# "A PROSPECTIVE RANDOMIZED CLINICAL STUDY TO COMPARE THE EFFECT OF BUPRENORPHINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE FOR POST OPERATIVE EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPEDIC SURGERIES"


**By**

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Dissertation submitted to BLDE (Deemed to be University), Vijayapura.

In partial fulfilment of the requirements for the award of the degree of

**DOCTOR OF MEDICINE**

**IN**

## ANAESTHESIOLOGY

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# ABSTRACT

**TITLE:-**

**"A PROSPECTIVE RANDOMIZED CLINICAL STUDY TO COMPARE THE EFFECT OF BUPRENORPHINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE FOR POSTOPERATIVE EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPEDIC SURGERIES."**

**INTRODUCTION:-**

Neuraxial block is commonly used for lower abdomen and lower limb procedures because it has several advantages over general anaesthesia. Epidural analgesia is one of the most widely accepted method for postoperative pain relief in orthopedic surgeries. In current day practice various adjuvants for local anesthetics are used for epidural analgesia to enhance the quality and duration of analgesia.

**AIMS & OBJECTIVES:-**

A Comparison of Buprenorphine versus Fentanyl with 0.5%Bupivacaine for postoperative epidural analgesia in Lower Limb orthopedic surgeries in Adults with respect to:

- Onset of analgesia.
- Duration of analgesia
- VAS scores and Hemodynamics
- side effects, if any

**METHODOLOGY:-**

Institutional ethical committee approval was taken. After obtaining written informed consent, 60 patients in the age group 20-60 years of either gender belonging to ASA I-II who were scheduled for lower limb orthopaedic procedures were enrolled in our study.The patients were divided into two groups of 30 each .

| | |
|---|---|
| GROUP A | 2ml 0.5% Bupivacaine + 1.5 mcg/kg Buprenorphine diluted with distilled water to 10ml |
| GROUP B | 2ml 0.5% Bupivacaine + 1mcg/kg Fentanyl diluted with distilled water to 10ml |

Postoperatively when the patient complained of pain and VAS score >4, study drug was given via epidural catheter and patient monitored. We recorded onset of analgesia, VAS scores, Pulse rate, Blood pressure, duration of analgesia, side effects if any at regular intervals for 24 hours.

**RESULTS:-**

In our study patient characteristics were comparable. The onset of analgesia was significantly faster ($p<0.001$) in Fentanyl Group (7.17±3.13 mins) as compared to Buprenorphine group (15.33±8.09 mins). While the duration of analgesia was 13.63±3.19 hours with Buprenorphine as compared to 3.73±1.14 hours with Fentanyl and was statistically significant ($p<0.001$). Side effects such as nausea ,vomiting , pruritis , sedation was seen in 9, 3, nil , nil patients respectively in the Buprenorphine group and 2 ,nil, 3, 2 patients respectively in the Fentanyl group.

**CONCLUSION:-**

Buprenorphine and Fentanyl are both safe and effective epidural adjuvants to Bupivacaine. Because of its faster onset of action and fewer side effects, we concluded that Fentanyl is a preferable choice.However, the duration of analgesia is longer with Buprenorphine.

**KEYWORDS:-**

Epidural analgesia, Bupivacaine , Buprenorphine , Fentanyl

# ABBREVIATIONS

| | | |
|---|---|---|
| ASA | - | American Society of Anaesthesiologists |
| CSF | - | Cerebrospinal fluid |
| ECG | - | Electrocardiogram |
| HR | - | Heart rate |
| BP | - | Blood pressure |
| SBP | - | Systolic blood pressure |
| DBP | - | Diastolic blood pressure |
| LA | - | Local anesthetic |
| IV | - | Intravenous |
| Inj. | - | Injection |
| NIBP | - | Noninvasive Blood Pressure |
| SPO2 | - | Oxygen Saturation |
| S.D | - | Standard deviation |
| VAS | - | Visual Analog Score |
| Mcg | - | Microgram |
| Mg | - | Milligram |
| Ml | - | Milliliter |
| Kg | - | Kilogram |
| Hrs | - | Hours |
| Mins | - | Minutes |
| PDPH | - | Postdural puncture headache |

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# INTRODUCTION

*"The proper management of pain remain, after all, the most important obligation, the main objective, and the crowning achievement of every physician"* – John Bonica , Father of Pain management.[1]

Pain is described as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" according to the Taxonomy Committee of the International Association for the Study of Pain, led by Merskey (1979)." [2]

Pain is a complex, multidimensional perception. It is a dynamic process that involves actions at multiple sites starting from peripheral tissue injury provoking peripheral sensitization leading to central sensitization. Ultimately the inflammatory response leads to release of chemical mediators that act synergistically to convert high thresh-hold nociceptors to low thresh-hold nociceptors.[3]

Prevention and treatment of postoperative pain plays an important role in reducing patient morbidity. It enables early ambulation, reduces morbidity, duration of hospital stay and improves the surgical outcome. The adequacy of postoperative pain control is one of the most important factors in determining safe discharge from Day care surgery.[4] Systemic analgesia by nature is associated with numerous side effects like drowsiness, dizziness, respiratory depression and disorientation. This may not allow the patient to ambulate early. Some drugs may cause nausea, vomiting andpruritis.

Orthopedic surgeries are usually indicated for musculoskeletal dysfunction like fractures, trauma, tumors, joint disorders, deformities or infections. The goal in these surgeries is to improve movement and stability and alleviate pain. Regional Anesthesia by Spinal and Epidural Anesthesia is the most widely used technique for orthopedic lower limb surgeries. Neuraxial Anesthesia has various advantages over general

anesthesia such as reduced need for sedatives, prevention of airway manipulation, better hemodynamic stability, reduced postoperative nausea vomiting and early ambulation. Epidural anesthesia has various advantages over spinal anesthesia such as prolonged duration of analgesia upto 48-72hours, reduced incidence of postdural puncture headache , better hemodynamic stability. Epidural anaesthesia using traditional local anaesthetics only, without adjuvants have a shorter duration of action. In the context of augmentation strategies for postoperative analgesia, a number of adjuvants have been used .This includes Opioids like Morphine, Pethidine ,Fentanyl and Buprenorphine and Non-opioids like Midazolam, Dexmeditomidine, Neostigmine, Tramadol and Clonidine. Amongst them Opioids have been the most studied and commonly used drugs.

Bupivacaine is the most commonly used local anesthetic drug for epidural analgesia. It is an amino-amide type of local anesthetic which acts by blocking sodium channels and preventing conduction of impulses. It has high potency, slow onset of action (5-8mins) and long duration of action (90-150mins).

Bromage *et al* published a paper in 1980 which concluded that epidural opioids are valuable adjuncts to local anesthetics to prolong postoperative analgesia.[5]

Buprenorphine is a thebaine derivative. It has a mixed agonist-antagonist action on opioid receptors. Its potency is 25-40 times more than Morphine.

Fentanyl is a synthetic phenylpiperidine derivative. It is 75-125 times more effective than morphine and works by stimulating the mu opioid receptors.

The purpose of this study is to compare postoperative epidural analgesia in lower limb orthopaedic surgeries between two opioid adjuvants to the local anesthetic Bupivacaine – Buprenorphine and Fentanyl.

## AIMS AND OBJECTIVES

**AIM:-**

To compare the effect of Buprenorphine and Fentanyl as adjuvants to Bupivacaine for postoperative Epidural Analgesia in lower limb orthopaedic surgeries.

**OBJECTIVES:-**

Primary objective:-

To compare the onset and duration of postoperative analgesia using buprenorphine and fentanyl with 0.5% Bupivacaine administered via epidural route .

Secondary objectives:-

1. To study changes in respiratory and hemodynamic parameters after administration of study drugs
2. To compare adverse effects if any between the two study drugs

# REVIEW OF LITERATURE

**History Of Epidural anesthesia[6]:-**

In 1901, Jean Enthuse Sicard and Fernand Cathelin became the first practitioners of caudal epidural anaesthesia when they individually injected cocaine through the sacral hiatus.

Archile Mario Dogliotti, a Spanish military surgeon, conducted abdominal surgery utilising single shot lumbar epidural anaesthetic 19 years later. After the needle had crossed the ligamentum flavum, he accurately recognised the epidural space by noting the immediate loss of resistance.

Aburel, Higson, and Edwards all devised continuous but inconvenient epidural blocking methods. Manual Martinez Curbelo, a Cuban anaesthesiologist, is credited with making the procedure more feasible. During a 1947 visit to the Mayo Clinic, he witnessed Tuohy administer continuous spinal block. Curbelo provided continuous segmental lumbar peridural anaesthesia using the Tuohy needle and a silk ureteral catheter. In recent years, several improvements of the Tuohy-Huber epidural needle have been created and are now used in modern anaesthetic practise.[6]

Ekenstam developed Bupivacaine in 1956, and Telivuo introduced it into clinical use in 1963. Because of its prolonged duration of action and differential sensory block at lower concentrations, bupivacaine has become quite popular for epidural anaesthesia and analgesia since then.[7]

After the discovery of opioid receptors in the dorsal horn of the spinal cord, which was initially hypothesised by Backett and Casy in 1954, the technique of epidural for postoperative pain treatment was revolutionised by the use of neuraxial opioids. The first studies about the use of spinal opioids in humans were published in 1979. To

optimise analgesia and reduce overall drug doses, opioids have been used as adjuvants to local anaesthetics.[8]

**Naulty JS** et al (1985) evaluated the suitability of Fentanyl for epidural use and the dosages required in a double blind, randomized study in 30, ASA-1 parturients following caesarean section . The patients were divided into 5 groups randomly to receive 0, 12.5, 25, 50,100 mcg of Fentanyl citrate through the epidural catheter. Level of sensory block, motor block and pain intensity was assessed. 50mcg Fentanyl produced pain scores of 0 within 9 minutes and 100mcg in 3-6mins.[9]

**Lanz**et al investigated Epidural Buprenorphine as a postoperative analgesic in a study on 158 patients for lower extremity orthopedic surgery. Post-operatively patients in Group 1 , 2 ,3 received either 0.15mg Buprenorphine in 15ml NS (n=37), 0.3mg buprenorphine in 15ml NS (n=37) , no further injections (control group, n=47) after 2%Mepivacaine for intraoperative anesthesia. A fourth group received 0.3mg epidural Buprenorphine in 15ml NS after intraoperative 0.5%Bupivacaine. They recorded postoperative pain quality and need for additional analgesics. They concluded that analgesia after use of Buprenorphine (both 0.15mg and 0.3mg) was superior to no injections (control group). Further Buprenorphine 0.3mg was superior to 0.15mg for analgesia upto 12 hours.Analgesia following bupivacaine anaesthesia with 0.3mg buprenorphine was comparable to analgesia after mepivacaine anaesthesia. [10]

**Review of previous studies:-**

1. **Dr. Santosh Kumar** et al undertook a prospective randomised trial to assess the effects of epidural bupivacaine with buprenorphine against epidural bupivacaine with fentanyl for lower limb surgeries. A total of 60 patients in the age range of 20-60 years belonging to ASA I-II who were scheduled for elective lower limb procedures were divided into two groups of 30 patients each. Group A received 150 mcg Buprenorphine and 0.5 percent Bupivacaine 15ml. Bupivacaine 0.5 percent 15ml with 50mcg Fentanyl was given to Group B. Sensory and motor blockade, quality and duration of postoperative analgesia, hemodynamic and respiratory parameters, and side effects such as nausea, vomiting, respiratory depression, and pruritis were all investigated . Both groups experienced a fast onset of sensory and motor blockade. The duration of analgesia in Group A was substantially longer than in Group B. (766.6 vs 471 minutes). Nausea and vomiting were more common in group A (40%) compared to group B (10%), while pruritus was more common in group B (10%) as opposed to none in group A. In comparison to epidural Fentanyl, epidural buprenorphine was found to provide greater postoperative analgesia for a longer period of time.[11]

2. **Giridhar Naik** et al in 2017 compared postoperative analgesia among epidural Tramadol, Fentanyl & Buprenorphine over first 24 hours in 60 patients undergoing lower limb or lower abdominal surgeries .Patients were divided into three groups (Group T , F and B) of 20 each. Group T patients received epidural top ups of Tramadol 1mg/kg diluted to 10ml with distilled water whenever they had pain for 24hrs from the first dose. Group F patients received epidural top ups of Fentanyl 1μg/kg diluted to 10ml with distilled water and Group B patients

received epidural top ups of Buprenorphine 3µg/kg diluted to 10ml with distilled water whenever they had pain for 24hrs from the first dose. In all the patients intensity of pain and pain relief following injection of the drug in epidural space was assessed. Quality of analgesia was similar with all the three drugs. Fentanyl had earliest onset of analgesia, but because of its shorter duration of analgesia it have to be given more frequently than tramadol and buprenorphine. Buprenorphine had prolonged duration of analgesia and hence required very less number of doses compared to tramadol and fentanyl.[12]

3. **Suraj Dhalae** et al conducted a Study of Epidural Bupivacaine plain versus Epidural Bupivacaine with Fentanyl for intra-operative analgesia in 2000. Sixty patients were divided into four groups (1, 2, 3, 4), each with 15 patients, and were given Epidural anaesthesia with 0.5 percent bupivacaine plain, 0.5 percent bupivacaine with 25 mcg Fentanyl, 0.5 percent bupivacaine with 50 mcg Fentanyl, and 0.5 percent bupivacaine with 75 mcg Fentanyl in groups 1, 2, 3, 4 respectively. Fentanyl was found to have a faster onset , as well as longer analgesia and greater sedation, and its drawbacks were reduced motor blockade, pruritis, and urinary retention. They came to the conclusion that Fentanyl 50 mcg with a longer duration of analgesia (256.66 minutes) was the best choice for optimal postoperative analgesia with lesser side effects. .[13]

4. In 1993, **Dhakshinamoorthy** and his colleagues compared fentanyl and buprenorphine as adjuvants to bupivacaine in epidural anaesthesia for lower abdomen and lower limb procedures. Group A received 0.5 percent bupivacaine 14-20 ml at 1.5 mg/kg with 300 mcg buprenorphine and Group B received 0.5 percent bupivacaine 14-20 ml with 50 mcg fentanyl at 1.5 mg/kg. When administered as an adjuvant to bupivacaine in epidural anaesthesia, they found

that epidural buprenorphine is more effective than fentanyl at delivering long-lasting, satisfying postoperative analgesia.[14]

5. **GM George** et al (2014) compared the analgesic efficacy of three different epidural solutions- Plain ropivacaine0.75% , 0.75% Ropivacaine with 50mcg Fentanyl and 0.75% Ropivacaine with 300mcg Buprenorphine. 102 parturients in the age group 20-35years scheduled for elective cesarean section under continous epidural anesthesia were included in the study. Onset of sensory block was faster in Fentanyl and Buprenorphine groups as compared to Plain Ropivacaine group (9.94±0.48, 10.72±0.26, 14.59±0.34 minutes respectively). Duration of analgesia was longer in Buprenorphine group (516.38 ± 29.14) compared to Fentanyl group (327.06 ±12.41) and Ropivacaine group ( 285.78 ± 10.10). They concluded that addition of both Buprenorphine and Fentanyl to Ropivacaine hastened the onset of sensory block, while addition of Buprenorphine provided prolonged postoperative analgesia.[15]

6. **Cohen S** et al conducted a study to compare the analgesia, plasma concentrations and side effects of Fentanyl and Buprenorphine among 78 parturients after elective cesarean section with epidural anaesthesia. Patients were divided into 3 groups of 26 patients each - Group1 received 0.015%Bupivacaine with 3mcg/ml Buprenorphine and 1mcg/ml epinephrine , Group 2 received 0.015%Bupivacaine with 3mcg/ml Fentanyl with 1mcg/ml epinephrine and Group 3 received 0.015%Bupivacaine with 3 mcg/ml fentanyl as epidural infusions. Plasma for estimation of opioid concentrations was obtained in few patients from each group at intervals of 48 hours during infusion and after infusion was stopped . They observed that pain relief was satisfactory and similar in all three groups. Respiratory and Hemodynamic stability was

maintained in all groups. Pruritis was more common in Fentanyl groups and vomiting was seen only with Buprenorphine. They discovered that average opioid plasma concentrations were less than 1.5ng/ml. They determined that epidural patient-controlled analgesia produced good analgesia, allowed early ambulation, and had no significant adverse effects in all three groups. There were no benefits to using epidural buprenorphine over epidural fentanyl.[16]

7. **WE Ackerman** in 1988 in his study evaluated and compared the duration of analgesia and side effects of equipotent doses of fentanyl (a pure agonist), buprenorphine (an agonist - antagonist) and butorphanol (an agonist – antagonist). He used 50µg of fentanyl, 0.3mg of buprenorphine and 2mg butorphanol epidurally for comparison in postoperative pain relief. The duration of analgesia was defined to be from the time of injection of epidural study solution until the patient experienced any pain (a score > 5 on a 0-10 verbal response scale). The duration of analgesia with buprenorphine was longer (388.06 ± 54.6 min.) as compared to butorphanol (117 ± 36.4 min.). Incidence of sedation was higher with butorphanol and no nausea / vomiting, disturbances in micturition or respiratory depression were noted in any group.[17]

8. **Hayashi H** et al (1993) investigated the analgesic efficacy and side effects of continuous epidural infusions of buprenorphine and fentanyl for postoperative pain management. 50 patients were included in the study who underwent upper or lower abdominal surgeries. They were divided into two groups – Buprenorphine group (B) received bolus injection of 0.1mg Buprenorphine+8ml saline followed by continous infusion of 0.8mg Buprenorphine+ 92ml saline @2ml/hour. Fentanyl group (F) received bolus injection of 0.1mg Fentanyl+6ml saline followed by a infusion of Fentanyl

0.6mg+84ml saline @2ml/hour. They concluded that the analgesic efficacy between the groups was not significantly different. When compared to the Buprenorphine group, the incidence of side effects such as nausea-vomiting, and dizziness was much lower in the Fentanyl group. i.e 11 vs 4 cases and 7 vs 1 case respectively.[18]

9. Receptor binding assays were undertaken in 1985 by **Boas RA** et alto learn more about fentanyl and buprenorphine's opioid binding properties. They used rat forebrain as source of opioid receptors to conduct Ligand binding assays. Fentanyl reached equilibrium rapidly(after 10 minutes) and dissociated equally rapidly (T1/2 =6.8 minutes) and completely within 1 hour. Buprenorphine, on the other hand, displayed a slow receptor association (30 minutes) with high affinity to numerous sites, with slow (T1/2=166 minutes) and incomplete dissociation (50 percent binding after 1 hour).Their results indicated that fentanyl has selective affinity for morphine (μ) receptors while buprenorphine has non-specific binding to opioid receptors. This study helped explain the differences in attaining full analgesic efficacy and duration of action of fentanyl and buprenorphine.[19]

10. **Kaetsu H** et al did a retrospective study on 177 patients for upper and lower abdominal surgeries to compare the efficacy of epidural administration of fentanyl and buprenorphine for postoperative pain relief. 73 patients in Fentanyl group (F) received fentanyl 0.1 mg with saline 8ml epidurally followed by a constant infusion of 0.025 mg/hr for 18-24hrs. 104 patients in Buprenorphine group(B) received Buprenorphine 0.2mg with saline 9ml epidurally . In the postoperative period , 33 patients (76.7%) in F group and 27 patients (52.9%) in B group obtained satisfactory analgesia ($p<0.05$). [20]

## ANATOMY OF VERTEBRAL COLUMN

The success of this study depends on a good anatomical knowledge of the spinal cord and vertebral column.

## VERTEBRAL COLUMN[21]:

The Vertebral column is made up of 33 vertebrae:-

TABLE 1:- TYPES OF VERTEBRAE

| | |
|---|---|
| CERVICAL | 7 (C1-C7) |
| THORACIC | 12 (T1-T12) |
| LUMBAR | 5 (L1-L5) |
| SACRUM | 5 (fused) |
| COCCYX | 4 (fused) |

There are 4 anatomical curvatures in the vertebral column namely, :-

Primary – Thoracic and sacral which are concave anteriorly.

Secondary- Cervical and Lumbar which are convex anteriorly.

The spinal canal extends from the foramen magnum upto the sacral hiatus.

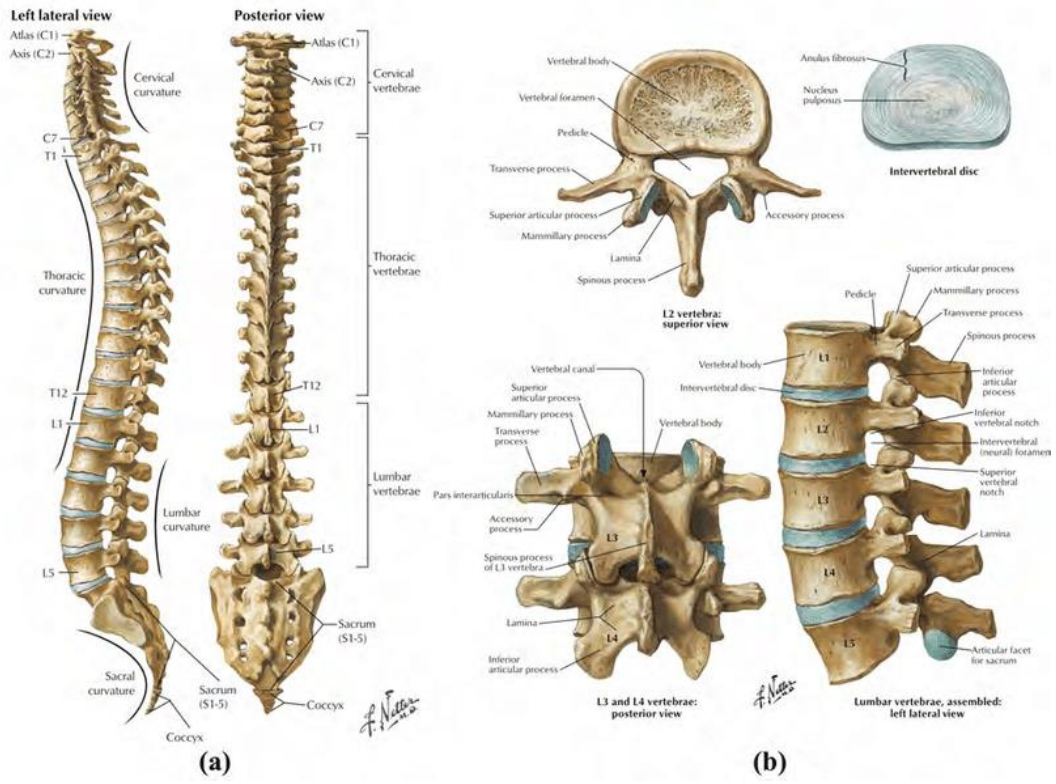



**FIGURE 1:- Lateral and Posterior View of Vertebral Column ; Parts of Lumbar vertebrae.**

**CERVICAL VERTEBRA:-**

The normal cervical vertebral body (C3-C6) is characterised by a small flattened triangular body with a relatively large vertebral foramen. The transverse process is short ans has the foramen transversarium which transmits the vertebral vessels .

The largest and most inferior cervical vertebra is the c7 vertebra. C7 has a large spinous process that protrudes posteriorly towards the skin at the back of the neck andcan be easily seen and felt making it a prominent landmark known as vertebra prominens.

**THORACIC VERTEBRA:-**

The typical thoracic vertebral body (T2-T8) is in the shape of heart, with the upper two vertebral bodies resembling cervical vertebrae and the lower thoracic vertebral bodies resembling lumbar vertebrae. Because the spinous processes of the mid thoracic vertebrae are caudally angulated, a pronounced cephalad angulation of the needle is required for passing in between the spines while executing a thoracic epidural in the midline route. T11 and T12 have spinous processes that are almost horizontal, short, and square in shape, similar to lumbar vertebrae.

**LUMBAR VERTEBRA :-**

The lumbar vertebra's body is big and in shape of kidney. The vertebral foramen is triangular in shape, larger than the thoracic vertebral foramen but smaller than the cervical vertebral foramen. The superior notches are shallow and the pedicles are thick. The transverse processes are narrow; their length increases from L1 to L3, then decreases from L4 to L5. As opposed to the thoracic area, the laminae are short, wide, and do not overlap. Spinous processes of the lumbar spine are horizontal and oblong . The lumbosacral angle is formed by the fifth lumbar vertebra, which is wedge-shaped and deeper in front than behind.

The intercristal line (Tuffier's line), which connects the tops of the iliac crests, runs through the body of the 4th lumbar vertebra and serves as a valuable landmark. The L3/L4 interspace is normally above this line, while the L4/L5 interspace is below. By flexing the patient's spine and widening the gap between the lumbar spinous processes, the interspace for lumbar puncture can be identified more easily.

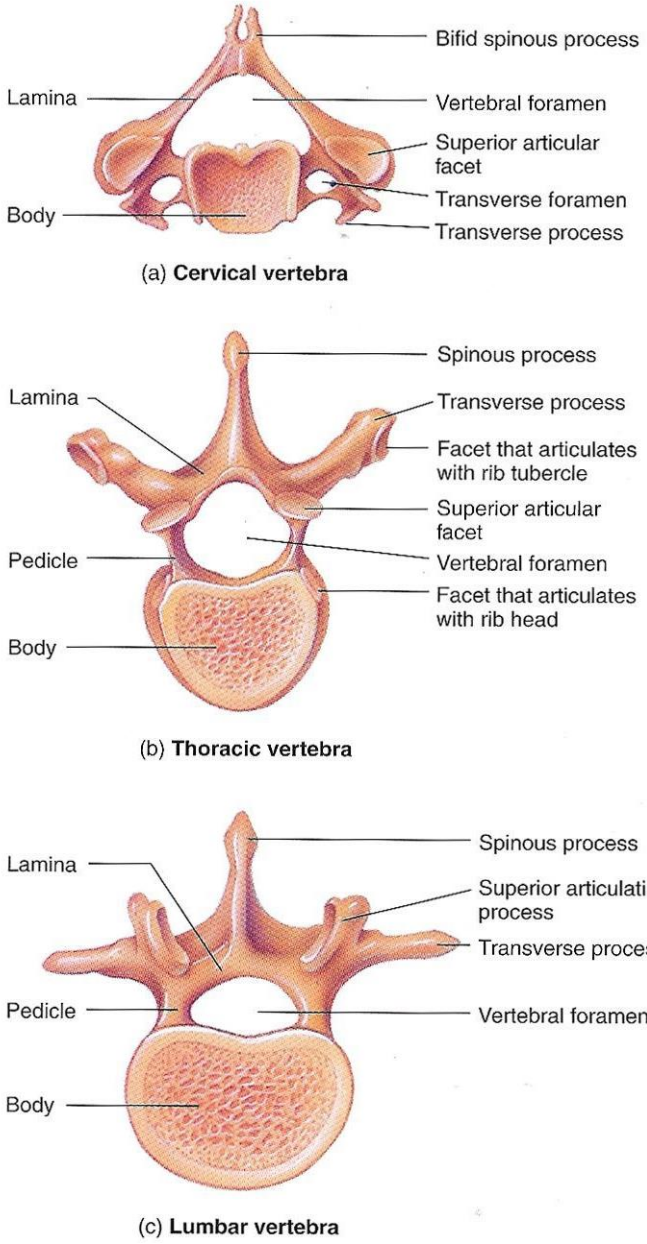



**FIGURE 2 :- TYPES OF VERTEBRA**

Several ligaments bind the spinal column together, providing stability and flexibility.

