE SCORE



Visual Analog Scale Score is **significantly lower** in group RD than group RF at 30 minutes,60 minutes, 90 minutes and 120 minutes after epidural administration (VAS <3). The difference in VAS scores between group RD and group RF is **statistically significant** at 5 minutes, 10 minutes,30 minutes,60 minutes, 90 minutes and 120 minutes (p<0.05).

Both groups are comparable in VAS score at baseline and 20 minutes and is **statistical non-significant** at these time points.

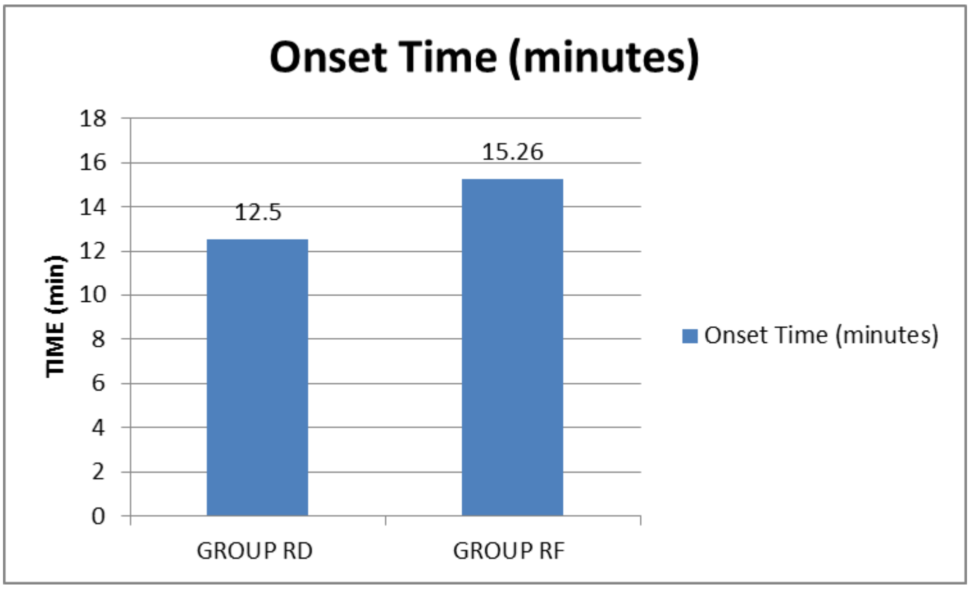
VARIABLES ASSOCIATED WITH DRUG

The following tables and bar diagrams compares onset time, local anaesthetic requirement, bolus frequency, duration of labor among patients in group RD and RF.

Table 7 . COMPARISON OF ANALGESIA ONSET TIME, LOCAL ANAESTHETIC REQUIREMENT, BOLUS FREQUENCY, DURATION OF LABOUR

VARIABLE	GROUP RD (n=34)		GROUP RF (n=34)		Mann-Whitney U test	p value
	Mean	Standard Deviation	Mean	Standard Deviation		
Onset Time of Analgesia (min)	12.50	1.31	15.26	1.46	101.00	0.001**
Total volume of anaesthetic solution (ml)	47.54	5.37	59.05	6.62	103.00	0.001**
Bolus Frequency	0.15	0.36	1.21	0.95	217.50	0.001**
Duration Between epidural and delivery of baby (min)	312.97	42.40	345.94	14.67	225.50	0.001**

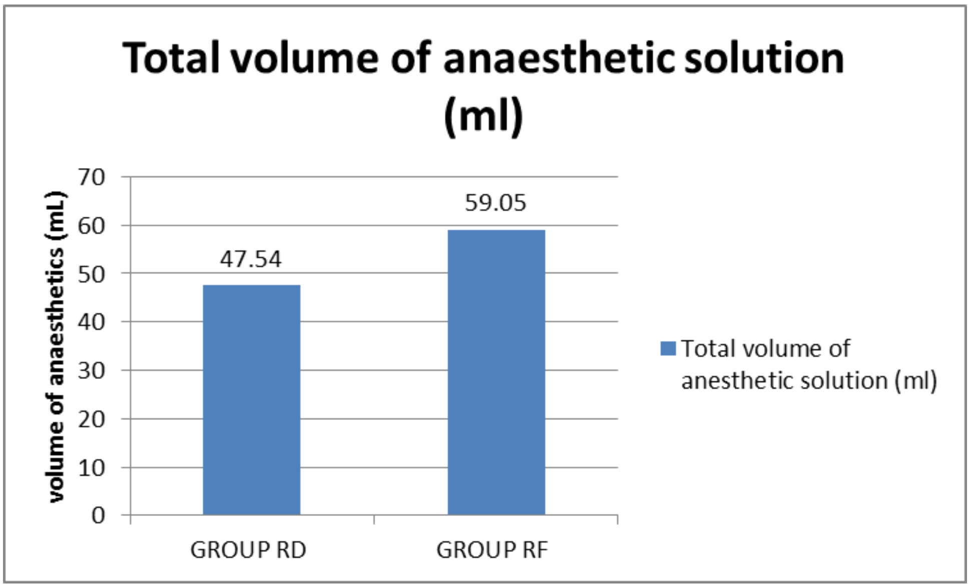
Graph 9. COMPARISON OF ONSET TIME OF ANALGESIA IN MINUTES



In group RD, the mean onset time of analgesia is 12.50 ±1.31 minutes and in group RF, the mean onset time is 15.26±1.46 minutes.

Group RD shows shorter time of onset of analgesia than group RF with P value 0.001 which is **statistically significant**.

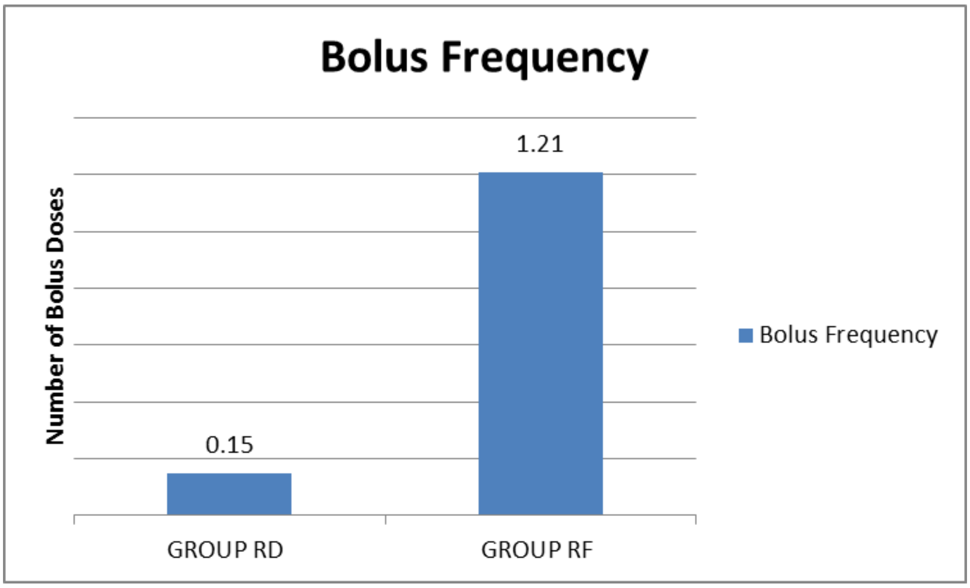
Graph 10. COMPARISON OF TOTAL VOLUME OF ANAESTHETIC SOLUTION



In group RD, the mean total volume of local anaesthetic solution required is 47.54 ±5.37 ml and in group RF, the mean total volume of local anaesthetic solution required is 59.05 ±6.62 ml.

Group RD shows lesser requirement of local anaesthetic than group RF with P value 0.001 which is **statistically significant**.

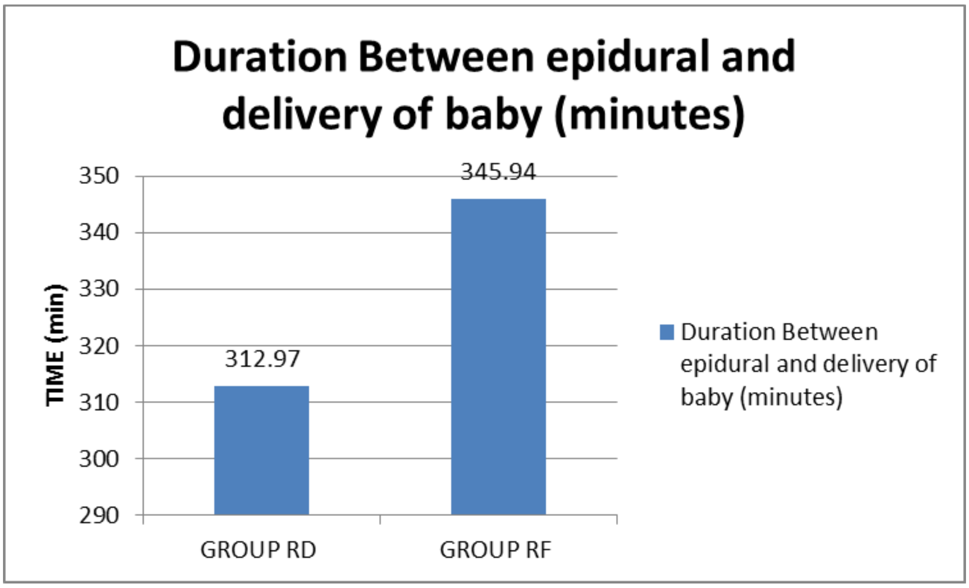
Graph 11. COMPARISON OF BOLUS FREQUENCY



In group RD, the mean bolus frequency is 0.15±0.36 and in group RF, the mean bolus frequency is 1.21 ±0.95.

Group RD shows lesser bolus frequency than group RF with P value 0.001 which is **statistically significant**.

Graph 12. COMPARISON OF DURATION BETWEEN EPIDURAL AND DELIVERY OF BABY (in minutes)



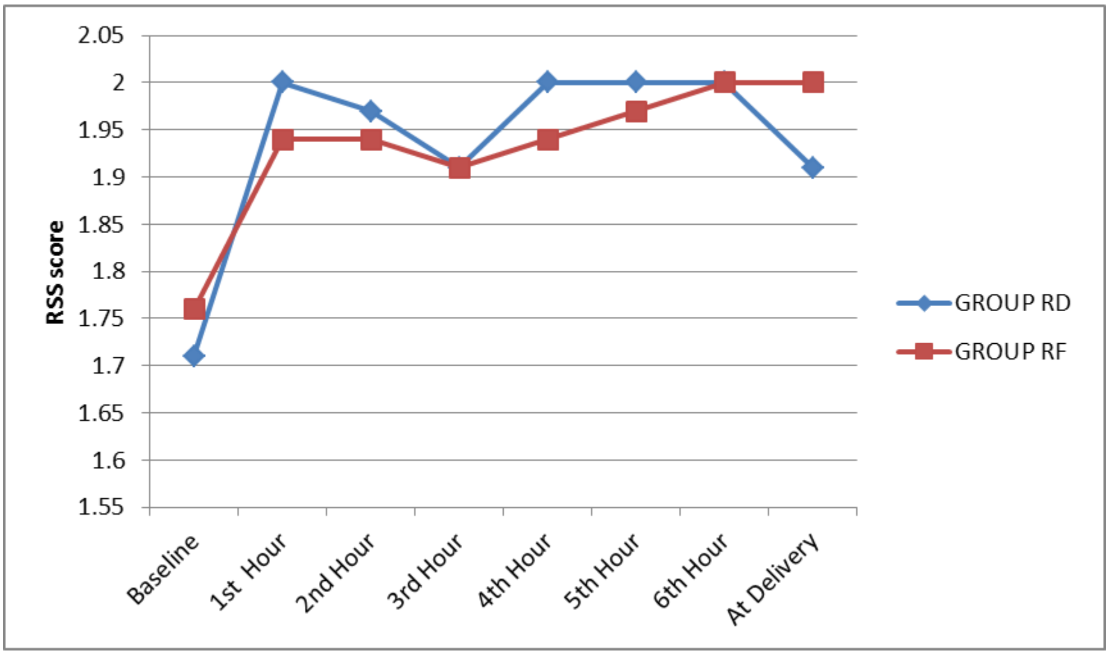
In group RD, the mean duration between epidural and delivery of baby is 312.97 ±42.40 minutes and in group RF, the mean duration between epidural and delivery of baby is 345.94 ±14.67 minutes.

Group RD shows shorter duration between epidural administration and delivery of baby than group RF with P value 0.001 which is **statistically significant.**

Table 8 . COMPARISON OF RAMSAY SEDATION SCALE SCORE

Ramsay Sedation Scale	GROUP RD (n=34)		GROUP RF (n=34)		Mann-Whitney U test	p value
	Mean	Standard Deviation	Mean	Standard Deviation		
Baseline	1.71	0.46	1.76	0.43	544.00	0.585
1st Hour	2.00	0.00	1.94	0.24	544.00	0.154
2nd Hour	1.97	0.17	1.94	0.24	561.00	0.558
3rd Hour	1.91	0.28	1.91	0.28	578.00	1.000
4th Hour	2.00	0.00	1.94	0.23	512.00	0.167
5th Hour	2.00	0.00	1.97	0.17	379.00	0.411
6th Hour	2.00	0.00	2.00	0.00	6.00	1.000
At Delivery	1.91	0.28	2.00	0.00	527.00	0.079

Graph 13. COMPARISON OF RAMSAY SEDATION SCALE SCORE



Both groups are comparable in Ramsay Sedation Scale values at baseline, 1st hour,2nd hour, 3rd hour,4th hour,5th hour, 6th hour and at delivery and is statistically **non- significant** at this time points.

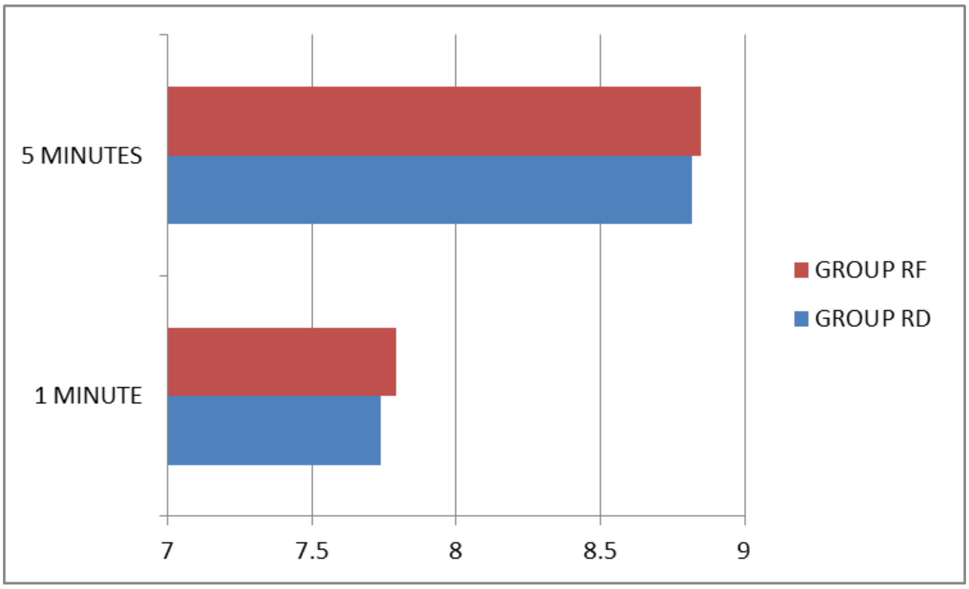
APGAR SCORE OF NEWBORN

The following tables and bar diagrams compares APGAR score among newborn in group RD and RF.

Table 9. COMPARISON OF APGAR SCORE OF BABIES

APGAR SCORE	GROUP RD (n=34)		GROUP RF (n=34)		Mann-Whitney U test	p value
	Mean	Standard Deviation	Mean	Standard Deviation		
1 MINUTE	7.74	0.51	7.79	0.48	545.00	0.565
5 MINUTES	8.82	0.39	8.85	0.36	561.00	0.744

Graph 14. COMPARISON OF APGAR SCORE OF BABIES



Both groups have comparable APGAR scores at 1 minute and 5 minutes and is **statistically insignificant**.

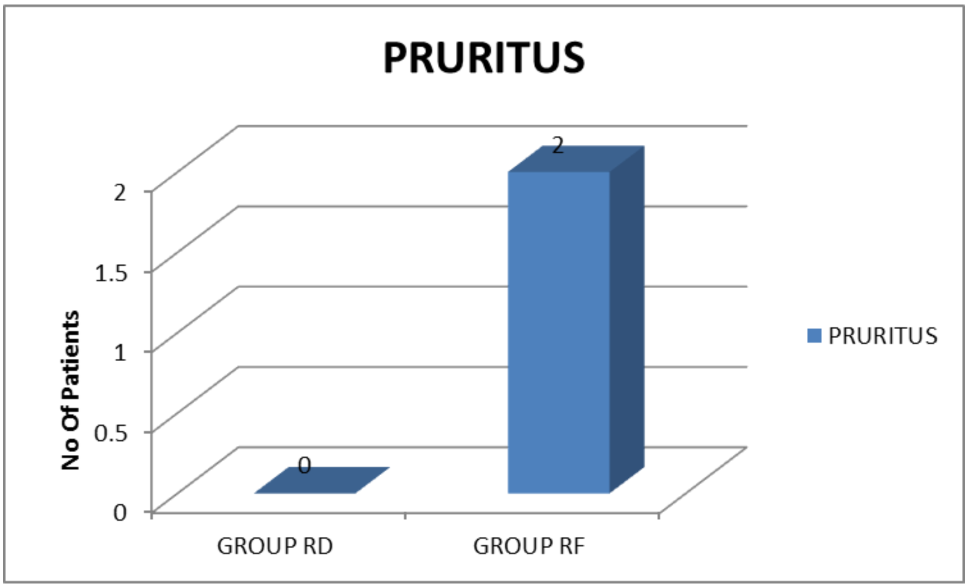
MATERNAL SIDE EFFECTS

The following tables and bar diagrams compares side effects among patients in group RD and RF.