They are :-

- **The Anterior Logitudnal Ligament**, which runs along the anterior aspect of the vertebral bodies from above downwards, extending from C2 to the upper sacral vertebrae , it is adherent to the intervertebral disc.

- **Posterior logitudnal ligament**: this ligament runs along the posterior surface of the vertebral bodies.
- **Supraspinous ligament**: ascends from the sacrum to the C7 vertebra, and is a strong fibrous cord linking the apices of spinous processes. Then it extends up to the external occipital protuberance as the ligamentumnuchae.
- **The interspinousligament** : It is a thin membranous ligament that connects the spinous processes shafts, joining anetriorly with the ligamentumflavumand posteriorly with the supraspinous ligament.
- **Ligamentumflavum**: It joins adjacent lamina by linking the downward edge of the above lamina to the cephalad edge of the below lamina. It is also known as the "yellow ligament." It is made up of yellow elastic fibres.

**SPINAL CANAL**

The spinal cord, which begins at the level of the foramen magnum and terminates below as the conusmedullaris, is a continuation of the medulla oblongata. It has a cylindrical shape and a length of 45 cm in adults. The spinal cord tapers into the conusmedullaris, which continues as the filumterminale, a thin thread-like tissue linked to the coccyx. The filumterminale is mainly the pia mater invested in a dura sheath. At birth Itends at the lower border of the L3 vertebra and rises to end at the lower border of the L1 vertebra in adults.

There are totally 31 pairs of symmetrically arranged spinal verve roots- Cervical-8, thoracic-12, lumbar-5, sacral-5, and coccygeal-1 . The elongation of nerve roots in the lumbar and sacral regions before they exit the intervertebral foramen forms the caudaequina.

The dura mater, arachanoid mater, and pia mater are the three meningeal coverings of the spinal cord.

- **DURAMATER:-**contains two layers- the internal meningeal layer made by cerebral dura, which is composed of dense fibrous tissue and the outer endosteal layer of the cerebral dura at the level of foramen magnum merges with the periosteum enclosing the skull , and then continues as periosteal lining of the vertebral canal. At the second sacral segment, the dura comes to an end (variably L5-S3). It covers the filumterminale and joins to the coccygeal periosteum. The dura is linked to the posterior longitudinal ligament anteriorly and extends laterally around the nerve roots, although it is free posteriorly**.**
- **ARACHANOID MATER:** a thin, fragile, nonvascular membrane that lines the duramater.
- **PIA MATER**: a vascular sheath of connective tissue that wraps around the spinal cord and protects it. The frontal section (lineasplendens) is thickened, and the ligamentumdenticulatum forms laterally and is linked to the duramater. An incomplete sheet of pia (posterior subarachnoid septum) connects it to the dura posteriorly. It pierces the dural sac inferiorly and adheres to the coccyx with a dura covering sheath.
- **SUBDURAL SPACE**: Between the arachnoid mater and the dura mater, there is a gap that harbors thin serous fluid. This space is subdural space
- **SUBARACHANOID SPACE**: It is the anatomical space between the arachanoid mater and the pia mater that contains cerebrospinal fluid and spinal nerve roots. Although the spinal cord in adults ends at the lower border of L1, the subarachnoid space extends till S2.

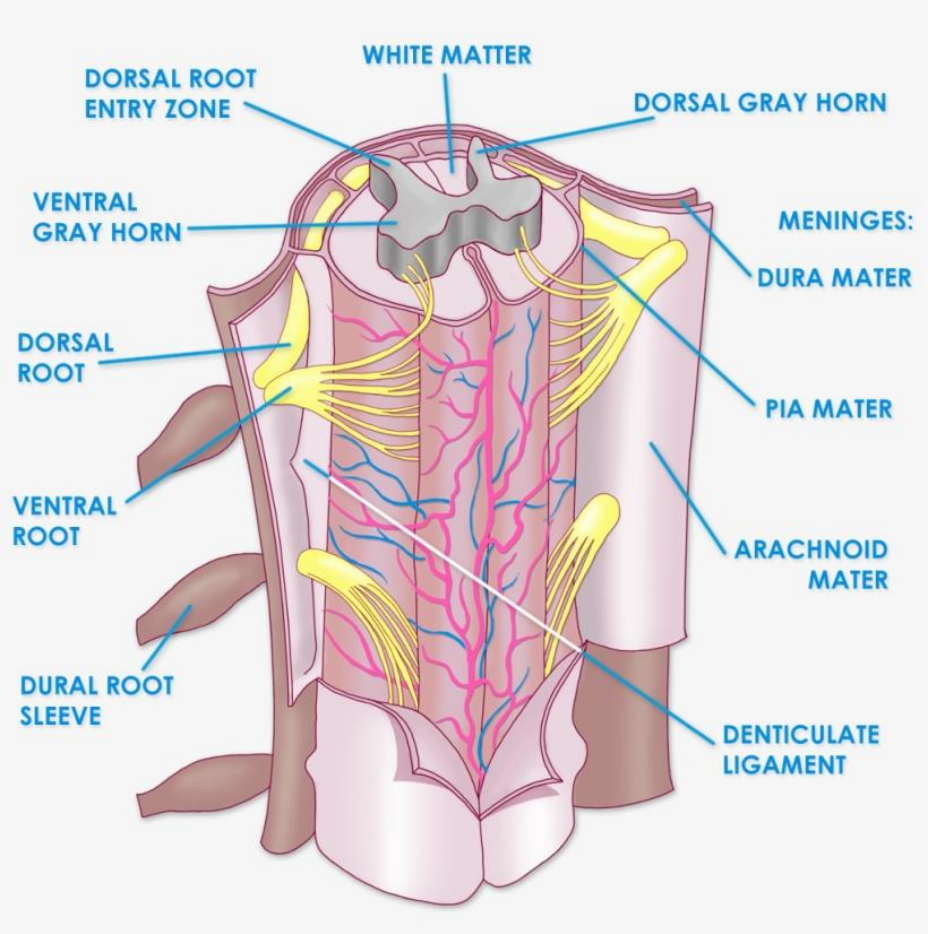



**FIGURE 3:- TRANSVERSE SECTION OF SPINAL CORD SHOWING THE MENINGES.**

## EPIDURAL ANESTHESIA

History:-

- 1885- Corning first performed peridural anesthesia with cocaine for pain relief of an extremity.
- Cathelin first used epidural anesthesia in sacral region. This is now called Caudal analgesia
- Lawen investigated the anatomy of the spinal and epidural areas.
- Curbelo first performed continousperidural anesthesia by means of a ureteral catheter.
- Crawford used peridural anesthesia for thoracic surgery.

**Definition:-**

Epidural anesthesia (Peridural or extradural) is anesthesia obtained by blocking spinal nerves in the epidural space as the nerves emerge from the dura and pass into the intervertebral foramina. The anesthetic solution is deposited outside the dura and therefore differs from the spinal or subdural anesthesia, where the solution is deposited in the subarachnaoid space. A segmental block is produced mainly of the spinal sensory and sympathetic nerve fibers. Motor fibers maybe partially or fully blocked.

Deposition of the anesthetic solution may be accomplished at the thoracic, lumbar or caudal area.

**ANATOMIC CONSIDERATIONS[22]:-**

The epidural space is a circular space surrounding the dural sac and all of its extensions. It extends from the foramen magnum to the coccyx.

**BOUNDARIES:-**

- Superior : The periosteal layer of the vertebral canal merges with the spinal dura at the foramen magnum.Inferior: upto the sacrococcygeal membrane.
- Lateral: intervertebral foramen and peduncles of the vertebra.
- Posterior: ligamentum flavum

The gap is larger and more easily distensible posteriorly, whereas the dura is closely attached to the periosteum of the vertebral bodies anteriorly. Up to the angle of the ribs, lateral extensions of the space accompany the spinal nerves through the intervertebral foramina into the paravertebral tissue.

The following structures are pierced to reach the epidural space in the midline sagittal plane:

1. Skin
2. Subcutaeneous tissue,
3. Supraspinous ligament
4. Interspinous ligament
5. FlavumLigamentum

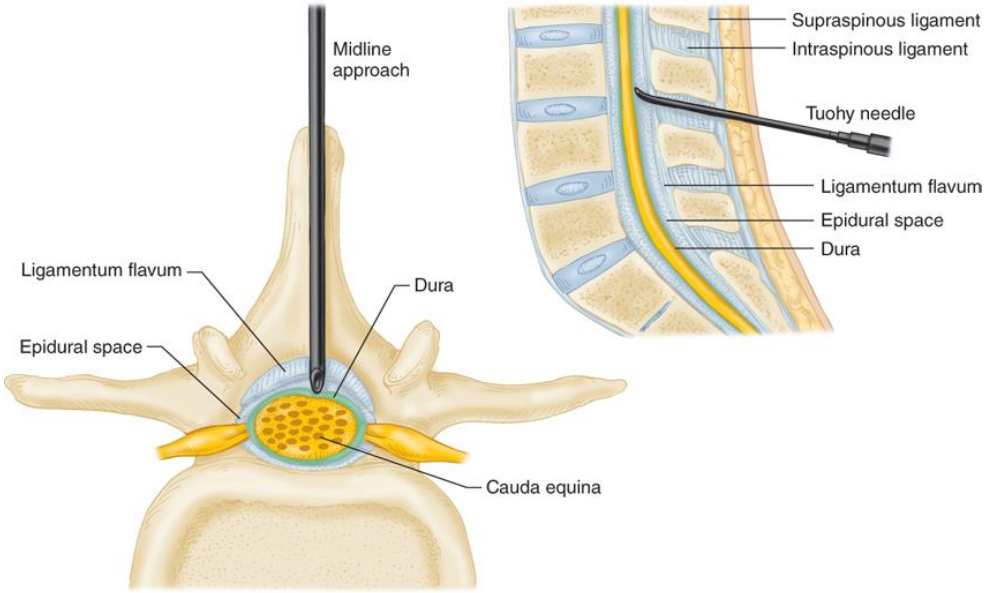





**FIGURE 4:- STRUCTURES PIERCED TO ENTER EPIDURAL SPACE.**

The vertebral column provides anatomic factors important in inserting the epidural needle. In the cervical and lumbar area , the spinous processes and more horizontal. However , in the thoracic region, they are oblique. In the mid region from T4 –T7 tips of the spine usually overlie the next lower vertebrae or interspace.

**CONTENTS:-**

1) **CONNECTIVE TISSUE:-**

- Significant amount present ventrally connecting the dura with posterior longitudinal ligament.
- The dura is connected to the ligamentumflavum dorsally by an unique midline fold of connective tissue known as the "plicamedianadorsalis." The midline band separates the epidural space into right and left halves, narrowing the space in the middle.
- The dorsomedian fold or strands of connective tissue must be separated in order to place an epidural needle. When a real dorsomedian band or membrane is present, a patchy and/or unilateral sort of block is conceivable.

2) **EPIDURAL FAT:-**

- Varying amounts distributed in random fashion more or so lateral and posterior region.
- Has affinity for lipid soluble drugs ( Bupivacaine and Etidocaine) thus competes with vascular and neural uptake – the drug remains in the fat for longer duration.
- The compliance of the epidural fat varies with persons and with increasing age – low compliance may result in drip back of injected local anesthetic

3) Areolar tissue

4) Spinal nerve roots with their dural sleeves.

5) Spinal arteries: the spinal branches of aortic ,subclavian and iliac artery crosses the epidural space in the region of dural cuff.

6) Epidural veins:-

- Large valveless veins which are part of internal vertebral venous plexus.

- They lie in the anterolateral part thus epidural needles should pierce the ligamentumflavum in midline
- Marked increase in intrabdominal pressure (pregnancy , abdominal mass) thus leads to obstruction of inferior vena cava resulting in rerouting of the venous return by way of epidural veins and then azygous vein above the level of obstruction. This leads to –
    - Increased chance of accidental puncture or catheter insertion into the veins
    - Increased surface area- more absorption of local anesthetics
    - Decreased epidural space volume thus requiring reduction of dose.

**7) Epidural lymphatics**

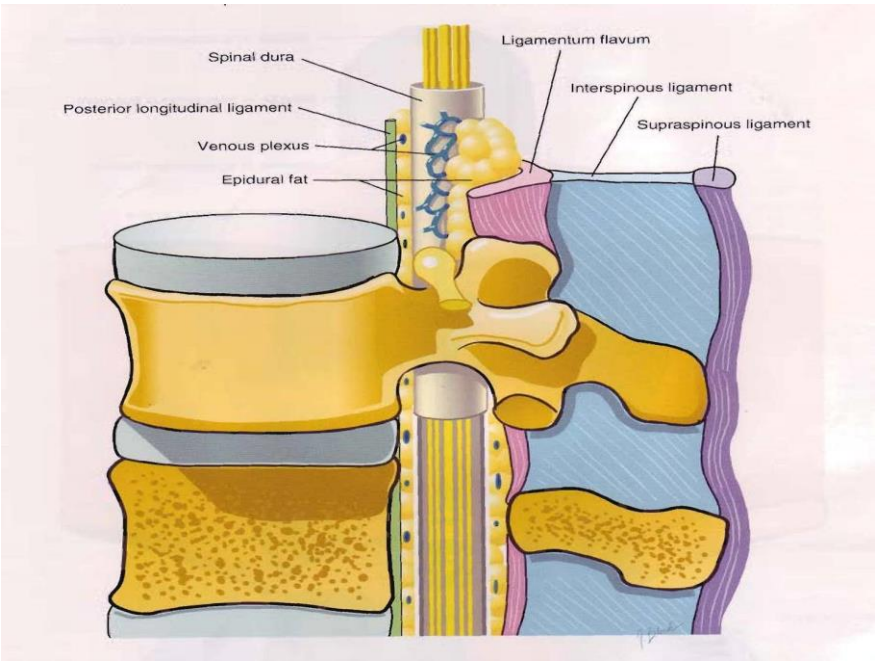



**FIGURE 5:- CONTENTS OF EPIDURAL SPACE**

**SIZE OF EPIDURAL SPACE:-**

**TABLE 2:- Regional epidural space width with dural thickness:-**

| | Epidural space (mm) | Thickness of Dura(mm) |
|---|---|---|
| Cervical | 1.0-1.5 | 1.5-2.0 |
| Upper thoracic | 2.5-3.0 | 1.0 |
| Lower thoracic | 4.0-5.0 | 1.0 |
| Lumbar | 5.0-.0 | 0.33-0.66 |

**DISTANCE TO EPIDURAL SPACE:-**

In 60% patients, the epidural space is to be found within 5.0 cm of the skin in the midline. In about 10% of patients, it maybe necessary to insert a needle to a depth of 6.0cm or more. A decrease of resistance at a depth of < 3.0 cm, on the other hand, is unlikely to detect the epidural space.

**Factors affecting depth of epidural space:-**

- Distance increases with increasing adipose tissue as seen in obese patients.
- Angle of the needle. If the needle is not perpendicular , the space will be located at a greater distance
- Position of the patient :-with the patient in lateral position , the skin may sag imperceptibly and the distance increases. With the patient in the sitting position , the depth of the space is slightly less.
- Ethnic origin:- Asian women have an average depth to the epidural space of 4.33cm which is less that of Caucasian women with a depth of 4.89cm.
- Edema:- clinically recognized edema in patients will increase the distance from the skin to the epidural space by an average of 0.75cm

**EPIDURAL SPACE IN CHILDREN:-**

In children under six years of age , the epidural space has spongy , gelatinous lobules and distinct spaces. This in in contrast to the densely packed fat globules and fibrous strands characteristic of the mature epidural space. Because of this difference , there is a more rapid longitudinal spread of drugs within the juvenile epidural space.

**PHYSIOLOGIC CONSIDERATIONS:-**

Originally, a negative extradural pressure was described in 1928 by Heldt and Moloney. This so called negative pressure in the epidural space is higher at places of firm attachment and in the thoracic area, lower in the lumbar region, and absent in the sacral region.

**CONE THEORY-**The needle inserted into the epidural space depresses the dura, resulting in a bigger epidural space, according to the cone theory. As a result, it's regarded as an artefact caused by the advancing needle's depression of the dura.

**TRANSMISSION THEORY-** The transmission theory proposes that intrapleural negative pressure is transmitted to the epidural space via the intervertebral foramina, resulting in negative pressure in the epidural space.

Anatomically, there is a free communication of the extradural space with the paravertebral space and in turn , the tissue pressure in this area is influenced by the intrapleural pressure. Factors that decrease the negative intrapleural pressure or raise the subarachnoid pressure will decrease the negative epidural pressure.

Marked flexion of the spinal column reduces the length of the anterior wall and elongates the posterior wall. Consequently, the capacity of the vertebral canal proper increases and results in a greater negative pressure. The negative pressure is greater in young people. In older patients with ligamentous changes and ankylosis of articulations , anterior flexion is limited.

The extradural pressure has been carefully measured in the relaxed patients. In the lower lumbar region , it amounts to about 0.5cmof H2O . the upper lumbar region , it amounts to about 1.0 cm of H20; and in the thoracic region , it varies from 1 to 3 cm of H2O with an average of 2.0 cm.

**SITE OF ACTION:-**

Three sites of action of local anesthetic agents have been identified:-

1. On the nerves as they traverse the epidural space
2. On the nerves as they pass out through the intervertebral foramina
3. On the nerves in the subrachanoid space- the agent having reached this area by diffusion through the dura.

After administration of 2% lignocaine solution , anesthesia appears in about 10minutes and is complete in 20 minutes. Sensory anesthesia of all modalities is complete , block of sympathetic fibers is partial , while motor paralysis is incomplete. The anesthesia lasts upto two hours and gradually disappears during the following two hours.

**VASCULAR ABSORPTION PHARMACOKINETICS:-**

Absorption of local anesthetics from the epidural space is biphasic. The intial or rapid absorption phase is characterized by short peak plasma times , rapidly attained and high peak concentrations. As the peak levels decline , a second slower phase of absorption continues lasting upto 3 hours. This slow absorption phase extends into the elimination half life phase, which appears to be prolonged.

**FACTORS DETERMING EXTENT OF EPIDURAL ANESTHESIA:-**

- Volume of solution
- Selection of appropriate interspace
- Speed of injection- slow rates diminish spread, and interrupted injection minimizes spread.
- Position of patient
- Effect of gravity- solutions tend to gravitate to dependant parts of the epidural space .
- Specific gravity of anesthetic solution

**VOLUME CAPACITY OF EPIDURAL SPACE:-**

The volume of solution required for an epidural anesthetic depends on the number of segments to be blocked and the site of injection. Spread or extent of anesthesia is commonly expressed as the segmental dose. That is 'dose spread' is the volume of analgesic solution injected in milliliters per number of dermatomes blocked or milliliters per spinal segment.

Cervical- 1.5ml

Thoracic – 2.0ml

Lumbar- 2.5ml

**DETECTION OF EPIDURAL SPACE[23]:-**

- Negative pressure techniques:-
    1. Hanging drop Sign
    2. Manometer technique
    3. Capillary Tube method
- Disappearance of resistance techniques:-
    1. Loss of resistance syringe

2. Balloon technique
3. Spring loaded syringe
4. Vertical tube of Dawkins
5. Brook's device

- Nerve Stimulation
- Ultrasound
- Fluoroscopy
- Epiduroscopy
- Pressure transducer guided method
- The sound created by the epidural needle as it passes through the interspinous ligament and ligamentumflavum which is amplified using auditory amplification.

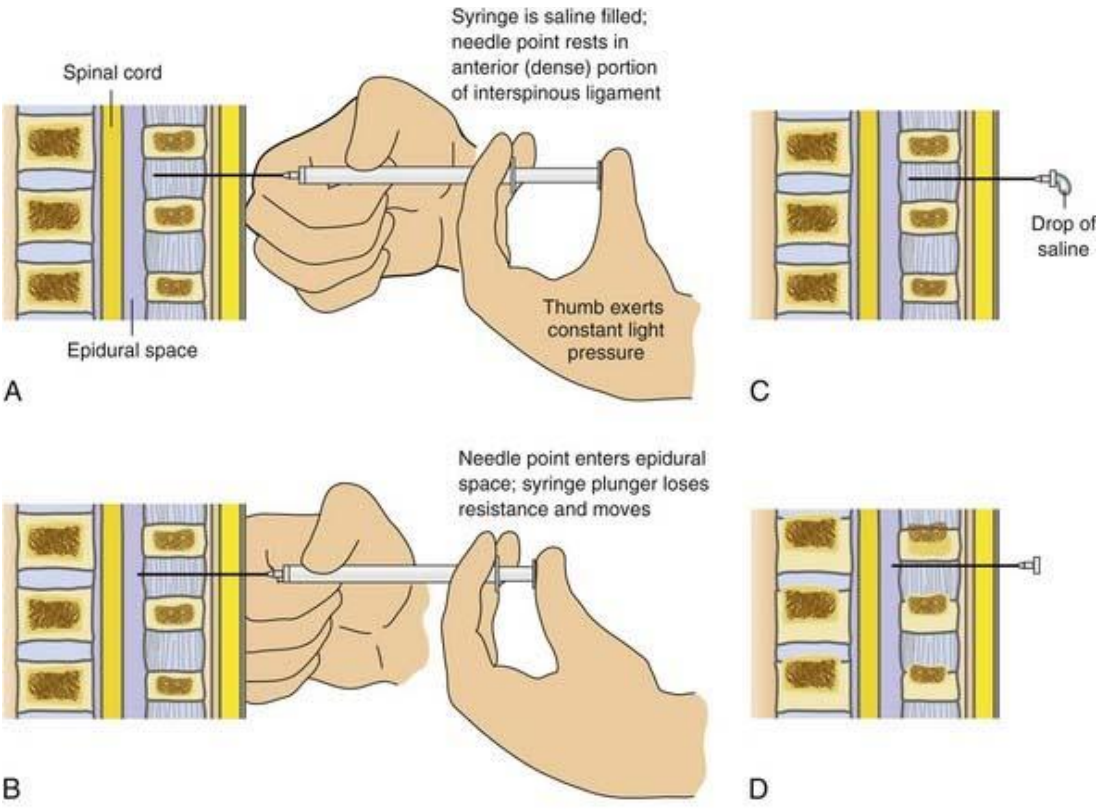



**FIGURE 6 :- TECHNIQUES OF IDENTIFICATION OF EPIDURAL SPACE**

**TABLE 3:- CHOICE OF EPIDURAL NEEDLES AND CATHETERS:-**

| EPIDURAL NEEDLES | CATHETERS |
|---|---|
| • Crawford point needle | 16, 18 , 19, 20 G |
| • Touhy needle Huber point | Nylon , polyurethane and Teflon |
| • Hustead needle | Single lumen (open end) |
| Others- Weiss , Cheng , Crawley | Multi orifice (blunt tip) |

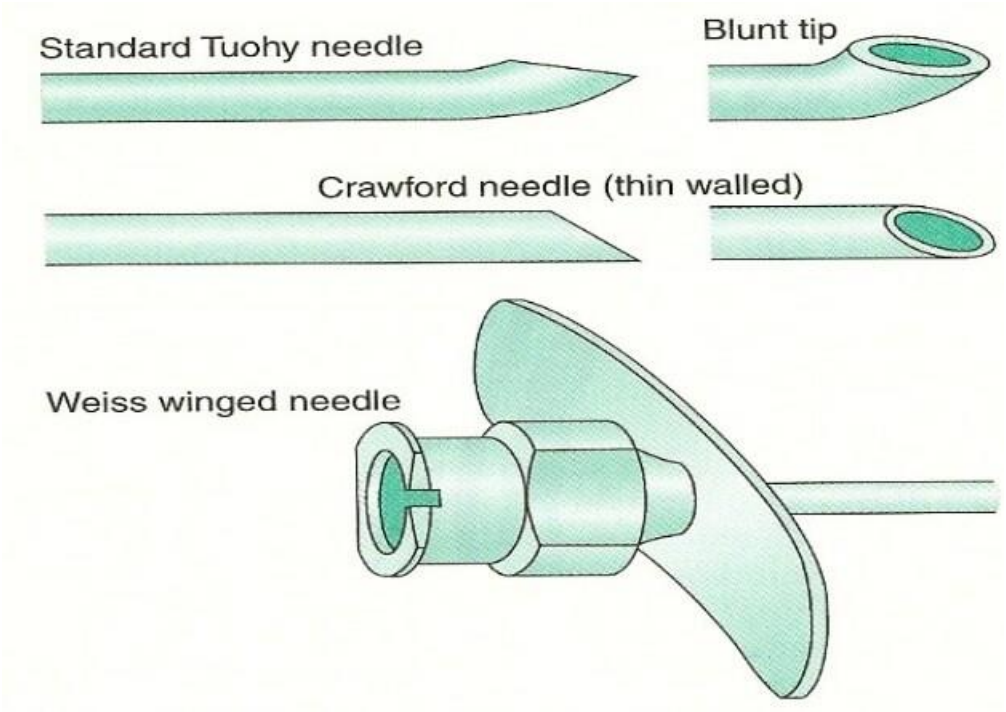



**FIGURE 7 :- TYPES OF EPIDURAL NEEDLE**

**INDICATIONS:-**

1. Surgery
    - Upper & lower abdominal surgery for intra and postoperative pain management
    - Urological surgeries
    - Thoracic surgeries.
2. Postoperative and post trauma pain relief.
3. Obstetric anesthesia and analgesia.
4. Diagnosis and management of chronic pain.
5. Epidural steroids and narcotics
6. Newer techniques - Epidural electrical stimulation.

**CONTRA INDICATIONS:-**

Absolute:

- Patient refusal
- Major coagulation disorders.
- Uncorrected hypovolemia
- Infection at site of injection
- Severe sepsis.

Relative:

- Pre-existing neurological deficit.
- Spine deformities.

**COMPLICATIONS:**

1. Director trauma to nerve and nerve roots.
2. Epidural hematoma
3. Abscess
4. Neurotoxicity
5. Anterior spinal artery spasm due to needle injury or by use of epinephrine.
6. Missed segments - patching uptake of blockade.
7. Inadequate motor block
8. Sacral sparing.
9. Inadvertent dural puncture
10. Subdural communication
11. Cannulation into an epidural vein.