Table 10. COMPARISON OF MATERNAL SIDE EFFECTS

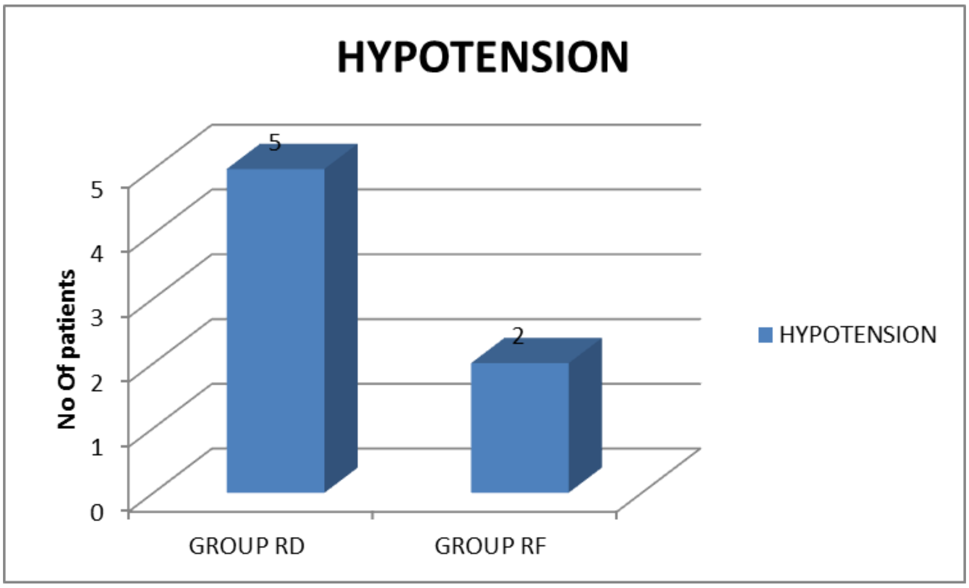
MATERNAL SIDE EFFECTS	GROUP RD (n=34) (%)	GROUP RF (n=34) (%)	Chi Square test	p value
PRURITUS	0 (0.0%)	2 (5.9%)	2.06	0.151
HYPOTENSION	5 (14.7%)	2 (5.9%)	1.43	0.231
NAUSEA/VOMITING	3 (8.8%)	5 (14.7%)	0.56	0.452
RESPIRATORY DEPRESSION	0 (0.0%)	0 (0.0%))	0	1.000
MATERNAL BRADYCARDIA	3 (8.8%)	0 (0.0%)	3.138	0.076
SHIVERING	3 (8.8%)	3 (8.8%)	0.00	1.000

Graph 15. COMPARISON OF MATERNAL PRURITUS



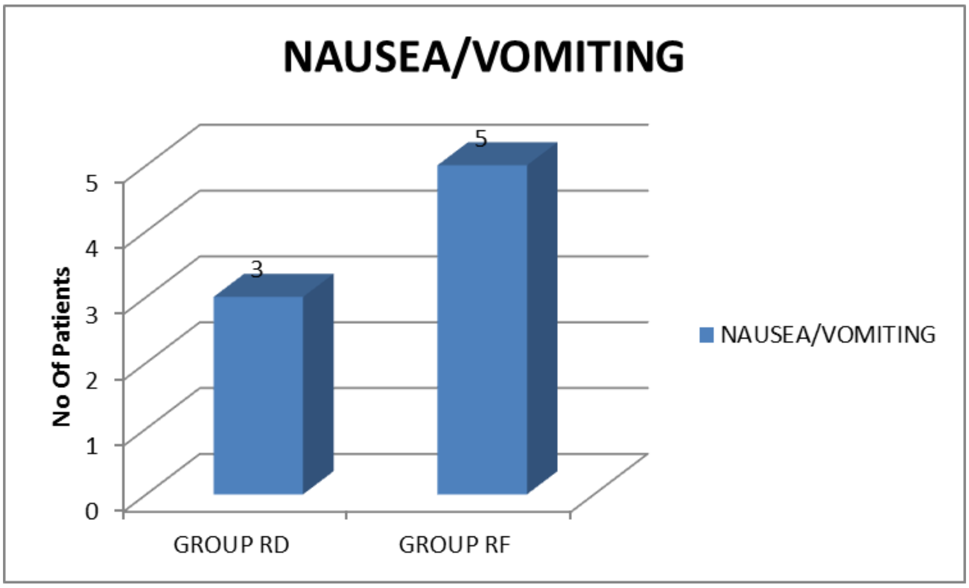
Pruritus was seen in no patients in group RD (0.0%) and 2 in group RF (5.9%). Group RF showed pruritus more than group RD which is **statistically insignificant** (p>0.05).

Graph 16. COMPARISON OF MATERNAL HYPOTENSION



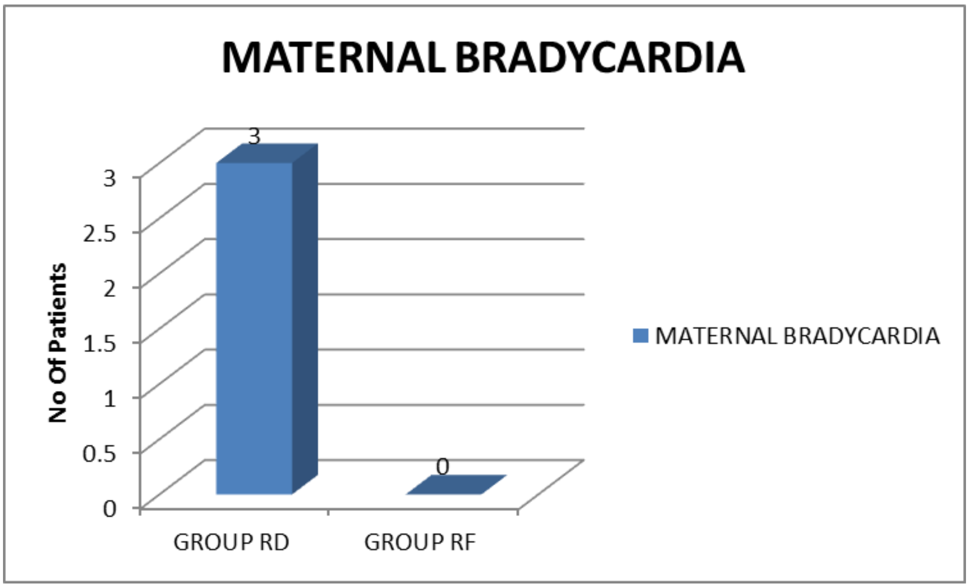
Hypotension was seen in 5 patients in group RD (14.7%) and 2 in group RF (5.9%).Group RD showed hypotension more than group RF which is **statistically insignificant** (p>0.05).

Graph 17. COMPARISON OF NAUSEA AND VOMITING



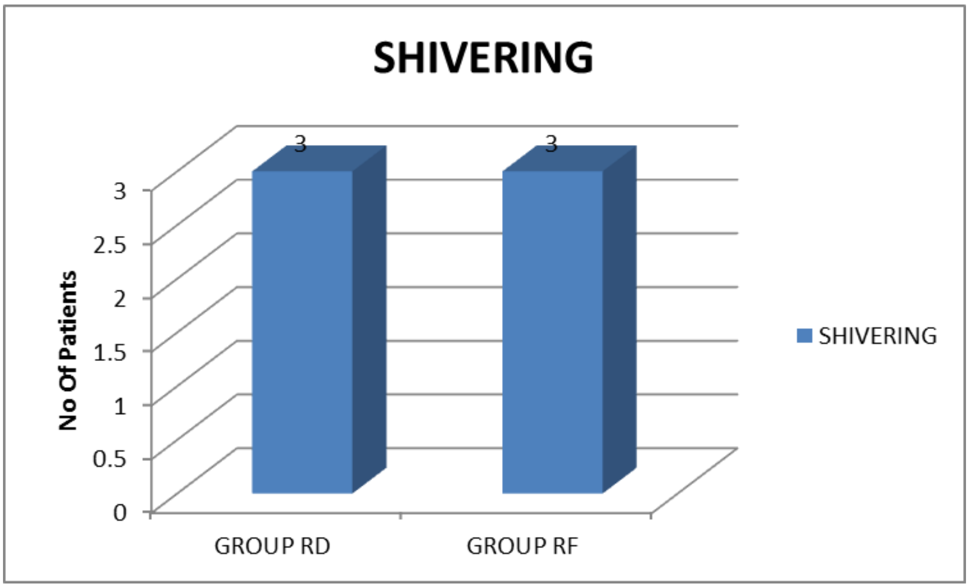
Nausea/vomiting was seen in 3 patients in group RD (8.8%) and 5 in group RF (14.7%).Group RF showed nausea/vomiting more than group RD which is **statistically insignificant** (p>0.05)

Graph 18. COMPARISON OF MATERNAL BRADYCARDIA



Bradycardia was seen in 3 patients in group RD (8.8%) and none in group RF (0%).Group RD showed maternal bradycardia more than group RF which is **statistically insignificant** (p>0.05).