# PHYSIOLOGY OF PAIN[24]

Pain is a distressing sensory and emotional experience that is linked to, or mimics, real or potential tissue damage.

Acute pain:- any pain of recent onset and probable limited duration of <12weeks Chronic pain- any pain of duration >12weeks.

Pain transmission from peripheral nociceptors to the spinal cord and higher structures of the CNS is a dynamic process involving several pathways , numerous receptors , neurotransmitters and secondary messengers.

**Theories of pain transmission:-**

1. Specific theory: According to this theory, there are specific pain receptors in the skin and specialized nerves and pathways which transmit painful stimuli from the periphery to spinal cord and then to the brain.
2. Pattern theory:- There were no pain receptors in this theory, and pain was caused by the summation of impulses elicited by heat stimuli or pressure applied to the skin. This theory, initially called as intense theory, was later renamed summation theory.
3. Gate control theory:- by Mezlack and Wall (1965) , impulses initiated by stimulation of skin pass to three spinal cord systems - the dorsal horn fibres , the substantia gelatinosa and the first central transmission cells (T cells) in dorsal horn.

**Pain pathway:-**

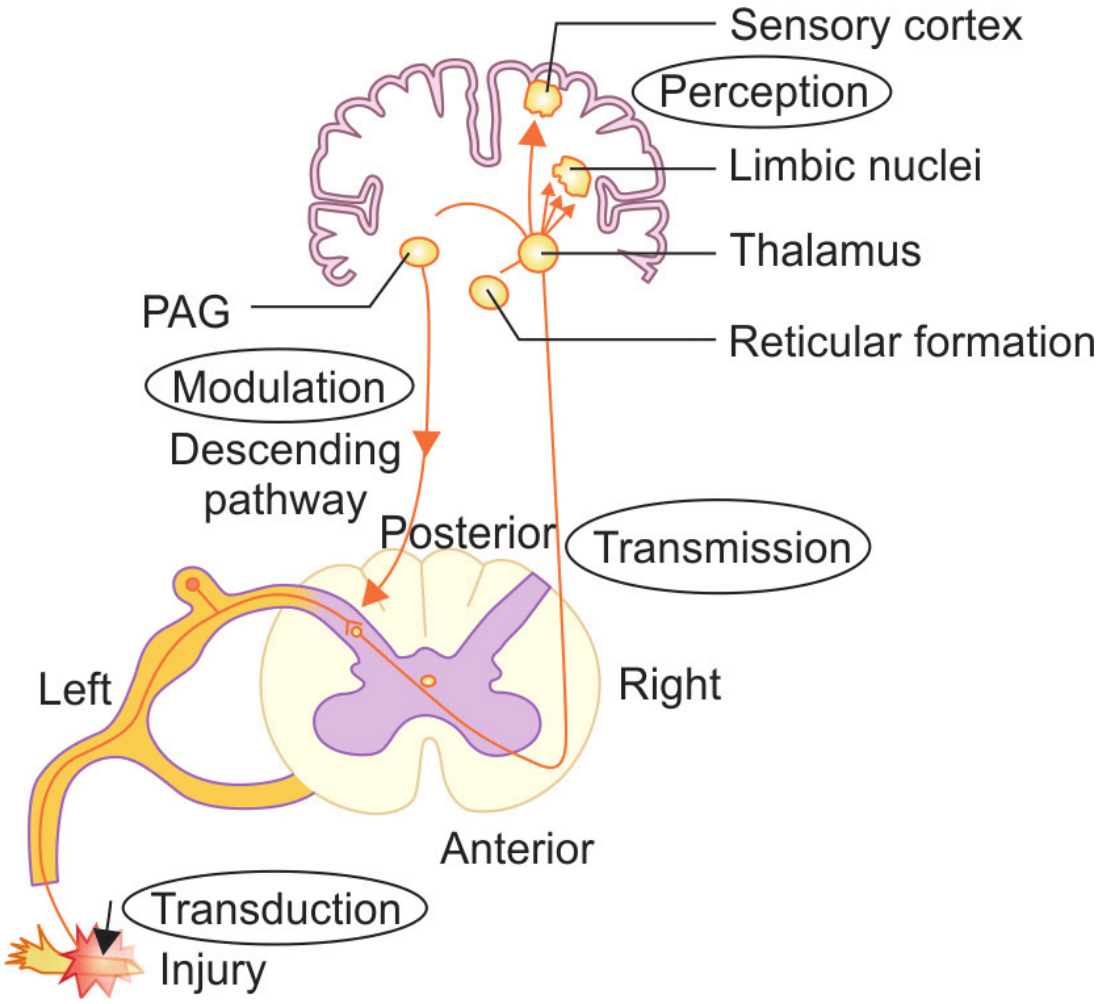



**FIGURE 8 :- PAIN PATHWAY**

Dorsal horn: The relay centre for nociception: The afferent fibers from peripheral nociceptors enter the spinal cord in the dorsal root, ascend or descend several segments in the Lissauer tract and synapse with the dorsal horn neurons for the primary integration of peripheral nociceptive information. The dorsal horn consists of 6 laminae

1. C fibers (unmyelinated) synapse with interneurons in Lamina Ⅰ (marginal layer) and Lamina Ⅱ ( substantia gelatinosa of Rolando)
2. Aδ fibers project to Laminae Ⅰ Ⅱ and Ⅴ
3. Aβ fibers terminate in LaminaeⅢ , Ⅳ and Ⅴ

4. Large diameter myelinated fibers also terminate in Laminae Ⅰ, Ⅳ, Ⅶand the ventral horn.
5. 2nd order wide dynamic range neurons are located in Lamina Ⅴ

The Lamina Ⅰ and LaminaeⅢ, Ⅳ projection neurons that express the NK-1 receptors are heavily innervated by Substance-P containing primary afferents.

The descending monoaminergic (serotinergic and norepinephrinergic) axons project from the brain through the dorsal horn , terminating in Laminae Ⅰ and Ⅱ and are involved in the descending pain modulation

**Gate Control Theory of Pain[25]:-**

It was proposed by Ronald Melzack and Patrick Wall in 1965

Painful information is projected to the Supraspinal brain region if the gate is open , whereas painful stimulus is not felt if the gate is closed by the simultaneous inhibitory impulses.

- Aδ and C fibers:-

-inhibit the inhibition

-open the gate

-transmission of painful stimuli

- Aβ fibers:-

-activate the inhibition

-close the gate

-inhibition of painful stimuli

**Ascending Pathways for pain transmission:-**

- Major pathways:-

- Spinothalamic tract (Thalamus)
- Spinomedullary Tract (Medulla oblongata)

- Spinobulbar tract (brainstem)
- Spinohypothalamic tract (hypothalamus and ventral forebrain)
    - Indirect projections:-
- Dorsal Column system
- Spinocervicothalamic pathway

Spinothalamic Tract:- About 85-90% of neuronal cells are found on the contraletral side. The axons of Spinothalamic tract cells cross in the dorsal and ventral spinal commissures to reach the white matter of contralateral spinal cord. Within one or two segments rostral to the cells of origin.

Descending pathways of pain modulation:-

-The Periaqueductal Gray(PAG) and Rostro Ventral Medulla(RVM) regions of the brainstem are the critical brain regions underlying descending pain modulation.

-Evidence demonstrates that descending pathways originating from certain supraspinal regions may concurrently promote and suppress nociceptive transmission through the dorsal horn , termed as the descending inhibition pathway (DI) and descending facilitation pathway (DF)

-The periaqueductal (PAG) neurons receive direct and indirect inputs from several brain structures.

-The RostroVentral Medulla (RVM) receives inputs from serotonin containing neurons of the dorsal raphe and neurotensinergic neurons of the PAG. The PAG and adjacent Nucleus Cuneiformis are major sources of input for the RVM.

-The Locus Ceruleus and the A5 and A7 noradrenegic cell groups are major noradrenergic projections to the dorsal horn

-The PAG-RVM system also contribute to hyperalgesia and allodynia in inflammatory and neuropathic models.

-there are 3 distinct populations of neurons in RVM system- ‘ON cells’ , ‘OFF cells’ , ‘Neutral cells’.

-The ‘ON cells’ exhibit net facilitatory effect on nociception and ‘OFF cells’ exhibit inhibitory effect.

-Also PAG-RVM system serves as one of the major brain sites underlying opiate induced analgesia.

-the μ opioid receptors are located in the ‘ON cells’ and the κ opioid receptors in the ‘OFF cells’

**OPIOID RECEPTORS[26]:-**

Discovery of specific opioid receptors was made by Snyder and Pert in 1973; Yaksh and Rudy 1976.

There are as many as 8 types of opioid receptors. In the CNS , 4 types are shown to exist , namely μ (Mu) , κ (kappa), σ (sigma) and δ (delta).

Relative densities of opioid receptors:-

- Primary Mu:-
  - Lamina Ⅰ/Ⅳ cortex
  - Dorsomedial and Ventral thalamus
  - Hypothalamus
  - Hippocampus
  - Mid brain Raphe
- Primary Delta:-
  - Lamina Ⅱ/Ⅲ/Ⅴ cortex
  - Amygdala
  - Nucleus accumbens
  - pontine nucleus
- Mixed Mu & Delta:-
  - Lamina Ⅵ cortex
  - Nucleus tractus solitaries
  - Substantia gelatinosa

Pharmacological properties associated with the type of receptors:-

μ: Receptors thought to mediate supraspinal analgesia, respiratory depression , euphoria and physical dependence.

K: receptors mediate dependence , dieresis , analgesia , respiratory depression , miosis, sedation.

σ :dysphoria, hallucination, respiratory and vasomotor stimulation

δ : respiratory depression.

**PHARMACOLOGY OF DRUGS:**

**BUPIVACAINE**[27]**:-**

In the year 1957 Ekemstam developed an amide-type local anaesthetic medication called Bupivacaine hydrochloride and first used clinically in 1963 by L.J. Telivuo.

**Chemical Structure** :-

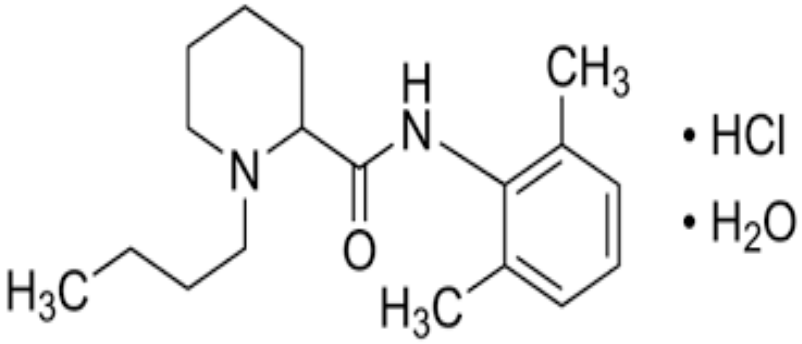



FIGURE 9 :- Chemical Structure of Bupivacaine

**Chemical name:** l-n-butyl-DL-piperidine-2-carboxylic acid-2, 6 dimethylanilide hydrochloride.

**Physicochemical properties:**

Molecular weight - 288 (base)

325 (chloride salt)

pKa value - 8.115

Plasma protein binding - 95%

Solubility: The base is just slightly soluble in water, whereas the hydrochloride is much readily soluble.

Stability and sterilisation: Bupivacaine is quite stable and can be autoclaved multiple times.

258°C is its melting point

Bupivacaine is 3 to 4 times more strong than lidocaine in terms of potency**.**

**Mechanism of action:-**

Local anaesthetics limit the passage of sodium ions through ion selective sodium channels in neuronal membranes, preventing nerve impulse transmission (conduction blockade). For local anaesthetic compounds, the sodium channel is a specific receptor. Local anaesthetic compounds occluding open sodium channels contribute little to total sodium permeability inhibition. When the permeability of sodium ion channels fails to rise, the rate of depolarization slows to the point where the threshold potential is not reached and an action potential is not transmitted. Because the concentration of local anaesthetics in CSF drops as the distance from the injection site increases, Different types of nerve fibres are sensitive to the effects of local anaesthetics in different ways, resulting in zones of differential anaesthesia.

The Cm refers to the lowest concentration of local anaesthesia required to stop nerve impulse conduction. Cm is influenced by nerve fibre diameter, with larger nerve fibres requiring a higher dosage of local anaesthetic to achieve conduction blocking. Cm is reduced by a high frequency of nerve stimulation or an increased tissue pH. Sensory anaesthesia is not always accompanied by skeletal muscle paralysis because the Cm of motor fibres is typically twice that of sensory fibres.

It is necessary to expose at least two and ideally three consecutive Ranvier nodes (about 1 cm) to an appropriate dosage of local anaesthetic for conduction blockage to occur in an A fibre. Despite the differences in sizes, both types of pain transmitting fibres (myelinated A delta and non myelinated C fibres) are blocked by similar concentrations of local anaesthetics. Despite being myelinated, preganglionic B fibres are more easily inhibited by local anaesthetics than any other fibre.

**Pharmacodynamics**:-

Bupivacaine takes 5 to 7 minutes to take effect, and it takes 15 to 25 minutes to achieve maximum anaesthesia..

The length of anaesthesia varies depending on the type of block; a peridural block lasts roughly 3.5 to 5 hours on average. It takes roughly 5 to 6 hours for nerve blocks.

**Pharmacokinetics**

- Distribution and absorption:

The place of injection and dosage, as well as the usage of epinephrine and the drug's pharmacologic features, all influence local anaesthetic absorption into the systemic circulation.

The velocity of tissue distribution and the rate of drug clearance define the final plasma concentration of a local anaesthetic.

The intrinsic local anaesthetic efficacy and redistribution are determined by lipid solubility. The local anaesthetic is eventually removed from the bloodstream through metabolism and excretion.

Bupivacaine has a 2.5-hour alpha half-life in plasma after reaching concentrations of 1.0 to 2.0 g/ml. The half-life of beta is around 4 to 5 hours.

- **Plasma Binding**:

The medicine binds to protein so well in plasma that it binds to it 95% of the time. The distribution and excretion of local anaesthetics will be influenced by protein binding. Protein binding is related to the lipid solubility of the local anaesthetic and is inversely proportional to the drug's plasma concentration.

The first pass lung extraction for Bupivacaine is dosage dependent, implying that the absorption process becomes saturated quickly. The mother and foetus may experience clinically significant transplacental transmission of local anaesthesia.

The rate and degree of diffusion of local anaesthetics across the placenta is influenced by plasma protein binding. Bupivacaine is 95 percent protein bound and has a concentration ratio of 0.32 between the umbilical vein and the maternal artery.

- **Metabolism**

Bupivacaine is metabolised at different rates by microsomal enzymes in the liver. Among the amide local anaesthetics, bupivacaine has the slowest metabolism. Aromatic hydroxylation, N-dealkylation, amide hydrolysis, and conjugation are all pathways for Bupivacaine metabolism.

- **systemic toxicity**

A local anaesthetic's systemic toxicity is caused by an excessive plasma concentration of the medication. The pace of drug entry into the systemic circulation compared to their redistribution to inactive tissue locations and elimination by metabolism determines plasma concentrations.

- **Toxicity of the Central Nervous System (CNS)**: It causes restlessness, vertigo, tinnitus, and difficulties focusing at first. Slurred speech and skeletal muscle twitching arise from increased focus. The onset of tonic-clonic seizures is commonly preceded by skeletal muscle twitching in the face and extremities. Before the commencement of seizures, there is drowsiness. Seizures are frequently followed by CNS depression, which might include hypotension and apnea. Seizures are usually associated with plasma concentrations of 4.5 to 5.5 micro g/ml.

- Selective cardiac toxicity: Protein binding sites (alpha1 acid glycoprotein and albumin) are quickly saturated after an inadvertent IV injection of Bupivacaine, leaving a large amount of unbound drug available for diffusion into the heart's conducting tissue. This can lead to dangerously low blood pressure, cardiac dysrhythmias, and atrioventricular heart block. Bupivacaine has a cardiotoxic plasma concentration of 8 to 10 g/ml. In individuals being treated with medicines that impede myocardial impulse propogation, the threshold for cardiac toxicity caused by Bupivacaine may be reduced (beta adrenoreceptor blockers, digitalis preparations, calcium channel blockers). Because of their ability to limit sodium ion inflow via sodium channels, it lowers the maximal depolarization rate of the ventricular action potential (Vmax). Bupivacaine has a far greater effect on Vmax than Lidocaine. On the ECG, the consequent delayed conduction of the 70 cardiac action potential manifests as P-R and QRS interval prolongation and reentry ventricular cardiac dysrhythmias. Bupivacaine's R enantiomer is more poisonous than its S counterpart.
- **Hepatotoxicity**: Bupivacaine infusions, whether continuous or intermittent, were linked to higher plasma concentrations of liver transaminase enzymes, which returned to normal after the infusion was stopped.

**BUPRENORPHINE**[28]**:-**

Buprenorphine is an opioid that is both an agonist and an antagonist. It is generated from the opium alkaloid thebaine. It has a 33-fold higher potency than morphine. Buprenorphine has a gradual onset of action, a peak effect that can take up to 3 hours to reach, and a lengthy duration of effect (up to 10 hours).

**Chemical Structure:-**

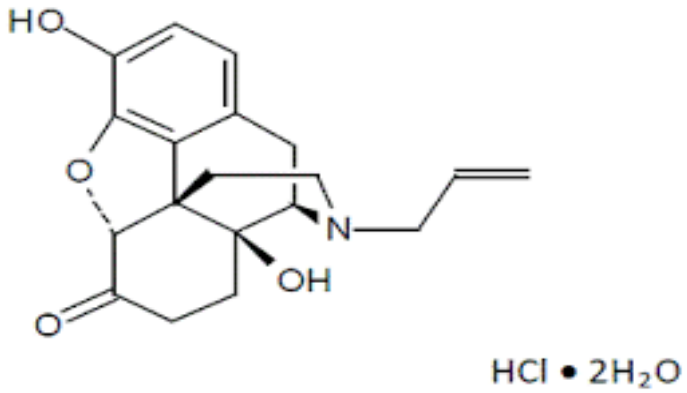



FIGURE 10:- Chemical Structure of Buprenorphine

**Physical properties:-**

It's sold commercially as a sterile solution containing 5% dextrose (1ml or 2ml ampoule containing 0.3 to 0.6 mg). It has a pH of 3.5 to 5.5 and is transparent. It should be kept away from light and at a temperature of no more than 400°C (15-300°C).

**Pharmacology**:

Buprenorphine is a powerful analgesic with a long half-life and low acute toxicity. The drug's potent agonist effects are counterbalanced by almost as potent antagonistic properties, resulting in self-limiting opiate effects and a low dependence risk. Buprenorphine's pharmacological profile is determined by its unique features at the receptor level. Buprenorphine, unlike Nalorphine and Pentazocine, possesses agonistic action at mu receptors for which Morphine acts as the ligand, but is classed as a Morphine-like partial agonist.

Buprenorphine's opiate agonist effects can be prevented with a pure antagonist like Naloxone, but only if the antagonist is administered before the Buprenorphine is given. Once the drug's effects are established, it's considerably more difficult to reverse them. This, combined with the medication's extended duration of action and moderate rate of association and dissociation with receptors, makes it a particularly stable medicine.

Buprenorphine has a distribution volume of 2.8 L/kg and a clearance rate of 20 ml/kg/min. Buprenorphine's metabolites, Buprenorphine-3-glucuronide and Norbuprenorphine, are much less powerful and have lower receptor affinity for mu receptors**.**

**Influence on the Respiratory System:**

Compared to pure agonist opiates, buprenorphine has a less pronounced effect on respiratory activity. Buprenorphine's respiratory depressive effects are dosage independent and reach a maximum at about 0.1 mg/kg, after which additional increases produce the same or reduced degrees of depression, whereas pure opiate agonists show a dose dependent drop in respiratory rate and arterial PaO2.

**Effect on Cardiovascular system:-**

The effects of buprenorphine on the cardiovascular system are minor and are clinically insignificant

**Clinical Uses:-**

Buprenorphine has at least 30 times the analgesic effectiveness of Morphine. The least dose for IM administration (0.3 mg) has been found to be at least as effective as 10 mg of Morphine, but with a 6-18 hour duration of action. A dosage of 0.3 mg to 0.6 mg is utilised for intramuscular and intravenous delivery.

Whether given IV or IM, the drug takes effect within 5-15 minutes, and a plasma level of 0.4 to 0.6 microgram/ml offers good analgesia. A dosage of 0.2 to 0.8 mg is utilised for sublingual delivery.

Buprenorphine, like any other agonist-antagonist drugs, is ineffective as a single anaesthetic, and its profile of receptor kinetics limits its utility when combined with other mu agonists.

**Buprenorphine (intrathecal and epidural):**

The high affinity of Buprenorphine for opiate receptors, which is 50 times stronger than that of morphine, and its lipid solubility, which is around 5 times greater than that of morphine, may explain its long duration of action and analgesic efficacy. High lipid solubility enhances both diffusion and ultimate concentration in the spinal cord while decreasing diffusion into the bloodstream. Cephalad distribution is limited by the high lipid solubility and affinity for opioid receptors, as well as the possibility of delayed breathing depression.

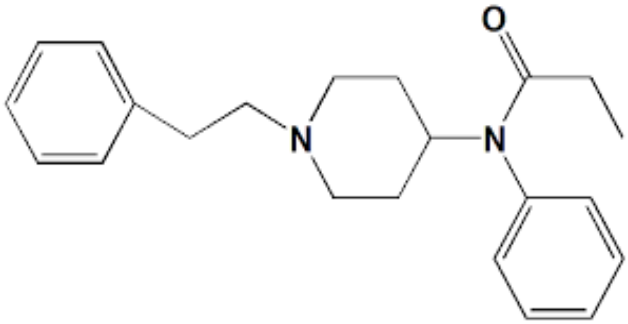
**Adverse effects** :Drowsiness, nausea, vomiting, and a decrease in breathing are among the side effects of Buprenorphine, which are comparable to those of Morphine but may last longer and be resistant to antagonism with Naloxone. Buprenorphine administration has been linked to pulmonary edoema. In contrast to other opioid agonist-antagonists, dysphoria is unlikely to occur after using this medication. Patients who are physically dependent on Buprenorphine experience milder withdrawal symptoms than those who are addicted to morphine, and the threat of abuse is low.

**FENTANYL**[29]**:-**

Fentanyl citrate is a synthetic phenylpiperidine opioid analgesic and chemical congener of the reversed ester of Pethidine. It is a safe, potent and rapidly acting

analgesic. Fentanyl is highly lipid soluble and has a low molecular weight. Fentanyl is widely available for parentral use and also in buccal, transdermal and aerosolized formulation. Fentanyl provides analgesia and relaxation. Fentanyl was first synthesized by Dr.Pauljanssen in 1960.

**CHEMICAL STRUCTURE:-**




Fentanyl

**FIGURE 11:- Chemical Structure of Fentanyl**

**Physical Properties:-**

Commercially available as sterile ampoules of Fentanyl citrate (2ml containing 100mcg of Fentanyl). It is transparent, with pH of 4.0 -7.5 andPka8.4. It should be protected stored at temperature less than $40^0$C (15- $30^0$C).

**MECHANISM OF ACTION:-**

Fentanyl is a μ receptor agonist with an analgesic potency superior to Morphine andPethidine. Analgesia is produced through interaction with μ receptors at supraspinal sites. It also binds to a much lesser degree to κ receptors located within the spinal cord. There is an evidence now that the gray mater of the spinal cord also contains opioid receptors and most of them are located in substantiagelatinosa i.e. 50%κ, 40%μ, 10%δ.

**PHARMACOKINETICS:-**

Protein binding -84 %

Clearance (ml/min) -1,530

Partition co-efficient -955

Elimination half time (t1/2)- 3.1 to 6.6hours

Context sensitive half life - 260mins

Effect site equilibrium- 6.8mins

**Routes of administration:-**

a. Orally as syrup or lozenges

b. I.V. route

c. Epidural route

d. Intrathecal route.

e. topical patches.

**Onset and duration of action:-**

a. I.V. – Onset in within 1-2min and duration of action is about 60mins.

b. Epidural – Duration is 3-4hours.

c. Intrathecal – Onset is within 5mins and duration is about 60mins.

**METABOLISM AND ELIMINATION:-**

Fentanyl is eliminated from body predominantly by the biotransformation in the liver and is metabolized mainly by N-Dealkylation to Norfentanyl which is pharmacologically inactive. Fentanyl is excreted by kidney in urine as its metabolites (less than 8% is excreted unchanged).

**PHARMACOLOGICAL ACTIONS:-**

1. Cardiovascular system:-
   a) Heart rate:- Due to stimulation of central vagal nucleus there is a decrease in the heart rate. It is dependent on dose and speed of injection. It can be effectively prevented by premedication with parasympatholytic agents such as glycopyrrolate or atropine. Fentanyl also blocks sympathetic stress response that includes increase in heart rate, by decreasing in CNS sympathetic vasoregulatory flow.
   b) Blood Pressure:- Minor fall in blood pressure seen mostly due to a reduction in systemic vascular resistance via centrally mediated reduction in sympathetic tone and often associated with bradycardia.
   c) Cardiac electrophysiological effects:- Fentanyl slows AV conduction, prolongs RR interval, AV node refractory period and the duration of purkinjefibres action potential.
   d) Coronary vasomotion and myocardial metabolism:- Fentanyl has no effect on coronary vasomotion or myocardial metabolism and does not diminish the ability of large coronary arteries or coronary arterioles to respond to vasoactive agents.
2. Respiratory system:- Fentanyl produces dose-related respiration depression . It causes decrease in minute volume, tidal volume and respiratory rate along with blunting of the ventilatory responses to hypercapnia and hypoxia.
3. Rigidity:-It is seen during I.V. induction of anaesthesia with larger doses of Fentanyl. However, no such complication is seen with intrathecal fentanyl .
4. Cerebral blood flow and intracranial pressure:- no change or modest reduction in cerebral blood flow and cerebral metabolic oxygen consumption seen.

5. Gastrointestinal tract:-decreases intestinal motility and may cause constipation. Also can increase the tone of sphincter of Oddi leading to increased pressure in biliary ducts, occasionally producing pain.
6. Drug interactions:-Neuraxial administration of opioids in conjunction with local anesthetic will improve the quality of intraoperative analgesia and prolong the duration of postoperative analgesia.

**THERAPEUTIC EFFICACY:-**

Fentanyl is both potent and safe. It has a therapeutic index of 323 , which is much greater than that of Pethidine and Morphine.