Graph 19. COMPARISON OF SHIVERING



Shivering was seen in 3 patients in group RD (8.8%) and 3 in group RF (8.8%).Both group are comparable in shivering and is **statistically insignificant** (p>0.05).

- Respiratory depression was not observed in any patient in both group RD and RF throughout the procedure.

DISCUSSION

Labor analgesia is a challenging path with gratifying outcomes. From chloroform in the 19th century to automated central neuraxial delivery systems in the 21st century, labor analgesia has evolved. The ideal drug for pain management during labor should provide a desirable sensory blockage with no motor block, no tachyphylaxis and unintended overdose or accidental intravenous delivery should have a suitable safety range.

The technique of epidural analgesia, which involves blocking a central nerve by injecting local anaesthetics close to the pain-transmitting nerve, is a popular choice for labor analgesia due to its clear benefits, high level of safety and ease of operation. Because epidural labor analgesia employs anaesthetics, there may be negative effects, including motor block, maternal hypotension, a prolonged second stage of labor and urinary retention.

Ropivacaine is a long-acting amide local anaesthetic having no adverse effects on the fetus and less harmful side effects on the central nervous system and is typically utilized in clinical practice for delivery. In order to prevent motor block, enhance the analgesic effect, lower the dosage of local anaesthetics and lessen the likelihood of associated adverse effects, it is currently standard practise to combine local anaesthetics with adjuvant medications. In order to provide epidural labor analgesia, fentanyl has frequently been utilized as an adjuvant to ropivacaine. Fentanyl as an opioid is known to cause side effects include headaches, vomiting, urine retention and respiratory depression. Dexmedetomidine, an α2-adrenoceptor agonist has been effectively utilized recently for epidural labor analgesia. Dexmedetomidine, in contrast to opioids, does not produce adverse effects including nausea, vomiting, respiratory depression or pruritus, yet it might result in bradycardia and hypotension. In our study, we investigated on the efficacy and safety of ropivacaine-dexmedetomidine versus ropivacaine-fentanyl in epidural labor analgesia.

In a study conducted by **Qiuju Cheng** et al [64] on analgesic effects of dexmedetomidine and sufentanil combined with ropivacaine in epidural analgesia during labor, it was found that group RD showed lower values than RS group in visual analog scale ($p < 0.05$).These results were similar to our study where Group RD displayed lower VAS scores compared with Group RF at most of the time points (5 minutes,10 minutes,30 minutes,60 minutes,90 minutes and 120 minutes) after epidural placement which was statistically significant. This could result from the fact that VAS scores were important parameter for assessing labor pain. The results indicate that the usage of Dexmedetomidine as adjuvant to local anaesthetic showed an higher analgesic effect compared to fentanyl as adjuvant.

The mechanism underlying epidural labor analgesia is that local anaesthetics block sodium channels in nerve membranes, inhibiting nerve transmission and preventing nerve impulses from traveling along these fibers. Analgesia is the outcome of blocking the pain impulse going through the epidural space nerve which mostly starts within minutes after epidural administration. **Koraki** et al [65] derived that the onset time of epidural Dexmedetomidine with ropivacaine was ~15 min. **E.C. Bang** et al [66] suggested that onset time of epidural fentanyl with ropivacaine varied from 8 minutes to 19 minutes according to increasing doses of fentanyl. In our study, shorter onset time of 12.50± 1.31 minutes was noticed in dexmedtomidine group whereas fentanyl group showed onset of analgesia in 15.26 ±1.46 minutes from the time of epidural administration.

Dexmedetomidine acts as an analgesic by activating the spinal cord $\alpha 2$ receptors causing prolonged analgesic effect and reducing total consumption of analgesia. In **Gehui Li** et al[55] study, the parturient women in Group ropivacaine+ dexmedetomidine required a lesser volume of injection and lesser local anaesthetics doses compared with Group ropivacaine + sufentanil ($P<0.05$). Similary in our study, the total amount of local anaesthetic requirement was significantly less in group RD than group RF.

Few researches suggest that as an α_2-adrenoceptor agonist, dexmedetomidine can cause contractions of smooth muscles in uterus and hasten the duration of the first stage of labor. A study done by **Tao Zhang** et al [59] compared the effects of dexmedetomidine (group D) and sufentanil (group S) and put forward that first-stage labor duration was shorter in group D ($p<0.05$).It was also observed in our study that duration between epidural administration to the delivery was shorter in group RD than in group RF which was statistically significant. One possible theory is that dexmedetomidine would reduce the early stage of labor by causing smooth muscle contractions in the uterus.

Hemodynamic stability is an important parameter to assess patient safety. In **Mohamed Fouad Selim** et al [67] study mean arterial pressure(MAP) and Heart Rate showed non significant decrease in Bupivacaine+ Dexmedetomidine(BD) group compared with Bupivacaine+Fentanyl (BF). The epidural groups showed decrease in HR were statistically significant at T20, T25 and T30.[67] There were no changes in SpO2 at any time in any of enrolled women. As of our study, maternal SBP,DBP and heart rate remained comparable in both groups in most of the observations. SBP showed significant difference only at 4 hours, while DBP remained comparable among the two groups. Significant difference in heart rate was noticed at 90 min after epidural administration in both groups. There was no significant fall in SpO2 at any time for both groups.

Dexmedetomidine is known to produce sedation by acting on α_2-adrenergic receptors, therefore monitoring sedation levels became important for the study. A good approach for evaluating and comparing sedative drug efficacy for patients is the Ramsay Sedation Scale scores. **Caifeng Li** et al[68] suggested that there is no significant difference in Ramsay Sedation Scale scores in dexmedetomidine and fentanyl group. In our study, similar results were found. There was no significant difference in RSS across the groups, and there was no evidence of profound sedation.

When used appropriately, the Apgar score serves as a tool for standardized assessment and defines the newborn state soon after birth. Additionally, it offers a way to record the shift from fetal to neonatal state and tells about the response to resuscitation. In **Mei Fan et al** [56] study, Apgar scores of newborns were high in both groups RD and RS. Similarly in our study, newborn Apgar scores at 1 and 5 minutes remained high in group RD and RF.

It is postulated that opioids cause several adverse effects like pruritus by medullary dorsal horn activation, antagonism of inhibitory transmitters and modulation of the serotonergic pathway[70] even though the exact reason is unclear. **Yafen Gao** et al [69] stated that compared with opioids, using dexmedetomidine as a local anaesthetic decreased the incidence of pruritus, nausea and vomiting without increasing the incidence of adverse events.[69] On the contrary, our study showed side effects in both the groups even though no statistical significance was derived. Maternal hypotension (14.7%), nausea/vomiting (8.8%), bradycardia (8.8%) and shivering (8.8%) was observed in group RD while pruritus (5.9%), hypotension (5.9%), nausea/vomiting (14.7%) and shivering (8.8%) was seen in group RF.

Our study has limitations in certain ways. First, other dosages should be tested in future trials as this study only evaluated the safety and efficacy of 0.1% ropivacaine in combination with 0.5mcg/ml dexmedetomidine and 2 µg/ml fentanyl. Second, our study was a single centre clinical trial. Large scale multi-centre studies can be done to verify results. Third, only primigravida were investigated in our study. Further studies with multigravida on larger groups can be done to testify results.

CONCLUSION

Dexmedetomidine as an adjuvant in epidural labor analgesia showed improved analgesic effect, quicker onset of action, reduced need of local anaesthetics, reduced bolus requirement compared to Fentanyl group. Ramsay sedation scale scores and APGAR scores were comparable results in both groups. The incidence of side effects in pregnant women and newborns was low in both groups.

The study concludes that Dexmedetomidine increases the effectiveness of local anaesthetics during epidural labor and is a safe alternative for labor pain.

SUMMARY

"A RANDOMISED CLINICAL TRIAL TO COMPARE THE EFFICACY AND SAFETY OF DEXMEDETOMIDINE-ROPIVACAINE VERSUS FENTANYL-ROPIVACAINE FOR EPIDURAL LABOR ANALGESIA"

This study was carried out from September 2022 to June 2024 in the Labor Room Complex, B.L.D.E (DU) Shri. B.M. Patil Medical College, Hospital and Research centre, Vijayapura.

This study aimed to compare the efficacy and safety of dexmedetomidine- ropivacaine versus fentanyl-ropivacaine for epidural labor analgesia in primigravida undergoing vaginal delivery. The objectives of the study were:

Primary Objectives: To compare Dexmedetomidine and Fentanyl as adjuvants in epidural analgesia in terms of the onset of epidural analgesia, duration of analgesia, rescue analgesic dose, visual analog scale (VAS) and maternal vitals – heart rate, blood pressure, oxygen saturation.

Secondary Objectives : To compare the two groups in terms of Ramsay Sedation Scale (RSS) scores,APGAR score of the baby and maternal side effects – pruritus, hypotension, nausea, vomiting, shivering, respiratory depression, bradycardia.

The study population of 68 were randomised using computer generated randomisation table into two groups

1) Group RD: receive 0.1% Ropivacaine +0.5 mcg/ml Dexmedetomidine

2) Group RF: receive 0.1% Ropivacaine + 2 mcg/ml Fentanyl

The observations were analysed statistically and the results are as follows:

The demographic variables were not statistically significant.