**INDICATION:-**

a. Cardiovascular procedures.

b. For prevention of surgery induced stress response.

c. Postoperative pain relief.

d. Analgesia for labour and delivery.

e. Sedation for patient on mechanical ventilators.

**CONTRAINDICATIONS AND CAUTIONS:-**

a. Should not be administered to patients on MAO inhibitors last dose within 24hrs.

b. Bronchial asthma.

c. Myasthenia gravis.

**Drug distribution:-**

a) Fentanyl is "lost" into the epidural space and epidural fat after administration of the drug, making it unavailable to the target tissue site in the spinal cord.
b) The CSF to epidural space transfer rate constant (kie) is the same as the meningeal permeability co-effective. Fentanyl octonol has a buffer distribution

coefficient of 955, which indicates that it has a hydrophobicity that is lesser than morphine.

c) Estimated apparent volume of distribution at the spinal cord (Vcord) applies to unbound, freely diffusible opioid in CSF. Vcord indicates the drugs octonal: buffering distribution coefficient is 23.58.

d) Vepi-fat - 45.88mland VCSF - 11.08ml. Hence, fentanyl's low nonionised fraction compared to Sufentanyl may lead to greater ion trapping.

**Potency:-**

Fentanyl when administered IV is 100times more potent in terms of dose than morphine, but is only 4 times more potent when administered intrathecally. It is less hydrophobic and has little rostral spread, which causes lesser respiratory depression as compared to morphine, which has a greater rostral CSF spread.

Fentanyl by virtue of its high volume of distribution in spinal cord and epidural space undergoes very low integral exposure within the spinal cord. Therefore , addition of vasoconstrictors would be beneficial to exposure, because most of the dose of fentanyl is lost into the epidural space.

**Side effects of fentanyl:-**

a. Bradycardia
b. Hypotension
c. Pruritis
d. Urinary retention
e. Respiratory depression
f. Hyperalgesia
g. Sexual dysfunction
h. Ocular dysfunction

i. Anaphylaxis

j. Shivering

k. Nausea

**Counter -measures for adverse effects:-**

a. Respiratory depression can be treated with Naloxone and by mechanical ventilation.

b. Pruritis, nausea and urinary retention which can be treated with Naloxone, antihistaminics, antiemeticsand catheterization.

c. Bradycardia counteracted by atropine or glycopyrrolate.

# MATERIALS AND METHODS

This study "A prospective randomized clinical study to compare the effect of Buprenorphine and Fentanyl as adjuvants to Bupivacaine for postoperative epidural analgesia in lower limb orthopedic surgeries" was conducted in Shri B M Patil Medical College Hospital & Research Centre, BLDE (Deemed to be university) between December 2019 and June 2021.

Ethical committee clearance (IEC:- 131/2019 , 22-11-2019) was taken.A total of 60 patients aged between twenty to sixty years of either gender belonging to ASA Grade I & II scheduled for orthopedic lower limb surgeries were enrolled. Written informed consent was obtained from the patients.

Patients were randomly divided into two groups of 30 each.

Group A – Buprenorphine group

Group B – Fentanyl group

**Sample size calculation:-**

Sixty (30per group) patients were required to have a 90% chance of detecting, as significant at the 5% level, an increase in the duration of analgesia from 471 min in the one group to 766min in the experimental group.[14]

Calculation based on the formula:

$n = f(\alpha/2, \beta) \times 2 \times \sigma 2 / (\mu 1 - \mu 2)\ 2$

Where $\mu 1$ and $\mu 2$ were the mean outcome in the study groups respectively, $\sigma$ was the standard deviation.

**INCLUSION CRITERIA**

- Patients aged between 20-60 years.
- Patients of either gender.
- Patients with ASA Grade I - II.
- Patients posted for lower limb orthopedic surgeries.

**EXCLUSION CRITERIA**

- Patient refusal
- Pregnant women.
- Patients with contra-indications for epidural anaesthesia.
- Patients with ASA Grade III and above.
- Patients with Cardio-Respiratory disorders
- Patients with Hepatic or Renal diseases.
- Patients with H/O convulsions or neurological deficits.
- Patients with Spinal deformities or Psychiatric diseases.

**EQUIPMENT USED:-**

- LOSS OF RESISTANCE SYRINGE
- 18G TUOHY EPIDURAL NEEDLE
- 25G QUINCKE SPINAL NEEDLE
- 18G EPIDURAL CATHETER WITH FILTER

**DRUGS USED:-**

- LIGNOCAINE 2%
- 2% LIGNOCAINE WITH ADRENALINE
- BUPIVACAINE HEAVY
- BUPIVACAINE HYDROCHLORIDE 0.5%
- FENTANYL 100mcg ampoule (preservative free)
- BUPRENORPHINE 300mcg ampoule (preservative free)

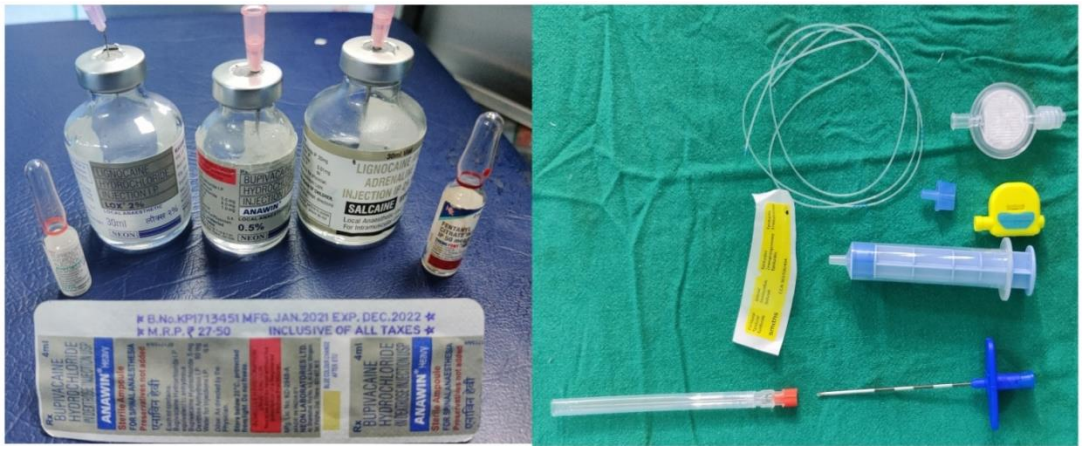



**FIGURE 12:- DRUGS & EQUIPMENT USED IN OUR STUDY**

**METHODOLOGY:-**

Pre-anaesthetic evaluation: Patients included in the study underwent thorough pre-operative evaluation which included the following :

- History: History of underlying medical illness, previous history of surgery, previous anaesthetic exposure and hospitalization.
- Physical examination :

1. General condition of the patient.
2. Vital signs- heart rate, blood pressure, respiratory rate, saturation
3. Weight
4. Examination of cardiovascular system, respiratory system, central nervous system and spine examination.

5. Airway assessment by Mallampati grading, cervical spine movement, mouth opening , neck movements.

- Investigations:-

  Complete Blood Counts, Serum Creatinine, Chest Xray, ECG , RBS , Serology, BT CT.

- Written Informed Consent:-

Before the procedure, a detailed written and informed consent was obtained from the patients.

**PROCEDURE**:

- Anesthesia machine, resuscitation equipment, emergency drugs were checked and kept ready before starting each case.
- Upon shifting the patient to the OT standard monitors were attached (pulse oximeter, NIBP, ECG) and baseline readings were noted.
- 20G IV Cannula was secured and all patients premedicated with Injection Ondansetron 0.15mg/kg IV.
- The patient wasplaced in sitting or lateral position. Under all aseptic precautions, after skin preparation, a local anaesthetic skin wheal was raised at L2- L3 / L3- L4 interspace with 2% lignocaine 2ml.
- using the 18G Tuohy needle by loss of resistance to air technique the epidural space was identified.
- 18G PORTEX epidural catheter was passed through the epidural needle till about 2-3 cms of the catheter was in the space and the catheter was fixed to the back using adhesive tape.

- 3ml of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter as a test dose and observed for any signs of intravascular or intrathecal injection.
- A 25G spinal needle was inserted at L3-L4 interspace and after confirming free flow of CSF spinal anesthesia given with appropriate dose of 0.5%Bupivacine heavy.
- The patient pulse rate, blood pressure, respiratory rate and oxygen saturation were monitored till termination of the surgery. At the termination of surgery, the patient was transferred to recovery room and monitoring continued.
- In the postoperative period, when the patient first complained of pain, intensity of pain was assessed using VAS scale. When the VAS score was >4, study drug was given through epidural catheter, as:

| | |
|---|---|
| GROUP A | 2ml 0.5% Bupivacaine + 1.5 mcg/kg Buprenorphine diluted with distilled water to 10ml |
| GROUP B | 2ml 0.5% Bupivacaine + 1mcg/kg Fentanyl diluted with distilled water to 10ml |

- The patient pulse rate, blood pressure, and oxygen saturation was recorded before injecting the drugs which was taken as the control value and subsequently monitored after 5mins , 10 mins, 15mins, 30mins , 45 mins , 60 mins, and then hourly for 8 hours and $4^{th}$ hourly upto 24hours.
- The intensity of pain and pain relief was assessed using VAS at 5,10,15,30,45,60 minutes and thereafter hourly for 8 hours and then at 4 hours interval for 24 hours postoperatively.
- As and when the patient complained of further pain during the period of observation, intensity of pain was assessed again using VAS to know the effect

of the study drug given earlier. If it was > 5, analgesia as per the ward protocol was given and the study ended at this stage.

- The patients were monitored during this period for any adverse effects like nausea , vomiting , hypotension , prurutis, sedation , respiratory depression. Incase of any adverse effects patients were managed by standard protocol.
- **Visual analog scale (VAS)[30]** consists of a 10cm scale with markings at 1cm distance on which the patient indicates the line that represents the intensity of pain he/she is experiencing. Mark '0' represents no pain and mark '10' represents worst possible pain. The numbers indicated by the patient is used to assessthe pain intensity.

**TABLE 4:- VAS SCORE INTERPRETATION**

| VAS SCORE INTERPRETATION | |
|---|---|
| 0-2 | No/slight pain |
| 2-5 | Mild pain |
| 5-7 | Moderate Pain |
| 7-9 | Severe pain |
| 10 | Worst possible pain |

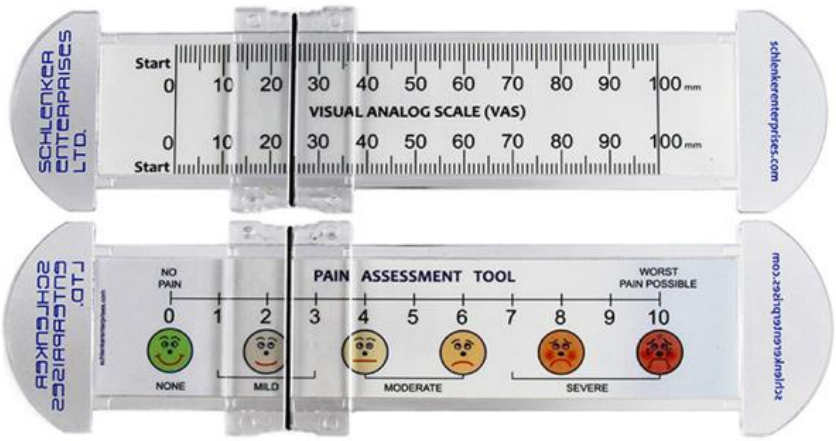



**FIGURE 13:- VAS SCALE**

**Definitions:-**

**Onset of analgesia**: the time interval from administration of the study drug (VAS score of >4) till VAS score came down to < 5.

**Duration of analgesia**: the time interval between onset of analgesia to when rescue analgesia is given.

**Hypotension**: fall of systolic BP by 20% from basal systolic BP

**Respiratory Depression:** bradypnoea is a more reliable early clinical sign of respiratory depression and Respiratory rate less than 10 was taken as respiratory depression.

All the observation and patient details were recorded in a proforma, a copy of which is enclosed.

**Statistical Methods:-**

The quantitative variables are expressed as mean±sd and compared between groups using unpaired t test.

Qualitative variables are compared between groups using Chi-square/Fisher's exact test. A p value < 0.05 is considered statistically significant.

The data was compiled meticulously and statistical analysis performed using IBM Statistical Package for Social Sciences (SPSS) version 20.0

**PROCEDURE OF EPIDURAL CATHETER INSERTION & SPINAL ANESTHESIA**

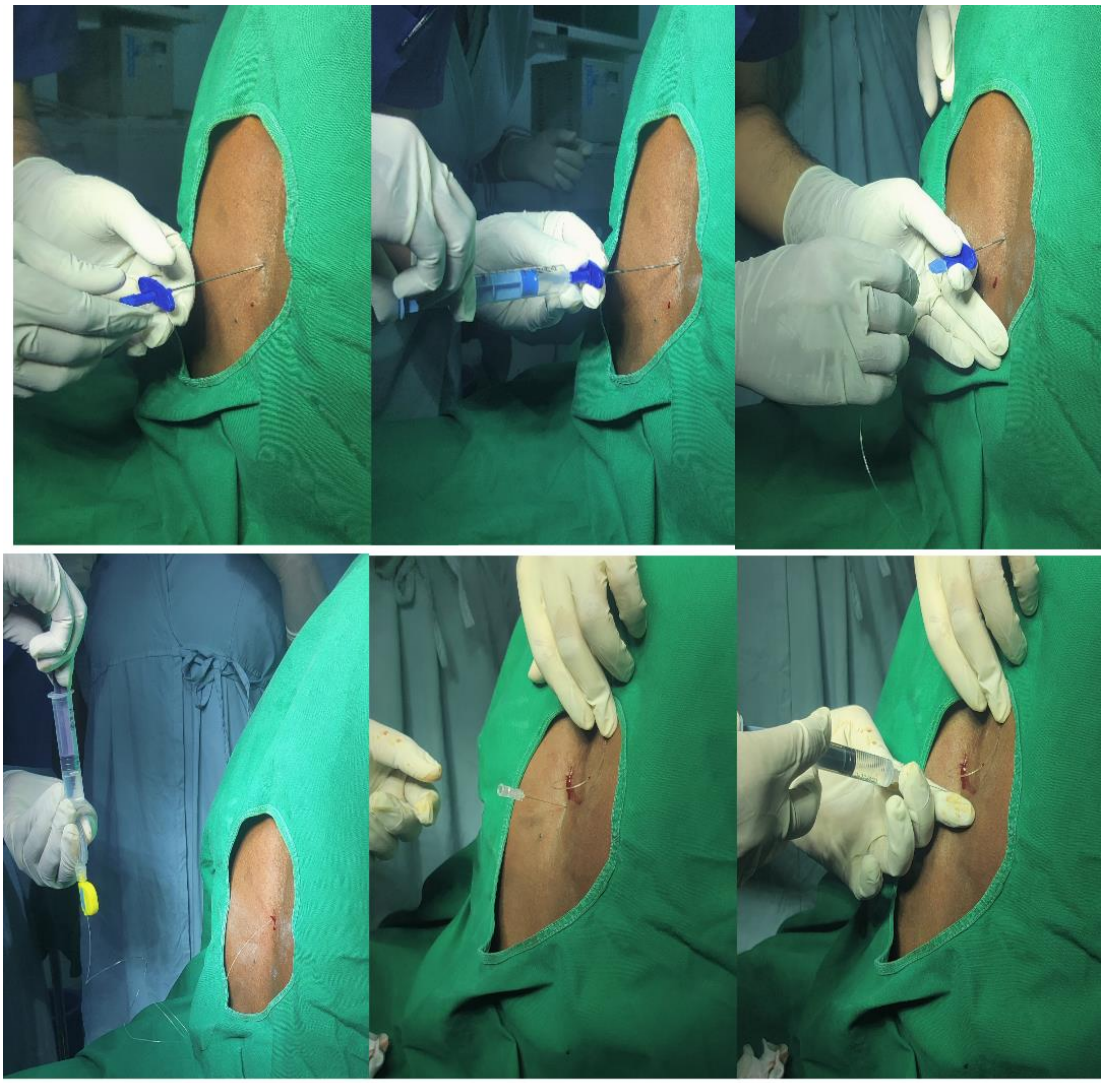


**FIGURE 14:- PROCEDURE OF EPIDURAL CATHETER INSERTION AND ADMINISTRATION SPINAL ANESTHESIA.**

# RESULTS

This study consists of 60 patients posted for lower limb orthopedic surgeries. They were randomly divided into two groups of 30 each.

GroupA:- 2ml 0.5% Bupivacaine + 1.5mcg/kg Buprenorphine diluted with distilled water to 10ml.

Group B:-2ml 0.5% Bupivacaine + 1mcg/kg Fentanyl diluted with distilled water to 10ml.

The onset of analgesia, duration of postoperative analgesia , pain scores , hemodynamics and side effects were compared and contrasted.

## DEMOGRAPHICAL DATA ANALYSIS:-

## AGE DISTRIBUTION:-

Patients included in our study belonged to the age group of 20-60 years.

**Table5:- Age Distribution**

| Age (years) | Group A | | Group B | |
|---|---|---|---|---|
| | N | % | n | % |
| 20 - 30 | 7 | 23.33% | 9 | 30.00% |
| 30 - 40 | 7 | 23.33% | 6 | 20.00% |
| 40 - 50 | 5 | 16.67% | 10 | 33.33% |
| 50 - 60 | 11 | 36.67% | 5 | 16.67% |
| **TOTAL** | **30** | **100%** | **30** | **100%** |

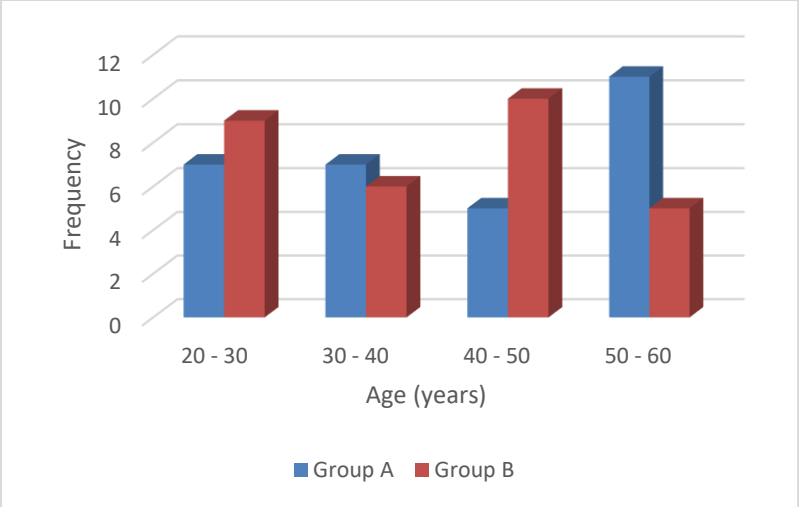



**FIGURE 15:- AGE DISTRIBUTION OF STUDY POPULATION**

**MEAN AGE AND WEIGHT COMPARISON:-**

The mean age of patients in Group A was 40.93±13.29 years and in Group B it was 38.57±11.41years. Samples in both group were not significantly different (p=0.231) and were age matched.

The mean weight of patients(in kgs) in Group A was 73.80±11.17 and in Group B was 70.57±11.83. Weight of patients in both groups were matched and not significantly different (p=0.140).

**Table 6:- Mean Age and Weight**

| | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| Age (years) | 40.93 | ±13.29 | 38.57 | ±11.41 | 0.231 |
| Weight (kg) | 73.80 | ±11.17 | 70.57 | ±11.83 | 0.140 |

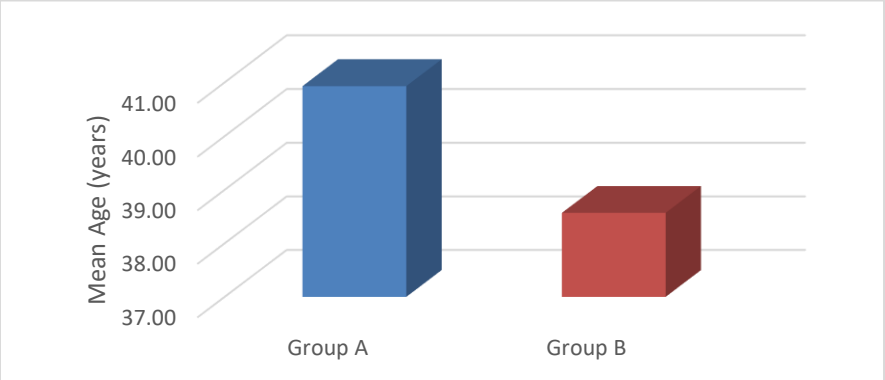



**FIGURE 16:- COMPARISON OF MEAN AGE BETWEEN STUDY GROUPS**

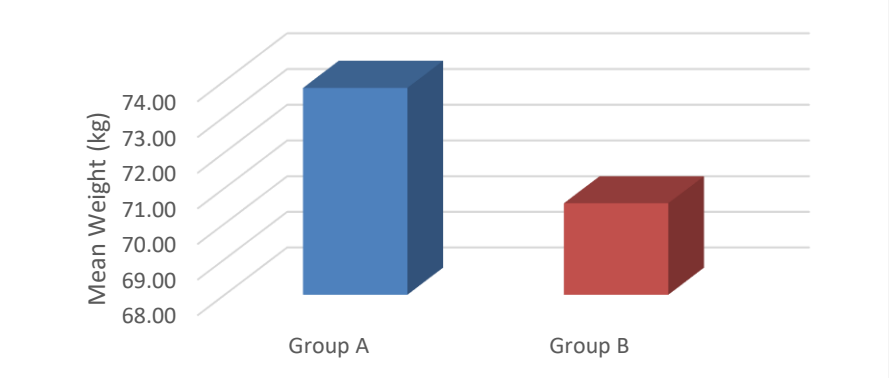



**FIGURE 17:- COMPARISON OF MEAN WEIGHT BETWEEN STUDY GROUPS**

**GENDER DISTRIBUTION:-**

In Group A, 20 patients (66.67%) were Male and 10 patients (33.33%) were female.

In Group B, 19 patients (63.33%) were Male and 11 patients (36.67%) were female.

There was no significant difference (p=0.393) in the gender distribution and samples were gender matched in both groups.

**Table 7:- Gender distribution**

| Gender | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Male | 20 | 66.67% | 19 | 63.33% | 0.393 |
| Female | 10 | 33.33% | 11 | 36.67% | |
| **TOTAL** | **30** | **100.00%** | **30** | **100.00%** | |

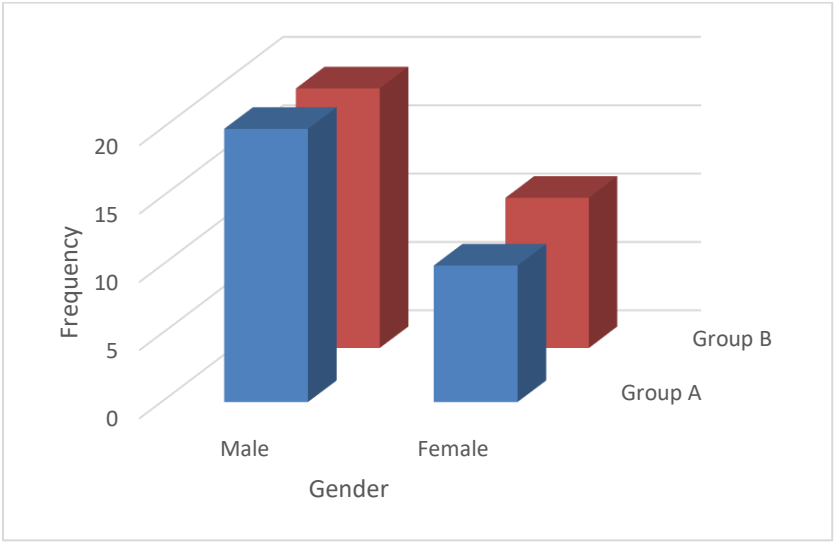



**FIGURE 18:- GENDER DISTRIBUTION OF STUDY POPULATION**

**ASA GRADES:-**

In Group A, 12 patients (40%) were ASA Ⅰ and 18 patients ( 60%) were ASA Ⅱ.

In Group B, 17 patients (56.67%) were ASA Ⅰ and 13 Patients (43.33%) were ASA Ⅱ.

There was no significant difference (p=0.098) in the ASA Grade between the two groups.

**TABLE 8:- ASA GRADE DISTRIBUTION**

| ASA Grade | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 1 | 12 | 40.00% | 17 | 56.67% | 0.098 |
| 2 | 18 | 60.00% | 13 | 43.33% | |
| **TOTAL** | **30** | **100.00%** | **30** | **100.00%** | |

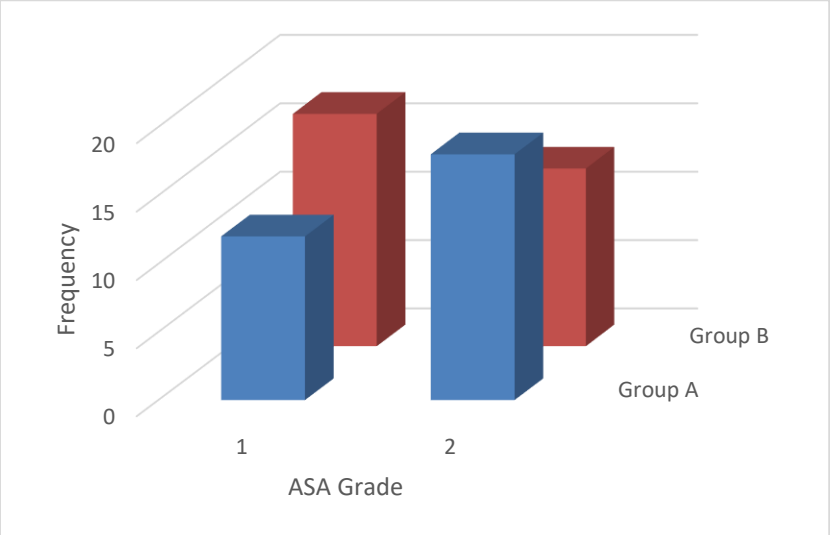



**FIGURE 19:- ASA GRADE DISTIBUTION BETWEEN STUDY GROUPS**

**COMPARISON OF BASELINE PARAMETERS:-**

During the preanesthetic evaluation we recorded the baseline pulse rate (beats/min), systolic and diastolic blood pressure (mmofHg), Respiratory rate(cycles/min ) and spo2 (%).

The Baseline parameters in both the groups had no significant difference and were matched.