The group RD showed shorter mean onset time of analgesia, less local anaesthetic requirement and less number of bolus doses than group RF which was statistically significant.

The duration from the administration of epidural to the delivery of baby was found to be significantly shorter in group RD than group RF.

VAS scores at 5 minutes, 10 minutes,30 minutes,60 minutes, 90 minutes and 120 minutes after epidural administration were higher in group RF than group RD which was statistically significant.

Maternal systolic blood pressure, diastolic blood pressure, heart rate and room air saturation remained comparable among both groups at most of the time periods.

Observations from Ramsay Sedation Scale values revealed that no excessive sedation was seen in our study in both the groups.

APGAR score of newborns in both the groups remained high suggesting no adverse effects on the baby.

In group RD, maternal hypotension , bradycardia, shivering , nausea and vomiting was observed whereas in group RF, pruritus, maternal hypotension, shivering, nausea and vomiting was seen.The study showed side effects in both the groups, which was not statistical significant.

Thus, our study indicates that dexmedetomidine-ropivacaine shows increased efficacy than fentanyl-ropivacaine for epidural labor analgesia and is a safe alternative for labor pain .

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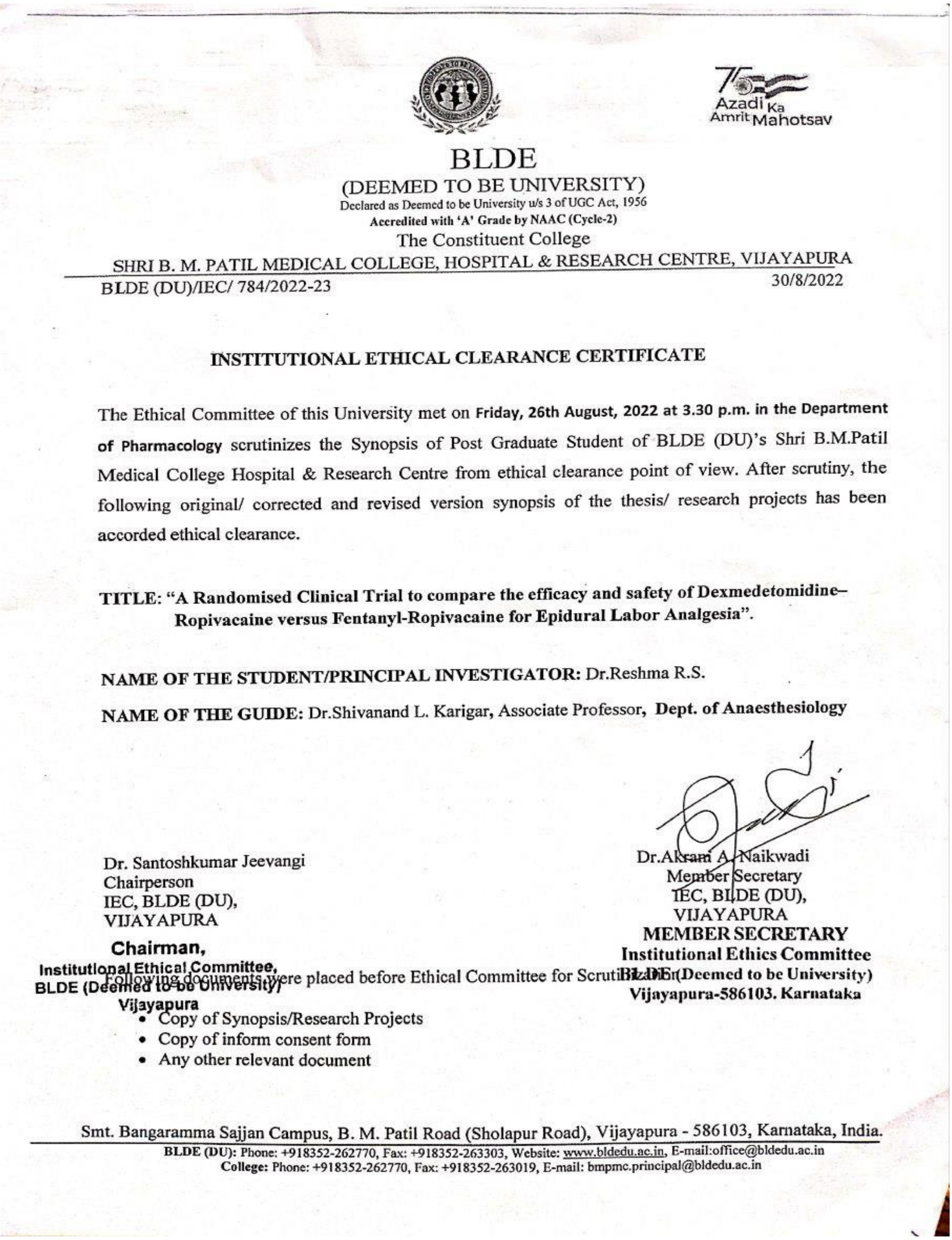
ANNEXURE I

ETHICAL COMMITTEE APPROVAL LETTER



Azadi Ka Amrit Mahotsav

BLDE
(DEEMED TO BE UNIVERSITY)
Declared as Deemed to be University u/s 3 of UGC Act, 1956
Accredited with 'A' Grade by NAAC (Cycle-2)
The Constituent College
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 784/2022-23 30/8/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Friday, 26th August, 2022 at 3.30 p.m. in the Department of Pharmacology** scrutinizes the Synopsis of Post Graduate Student of BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "A Randomised Clinical Trial to compare the efficacy and safety of Dexmedetomidine–Ropivacaine versus Fentanyl-Ropivacaine for Epidural Labor Analgesia".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: Dr.Reshma R.S.

NAME OF THE GUIDE: Dr.Shivanand L. Karigar, Associate Professor, **Dept. of Anaesthesiology**

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

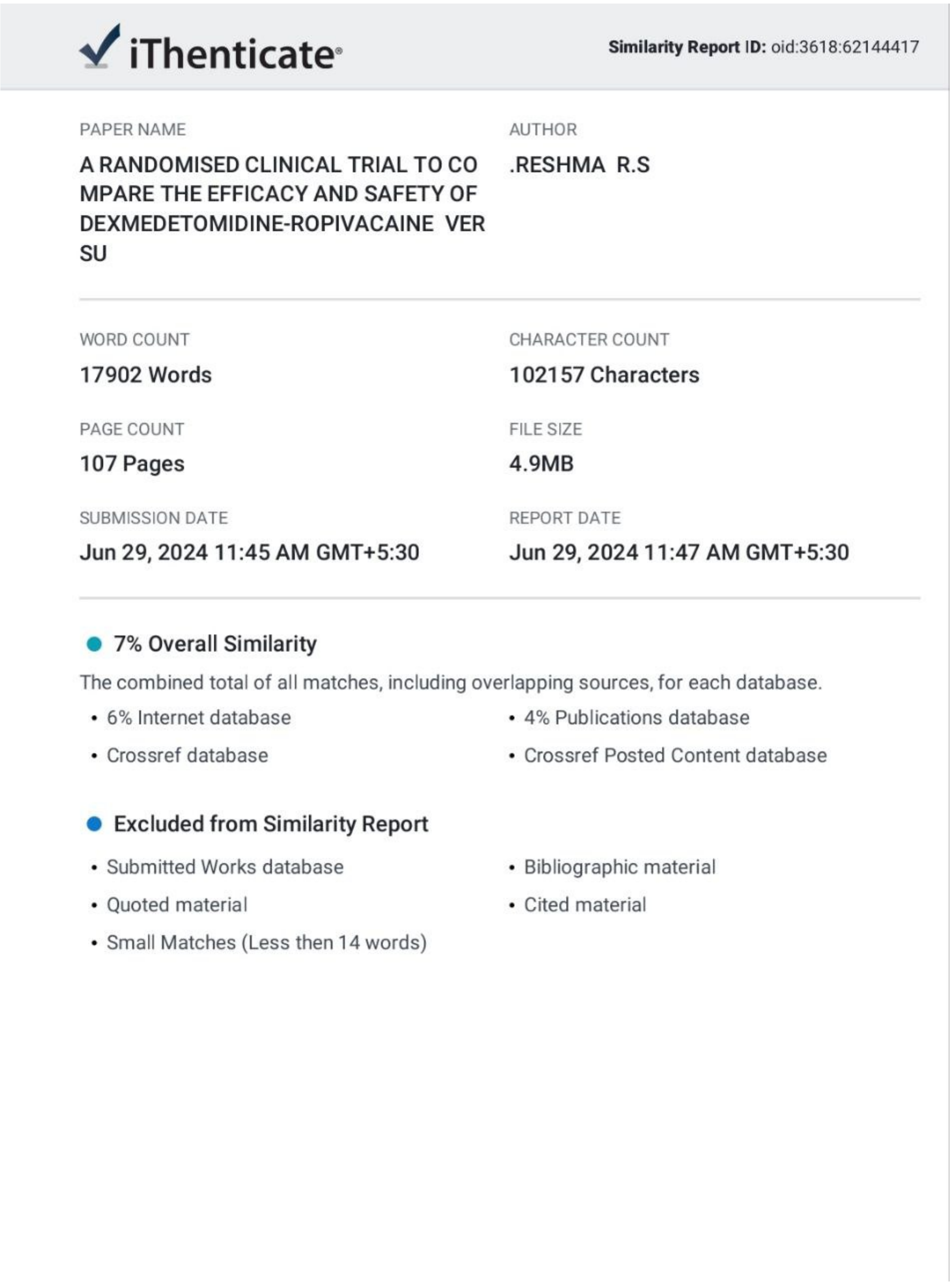
Following documents were placed before Ethical Committee for Scrutinization:

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

ANNEXURE II

PLAGIARISM CERTIFICATE



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PAPER NAME

A RANDOMISED CLINICAL TRIAL TO COMPARE THE EFFICACY AND SAFETY OF DEXMEDETOMIDINE-ROPIVACAINE VERSU

AUTHOR

.RESHMA R.S

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ANNEXURE III

PATIENT INFORMED CONSENT FORM

B.L.D.E (DU) S.H.R.I. B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA - 586103, KARNATAKA

TITLE OF THE PROJECT: A Randomised Clinical Trial To Compare The Efficacy And Safety Of Dexmedetomidine-Ropivacaine Versus Sufentanyl-Ropivacaine For Epidural Labour Analgesia

PRINCIPAL INVESTIGATOR: Dr. RESHMA R S
Department of Anaesthesiology
BLDE University Shri B M Patil Medical
College & Research Centre,
Solapur Road ,Vijayapura-03
E mail: reshmarajs001@gmail.com

POST GRADUATE GUIDE : Dr. Shivanand L Karigar
M.D Anaesthesiology
Professor
Department of Anaesthesiology
BLDE University Shri B M Patil Medical College &
Research Centre, Solapur Road, Vijayapura-03

CO-GUIDE: Dr.Shreedevi Kori
M.S.Obstetrics and Gynaecology
Associate Professor
Department of Obstetrics & Gynaecology
BLDE University Shri B M Patil Medical College &
Research Centre, Solapur Road , Vijayapura-03

PURPOSE OF RESEARCH:

I have been informed that this study is to compare the efficacy and safety of dexmedetomidine-ropivacaine versus sufentanyl-ropivacaine for epidural labour analgesia.

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

PROCEDURE:

I understand that I will be participating in the study to compare the efficacy and safety of dexmedetomidine-ropivacaine versus sufentanyl-ropivacaine for epidural labour analgesia.

RISKS AND DISCOMFORTS:

I understand that my ward may experience some discomfort during the procedure and I understand that necessary measures will be taken to reduce them.

BENEFITS:

I understand that my ward participating in this study will help in finding the efficacy and safety of dexmedetomidine-ropivacaine versus sufentanyl-ropivacaine for epidural labour analgesia.

CONFIDENTIALITY:

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

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

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. RESHMA R S is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation. If during this study ,or later I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me for keep for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

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

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

INJURY STATEMENT:

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

I understand that by my agreement to participate in this study, I am not waiving my legal rights. I have explained to____ the purpose of this research , the procedure required and the possible risk and benefits, to the best of my ability in patients own language.

DATE Dr. RESHMA R S (investigator)

PATIENT/PARENT SIGNATURE Witness

STUDY SUBJECT CONSENTSTATEMENT:

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

I have been explained all the above in detail in my own language and I understand the same.

Therefore I agree to give my consent to participate as a subject in this research project.

______________________ _______________

(Participant) (Date)

________________________ ________________

(Witness to above signature) (Date

ANNEXURE IV

PROFORMA

STUDY: A RANDOMISED CLINICAL TRIAL TO COMPARE THE EFFICACY AND SAFETY OF DEXMEDETOMIDINE-ROPIVACAINE VERSUS FENTANYL-ROPIVACAINE FOR EPIDURAL LABOR ANALGESIA

PATIENT DETAILS

Name Age Sex Height Weight

BMI Ward Group allotted by randomisation: RD /RF

Diagnosis

Surgical Procedure

Past History

General Physical Examination:

Pallor Icterus Cyanosis Clubbing Lymphadenopathy Edema

Airway Examination

Mallampati Grade:

Vital parameters

Pulse Blood Pressure Respiratory Rate Temperature

Systemic Examination

CVS

RS

CNS

PA

Spine Examination

Investigations

Hemoglobin: T.L.C.: Platelet count:

Bleeding time/ clotting time :

Urine routine: H.I.V.: HbsAg:

A.S.A. grade

Parameters:

TABLE 1- REQUIREMENT OF DRUG

PARAMETERS	GROUP RD/ GROUP RF
Time of Onset of Analgesia	
Duration from bolus to delivery	
Rescue analgesia doses given	

TABLE 2- VISUAL ANALOG SCALE SCORE

TIMING	GROUP RD/ GROUP RF
Baseline	
5 minutes	
10 minutes	
20 minutes	
30 minutes	
60 minutes	
90 minutes	
120 minutes	

TABLE 3- HAEMODYNAMIC PARAMETERS

Timing	GROUP RD/ GROUP RF			
	Systolic Blood Pressure	Diastolic Blood Pressure	Heart Rate	Oxygen Saturation
Baseline				
5 minutes				
10 minutes				
20 minutes				
30 minutes				
60 minutes				
90 minutes				
2 hours				
4 hours				
6 hours				
At time of delivery				

TABLE 4- RAMSAY SEDATION SCALE SCORE

TIMINGS	SCORE	GROUP RD/GROUP RF
	1- Anxious, agitated or restless 2- Cooperative, oriented, tranquil & alert 3- Responds to command only 4- Brisk response to light tactile stimuli or loud auditory stimuli 5- Sluggish response to light tactile stimuli or loud auditory stimuli 6- Asleep , no response	

TABLE 5- MATERNAL SIDE EFFECTS

SIDE EFFECTS	GROUP RD/ GROUP RF
Pruritus	
Hypotension	
Nausea/ Vomiting	
Respiratory Depression	
Maternal Bradycardia	
Shivering	

TABLE 6- APGAR SCORE

	At 1 minute	At 5 minutes
GROUP RD		
GROUP RF		

ANNEXURE V

BIO-DATA

BIODATA OF GUIDE

Name: DR. SHIVANAND L KARIGAR

Present Designation: Professor

Department: Department of ANESTHESIOLOGY

Date of birth: 20/07/1982

Qualification: M.B.B.S., M.D. Anaesthesia, FIPM.

Undergraduate: M.B.B.S., JAWAHARLAL NEHRU MEDICAL COLLEGE, BELGAUM, KARNATAKA, Pass out of 2006

Postgraduate: M.D. Anaesthesia, JAWAHARLAL NEHRU MEDICAL COLLEGE, BELGAUM, KARNATAKA, Pass out of 2011

Correspondence: DEPARTMENT OF ANAESTHESIA, BLDE UNIVERSITY, SHRI B. M. PATIL MEDICAL COLLEGE VIJAYAPURA, 586103, KARNATAKA

Contact Number: 9164319345

Teaching Experience: 13 Years

Publications: 30 (Research Publications and case reports)

Research Projects: 1 Completed and 4 Ongoing Research Project

BIO-DATA OF CO-GUIDE

Name: DR. SHREEDEVI KORI

Present Designation: Associate Professor

Department: Department of Obstetrics and Gynaecology

Date of birth: 04/02/1985

Qualification: M.B.B.S., MS OBG

Undergraduate: M.B.B.S., AL-AMEEN MEDICAL COLLEGE, VIJAYAPURA, KARNATAKA, Pass Out of 2008

Postgraduate: M.S.OBG, S.H.R.I. B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, Pass Out of 2013

Correspondence: DEPARTMENT OF OBSTETRICS & GYNAECOLOGY, BLDE UNIVERSITY, SHRI B. M. PATIL MEDICAL COLLEGE VIJAYAPURA, 586103, KARNATAKA

Contact Number: 9538846839

Teaching Experience: 10 Years

Publications:20 Research Publications and 10 Case Reports

Research Projects: 1 completed and 3 ongoing Research Projects

BIODATA OF INVESTIGATOR:

Name: Dr. RESHMA R S

K.M.C. Registration No.: 135479

Date of Birth: 25/08/1995

Present Designation: Post Graduate/Junior Resident

Department: Anaesthesiology

College: BLDE (DEEMED TO BE UNIVERSITY), SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA, KARNATAKA, INDIA – 586103.