**TABLE 9:-BASELINE PARAMETERS**

| Baseline Parameters | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| Pulse Rate | 83.77 | ±10.21 | 80.97 | ±8.42 | 0.126 |
| Blood Pressure (S) | 123.67 | ±10.33 | 123.00 | ±11.79 | 0.408 |
| Blood Pressure (D) | 79.33 | ±9.07 | 79.67 | ±8.5 | 0.442 |
| Respiratory Rate | 15.07 | ±1.53 | 14.77 | ±1.28 | 0.207 |
| $SpO_2$ | 99.00 | ±1.17 | 99.33 | ±0.8 | 0.102 |

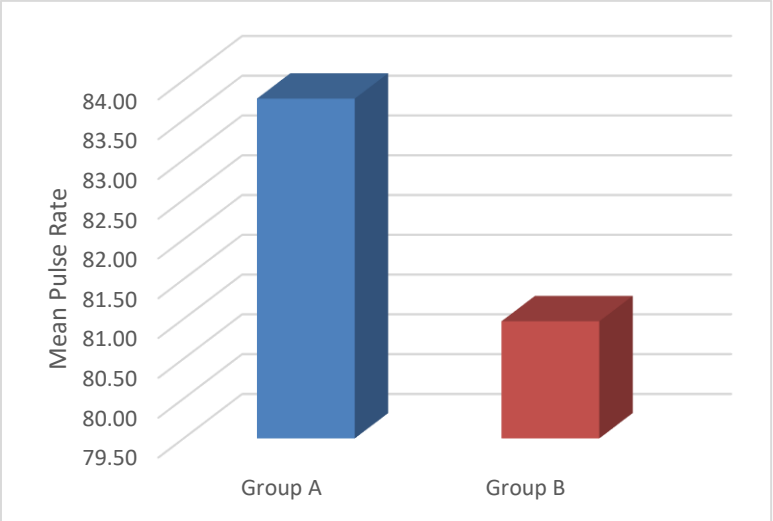



**FIGURE 20:- COMPARISON OF BASELINE PULSE RATE**

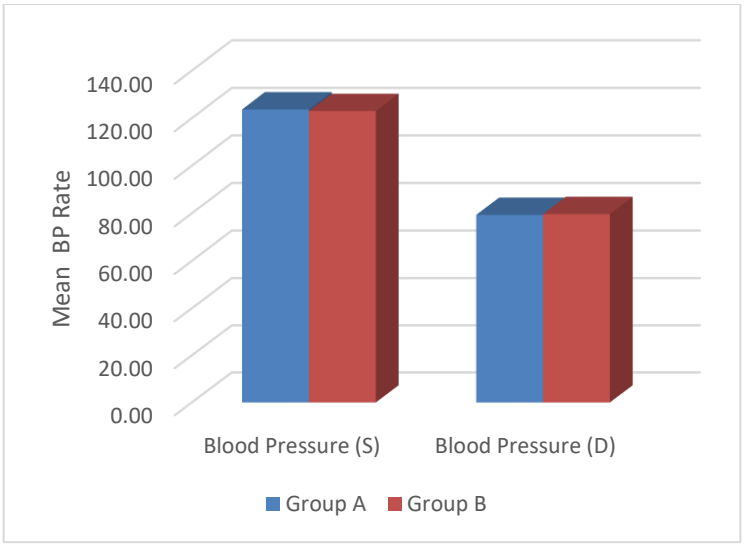



**FIGURE 21:- COMPARISON OF BASELINE BLOOD PRESSURE**

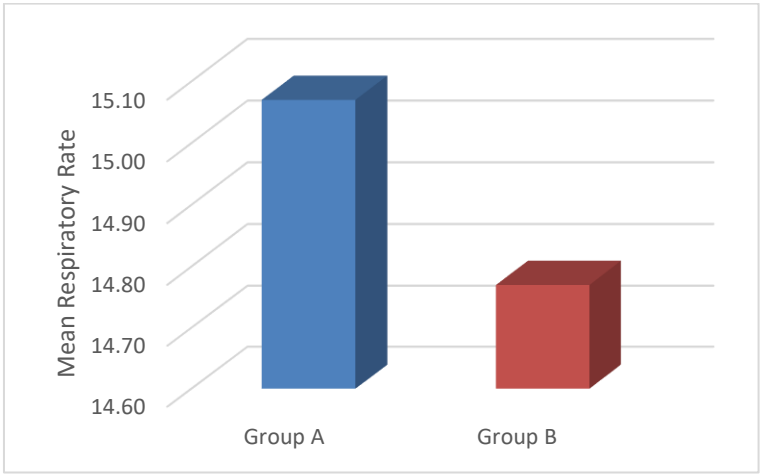



**FIGURE 22:- COMPRASION OF BASELINE RESPIRATORY RATE**

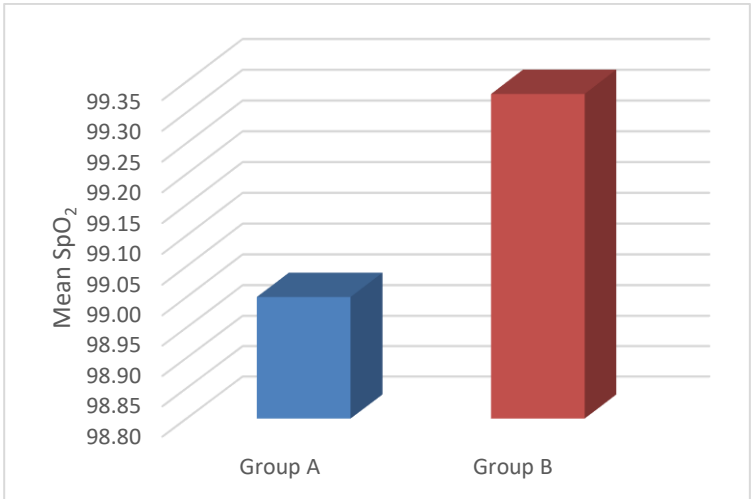



**FIGURE 23:- COMPARISON OF BASELINE SpO2**

**ONSET OF ANALGESIA:-**

**TABLE 10:- MEAN ONSET OF ANALGESIA (in minutes)**

| | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| Onset of Analgesia (mins) | 15.33 | ±8.09 | 7.17 | ±3.13 | <0.001 |

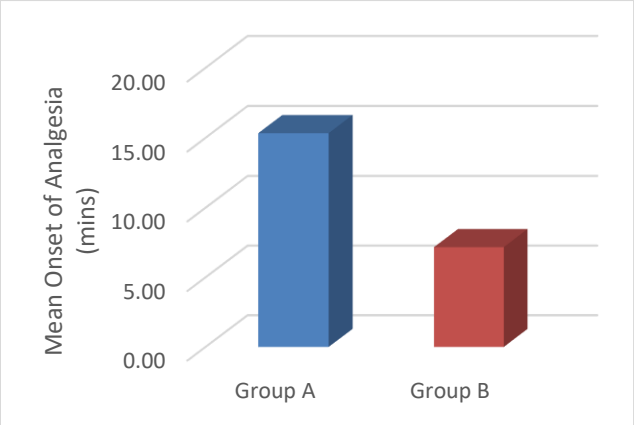



**FIGURE 24:- COMPARISON OF MEAN ONSET OF ANALGESIA BETWEEN STUDY GROUPS.**

The mean time of onset of analgesia in Group A was 15.33±8.09 minutes compared to 7.17±3.13 minutes in Group B.

Statistical analysis showed that onset of analgesia in Group B was earlier than Group A and strongly statistically significant ($p<0.001$).

**DURATION OF ANALGESIA** :-

**TABLE 11:- DURATION OF ANALGESIA (in hours)**

| | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| Duration of Analgesia (hrs) | 13.63 | ±3.19 | 3.73 | ±1.14 | <0.001 |

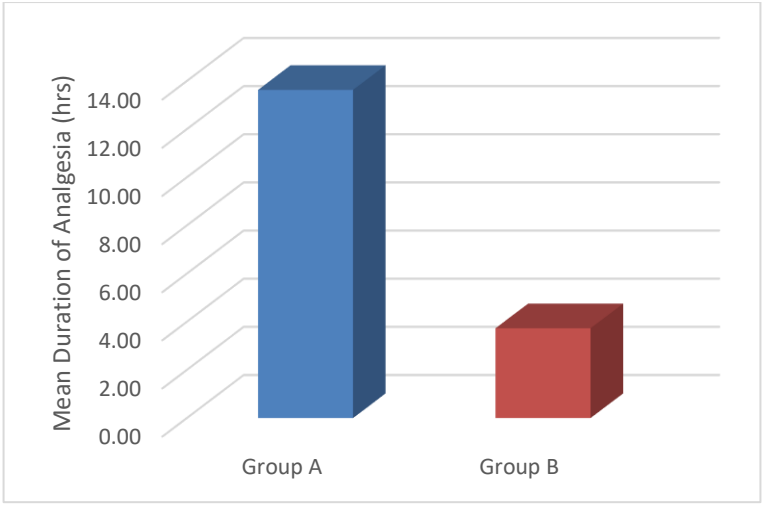



**FIGURE 25:- COMPARISON OF DURATION OF ANALGESIA BETWEEN STUDY GROUPS.**

In our study the time duration from the onset of Analgesia to the need for rescue analgesia (VAS ≥5) is taken as the Duration of Analgesia (in hours).

The mean duration of analgesia in Group A was 13.63±3.19 hours and in Group B it was 3.73±1.14 hours.

Statistical analysis showed a strongly significant difference in duration of analgesia between the two groups ($p<0.001$).

**COMPARISON OF VAS SCORES :-**

The VAS Scores were recorded at 0 , 5 , 10 , 15 , 30 , 45, 60 minutes and then hourly for 8 hours and then 4$^{th}$ hourly upto 24 hours after the epidural administration of study drugs.

**TABLE 12:- COMPARISON OF VAS SCORES FOR 24 HOURS**

| VAS Score | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| 0mins | 7.43 | ±1.07 | 7.33 | ±1.09 | 0.361 |
| 5mins | 6.37 | ±1.33 | 3.83 | ±1.95 | <0.001 |
| 10mins | 4.87 | ±1.89 | 2.30 | ±1.42 | <0.001 |
| 15mins | 3.47 | ±1.76 | 1.73 | ±1.17 | <0.001 |
| 30mins | 2.17 | ±1.26 | 1.43 | ±1.1 | 0.010 |
| 45mins | 1.50 | ±1.01 | 1.00 | ±0.95 | 0.026 |
| 60mins | 0.90 | ±0.76 | 1.27 | ±1.2 | 0.081 |
| 2hrs | 1.20 | ±0.81 | 2.47 | ±1.66 | <0.001 |
| 3hrs | 1.33 | ±0.88 | 4.03 | ±1.63 | <0.001 |
| 4hrs | 2.00 | ±0.83 | 5.27 | ±1.57 | <0.001 |
| 5hrs | 2.23 | ±0.9 | 5.80 | ±1.69 | <0.001 |
| 6hrs | 2.70 | ±1.02 | 6.23 | ±1.17 | <0.001 |
| 7hrs | 3.27 | ±0.94 | 6.27 | ±1.31 | <0.001 |
| 8hrs | 3.70 | ±1.12 | 6.67 | ±1.21 | <0.001 |
| 12hrs | 4.53 | ±1.25 | 6.80 | ±1.4 | <0.001 |
| 16hrs | 5.70 | ±1.29 | 6.37 | ±1.45 | 0.032 |
| 20hrs | 6.63 | ±1.03 | 5.87 | ±1.25 | 0.006 |
| 24hrs | 6.60 | ±1.04 | 6.03 | ±1.33 | 0.035 |

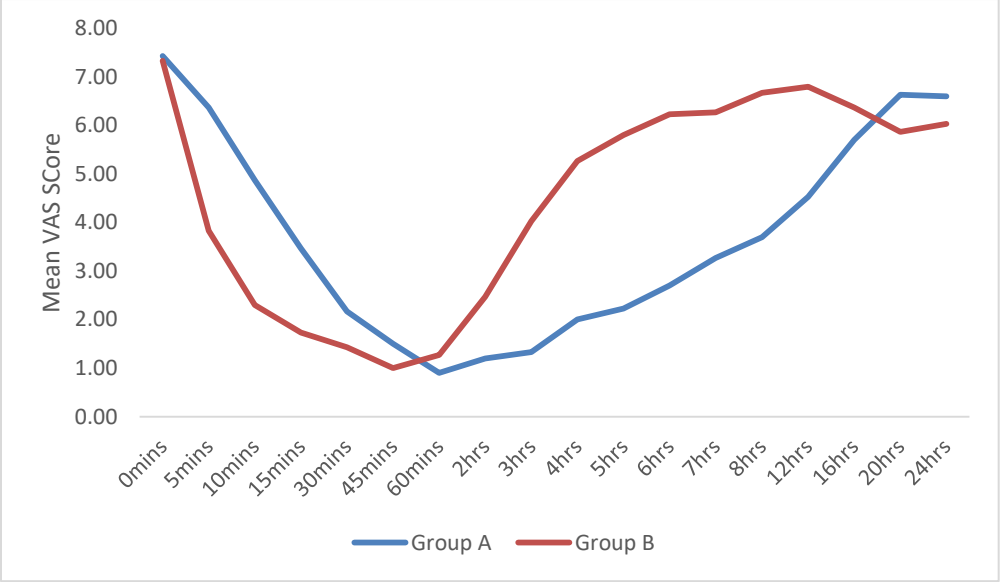



**FIGURE 26:- LINE DIAGRAM TO COMPARE MEAN VAS SCORES BETWEEN STUDY GROUPS**

As seen from table, VAS score indicating the quality of pain relief was compared between the two groups at different time intervals for the first 24 hours. After administration of study drugs the VAS scores in both the groups reduced to below 5. In the Fentanyl group the VAS scores started increasing again from 3$^{rd}$ hour onwards. Whereas the VAS scores remained low upto 12-16hours in the Buprenorphine group.

**PULSE RATE VARIATION:-**

**TABLE 13:- VARIATION IN PULSE RATE**

| Pulse Rate (Beats per minute) | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| 0mins | 81.23 | ±8.99 | 81.73 | ±9.34 | 0.417 |
| 5mins | 82.93 | ±8.54 | 81.20 | ±9.14 | 0.226 |
| 10mins | 83.27 | ±7.88 | 82.30 | ±8.62 | 0.326 |
| 15mins | 80.60 | ±7.1 | 79.40 | ±7.62 | 0.265 |
| 30mins | 78.90 | ±7.07 | 79.10 | ±6.79 | 0.456 |
| 45mins | 77.13 | ±7.55 | 77.73 | ±6.72 | 0.373 |
| 60mins | 78.97 | ±5.01 | 79.47 | ±6.39 | 0.369 |
| 2hrs | 78.97 | ±5.14 | 79.63 | ±6.56 | 0.331 |
| 3hrs | 81.13 | ±5.28 | 79.33 | ±5.27 | 0.096 |
| 4hrs | 79.50 | ±4.64 | 79.03 | ±5.18 | 0.357 |
| 5hrs | 78.80 | ±4.74 | 79.73 | ±6.73 | 0.268 |
| 6hrs | 78.03 | ±6.44 | 82.90 | ±8.35 | 0.007 |
| 7hrs | 77.37 | ±6.85 | 81.37 | ±7.95 | 0.021 |
| 8hrs | 76.30 | ±4.76 | 80.00 | ±7.5 | 0.013 |
| 12hrs | 80.40 | ±5.33 | 80.97 | ±7.05 | 0.363 |
| 16hrs | 81.50 | ±5.64 | 82.17 | ±6.14 | 0.332 |
| 20hrs | 81.50 | ±6.1 | 83.13 | ±5.31 | 0.136 |
| 24hrs | 80.67 | ±5.77 | 82.00 | ±4.03 | 0.152 |


**FIGURE 27:- COMPARISON OF PULSE RATE BETWEEN THE STUDY GROUPS**

Variation of pulse rate was studied in both the groups for 24 hours. Pulse rate remained stable in both the groupsupto 24 hours after administration of study drugs.Statistically there was no significant difference in the pulse rate between the two groups with p >0.05.

## VARIATION IN BLOOD PRESSURE:-

### TABLE 14:- VARIATION IN SYSTOLIC BLOOD PRESSURE

| Blood Pressure (Systolic) - mmHg | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| 0mins | 122.93 | ±10.25 | 125.27 | ±12.93 | 0.221 |
| 5mins | 121.80 | ±11.05 | 121.33 | ±13.74 | 0.443 |
| 10mins | 119.00 | ±9.49 | 118.13 | ±12.6 | 0.382 |
| 15mins | 118.20 | ±10.15 | 115.80 | ±9.16 | 0.170 |
| 30mins | 116.60 | ±8.09 | 114.40 | ±8.62 | 0.156 |
| 45mins | 119.27 | ±6.8 | 115.07 | ±6.05 | 0.007 |
| 60mins | 115.13 | ±8.11 | 119.13 | ±8.08 | 0.030 |
| 2hrs | 116.67 | ±6.57 | 120.73 | ±7.29 | 0.013 |
| 3hrs | 116.33 | ±7.7 | 119.40 | ±10.21 | 0.097 |
| 4hrs | 119.13 | ±9.03 | 123.60 | ±8.92 | 0.029 |
| 5hrs | 121.53 | ±8.48 | 125.47 | ±9.78 | 0.051 |
| 6hrs | 119.73 | ±7.98 | 124.87 | ±8.51 | 0.010 |
| 7hrs | 118.27 | ±7.5 | 124.53 | ±9.17 | 0.003 |
| 8hrs | 119.47 | ±7.45 | 122.80 | ±8.03 | 0.050 |
| 12hrs | 120.33 | ±8.84 | 126.07 | ±9.21 | 0.008 |
| 16hrs | 119.80 | ±9.46 | 125.00 | ±7.42 | 0.011 |
| 20hrs | 120.67 | ±9.44 | 122.80 | ±8.54 | 0.181 |
| 24hrs | 121.53 | ±8.4 | 122.13 | ±8.25 | 0.391 |

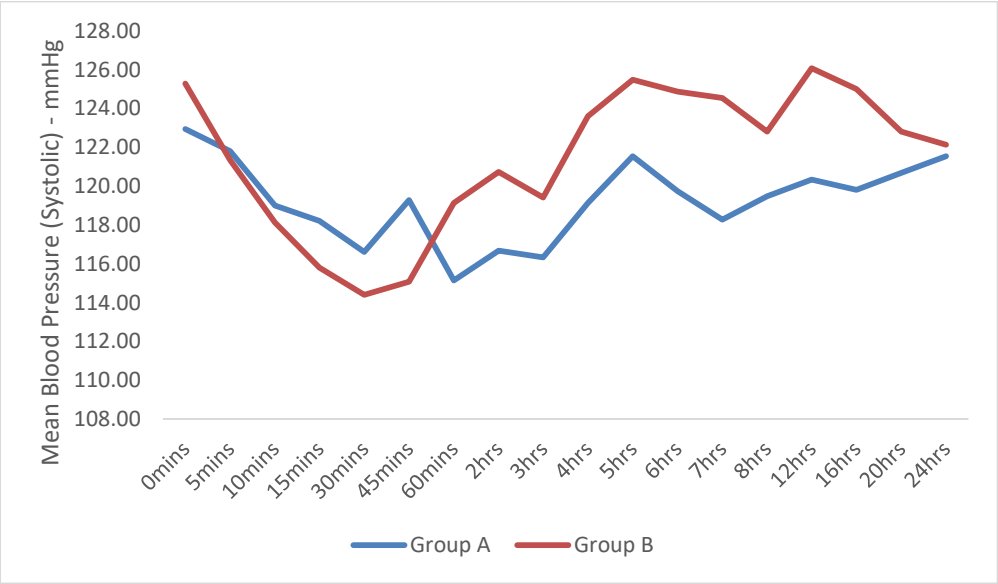



**FIGURE 28:- COMPARISON OF SYSTOLIC BLOOD PRESSURE BETWEEN THE STUDY GROUPS**

**TABLE 15:- VARIATION IN DIASTOLIC BLOOD PRESSURE**

| Blood Pressure (Diastolic) - mmHg | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| 0mins | 78.33 | ±9.5 | 79.53 | ±9.67 | 0.315 |
| 5mins | 78.67 | ±8.19 | 75.47 | ±10.54 | 0.097 |
| 10mins | 77.67 | ±6.26 | 73.73 | ±9.72 | 0.034 |
| 15mins | 76.33 | ±4.9 | 72.47 | ±6.9 | 0.008 |
| 30mins | 76.67 | ±5.47 | 72.80 | ±6.78 | 0.009 |
| 45mins | 76.33 | ±7.18 | 71.00 | ±4.81 | <0.001 |
| 60mins | 77.33 | ±7.85 | 73.47 | ±4.07 | 0.010 |
| 2hrs | 79.33 | ±7.85 | 73.53 | ±5.65 | <0.001 |
| 3hrs | 79.33 | ±6.4 | 76.07 | ±7.42 | 0.036 |
| 4hrs | 81.00 | ±7.59 | 77.53 | ±6.03 | 0.027 |
| 5hrs | 79.33 | ±6.4 | 77.87 | ±6.1 | 0.184 |
| 6hrs | 79.60 | ±7.19 | 76.53 | ±8.65 | 0.070 |
| 7hrs | 78.67 | ±5.07 | 76.80 | ±5.84 | 0.096 |
| 8hrs | 78.00 | ±5.51 | 76.47 | ±6.47 | 0.164 |
| 12hrs | 77.00 | ±6.51 | 78.87 | ±6.53 | 0.136 |
| 16hrs | 80.00 | ±5.87 | 78.73 | ±6.63 | 0.218 |
| 20hrs | 79.00 | ±6.07 | 77.00 | ±7.23 | 0.125 |
| 24hrs | 80.33 | ±6.15 | 76.27 | ±6.78 | 0.009 |

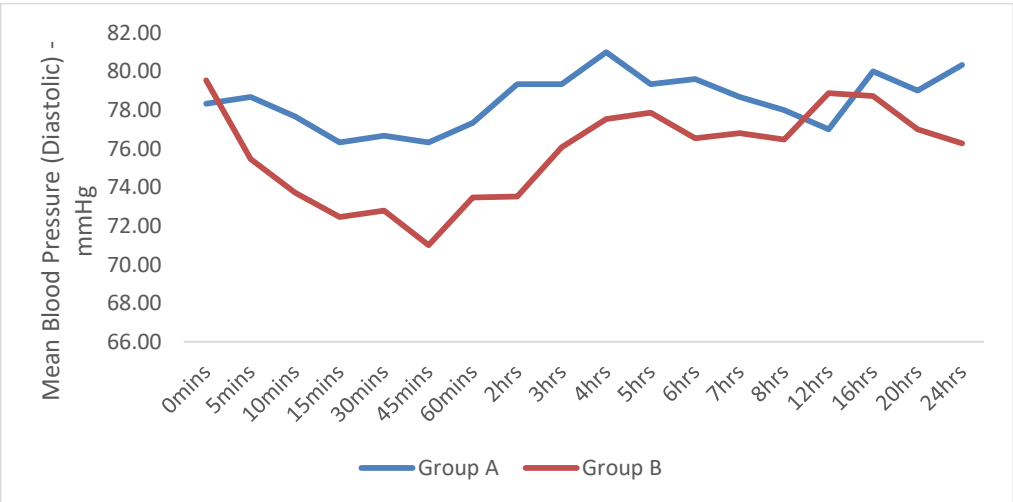



**FIGURE 29:- COMPARISON OF DIASTOLIC BLOOD PRESSURE BETWEEN THE STUDY GROUPS**

**TABLE 16:- VARIATION IN MEAN ARTERIAL PRESSURE**

| Mean Arterial Pressure | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | mean | ±sd | mean | ±sd | |
| 0mins | 93.20 | ±8.44 | 94.78 | ±10.34 | 0.260 |
| 5mins | 93.04 | ±7.73 | 90.76 | ±10.64 | 0.172 |
| 10mins | 91.44 | ±6.24 | 88.53 | ±9.22 | 0.079 |
| 15mins | 90.29 | ±5.2 | 86.91 | ±6.79 | 0.017 |
| 30mins | 89.98 | ±5.45 | 86.67 | ±5.8 | 0.013 |
| 45mins | 90.64 | ±5.74 | 85.69 | ±4.1 | <0.001 |
| 60mins | 89.93 | ±6.26 | 88.69 | ±3.93 | 0.180 |
| 2hrs | 91.78 | ±5.74 | 89.27 | ±5.03 | 0.039 |
| 3hrs | 91.67 | ±4.64 | 90.51 | ±7.06 | 0.228 |
| 4hrs | 93.71 | ±5.52 | 92.89 | ±6.24 | 0.295 |
| 5hrs | 93.40 | ±5.94 | 93.73 | ±5.95 | 0.414 |
| 6hrs | 92.98 | ±5.78 | 92.64 | ±7.36 | 0.423 |
| 7hrs | 91.87 | ±4.04 | 92.71 | ±4.89 | 0.234 |
| 8hrs | 91.82 | ±4.38 | 91.91 | ±5.28 | 0.471 |
| 12hrs | 91.44 | ±5.57 | 94.60 | ±6.25 | 0.022 |
| 16hrs | 93.27 | ±5.41 | 94.16 | ±5.7 | 0.269 |
| 20hrs | 92.89 | ±6.24 | 92.27 | ±6.5 | 0.353 |
| 24hrs | 94.07 | ±5.66 | 91.56 | ±6.09 | 0.052 |


**FIGURE 30:- COMPARISON OF MEAN ARTERIAL PRESSURE BETWEEN THE STUDY GROUPS**

From the above tables we noted that Blood pressure ( Systolic , Diastolic and Mean Arterial pressure) remained stable with no significant hypotension in either of the groups.