Phone: 8762343213,9496381213

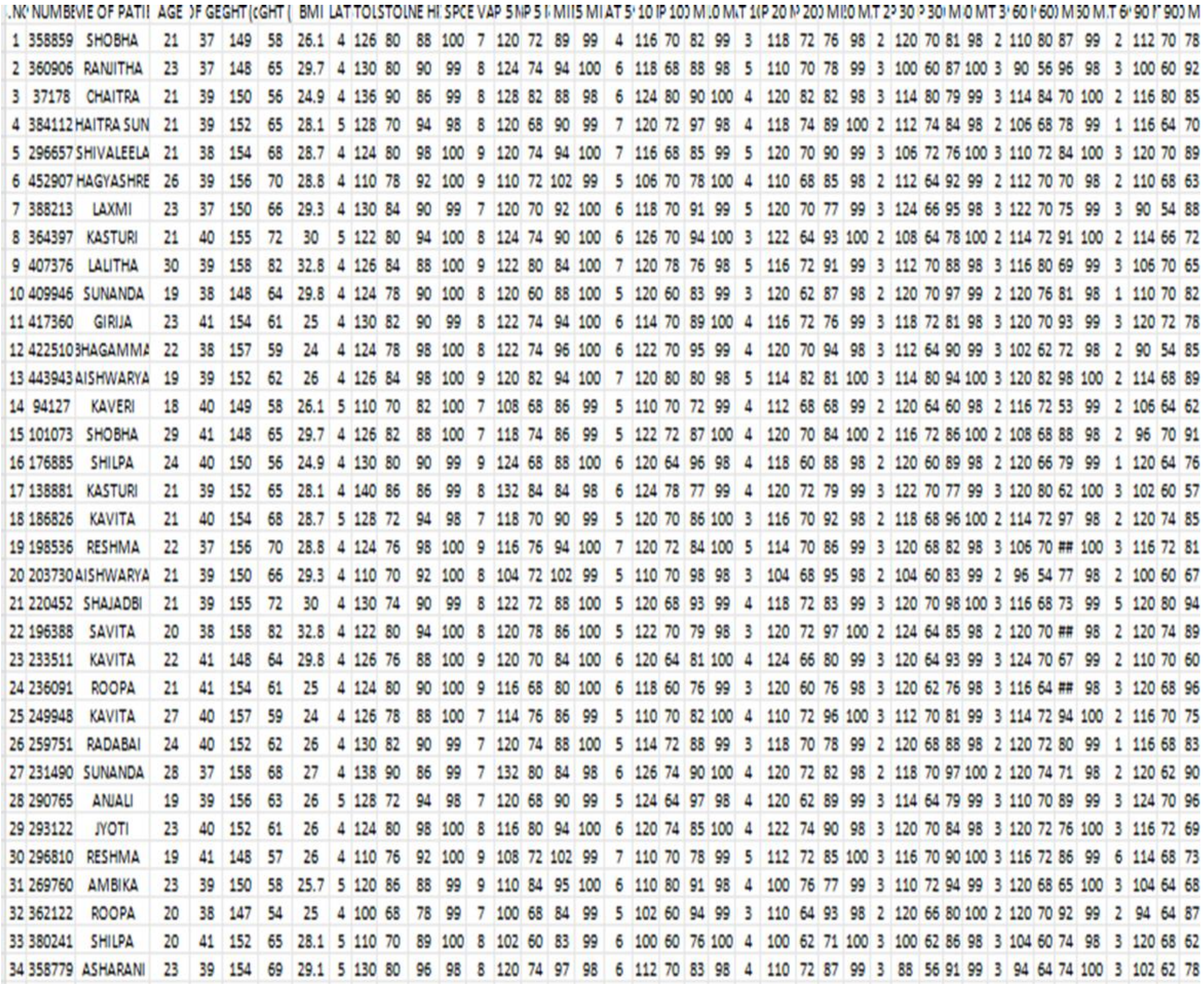
Email address: reshmarajs001@gmail.com

Qualification: M.B.B.S., Dr B R AMBEDKAR MEDICAL COLLEGE BANGALORE, Pass Out of 2020

ANNEXURE VI

MASTERCHART

MASTER CHART – GROUP RD



.NO	NUMBE	ME OF PATI	AGE	)F GE	GHT (c	GHT (	BMI	LAT	TOL	STO	NE HI	SPCE	VAP	5 M	P 5	MI	5 MI	AT 5	10	P 10	) M	.0 M	T 1	P 20	M 20	) MI	0 M	T 2	30	P 30	M	0 MT	T 3	60	60	) M	0 M	T 6	90	90	) M
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5	296657	SHIVALEELA	21	38	154	68	28.7	4	124	80	98	100	9	120	74	94	100	7	116	68	85	99	5	120	70	90	99	3	106	72	76	100	3	110	72	84	100	3	120	70	89
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8	364397	KASTURI	21	40	155	72	30	5	122	80	94	100	8	124	74	90	100	6	126	70	94	100	3	122	64	93	100	2	108	64	78	100	2	114	72	91	100	2	114	66	72
9	407376	LALITHA	30	39	158	82	32.8	4	126	84	88	100	9	122	80	84	100	7	120	78	76	98	5	116	72	91	99	3	112	70	88	98	3	116	80	69	99	3	106	70	65
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11	417360	GIRIJA	23	41	154	61	25	4	130	82	90	99	8	122	74	94	100	6	114	70	89	100	4	116	72	76	99	3	118	72	81	98	3	120	70	93	99	3	120	72	78
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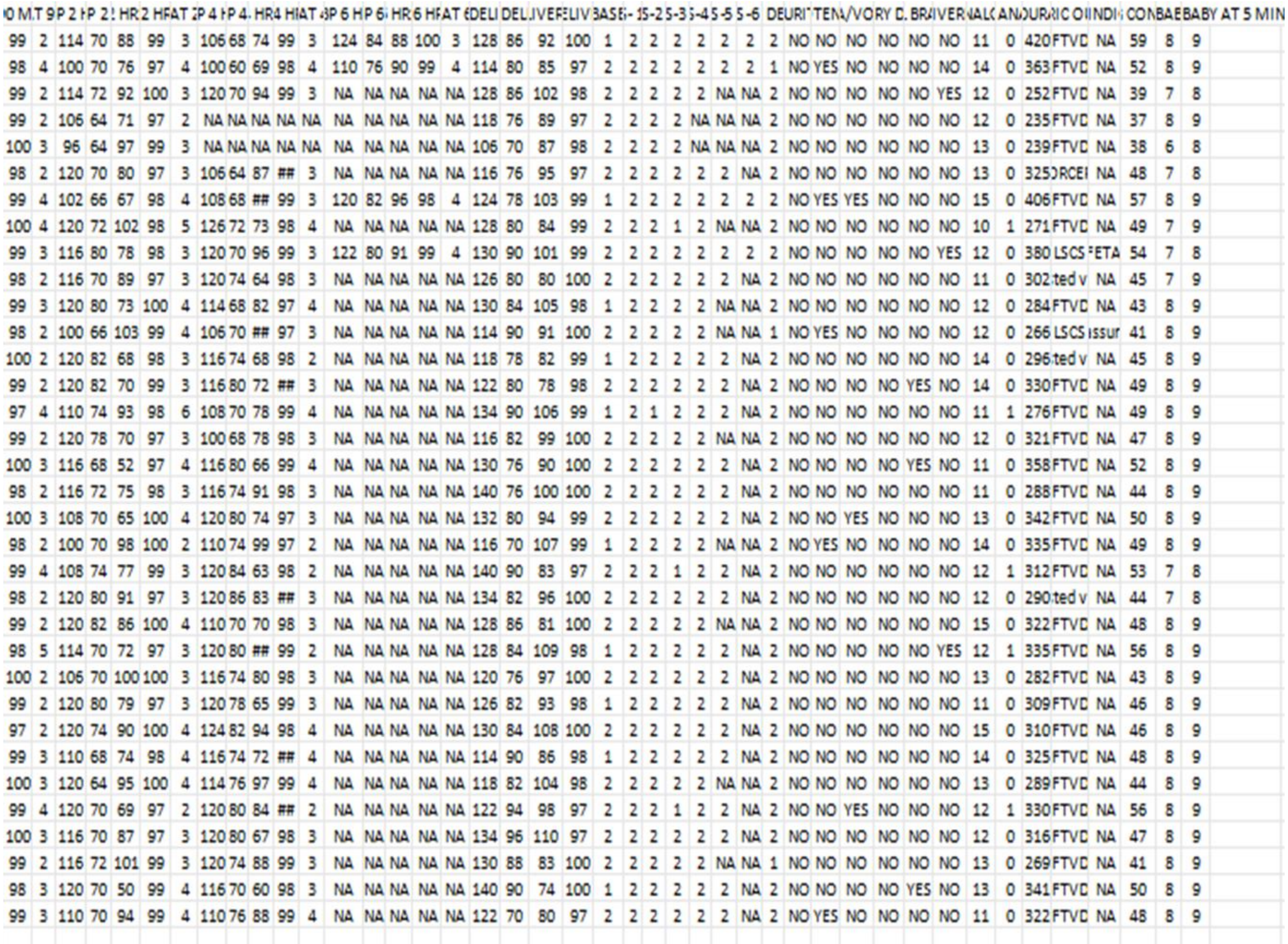

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99	2	114	70	88	99	3	106	68	74	99	3	124	84	88	100	3	128	86	92	100	1	2	2	2	2	2	2	2	NO	NO	NO	NO	NO	NO	11	0	420	FTVD	NA	59	8	9
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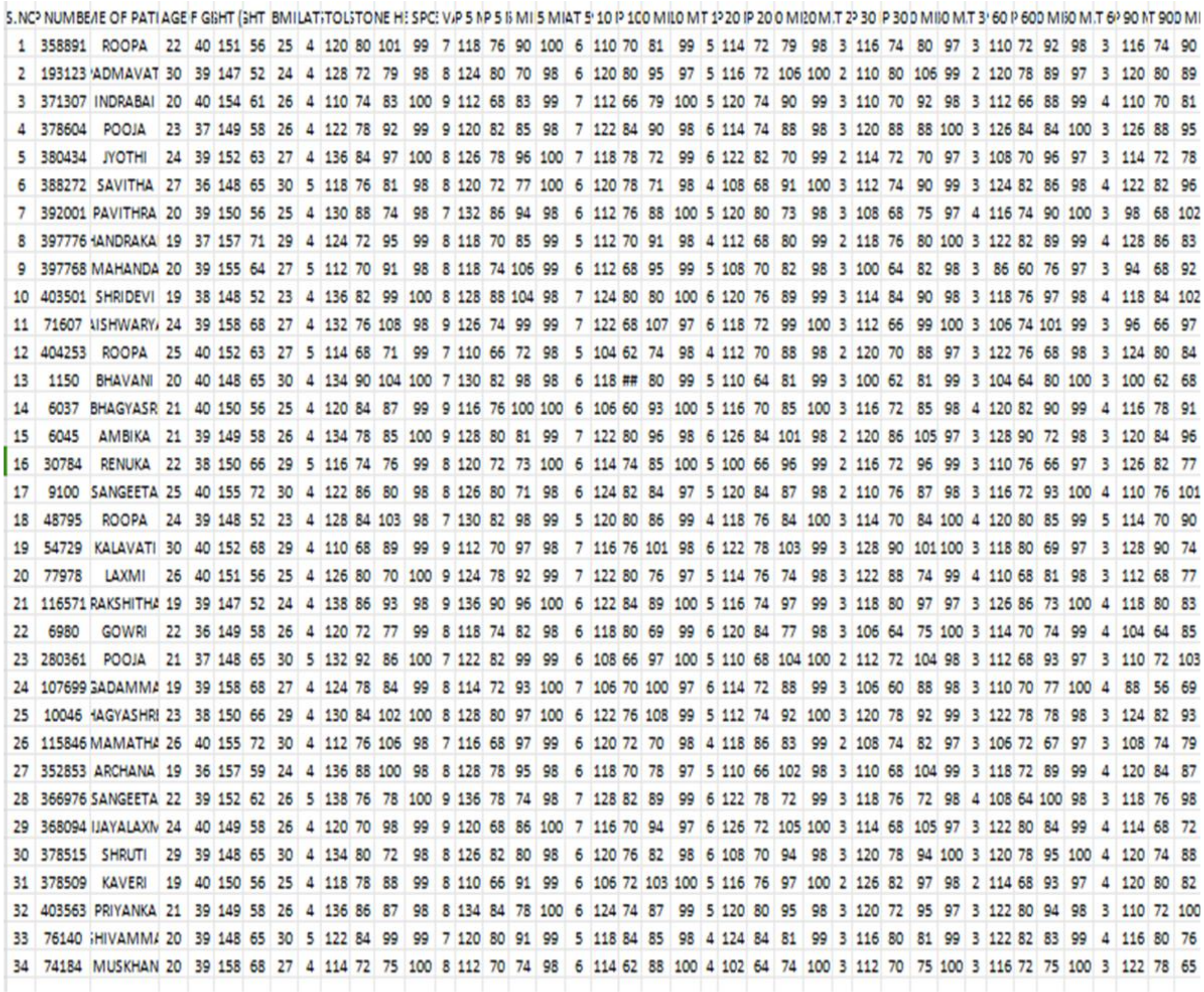
MASTER CHART- GROUP RF



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2	193123	PADMAVAT	30	39	147	52	24	4	128	72	79	98	8	124	80	70	98	6	120	80	95	97	5	116	72	106	100	2	110	80	106	99	2	120	78	89	97	3	120	80	89
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6	388272	SAVITHA	27	36	148	65	30	5	118	76	81	98	8	120	72	77	100	6	120	78	71	98	4	108	68	91	100	3	112	74	90	99	3	124	82	86	98	4	122	82	96
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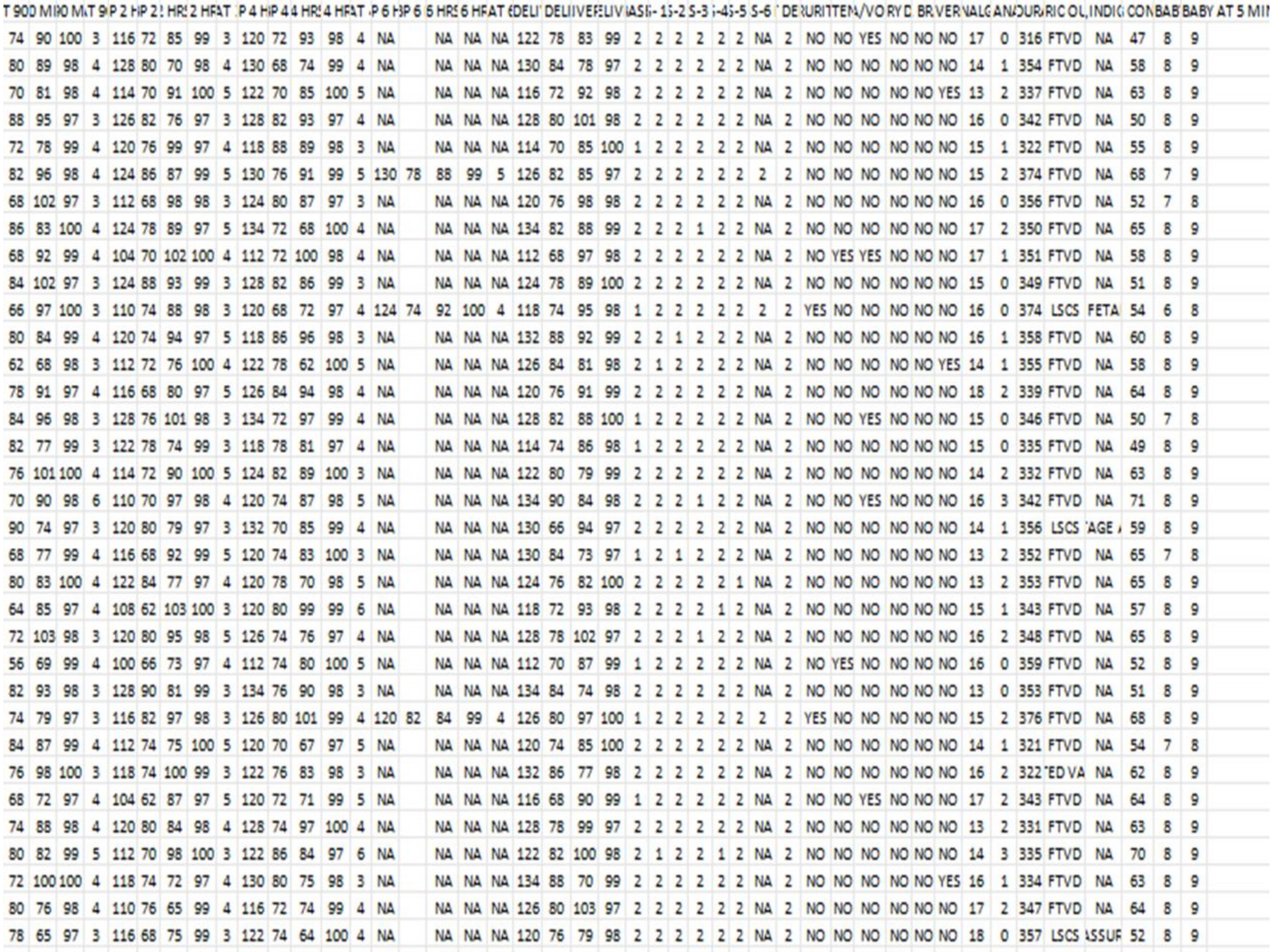
33	76140	SHIVAMMA	20	39	148	65	30	5	122	84	99	99	7	120	80	91	99	5	118	84	85	98	4	124	84	81	99	3	116	80	81	99	3	122	82	83	99	4	116	80	76
34	74184	MUSKHAN	20	39	158	68	27	4	114	72	75	100	8	112	70	74	98	6	114	62	88	100	4	102	64	74	100	3	112	70	75	100	3	116	72	75	100	3	122	78	65



T 900	MI	0 M	T 9	P 2	HP 2	HR	2 HF	AT	P 4	HP 4	4 HR	4 HF	AT	P 6	HP 6	6 HR	6 HF	AT	DELI	DELI	IVE	LIV	ASI	- 1	-2	S-3	-4	-5	S-6	DE	URI	TTEN	/VO	RY D	BR	VER	VALG	AN	DUR	RIC OL,	INDIG	CON	BAB	BABY AT 5 MIN
74	90	100	3	116	72	85	99	3	120	72	93	98	4	NA		NA	NA	NA	122	78	83	99	2	2	2	2	2	2	NA	2	NO	NO	YES	NO	NO	NO	17	0	316	FTVD	NA	47	8	9
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