**SIDE EFFECTS:-**

TABLE 17:- COMPARISON OF SIDE EFFECTS

| Side effects | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Nausea | 9 | 30.00% | 2 | 6.67% | 0.010 |
| Vommiting | 3 | 10.00% | 0 | 0.00% | 0.038 |
| Pruritis | 0 | 0.00% | 3 | 10.00% | 0.038 |
| Respiratory depression | 0 | 0.00% | 0 | 0.00% | - |
| Sedation | 0 | 0.00% | 2 | 6.67% | 0.075 |
| Hypotension | 0 | 0.00% | 0 | 0.00% | - |

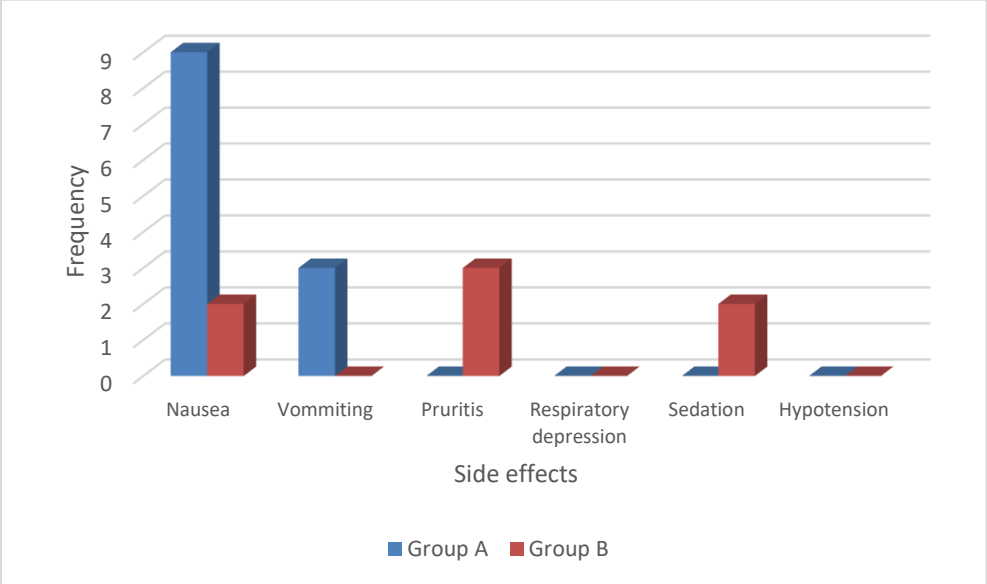



**FIGURE 31:- COMPARISON OF SIDE EFFECTS BETWEEN STUDY GROUPS**

From the above table it can be observed:-

Nausea was seen in 9 patients (30%) in Group A and in 2 patients(6.67%) in Group B which was statistically significant (p=0.010)

Vomiting was seen in 3 patients (10%) in Group A and none in Group B which was statistically significant (p=0.038)

Pruritis was observed in 3 patients(10%) in Group B as compared to none in Group A which was statistically significant (p=0.038)

Respiratory depression was not seen in any patient in either groups.

Sedation was seen in 2 patients (6.67%) in Group B and none in Group A and was statistically not significant (p=0.075)

Hypotension was not seen in any patient in either groups.

Urinary retention could not be studied as most of the patients in the study had indwelling urinary catheter .

# DISCUSSION

Pain is defined as " an unpleasant sensory and emotional experience associated with actualor potential tissue damage or explained in terms of such damage" by the International Association for the study of pain.

To relieve pain during and after surgery and the associated physiological effectshas been the main aim of every anaesthesiologist. General anesthesia can be given for all surgeries but it comes with its own set of disadvantages such as airway manipulation, poly-pharmacy, postoperative nausea &vomiting etc.[31] which can be reduced with regional anesthesia (intrathecal and epidural) especially for lower limb and lower abdominal surgeries which also provides the added benefit of better sensory and motor blockade, prolonged post-operative analgesia , ideal operating conditions and faster recovery. Of these two, epidural anesthesia has the added advantage of better hemodynamic stability, longer duration of post-operative analgesia owing to indwelling catheter use and reduced incidence of PDPH.

The discovery of opioid receptors in the spinal cord by Yaksh and Rudy in 1976 has revolutionized their use as adjuvants for local anaesthetics to hasten the block onset and prolong the duration of analgesia.[32]

In our study we have compared the effect of two opioids – Buprenorphine which is a thebaine derivative and a partial μ agonist and antagonist with Fentanyl which is a phenyl piperidine derivative and pure μ agonist along with the local anesthetic 0.5% Bupivacaine in epidural analgesia in lower limb orthopedic surgeries.

60 patients undergoing orthopedic lower limb surgeries under spinal anesthesia with epidural catheter in situ for postoperative analgesia were randomly selected for the study. The patients were randomly divided in two groups of 30 each.

In our study the demographic profile of the two groups were comparable in terms of age, gender, weight and ASA grade distribution. The baseline parameters such as pulse rate, systolic and diastolic blood pressure, respiratory rate and spo2 were comparable in both the groups.

In the postoperative period when the patient complained of pain (VAS score of>4), the study began. The following observations were made:

**MEAN ONSET OF ANALGESIA:-**

The mean onset of analgesia (VAS score less than 5) was 15.33±8.09 minutes in Group A(Buprenorphine) as compared to 7.17±3.13 minutes in Group B (Fentanyl) and there was a significant statistical difference ($p<0.001$) . The faster onset of pain relief in Fentanyl group can be attributed to its high lipid solubility. The faster onset of analgesia in the Fentanyl group we observed was comparable with the results obtained from the study done by SurajDhalae and his colleagues in 2000.[13] They studied epidural analgesia with 0.5% Bupivacaine and 50mcg Fentanyl and found that the mean onset of analgesia was 9.53±1.12 minutes, when compared to 0.5% Bupivacaine alone which was 11.26±0.79 minutes ($p<0.01$).

Boas RA et al evaluated the opioid receptor binding properties of fentanyl and buprenorphine in their study. Fentanyl receptor binding reached equilibrium fast (within 10 minutes) and dissociated rapidly (T 1/2 = 6.8 minutes) and entirely (100 percent by 1 hr). Buprenorphine, on the other hand, demonstrated sluggish receptor association (30 minutes) with high affinity for numerous sites, and slow (T 1/2 = 166 minutes) and incomplete dissociation (50 percent binding after 1 hr).These findings offer an explanation for the difference in onset of analgesia with fentanyl and buprenorphine .[19]

**DURATION OF ANALGESIA:-**

In our study the duration of analgesia is taken as the time from administration of study drugs epidurallyupto the time when patient complains of pain and VAS Score is more than equal to 5. We observed that patients who received Buprenorphine as adjuvant did not require rescue analgesia for more than 12 hours (mean 13.63±3.19 hours) as compared to 3-4 hours (mean 3.73 ± 1.14 hours) in those who received Fentanyl.

**This could be correlated with:**

1. D.Kumar, N.Dev, and N.Gupta found that 0.15mg Buprenorphine with 10 ml of 0.9 percent saline had a longer duration of action 13.1 hours (range 8-12 hours) than 10mg Ketamine with 10 ml of 0.9 percent saline, which had a mean duration of 5.2 hours in their study comparing epidural buprenorphine and epidural Ketamine for postoperative pain relief. [33]
2. Koshi T et al in 1994 compared epidural morphine and epidural buprenorphine for postoperative pain relief and found that longer duration of pain relief was with buprenorphine (19.9±8 hours). [34]
3. Rutter DV et al in 1981 reported that 100µg of epidural fentanyl for postoperative pain relief has a relatively shorter duration of action i.e by 3rd hour almost 50% of patients complained of increase in pain.[35]

Longer duration of action and greater analgesic efficacy of epidural buprenorphine can be attributed to its property of high affinity for spinal receptors. Smaller doses of buprenorphine have shown to produce a high concentration of the drug at the receptors. High lipid solubility of Buprenorphine facilitates its diffusion into the spinal cord. The diffusion into the blood stream from the spinal cord is slow and does not approach the bulbar Centers.[36]

**VAS SCORES:-**

The visual analogue pain score (VAS) was noted at 0, 5, 10 ,15 , 30 , 45 , 60 mins and then hourly for 8 hours and then 4$^{th}$ hourly upto 24hours after administration of study drugs.

At the end of first hour, Group A and Group B had excellent pain scores with mean VAS scores of 0.90 ± 0.76 and 1.27± 1.2 respectively.

The mean VAS scores remained less than 5 for upto 12 hours in Group A as compared to upto 3 hours in Group B. The increase in VAS Score above 5 indicated the need for rescue analgesia.

Our findings were comparable with the study conducted by Arun Kumar Gupta et al in 2015. They assessed pain quality by VAS scores and observed that within 15 minutes 100% of the patients in the fentanyl group had complete pain relief and it lasted till 2 hours. In Buprenorphine group within 15 minutes 60% patients had satisfactory analgesia, but within 30 minutes all patients (100%) had satisfactory analgesia which lasted beyond 6 hours (upto 24-30 hours).[37]

**HEMODYNAMIC STABILITY:-**

Pulse rate remained stable in the range of 64-101/min in Group A and 68-110/min in Group B.

Mean arterial pressure decreased from the baseline in both the groups but never went below 65mmofHg.

UshaRathi, M. Singh, M.Pramanik in 1993 conducted a study on postoperative analgesic efficacy with different doses of extradural buprenorphine for herniorrhaphy, where Group A (control) received 2 percent lignocaine plain , Group B received 0.15 mg buprenorphine with 2 percent lignocaine and Group C received 0.3 mg buprenorphine with 2 percent lignocaine. They reported that 0.3mg dose of

Buprenorphine was preferable for single shot epidural injection which provided both good quality anaesthesia and postoperative analgesia with hemodynamic stability which correlates with our observation[38]

Gough et al., in 1988 used epidural fentanyl 1.5µg/ kg body weight in 10ml of sterile solution and concluded that the range of mean(S.D) of cardio- respiratory variables like heart rate, systolic BP, diastolic BP and Respiratory rate varied negligibly from basal recordings.[39]

**SIDE EFFECTS:-**

Nausea and vomiting, pruritis, Urinary retention and Depression of ventilation are the four classic side effects of opioids.[40]These can be attributed to the presence of drug either in CSF or in the systemic circulation. Most side effects are dose dependant.

Opioids cause nausea and vomiting by directly stimulating the CTZ in the area postrema of the medulla. However, this is dose-dependent, and tolerance develops quickly. Anticholinergics and phenothiazines, particularly those that are antagonists at dopamine receptors, can be used to treat this emetic effect.[40]

One of the most frequent side effects of neuraxial opioids is pruritus. It can be generalized, but it's more likely to affect the face, neck, or upper thorax. The incidence varies greatly; severe pruritus is uncommon, but maybe seen in obstetric patients. The mechanism of pruritus is probably due to the cephalad migration of the opioids within the CSF and their interaction with opioid receptors in trigeminal nucleus rather than the histamine release from mast cells. Opioid antagonist Naloxone is effective in relieving this pruritus.

Urinary retention as an adverse effect of opioid use is caused by their action on the receptors in the sacral spinal cord. This interaction leads to inhibition of sacral parasympathetic nervous system outflow, causingdetrusor muscle relaxation and an

increase in maximum bladder capacity, finally resulting in urinary retention. Nalaxone causes a reduction in functional bladder capacity andpromotes an increase in detrusor contractility thus antagonizing the opioid action.

The patients in our study were observed for any side effects like nausea and vomiting, pruritis, respiratory depression, hypotension and sedation in both the groups.

**Nausea and vomiting**

In our study 9 patients (30%) had nausea and 3 patients (10%) developed vomiting in group A whereas in group B only 2 patients (6.67 %) had nausea with no incidence of vomiting. Morphine and related opioid congeners induce nausea by direct stimulation of CTZ and are reported to cause delay in gastric emptying.

Hayashi H, Nishiuchi T, and Tamura H studied postoperative pain relief with epidural buprenorphine and fentanyl in 1993 and found no difference in their analgesic efficacies, but the incidence of nausea and vomiting was significantly lower in fentanyl compared to buprenorphine, which was comparable to our study.[18]

**Pruritus**

In our study,Group A showed no incidence of pruritis while 3 patients (10%) in Group B developed pruritis. In a study by Lytle SA et al in 1991 using epidural fentanyl 50µg , they reported that 4% of patients had pruritis which correlates with our study .[41]

**Respiratory depression**

Gaffud et al (1986) in their study found that there was no respiratory depression with the use of epidural fentanyl. But Harcuset al[42] reported that respiratory depression is a common problem with use of buprenorphine. In our study also no respiratory depression was seen in any patient who received epidural fentanyl or buprenorphine. The oxygen saturation was maintained above 98% in both the groups.

In 1994, Koshi et al studied postoperative analgesia and side effects of epidural morphine versus epidural buprenorphine and reported that with epidural buprenorphine, the incidence of respiratory depression was zero.[34]

**Sedation-** was observed only in fentanyl group which constituted 6.67% and none of the patients in buprenorphine group. Majority of the patients had mild sedation(patient awake but drowsy). This was not statistically significant (p=0.075).

Drowsiness with fentanyl has been reported in many studies. Stephen Naulty et al[43] , reported drowsiness as one of the common side effects in a study of extradural fentanyl. Scott et al and Sylvie Rostening et al (1991) have also reported similar findings in their studies.

**Hypotension**

In our study none of the patients had significant hypotension in either of the groups.

# SUMMARY

This study was done to compare the effects of two opioids- buprenorphine and fentanyl, as adjuvant to the local anesthetic Bupivacaine for postoperative epidural analgesia in lower limb orthopedic surgeries. Sixty adult patients between twenty and sixty years of age of either gender of ASA status I - II scheduled for lower limb orthopedic surgeries satisfying the inclusion criteria were selected and randomly divided into 2 groups- Group A and Group B.

Surgery was performed under spinal anesthesia with epidural catheter insitu. Vital parameters were monitored intra-operatively. Postoperatively when the patient complained of pain and VAS score was more than or equal to 5 , study drugs were given via epidural catheter.Group A received 1.5mcg/kg Buprenorphine with 2ml 0.5% Bupivacaine diluted with distilled water to 10ml. Group B received 1mcg/kg Fentanyl with 2ml 0.5%Bupivacaine diluted with distilled water to 10ml. VAS scores, Pulse rate , Blood pressure , Side effects were noted at intervals of 5 , 10 , 15 , 30 , 45 , 60 minutes and then hourly for 8 hours and $4^{th}$ hourly upto 24 hours.

In this study,

1. The mean time of onset of analgesia was faster in Fentanyl group (15.33 ±8.09mins) than in Buprenorphine group (7.17 ±3.13mins).
2. The duration of analgesia was longer in Buprenorphine group (13.63±3.19 hours) than in Fentanyl group (3.73±1.14 hours).
3. Hemodynamic parameters such as pulse rate, systolic and diastolic blood pressure and mean arterial pressure remained stable throughout the study period in both groups.
4. Side effects such as nausea and vomiting was seen in 9 and 3 patients respectively in the Buprenorphine group whereas in fentanyl group 2 patients had nausea and

none had vomiting. Sedation and pruritis were seen only with fentanyl in 2 and 3 patients respectively.

Thus, Fentanyl as an adjuvant to Bupivacaine has a faster onset and recovery, resulting in a shorter duration of analgesia than Buprenorphine, which has a slower onset but a longer duration of analgesia, with no significant variations in haemodynamic parameters between the two groups.

# CONCLUSION

In this comparative study between Buprenorphine and Fentanyl used as adjuvants to Bupivacaine for postoperative Epidural Analgesia in lower limb orthopaedic surgeries we conclude that :-

1. Both Fentanyl and Buprenorphine are safe and effective opioids which can be used as adjuvants to Epidural Bupivacaine.
2. Fentanyl is a better adjuvant to Bupivacaine with faster onset of analgesia and lesser incidence of side effects.
3. The duration of analgesia is longer with buprenorphine as compared to fentanyl.

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# CONSENT FORM

**PURPOSE OF RESEARCH:**

I have been informed that this study is **"TO STUDY THE EFFECT OF BUPRENORPHINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE FOR POSTOPERATIVE EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPEDIC SURGERIES"**I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

**PROCEDURE:**

I understand that I will be participating in the study: **"TO STUDY THE EFFECT OF BUPRENORPHINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE FOR POSTOPERATIVE EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPEDIC SURGERIES"**

**CONFIDENTIALITY:**

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

**REQUEST FOR MORE INFORMATION:**

I understand that I may ask more questions about the study at any time **Dr. NAMRATHA B M** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this

study, which might influence my continued participation. If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me for keep for careful reading.

**REFUSAL OR WITHDRAWL OF PARTICIPATION:**

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

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

**INJURY STATEMENT:**

I understand that in the unlikely event of injury to me/my ward, resulting directly due to my participation in this study, such injury will be reported promptly, then medical treatment would be available to me, but no further compensation will be provided. I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

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

Date: **Dr. NAMRATHA**

(Investigator)

**STUDY SUBJECT CONSENT STATEMENT:**

I confirm that **Dr. NAMRATHA B M** has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

# PROFORMA

**STUDY:- "A PROSPECTIVE RANDOMIZED CLINICAL STUDY TO COMPARE THE EFFECT OF BUPRENORPHINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE FOR POSTOPERATIVE EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPEDIC SURGERIES."**

**PATIENT DETAILS:** **DATE:-**

I. Name: Age/ Sex: I.PNo: Weight:

Group allotted by randomization: Group A / Group B

II. 1. Type of the surgery:

2. Indication:

III. Significant History:

IV. General Physical Examination:

Pallor:

Icterus:

Cyanosis:

Clubbing:

Koilonychia:

Lymphadenopathy:

Oedema:

Teeth: Dentures:

V. Vital Parameters

Pulse: Blood Pressure:

Respiratory Rate: Temperature:

VI. Systemic Examination

1. CVS2.RS:

3. CNS 4.Per Abdomen:

VII. Airway Assessment:

Mallampati Grade: Cervical Spine:

Mouth opening: Neck Movement:

VIII. ASA Grade:

IX. Investigation

Hemoglobin: TLC:

S. Urea: S. Creatinine:

RBS: Platelet count:

Urine Routine:

Chest Xray: ECG:

X.

- Anaesthesia start time:

- Surgery start time:

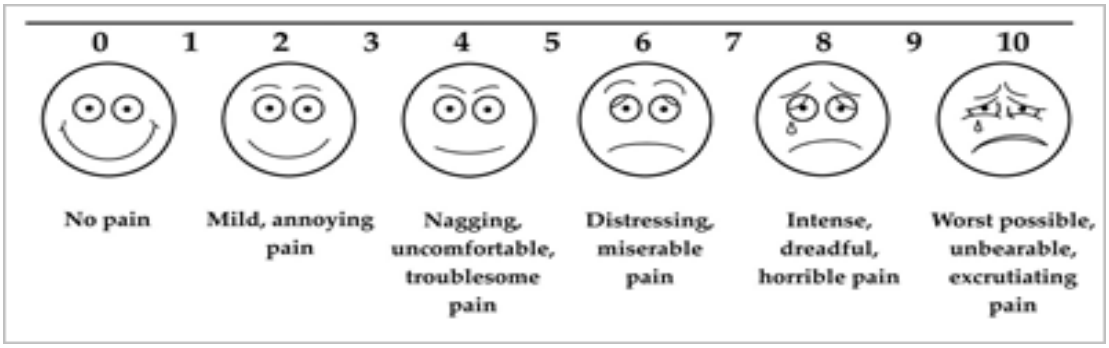
- Surgery end time:

- Time of first complaint of pain in postoperative period:

| **POST OP EDIDURAL ANAESTHESIA** | |
|---|---|
| TIME AT WHICH FIRST EPIDURAL DOSE GIVEN | |
| VITALS BEFORE DOSE | PR- |
| | BP- |
| | SPO2- |
| VITALS AFTER DOSE | PR- |
| | BP- |
| | SPO2- |
| DURATION OF POST OP ANALGESIA (TIME OF RESCUE ANALGESIA) | |
| QUALITY OF ANALGESIA(VAS SCORE) | |
| SIDE EFFECTS IF ANY | |

| TIME | VAS | PR | BP |
|---|---|---|---|
| 0 | | | |
| 5 | | | |
| 10 | | | |
| 15 | | | |
| 30 | | | |
| 45 | | | |
| 60 | | | |
| 2 HOUR | | | |
| 3 HOUR | | | |
| 4 HOUR | | | |
| 5 HOUR | | | |
| 6 HOUR | | | |
| 7 HOUR | | | |
| 8 HOUR | | | |
| 12 HOUR | | | |
| 16 HOUR | | | |
| 20 HOUR | | | |
| 24 HOUR | | | |

Visual analogue scale:

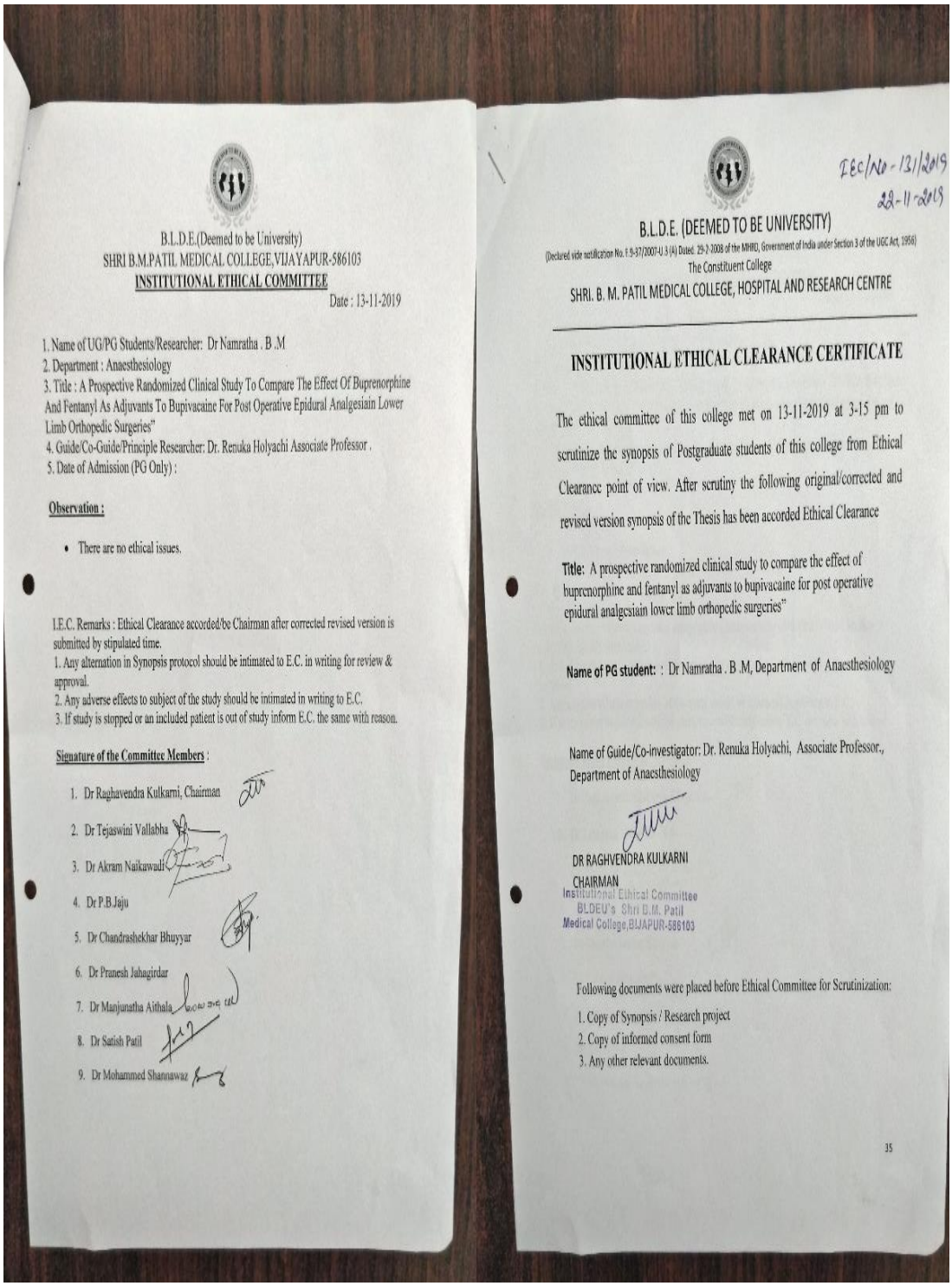



**COMMENTS:-**

**PRIMARY INVESTIGATOR SIGNATURE:-**

**GUIDE SIGNATURE:-**

# ETHICAL COMMITTEE CLEARANCE CERTICATE



B.L.D.E.(Deemed to be University)
SHRI B.M.PATIL MEDICAL COLLEGE,VIJAYAPUR-586103
**INSTITUTIONAL ETHICAL COMMITTEE**
Date : 13-11-2019

1. Name of UG/PG Students/Researcher: Dr Namratha . B .M
2. Department : Anaesthesiology
3. Title : A Prospective Randomized Clinical Study To Compare The Effect Of Buprenorphine And Fentanyl As Adjuvants To Bupivacaine For Post Operative Epidural Analgesiain Lower Limb Orthopedic Surgeries"
4. Guide/Co-Guide/Principle Researcher: Dr. Renuka Holyachi Associate Professor .
5. Date of Admission (PG Only) :

**Observation :**

- There are no ethical issues.

I.E.C. Remarks : Ethical Clearance accorded/be Chairman after corrected revised version is submitted by stipulated time.
1. Any alternation in Synopsis protocol should be intimated to E.C. in writing for review & approval.
2. Any adverse effects to subject of the study should be intimated in writing to E.C.
3. If study is stopped or an included patient is out of study inform E.C. the same with reason.

**Signature of the Committee Members** :

1. Dr Raghavendra Kulkarni, Chairman
2. Dr Tejaswini Vallabha
3. Dr Akram Naikawadi
4. Dr P.B.Jaju
5. Dr Chandrashekhar Bhuyyar
6. Dr Pranesh Jahagirdar
7. Dr Manjunatha Aithala
8. Dr Satish Patil
9. Dr Mohammed Shannawaz

IEC/NO-131/2019
22-11-2019

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-7-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

## INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 13-11-2019 at 3-15 pm to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

**Title:** A prospective randomized clinical study to compare the effect of buprenorphine and fentanyl as adjuvants to bupivacaine for post operative epidural analgesiain lower limb orthopedic surgeries"

**Name of PG student:** : Dr Namratha . B .M, Department of Anaesthesiology

Name of Guide/Co-investigator: Dr. Renuka Holyachi, Associate Professor., Department of Anaesthesiology

DR RAGHVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103

Following documents were placed before Ethical Committee for Scrutinization:

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

35

# MASTERCHART GROUP A:- BUPRENORPHINE GROUP

| SI NO | NAME | IP NO | DATE | Age | Sex | Weight (kg) | ASA | DIAGNOSIS | PROCEDURE | DURATION (hours) | Baseline | | | | | VAS before epidural dose (0) | VAS SCORE | | | | | | | | | | | | | | | Onset of Analgesia (mins) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | PR | BP (S) | BP (D) | RR | SPO2 | | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | |
| 1 | NAGAMMA | 3251 | 5/2/2020 | 60 | F | 80 | 2 | LT NECK OF FEMUR # | LT BIPOLAR HEMIARTHROPLASTY | 3 | 90 | 140 | 80 | 15 | 98 | 6 | 5 | 4 | 4 | 3 | 1 | 1 | 1 | 0 | 3 | 4 | 4 | 5 | 7 | 7 | 5 | 6 | 8 | 10 |
| 2 | SUMITHRA | 5020 | 19/2/20 | 44 | F | 66 | 2 | LT HIP OSTEO-ARTHRITIS | LT TOTAL HIP REPLACEMENT | 4 | 88 | 120 | 90 | 14 | 100 | 7 | 7 | 6 | 4 | 4 | 1 | 0 | 1 | 1 | 1 | 2 | 2 | 2 | 4 | 5 | 7 | 6 | 7 | 15 |
| 3 | VISHWANATH | 12033 | 27/4/20 | 23 | M | 72 | 1 | RT FEMUR SHAFT # | ORIF WITH IMIL NAILING | 2 | 90 | 130 | 90 | 14 | 99 | 6 | 6 | 5 | 4 | 3 | 3 | 1 | 2 | 2 | 2 | 2 | 3 | 4 | 4 | 6 | 6 | 7 | 6 | 15 |
| 4 | RUDRAPPA | 14772 | 17/6/20 | 45 | M | 70 | 1 | RT FEMUR SHAFT # WITH MEDIAL MALLEOLUS # | ORIF WITH PLATING WITH CC SCREW | 2 | 102 | 110 | 70 | 20 | 96 | 7 | 7 | 6 | 6 | 3 | 1 | 0 | 1 | 1 | 2 | 2 | 3 | 3 | 3 | 7 | 6 | 6 | 7 | 30 |
| 5 | GIRIJABAI | 14800 | 18/6/20 | 30 | F | 56 | 1 | RT KNEE COMPLETE ACL TEAR | ARTHROSCOPIC ACL RECONSTRUCTION | 4 | 70 | 110 | 70 | 14 | 99 | 8 | 7 | 6 | 4 | 2 | 2 | 2 | 1 | 1 | 1 | 3 | 3 | 3 | 4 | 6 | 6 | 6 | 6 | 15 |
| 6 | UMABAI | 14584 | 25/6/20 | 50 | F | 68 | 2 | RT DISTAL FEMUR # | CR WITH EX FIX WITH LIMB RECONSTRUCTION | 4.5 | 84 | 120 | 70 | 16 | 100 | 9 | 6 | 6 | 3 | 3 | 3 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 4 | 4 | 7 | 9 | 8 | 15 |
| 7 | SHIVAPPA | 15552 | 3/7/2020 | 45 | M | 55 | 2 | RT FEMUR SHAFT # WITH RT TIBIA # | ORIF WITH PLATING WITH CC SCREW | 3 | 98 | 120 | 70 | 14 | 100 | 8 | 8 | 6 | 4 | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 2 | 3 | 4 | 6 | 7 | 6 | 7 | 15 |
| 8 | ABDUL | 5904 | 18/9/20 | 42 | M | 94 | 1 | RT DISTAL COMPOUND FEMUR # | ORIF WITH PLATING | 4 | 98 | 120 | 80 | 16 | 99 | 7 | 7 | 3 | 3 | 3 | 1 | 1 | 1 | 0 | 3 | 3 | 4 | 4 | 4 | 4 | 5 | 8 | 8 | 10 |
| 9 | MANIKANTA | 5738 | 25/9/20 | 24 | M | 82 | 2 | TB LT HIP | DIAGNOSTIC ARTHROSCOPY | 3 | 72 | 110 | 70 | 14 | 100 | 6 | 6 | 3 | 3 | 1 | 1 | 0 | 1 | 1 | 3 | 3 | 4 | 4 | 4 | 4 | 6 | 6 | 7 | 10 |
| 10 | RAVI | 6101 | 25/9/20 | 49 | M | 74 | 2 | LT PROXIMAL TIBIA # | ORIF WITH PLATING | 2.5 | 80 | 110 | 70 | 16 | 99 | 6 | 4 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 3 | 3 | 7 | 7 | 6 | 5 |
| 11 | MAHADEVI | 6817 | 25/9/20 | 57 | F | 70 | 2 | RT IT # | CRIF WITH PFN | 3 | 88 | 130 | 80 | 14 | 98 | 7 | 7 | 7 | 5 | 4 | 1 | 1 | 1 | 2 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 6 | 6 | 30 |
| 12 | NINGAPPA | 7963 | 29/9/20 | 25 | M | 84 | 1 | RT FEMUR SHAFT # WITH RT TIBIA # | RT CRIF WITH IMIL NAILING WITH RT TIBIA PLATING | 4 | 78 | 120 | 80 | 14 | 99 | 7 | 7 | 6 | 6 | 3 | 3 | 1 | 1 | 3 | 2 | 2 | 3 | 3 | 3 | 4 | 8 | 7 | 8 | 30 |
| 13 | SIDAPPA | 3058 | 30/9/20 | 27 | M | 78 | 1 | RT SHAFT OF FEMUR # | ORIF WITH IMIL NAILING | 3 | 72 | 120 | 70 | 14 | 100 | 8 | 6 | 6 | 4 | 4 | 2 | 2 | 2 | 3 | 3 | 3 | 4 | 4 | 4 | 5 | 6 | 7 | 7 | 15 |
| 14 | CHANDAWWA | 10750 | 11/10/2020 | 30 | F | 66 | 2 | LT SUBTROCHANTERIC FEMUR # | CRIF WITH LONG PFN | 3 | 83 | 130 | 80 | 15 | 100 | 9 | 7 | 5 | 4 | 1 | 1 | 0 | 0 | 0 | 2 | 2 | 2 | 4 | 4 | 4 | 5 | 9 | 8 | 15 |
| 15 | GOURANGA | 10469 | 21/10/20 | 24 | M | 88 | 1 | LT SHAFT OF FEMUR # | ORIF WITH IMIL NAILING WITH BONE GRAFT | 3 | 72 | 130 | 90 | 16 | 99 | 7 | 6 | 4 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 4 | 6 | 6 | 10 |
| 16 | ANIL JADAV | 10460 | 17/11/20 | 30 | M | 72 | 2 | N/C/O RT NECK OF FEMUR # WITH IMPLANT IN SITU | TOTAL HIP ARTHROPLASTY | 3.5 | 86 | 110 | 90 | 14 | 100 | 8 | 6 | 4 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 2 | 4 | 4 | 4 | 4 | 4 | 7 | 5 | 10 |
| 17 | LAXMAN | 18683 | 30/11/20 | 36 | M | 75 | 1 | LT DISTAL FEMUR # | ORIF WITH PLATING | 2.5 | 98 | 140 | 90 | 16 | 98 | 9 | 8 | 5 | 4 | 1 | 1 | 1 | 3 | 1 | 1 | 2 | 2 | 2 | 2 | 4 | 6 | 5 | 5 | 15 |
| 18 | HANUMANTH | 30350 | 26/12/20 | 60 | M | 79 | 2 | LT NECK OF FEMUR # | LT BIPOLAR HEMIARTHROPLASTY | 3 | 89 | 130 | 70 | 14 | 100 | 6 | 5 | 4 | 4 | 3 | 3 | 0 | 2 | 2 | 4 | 5 | 5 | 6 | 6 | 7 | 8 | 6 | 7 | 10 |
| 19 | MOHAMMAD AZIM | 34272 | 11/1/2021 | 35 | M | 85 | 2 | RT TIBIA # WITH LT PATELLA # | RT ORIF WITH PLATING WITH LT TENSION BAND WIRING | 3.5 | 88 | 110 | 70 | 15 | 98 | 8 | 5 | 3 | 2 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 2 | 4 | 3 | 6 | 7 | 10 |
| 20 | SATISH | 47211 | 18/1/21 | 20 | M | 72 | 1 | RT KNEE COMPLETE ACL TEAR | ARTHROSCOPIC ACL RECONSTRUCTION | 3 | 74 | 140 | 90 | 16 | 99 | 9 | 8 | 8 | 6 | 4 | 4 | 3 | 3 | 3 | 3 | 2 | 3 | 3 | 3 | 3 | 6 | 7 | 6 | 30 |
| 21 | SHANTAPPA | 69469 | 26/01/21 | 22 | M | 76 | 1 | RT DISTAL FEMUR # | ORIF WITH PLATING | 3 | 90 | 120 | 80 | 18 | 100 | 7 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 2 | 1 | 2 | 2 | 3 | 6 | 6 | 5 | 5 |
| 22 | SHASHIKALA | 64443 | 2/2/2021 | 50 | F | 54 | 2 | LT KNEE OSTEOARTHRITIS | TOTAL KNEE REPLACEMENT | 4 | 69 | 130 | 90 | 14 | 99 | 8 | 8 | 4 | 1 | 1 | 0 | 0 | 1 | 1 | 2 | 2 | 4 | 4 | 4 | 6 | 6 | 7 | 7 | 10 |
| 23 | RAJAMBI | 69346 | 2/2/2021 | 53 | F | 50 | 2 | RT IT # WITH LT PROXIMAL TIBIA # | RT CRIF WITH PFN & LT ORIF WITH PLATING | 3.5 | 78 | 120 | 70 | 14 | 100 | 8 | 6 | 3 | 3 | 2 | 1 | 0 | 0 | 1 | 1 | 1 | 3 | 3 | 4 | 4 | 6 | 9 | 8 | 10 |
| 24 | SUSHILABAI | 76919 | 8/2/2021 | 55 | F | 68 | 2 | LT NECK OF FEMUR # | BIPOLAR HEMIARTHROPLASTY | 3 | 80 | 130 | 70 | 14 | 100 | 7 | 7 | 6 | 4 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 3 | 7 | 6 | 6 | 15 |
| 25 | MALLAPPA | 96547 | 14/2/21 | 58 | M | 90 | 2 | RT IT# WITH SUBTROCHANTERIC EXTENSION | CRIF WITH LONG PFN | 2.5 | 89 | 140 | 90 | 16 | 97 | 9 | 7 | 7 | 3 | 0 | 1 | 1 | 0 | 0 | 2 | 1 | 2 | 3 | 3 | 4 | 7 | 7 | 6 | 15 |
| 26 | NAGESH | 93397 | 22/2/21 | 35 | M | 84 | 1 | LT HIP AVASCULAR NECROSIS | LT TOTAL HIP REPLACEMENT | 3.5 | 82 | 110 | 70 | 15 | 98 | 6 | 3 | 3 | 1 | 1 | 1 | 1 | 2 | 1 | 2 | 2 | 2 | 3 | 3 | 4 | 6 | 7 | 4 | 5 |
| 27 | ANNAPPA | 123426 | 5/3/2021 | 58 | M | 67 | 1 | RT NECK OF FEMUR # | RT TOTAL HIP ARTHROPLASTY | 3.5 | 65 | 120 | 80 | 12 | 96 | 8 | 7 | 7 | 7 | 4 | 2 | 2 | 1 | 2 | 2 | 1 | 1 | 4 | 4 | 4 | 4 | 6 | 6 | 30 |
| 28 | RAJENDRA | 156497 | 26/3/21 | 56 | M | 77 | 2 | RT NECK OF FEMUR # | RT TOTAL HIP ARTHROPLASTY | 4 | 76 | 140 | 100 | 17 | 100 | 6 | 6 | 5 | 3 | 2 | 1 | 1 | 2 | 2 | 2 | 3 | 3 | 4 | 6 | 6 | 5 | 7 | 7 | 15 |
| 29 | AMEERBI | 166776 | 31/3/21 | 50 | F | 92 | 2 | RT NECK OF FEMUR # | RT BIPOLAR HEMIARTHROPLASTY | 3.5 | 104 | 130 | 80 | 16 | 99 | 9 | 9 | 9 | 6 | 2 | 1 | 0 | 0 | 0 | 0 | 2 | 2 | 2 | 3 | 4 | 4 | 6 | 7 | 30 |
| 30 | DANESH | 5744 | 15/4/21 | 35 | M | 70 | 2 | D LT DISTAL FEMUR COMMUNITED # WITH PATEL | EX FIX REMOVAL WITH ORIF PLATING WITH TBW | 4 | 80 | 120 | 80 | 15 | 100 | 7 | 6 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 3 | 3 | 3 | 4 | 4 | 5 | 7 | 10 |

| PULSE RATE ( beats/minute) | | | | | | | | | | | | | | | | | | SBP (mmofHg) | | | | | | | | | | | | | | | | | | DBP (mmofHg) | | | | | | | | | | | | | | | | | | Time of rescue analgesia (hrs) | Side Effects | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | 0 | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | 0 | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | | Nausea | Vomming | Pruritis | Respiratory depression | Sedation | Hypotension |
| 80 | 88 | 85 | 80 | 79 | 72 | 76 | 70 | 75 | 78 | 81 | 85 | 89 | 82 | 86 | 86 | 88 | 87 | 120 | 120 | 110 | 110 | 120 | 130 | 120 | 120 | 110 | 110 | 130 | 120 | 120 | 120 | 110 | 110 | 110 | 120 | 80 | 80 | 80 | 80 | 80 | 90 | 80 | 80 | 70 | 80 | 90 | 90 | 80 | 90 | 70 | 70 | 80 | 80 | 7.5 | Y | N | N | N | N | N |
| 72 | 78 | 80 | 82 | 74 | 70 | 68 | 73 | 78 | 80 | 84 | 88 | 72 | 68 | 73 | 76 | 75 | 71 | 120 | 120 | 120 | 110 | 110 | 110 | 110 | 120 | 120 | 120 | 120 | 110 | 120 | 120 | 120 | 120 | 130 | 120 | 70 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 80 | 80 | 70 | 70 | 70 | 80 | 80 | 80 | 10 | N | N | N | N | N | N |
| 80 | 82 | 82 | 74 | 72 | 70 | 74 | 76 | 82 | 86 | 84 | 80 | 82 | 84 | 86 | 89 | 88 | 84 | 130 | 120 | 120 | 120 | 110 | 110 | 110 | 120 | 120 | 120 | 130 | 130 | 110 | 120 | 120 | 120 | 130 | 130 | 80 | 80 | 80 | 70 | 70 | 70 | 80 | 80 | 90 | 90 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 90 | 12 | Y | Y | N | N | N | N |
| 90 | 92 | 90 | 88 | 86 | 85 | 80 | 76 | 76 | 78 | 76 | 68 | 73 | 82 | 80 | 78 | 75 | 79 | 130 | 130 | 130 | 140 | 120 | 120 | 120 | 110 | 120 | 130 | 120 | 122 | 130 | 130 | 128 | 130 | 140 | 120 | 90 | 90 | 80 | 80 | 80 | 80 | 90 | 90 | 90 | 90 | 80 | 80 | 80 | 80 | 80 | 80 | 90 | 90 | 11 | N | N | N | N | N | N |
| 68 | 82 | 90 | 86 | 80 | 82 | 78 | 82 | 80 | 81 | 82 | 87 | 74 | 78 | 82 | 84 | 84 | 88 | 110 | 112 | 112 | 120 | 120 | 120 | 110 | 110 | 110 | 110 | 110 | 110 | 110 | 110 | 120 | 120 | 110 | 110 | 60 | 70 | 70 | 80 | 80 | 70 | 70 | 70 | 80 | 70 | 80 | 80 | 80 | 80 | 80 | 90 | 70 | 80 | 10.5 | N | N | N | N | N | N |
| 76 | 79 | 76 | 75 | 69 | 64 | 72 | 74 | 78 | 68 | 73 | 74 | 78 | 82 | 80 | 80 | 78 | 76 | 120 | 120 | 120 | 120 | 110 | 130 | 120 | 120 | 120 | 110 | 110 | 120 | 122 | 120 | 130 | 120 | 110 | 120 | 70 | 70 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 80 | 70 | 80 | 80 | 80 | 80 | 80 | 15 | N | N | N | N | N | N |
| 100 | 102 | 98 | 96 | 90 | 88 | 82 | 85 | 89 | 76 | 72 | 76 | 88 | 84 | 82 | 82 | 84 | 80 | 120 | 110 | 112 | 110 | 120 | 120 | 124 | 120 | 110 | 120 | 110 | 110 | 120 | 124 | 120 | 130 | 120 | 110 | 90 | 90 | 80 | 80 | 80 | 80 | 90 | 70 | 80 | 70 | 78 | 80 | 80 | 80 | 90 | 80 | 80 | 80 | 12 | Y | N | N | N | N | N |
| 88 | 86 | 89 | 84 | 80 | 79 | 74 | 78 | 86 | 88 | 71 | 82 | 80 | 78 | 86 | 94 | 88 | 89 | 120 | 120 | 110 | 100 | 110 | 120 | 120 | 120 | 118 | 110 | 118 | 118 | 120 | 120 | 110 | 110 | 120 | 120 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 16 | N | N | N | N | N | N |
| 83 | 89 | 86 | 85 | 80 | 78 | 84 | 88 | 82 | 84 | 86 | 88 | 76 | 73 | 74 | 80 | 82 | 79 | 110 | 110 | 130 | 130 | 120 | 120 | 110 | 110 | 110 | 120 | 120 | 110 | 110 | 120 | 120 | 120 | 110 | 120 | 90 | 90 | 90 | 80 | 90 | 90 | 80 | 80 | 80 | 90 | 90 | 90 | 80 | 80 | 80 | 90 | 70 | 80 | 13 | Y | N | N | N | N | N |
| 82 | 84 | 86 | 76 | 79 | 70 | 74 | 80 | 83 | 80 | 79 | 75 | 73 | 72 | 75 | 75 | 75 | 74 | 120 | 120 | 110 | 110 | 118 | 116 | 118 | 120 | 120 | 130 | 130 | 130 | 120 | 120 | 110 | 110 | 120 | 110 | 80 | 80 | 80 | 70 | 70 | 70 | 70 | 80 | 70 | 70 | 90 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 15 | N | Y | N | N | N | N |
| 74 | 78 | 76 | 74 | 78 | 80 | 82 | 80 | 76 | 75 | 78 | 68 | 73 | 82 | 80 | 78 | 75 | 74 | 130 | 120 | 118 | 116 | 116 | 120 | 120 | 110 | 110 | 120 | 120 | 120 | 130 | 130 | 130 | 120 | 130 | 130 | 70 | 70 | 70 | 70 | 70 | 70 | 70 | 80 | 80 | 80 | 70 | 80 | 80 | 80 | 70 | 80 | 80 | 70 | 16.5 | N | N | N | N | N | N |
| 90 | 95 | 92 | 88 | 86 | 82 | 84 | 86 | 80 | 82 | 80 | 85 | 68 | 73 | 86 | 90 | 99 | 94 | 120 | 122 | 120 | 120 | 110 | 114 | 120 | 120 | 130 | 120 | 120 | 120 | 110 | 110 | 110 | 100 | 110 | 116 | 90 | 90 | 80 | 80 | 80 | 90 | 90 | 80 | 80 | 90 | 90 | 80 | 80 | 80 | 90 | 70 | 80 | 80 | 14 | N | N | N | N | N | N |
| 76 | 78 | 83 | 76 | 72 | 74 | 86 | 83 | 88 | 86 | 85 | 78 | 86 | 74 | 78 | 76 | 80 | 73 | 118 | 110 | 110 | 120 | 130 | 120 | 120 | 120 | 118 | 120 | 120 | 120 | 110 | 110 | 130 | 130 | 120 | 130 | 70 | 80 | 80 | 80 | 80 | 70 | 70 | 70 | 80 | 80 | 80 | 70 | 70 | 70 | 80 | 80 | 80 | 80 | 12 | N | N | N | N | N | N |
| 82 | 88 | 80 | 78 | 82 | 84 | 82 | 76 | 88 | 82 | 80 | 77 | 74 | 78 | 81 | 80 | 79 | 80 | 130 | 130 | 130 | 130 | 134 | 130 | 130 | 128 | 120 | 130 | 130 | 120 | 120 | 120 | 120 | 134 | 130 | 130 | 80 | 80 | 80 | 70 | 80 | 70 | 70 | 90 | 80 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 16 | N | N | N | N | N | N |
| 88 | 80 | 74 | 76 | 73 | 83 | 76 | 70 | 84 | 86 | 82 | 78 | 80 | 78 | 86 | 86 | 84 | 80 | 130 | 130 | 120 | 120 | 110 | 110 | 100 | 110 | 110 | 110 | 120 | 130 | 120 | 120 | 120 | 110 | 120 | 120 | 90 | 80 | 80 | 70 | 80 | 80 | 80 | 80 | 80 | 90 | 80 | 80 | 70 | 70 | 70 | 90 | 90 | 80 | 16.5 | Y | N | N | N | N | N |
| 76 | 78 | 80 | 71 | 72 | 70 | 82 | 70 | 75 | 76 | 74 | 78 | 74 | 78 | 87 | 89 | 76 | 87 | 110 | 112 | 112 | 120 | 110 | 110 | 100 | 100 | 120 | 120 | 110 | 110 | 110 | 120 | 110 | 110 | 110 | 110 | 80 | 80 | 80 | 70 | 70 | 70 | 80 | 90 | 80 | 90 | 80 | 90 | 90 | 80 | 70 | 70 | 70 | 70 | 18 | N | N | N | N | N | N |
| 96 | 80 | 82 | 80 | 86 | 80 | 76 | 76 | 72 | 73 | 76 | 72 | 68 | 73 | 82 | 80 | 80 | 78 | 140 | 140 | 130 | 130 | 130 | 130 | 120 | 120 | 130 | 130 | 140 | 140 | 130 | 130 | 120 | 130 | 120 | 130 | 90 | 80 | 90 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 90 | 100 | 90 | 90 | 90 | 80 | 80 | 90 | 13 | N | N | N | N | N | N |
| 80 | 82 | 78 | 76 | 74 | 70 | 80 | 80 | 78 | 82 | 80 | 82 | 80 | 78 | 86 | 82 | 84 | 80 | 130 | 120 | 110 | 110 | 110 | 120 | 120 | 120 | 120 | 114 | 114 | 120 | 110 | 100 | 110 | 110 | 120 | 120 | 80 | 70 | 70 | 80 | 80 | 70 | 70 | 60 | 70 | 70 | 70 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 6 | N | N | N | N | N | N |
| 90 | 96 | 95 | 90 | 89 | 84 | 80 | 78 | 80 | 82 | 78 | 86 | 74 | 71 | 76 | 72 | 72 | 76 | 110 | 130 | 130 | 130 | 120 | 120 | 110 | 110 | 110 | 120 | 120 | 114 | 116 | 120 | 122 | 120 | 130 | 130 | 80 | 90 | 80 | 80 | 80 | 80 | 80 | 80 | 90 | 90 | 80 | 80 | 80 | 80 | 80 | 80 | 70 | 90 | 20 | N | N | N | N | N | N |
| 70 | 71 | 72 | 74 | 68 | 64 | 72 | 75 | 68 | 73 | 66 | 68 | 73 | 78 | 86 | 90 | 88 | 85 | 140 | 140 | 120 | 120 | 110 | 118 | 120 | 120 | 124 | 120 | 130 | 130 | 130 | 120 | 130 | 140 | 130 | 130 | 70 | 70 | 70 | 70 | 70 | 70 | 80 | 80 | 70 | 70 | 70 | 70 | 70 | 70 | 70 | 80 | 80 | 70 | 15.5 | N | N | N | N | N | N |
| 88 | 82 | 88 | 72 | 75 | 79 | 80 | 82 | 89 | 74 | 78 | 78 | 86 | 74 | 78 | 79 | 78 | 78 | 120 | 110 | 108 | 110 | 110 | 110 | 110 | 110 | 100 | 110 | 110 | 110 | 110 | 120 | 120 | 110 | 110 | 120 | 80 | 70 | 70 | 70 | 70 | 80 | 80 | 90 | 90 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 80 | 80 | 14 | Y | N | N | N | N | N |
| 68 | 70 | 72 | 78 | 80 | 76 | 78 | 80 | 82 | 80 | 78 | 74 | 75 | 68 | 73 | 75 | 76 | 80 | 100 | 100 | 110 | 110 | 120 | 120 | 120 | 118 | 110 | 120 | 120 | 120 | 110 | 110 | 120 | 120 | 110 | 110 | 60 | 60 | 60 | 70 | 70 | 80 | 80 | 80 | 80 | 90 | 70 | 70 | 80 | 80 | 70 | 80 | 70 | 80 | 12 | Y | N | N | N | N | N |
| 78 | 80 | 82 | 85 | 76 | 64 | 78 | 80 | 82 | 80 | 78 | 69 | 68 | 73 | 74 | 80 | 82 | 80 | 120 | 120 | 118 | 118 | 120 | 120 | 120 | 120 | 110 | 120 | 120 | 120 | 110 | 110 | 120 | 130 | 130 | 130 | 70 | 70 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 16 | N | N | N | N | N | N |
| 80 | 78 | 83 | 86 | 80 | 78 | 80 | 82 | 86 | 77 | 78 | 76 | 70 | 72 | 70 | 70 | 74 | 72 | 130 | 130 | 120 | 120 | 120 | 130 | 100 | 110 | 110 | 110 | 130 | 130 | 130 | 110 | 110 | 110 | 120 | 120 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 90 | 80 | 80 | 80 | 80 | 80 | 90 | 80 | 80 | 14.5 | N | N | N | N | N | N |
| 88 | 90 | 92 | 88 | 86 | 80 | 82 | 88 | 86 | 84 | 80 | 82 | 94 | 73 | 76 | 80 | 86 | 89 | 140 | 150 | 150 | 140 | 130 | 130 | 128 | 130 | 130 | 140 | 140 | 130 | 130 | 120 | 150 | 120 | 120 | 130 | 90 | 90 | 80 | 80 | 80 | 80 | 80 | 90 | 80 | 70 | 80 | 70 | 80 | 80 | 80 | 80 | 90 | 90 | 15 | Y | Y | N | N | N | N |
| 80 | 78 | 80 | 82 | 86 | 88 | 82 | 84 | 86 | 80 | 78 | 75 | 84 | 78 | 86 | 84 | 86 | 88 | 120 | 110 | 110 | 110 | 100 | 110 | 110 | 120 | 120 | 116 | 124 | 120 | 120 | 120 | 110 | 120 | 110 | 110 | 80 | 70 | 70 | 80 | 70 | 70 | 70 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 80 | 80 | 13.5 | N | N | N | N | N | N |
| 64 | 65 | 69 | 70 | 64 | 66 | 70 | 72 | 76 | 78 | 80 | 82 | 72 | 76 | 77 | 80 | 79 | 76 | 110 | 120 | 120 | 112 | 112 | 120 | 110 | 110 | 120 | 120 | 110 | 110 | 120 | 130 | 120 | 120 | 110 | 120 | 60 | 70 | 70 | 70 | 70 | 60 | 60 | 70 | 70 | 70 | 70 | 60 | 80 | 70 | 70 | 80 | 70 | 70 | 17 | N | N | N | N | N | N |
| 74 | 76 | 78 | 76 | 80 | 82 | 81 | 85 | 86 | 84 | 90 | 88 | 86 | 83 | 87 | 87 | 89 | 85 | 130 | 120 | 120 | 110 | 110 | 110 | 100 | 110 | 100 | 100 | 120 | 110 | 110 | 120 | 120 | 130 | 120 | 130 | 70 | 80 | 80 | 80 | 70 | 70 | 70 | 70 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 12.5 | N | N | N | N | N | N |
| 98 | 101 | 102 | 97 | 95 | 90 | 88 | 80 | 84 | 74 | 78 | 68 | 73 | 78 | 86 | 84 | 86 | 80 | 140 | 140 | 130 | 130 | 128 | 120 | 120 | 124 | 120 | 114 | 120 | 118 | 120 | 130 | 120 | 130 | 140 | 140 | 90 | 90 | 80 | 80 | 80 | 80 | 100 | 90 | 90 | 90 | 80 | 80 | 80 | 80 | 80 | 90 | 90 | 90 | 8 | Y | N | N | N | N | N |
| 78 | 80 | 78 | 75 | 76 | 82 | 88 | 80 | 79 | 78 | 79 | 74 | 78 | 68 | 73 | 79 | 75 | 78 | 120 | 118 | 110 | 100 | 110 | 120 | 114 | 120 | 120 | 140 | 130 | 120 | 120 | 130 | 130 | 110 | 130 | 110 | 80 | 80 | 80 | 70 | 70 | 70 | 70 | 70 | 80 | 80 | 80 | 80 | 70 | 70 | 90 | 80 | 80 | 80 | 17 | N | N | N | N | N | N |

# MASTERCHART GROUP B :- FENTANYL GROUP

| SI NO | NAME | IP NO | DATE | Age | Sex | Weight (kg) | ASA | DIAGNOSIS | PROCEDURE | DURATION (hours) | Baseline | | | | | VAS before epidural dose (0) | VAS SCORE | | | | | | | | | | | | | | | | Onset of Analgesia (mins) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | PR | BP (S) | BP (D) | RR | SPO2 | | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | |
| 1 | SANJU | 508 | 11/1/2020 | 28 | M | 70 | 1 | LT TIBIA PLATEAU # | ORIF WITH PLATING | 2 | 78 | 130 | 90 | 14 | 100 | 7 | 5 | 0 | 0 | 4 | 2 | 1 | 1 | 4 | 6 | 8 | 8 | 5 | 4 | 6 | 8 | 6 | 6 | 10 |
| 2 | ANAND | 1723 | 27/1/20 | 38 | M | 68 | 2 | RT NECK OF FEMUR # + RT DISTAL FEMUR & TIBIA # | ORIP WITH CC SCREW AND DHS | 5 | 80 | 110 | 70 | 14 | 99 | 8 | 3 | 2 | 0 | 1 | 0 | 1 | 4 | 5 | 5 | 6 | 6 | 5 | 7 | 7 | 6 | 8 | 7 | 5 |
| 3 | KASTURI | 3157 | 12/2/2020 | 35 | F | 57 | 1 | LT HIP OSTEOARTHRITIS | LT TOTAL HIP REPLACEMENT | 4 | 72 | 120 | 90 | 15 | 99 | 7 | 2 | 2 | 2 | 2 | 1 | 3 | 6 | 5 | 6 | 6 | 8 | 6 | 7 | 8 | 6 | 6 | 7 | 5 |
| 4 | YALLAWA | 11145 | 20/4/20 | 55 | F | 55 | 2 | RT FEMUR SHAFT # | CRIF WITH NAILING | 4 | 72 | 130 | 80 | 16 | 100 | 6 | 3 | 1 | 1 | 0 | 0 | 0 | 2 | 3 | 7 | 7 | 5 | 6 | 6 | 8 | 4 | 5 | 6 | 5 |
| 5 | GURUPADAPPA | 13159 | 20/5/20 | 49 | M | 80 | 1 | LT TRIMALLEOLAR # | ORIF WITH PLATING/SCREW | 2 | 82 | 100 | 70 | 14 | 100 | 6 | 4 | 2 | 2 | 0 | 0 | 1 | 4 | 5 | 6 | 4 | 5 | 6 | 6 | 7 | 6 | 4 | 5 | 5 |
| 6 | DUNDAWWA | 12906 | 23/5/20 | 40 | F | 66 | 1 | RT DISTAL TIBIA FIBULA # WITH BIMALLEOLAR # | ORIF WITH PLATING/ CC SCREW | 2.5 | 78 | 110 | 70 | 12 | 100 | 7 | 2 | 1 | 1 | 2 | 2 | 3 | 3 | 4 | 4 | 6 | 6 | 7 | 7 | 8 | 7 | 7 | 8 | 5 |
| 7 | MAHANTAPPA | 13069 | 26/5/20 | 45 | M | 72 | 1 | LT SUB-TROCHANTERIC FEMUR # | CRIF WITH LONG PFN | 2 | 70 | 110 | 70 | 14 | 99 | 9 | 6 | 3 | 1 | 1 | 0 | 2 | 2 | 5 | 6 | 5 | 6 | 6 | 5 | 8 | 8 | 8 | 6 | 10 |
| 8 | AMIN | 1276 | 2/9/2020 | 28 | M | 94 | 1 | LT FEMUR SHAFT # | CRIF WITH NAILING | 2 | 82 | 110 | 70 | 16 | 99 | 7 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 3 | 3 | 6 | 6 | 5 | 7 | 7 | 5 | 6 | 5 |
| 9 | SATEESH | 1539 | 3/9/2020 | 21 | M | 85 | 1 | LT FEMUR SHAFT # | CRIF WITH IMIL NAILING | 2.5 | 70 | 130 | 80 | 16 | 98 | 6 | 1 | 1 | 1 | 0 | 0 | 0 | 3 | 6 | 4 | 6 | 6 | 4 | 5 | 3 | 4 | 5 | 5 | 5 |
| 10 | KALLAPPA | 2363 | 8/9/2020 | 59 | M | 82 | 2 | LT NECK OF FEMUR # | LT HEMIARTHROPLASTY | 3.5 | 80 | 140 | 90 | 16 | 99 | 8 | 5 | 2 | 2 | 1 | 1 | 1 | 1 | 5 | 6 | 6 | 4 | 5 | 7 | 7 | 6 | 7 | 8 | 10 |
| 11 | BAVASAB | 4775 | 16/9/20 | 42 | M | 78 | 2 | LT TIBIA FIBULA COMPOUND # | CRIF WITH NAILING | 2 | 74 | 130 | 90 | 15 | 100 | 9 | 6 | 4 | 2 | 3 | 2 | 2 | 1 | 2 | 7 | 7 | 8 | 9 | 8 | 9 | 8 | 7 | 7 | 10 |
| 12 | SHIVAMMA | 5698 | 18/9/20 | 54 | F | 59 | 2 | RT PROXIMAL TIBIA SHAFT WITH FIBULA # | CRIF WITH NAILING | 2.5 | 86 | 130 | 70 | 14 | 100 | 7 | 3 | 1 | 1 | 1 | 0 | 0 | 3 | 4 | 5 | 5 | 7 | 6 | 7 | 7 | 6 | 6 | 8 | 5 |
| 13 | SANGAPPA | 6603 | 21/9/20 | 28 | M | 64 | 2 | RT COMPOUND TIBIA FIBULA # | CRIF WITH NAILING | 3 | 88 | 120 | 80 | 16 | 99 | 9 | 4 | 3 | 3 | 2 | 1 | 1 | 6 | 4 | 5 | 6 | 7 | 7 | 6 | 7 | 3 | 3 | 6 | 5 |
| 14 | DILIP | 6982 | 30/9/20 | 40 | M | 83 | 2 | RT FEMUR SHAFT # | CRIF WITH IMIL NAILING | 2.5 | 80 | 110 | 70 | 14 | 100 | 8 | 1 | 2 | 2 | 1 | 1 | 0 | 0 | 2 | 4 | 6 | 6 | 5 | 6 | 6 | 7 | 8 | 3 | 5 |
| 15 | CHANAMALLAPPA | 673 | 6/9/2020 | 25 | M | 75 | 1 | T TIBIA FIBULA # WITH PATELLA # WITH CLW OVER RT KNI | CRIF WITH EX FIX | 3 | 86 | 110 | 70 | 14 | 100 | 6 | 6 | 5 | 4 | 2 | 2 | 1 | 1 | 4 | 6 | 6 | 7 | 7 | 8 | 6 | 7 | 7 | 6 | 15 |
| 16 | SHIVANAND | 11027 | 9/10/2020 | 42 | M | 80 | 2 | OMPOUND TIBIA WITH PATELLA # WITH FIBULA SEGMENT | RT KNEE SPARRING EX FIX | 2 | 81 | 120 | 70 | 16 | 99 | 6 | 1 | 1 | 1 | 0 | 0 | 0 | 2 | 2 | 3 | 1 | 7 | 6 | 6 | 7 | 5 | 6 | 7 | 5 |
| 17 | KIRAN TELI | 12135 | 15/10/20 | 25 | M | 72 | 1 | BILATERAL HIP AVN | RT HIP ARTHROSCOPIC CONE DECOMPRESSION | 3 | 84 | 130 | 90 | 15 | 98 | 7 | 2 | 1 | 1 | 2 | 1 | 0 | 2 | 7 | 7 | 8 | 5 | 4 | 5 | 7 | 7 | 6 | 7 | 5 |
| 18 | MALLAMMA | 5015 | 31/10/20 | 56 | F | 70 | 2 | LT NECK OF FEMUR # | LT BIPOLAR HEMIARTHROPLASTY | 2.5 | 90 | 130 | 80 | 14 | 100 | 9 | 3 | 1 | 2 | 1 | 1 | 1 | 3 | 5 | 6 | 6 | 7 | 6 | 8 | 7 | 6 | 5 | 6 | 5 |
| 19 | TIPANNA | 3414 | 17/11/20 | 35 | M | 75 | 1 | O/C/O RT NOF # WITH DHS IMPLANT FAILURE | RT IMPLANT REMOVAL WITH TFN NAILING | 3.5 | 64 | 140 | 90 | 16 | 99 | 8 | 1 | 1 | 0 | 0 | 0 | 0 | 3 | 3 | 4 | 8 | 6 | 7 | 8 | 9 | 8 | 6 | 5 | 5 |
| 20 | KAVITA | 18669 | 19/11/20 | 22 | F | 52 | 1 | RT BIMALLEOLAR # WITH LT TIBIAL PLATEAU # | RT ORIF WITH PLATING WITH LT CRIF WITH CC SCREW | 3.5 | 77 | 120 | 80 | 14 | 100 | 9 | 4 | 2 | 1 | 2 | 1 | 1 | 0 | 3 | 5 | 5 | 6 | 9 | 9 | 8 | 7 | 6 | 7 | 5 |
| 21 | SUMAN | 18965 | 20/11/20 | 26 | M | 66 | 1 | RT DISTAL FEMUR COMMUNITED OPEN # | ORIF WITH EX FIX | 3 | 78 | 140 | 90 | 14 | 99 | 7 | 6 | 4 | 2 | 2 | 1 | 1 | 4 | 6 | 6 | 3 | 6 | 7 | 8 | 9 | 9 | 7 | 6 | 10 |
| 22 | GANGABAI | 22842 | 5/12/2020 | 40 | F | 58 | 2 | LT NECK OF FEMUR # | LT BIPOLAR HEMIARTHROPLASTY | 2.5 | 87 | 120 | 80 | 14 | 100 | 6 | 6 | 2 | 1 | 1 | 0 | 1 | 3 | 2 | 2 | 3 | 7 | 8 | 9 | 8 | 6 | 5 | 7 | 10 |
| 23 | SHARADA | 28755 | 4/1/2021 | 59 | F | 64 | 2 | LT NECK OF FEMUR # | LT HEMIARTHROPLASTY | 3.5 | 85 | 150 | 90 | 18 | 97 | 7 | 3 | 2 | 1 | 1 | 2 | 2 | 1 | 4 | 6 | 8 | 6 | 5 | 6 | 6 | 7 | 5 | 6 | 5 |
| 24 | IRANNA | 30289 | 7/1/2021 | 34 | M | 98 | 1 | RT COMPLETE ACL TEAR WITH MEDIAL MENISCAL TEAR | ARTHROSCOPIC ACL RECONSTRUCTION | 2.5 | 82 | 130 | 70 | 15 | 100 | 6 | 6 | 4 | 4 | 4 | 3 | 4 | 2 | 2 | 4 | 5 | 5 | 6 | 7 | 6 | 7 | 6 | 6 | 10 |
| 25 | MALLIKARJUN | 52664 | 18/1/21 | 49 | M | 65 | 2 | RT NECK OF FEMUR # | RT TOTAL HIP REPLACEMENT | 3 | 104 | 120 | 90 | 14 | 99 | 8 | 8 | 6 | 4 | 3 | 3 | 2 | 2 | 4 | 6 | 8 | 8 | 7 | 6 | 5 | 7 | 6 | 5 | 15 |
| 26 | MADHU | 56619 | 28/1/21 | 24 | F | 48 | 1 | RT KNEE COMPLETE ACL TEAR | ARTHROSCOPIC ACL RECONSTRUCTION | 4 | 100 | 110 | 80 | 15 | 100 | 8 | 4 | 2 | 2 | 1 | 2 | 1 | 1 | 5 | 9 | 7 | 8 | 9 | 7 | 6 | 6 | 6 | 6 | 5 |
| 27 | KASTURI | 110837 | 23/2/21 | 32 | F | 68 | 1 | LT KNEE COMPLETE ACL TEAR | ARTHROSCOPIC ACL RECONSTRUCTION | 3 | 80 | 120 | 90 | 16 | 98 | 7 | 3 | 1 | 1 | 0 | 0 | 0 | 2 | 3 | 2 | 7 | 7 | 7 | 6 | 7 | 8 | 4 | 5 | 5 |
| 28 | NEELAPPA | 122315 | 4/3/2021 | 40 | M | 71 | 1 | RT IT # | RT ORIF WITH DHS | 3 | 88 | 130 | 70 | 14 | 99 | 9 | 7 | 4 | 3 | 2 | 2 | 4 | 6 | 7 | 6 | 6 | 5 | 6 | 7 | 4 | 3 | 4 | 2 | 10 |
| 29 | DYAMAWWA | 105298 | 4/3/2021 | 48 | F | 60 | 2 | LT FEMORAL HEAD AVASCULAR NECROSIS | LT TOTAL HIP REPLACEMENT | 3.5 | 72 | 130 | 80 | 16 | 100 | 6 | 3 | 3 | 2 | 1 | 1 | 2 | 3 | 4 | 7 | 6 | 5 | 5 | 7 | 6 | 6 | 5 | 5 | 5 |
| 30 | SIDRAMAPPA | 131973 | 10/3/2021 | 38 | M | 82 | 1 | T DISTAL TIBIA COMMUNITED # WITH TIBIA SEGMENTAL | LT CRIF WITH IMIL NAILING | 3 | 79 | 110 | 80 | 12 | 100 | 7 | 5 | 4 | 4 | 2 | 1 | 3 | 3 | 6 | 5 | 6 | 4 | 6 | 7 | 5 | 6 | 7 | 7 | 10 |

| PULSE RATE (beats/minute) | | | | | | | | | | | | | | | | | | SBP (mmoHg) | | | | | | | | | | | | | | | | | | DBP (mmoHg) | | | | | | | | | | | | | | | | | | Time of rescue analgesia (hrs) | Side Effects | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | 0 | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | 0 | 5 | 10 | 15 | 30 | 45 | 60 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 12 | 16 | 20 | 24 | | Nausea | Vomniing | Pruritis | Respiratory depression | Sedation | Hypotension |
| 86 | 86 | 89 | 80 | 78 | 75 | 78 | 80 | 79 | 82 | 84 | 88 | 85 | 80 | 88 | 89 | 86 | 88 | 130 | 120 | 120 | 110 | 110 | 110 | 110 | 120 | 128 | 140 | 130 | 128 | 120 | 120 | 140 | 130 | 118 | 130 | 90 | 80 | 80 | 80 | 80 | 70 | 80 | 78 | 80 | 90 | 90 | 80 | 80 | 90 | 90 | 90 | 80 | 70 | 4 | N | N | N | N | N | N |
| 110 | 108 | 104 | 100 | 98 | 96 | 95 | 90 | 88 | 86 | 88 | 78 | 80 | 82 | 89 | 89 | 92 | 86 | 110 | 100 | 100 | 110 | 110 | 120 | 110 | 108 | 130 | 128 | 120 | 128 | 110 | 110 | 120 | 120 | 120 | 110 | 80 | 80 | 80 | 80 | 80 | 70 | 70 | 70 | 90 | 70 | 80 | 80 | 70 | 70 | 70 | 72 | 70 | 80 | 3 | N | N | N | N | N | N |
| 88 | 88 | 90 | 86 | 82 | 78 | 89 | 86 | 85 | 86 | 89 | 68 | 73 | 68 | 73 | 78 | 75 | 81 | 120 | 120 | 118 | 120 | 120 | 122 | 110 | 130 | 120 | 120 | 130 | 130 | 140 | 130 | 126 | 130 | 118 | 120 | 70 | 60 | 70 | 60 | 60 | 70 | 70 | 80 | 84 | 80 | 70 | 60 | 70 | 70 | 80 | 80 | 80 | 80 | 2 | N | N | N | N | N | N |
| 77 | 76 | 78 | 80 | 75 | 74 | 72 | 75 | 78 | 79 | 76 | 92 | 90 | 88 | 94 | 86 | 88 | 85 | 130 | 120 | 130 | 120 | 120 | 118 | 118 | 120 | 112 | 140 | 150 | 120 | 130 | 130 | 128 | 128 | 130 | 120 | 80 | 70 | 70 | 70 | 74 | 70 | 80 | 80 | 70 | 80 | 90 | 70 | 70 | 80 | 80 | 70 | 70 | 80 | 4 | N | N | Y | N | N | N |
| 84 | 82 | 80 | 85 | 86 | 80 | 82 | 84 | 86 | 84 | 82 | 82 | 90 | 86 | 80 | 82 | 84 | 88 | 100 | 100 | 110 | 100 | 112 | 120 | 118 | 120 | 128 | 130 | 140 | 130 | 130 | 120 | 130 | 120 | 120 | 130 | 60 | 60 | 60 | 66 | 70 | 60 | 70 | 70 | 80 | 80 | 80 | 90 | 70 | 70 | 80 | 80 | 80 | 70 | 3 | N | N | N | N | N | N |
| 69 | 69 | 70 | 72 | 74 | 70 | 68 | 70 | 72 | 78 | 68 | 73 | 80 | 82 | 91 | 94 | 87 | 88 | 110 | 100 | 100 | 120 | 90 | 110 | 110 | 112 | 112 | 110 | 128 | 120 | 120 | 120 | 130 | 130 | 120 | 120 | 70 | 60 | 70 | 70 | 80 | 70 | 70 | 72 | 70 | 80 | 80 | 90 | 80 | 90 | 90 | 80 | 70 | 80 | 5 | N | N | N | N | N | N |
| 88 | 88 | 85 | 82 | 84 | 80 | 82 | 83 | 80 | 82 | 84 | 102 | 98 | 96 | 80 | 85 | 84 | 80 | 112 | 120 | 110 | 110 | 100 | 120 | 130 | 120 | 140 | 130 | 118 | 124 | 120 | 120 | 110 | 120 | 130 | 130 | 70 | 70 | 60 | 66 | 74 | 70 | 70 | 80 | 90 | 90 | 80 | 70 | 80 | 70 | 90 | 90 | 60 | 70 | 3 | N | N | N | N | N | N |
| 76 | 75 | 74 | 70 | 72 | 70 | 73 | 74 | 73 | 70 | 75 | 86 | 89 | 86 | 90 | 88 | 82 | 80 | 110 | 110 | 100 | 100 | 110 | 114 | 114 | 110 | 100 | 116 | 120 | 130 | 120 | 110 | 120 | 110 | 112 | 110 | 70 | 70 | 60 | 60 | 60 | 68 | 70 | 70 | 60 | 70 | 70 | 80 | 80 | 70 | 70 | 80 | 80 | 70 | 6 | Y | N | N | N | N | N |
| 90 | 90 | 94 | 94 | 89 | 86 | 88 | 84 | 82 | 81 | 82 | 89 | 86 | 85 | 82 | 81 | 86 | 85 | 128 | 140 | 130 | 120 | 124 | 120 | 120 | 110 | 110 | 120 | 130 | 130 | 140 | 130 | 120 | 130 | 130 | 130 | 80 | 80 | 70 | 70 | 80 | 70 | 78 | 80 | 80 | 70 | 80 | 80 | 80 | 70 | 80 | 80 | 70 | 70 | 3 | N | N | N | N | N | N |
| 83 | 81 | 86 | 84 | 86 | 85 | 80 | 96 | 80 | 82 | 68 | 73 | 80 | 82 | 75 | 79 | 81 | 80 | 150 | 140 | 130 | 130 | 130 | 120 | 140 | 140 | 138 | 130 | 130 | 140 | 140 | 120 | 150 | 130 | 120 | 130 | 90 | 90 | 100 | 90 | 80 | 80 | 80 | 90 | 70 | 80 | 80 | 70 | 70 | 80 | 80 | 80 | 70 | 80 | 3 | N | N | N | N | Y | N |
| 78 | 78 | 84 | 72 | 76 | 77 | 76 | 73 | 74 | 76 | 77 | 78 | 76 | 74 | 84 | 80 | 78 | 79 | 140 | 130 | 130 | 120 | 124 | 120 | 130 | 130 | 110 | 120 | 130 | 120 | 120 | 130 | 140 | 130 | 130 | 120 | 90 | 80 | 78 | 80 | 90 | 80 | 70 | 70 | 90 | 78 | 70 | 72 | 80 | 80 | 90 | 80 | 80 | 70 | 4 | N | N | N | N | N | N |
| 69 | 68 | 70 | 72 | 72 | 70 | 73 | 72 | 75 | 80 | 82 | 83 | 68 | 73 | 70 | 72 | 76 | 74 | 130 | 140 | 140 | 120 | 120 | 110 | 130 | 130 | 128 | 124 | 130 | 130 | 120 | 118 | 120 | 130 | 140 | 120 | 80 | 70 | 80 | 70 | 70 | 76 | 70 | 72 | 70 | 80 | 78 | 80 | 70 | 80 | 70 | 82 | 80 | 68 | 3.5 | N | N | N | N | N | N |
| 75 | 75 | 76 | 74 | 72 | 70 | 72 | 74 | 74 | 72 | 74 | 78 | 83 | 76 | 72 | 72 | 75 | 74 | 118 | 120 | 110 | 110 | 112 | 110 | 130 | 120 | 120 | 130 | 130 | 100 | 120 | 110 | 120 | 120 | 120 | 130 | 80 | 68 | 72 | 70 | 76 | 70 | 80 | 74 | 70 | 84 | 80 | 60 | 70 | 72 | 80 | 68 | 80 | 90 | 2 | N | N | N | N | N | N |
| 86 | 86 | 90 | 86 | 85 | 86 | 86 | 86 | 84 | 83 | 80 | 80 | 82 | 98 | 75 | 80 | 89 | 84 | 112 | 110 | 110 | 120 | 120 | 110 | 110 | 120 | 112 | 110 | 110 | 120 | 120 | 130 | 120 | 120 | 110 | 110 | 70 | 66 | 60 | 70 | 72 | 70 | 80 | 70 | 72 | 70 | 68 | 68 | 70 | 70 | 64 | 60 | 70 | 68 | 4.5 | N | N | N | N | N | N |
| 68 | 68 | 70 | 73 | 70 | 68 | 70 | 72 | 70 | 70 | 73 | 80 | 74 | 76 | 84 | 80 | 78 | 76 | 110 | 100 | 110 | 114 | 112 | 110 | 120 | 112 | 110 | 130 | 120 | 110 | 120 | 130 | 130 | 120 | 120 | 118 | 70 | 60 | 64 | 70 | 72 | 60 | 68 | 60 | 70 | 70 | 76 | 70 | 80 | 80 | 76 | 80 | 84 | 70 | 4 | N | N | Y | N | N | N |
| 83 | 82 | 88 | 82 | 84 | 85 | 85 | 82 | 83 | 80 | 84 | 94 | 80 | 82 | 70 | 83 | 85 | 82 | 116 | 112 | 110 | 110 | 120 | 118 | 120 | 120 | 110 | 120 | 130 | 130 | 120 | 120 | 110 | 120 | 112 | 120 | 70 | 66 | 70 | 70 | 72 | 68 | 70 | 70 | 78 | 72 | 90 | 80 | 70 | 70 | 80 | 76 | 78 | 80 | 6 | N | N | N | N | N | N |
| 86 | 86 | 88 | 86 | 84 | 82 | 80 | 79 | 80 | 82 | 84 | 68 | 73 | 68 | 73 | 78 | 79 | 82 | 140 | 130 | 120 | 120 | 110 | 120 | 130 | 128 | 120 | 120 | 130 | 140 | 120 | 120 | 120 | 110 | 130 | 130 | 90 | 90 | 88 | 70 | 70 | 70 | 72 | 72 | 80 | 70 | 76 | 100 | 80 | 72 | 78 | 80 | 88 | 90 | 3 | N | N | N | N | N | N |
| 90 | 90 | 96 | 88 | 86 | 84 | 82 | 86 | 84 | 83 | 86 | 82 | 86 | 80 | 82 | 82 | 86 | 83 | 130 | 120 | 118 | 110 | 120 | 120 | 114 | 120 | 130 | 140 | 120 | 120 | 130 | 130 | 128 | 140 | 120 | 110 | 80 | 72 | 68 | 70 | 74 | 70 | 74 | 78 | 80 | 88 | 80 | 80 | 74 | 70 | 76 | 80 | 78 | 70 | 2.5 | N | N | N | N | N | N |
| 68 | 68 | 68 | 70 | 73 | 70 | 70 | 72 | 70 | 70 | 73 | 80 | 74 | 76 | 84 | 80 | 76 | 78 | 140 | 140 | 130 | 140 | 120 | 120 | 110 | 120 | 110 | 140 | 120 | 120 | 150 | 140 | 130 | 130 | 140 | 120 | 90 | 94 | 88 | 86 | 78 | 80 | 78 | 70 | 80 | 82 | 80 | 80 | 80 | 80 | 80 | 80 | 88 | 90 | 5 | N | N | N | N | N | N |
| 76 | 76 | 78 | 76 | 78 | 76 | 80 | 80 | 78 | 82 | 86 | 71 | 72 | 74 | 84 | 80 | 78 | 81 | 130 | 120 | 110 | 110 | 110 | 112 | 120 | 124 | 120 | 120 | 110 | 130 | 128 | 130 | 120 | 128 | 124 | 130 | 76 | 76 | 70 | 72 | 68 | 70 | 74 | 70 | 70 | 80 | 70 | 76 | 74 | 72 | 70 | 80 | 80 | 80 | 3.5 | N | N | N | N | N | N |
| 73 | 71 | 75 | 70 | 70 | 72 | 74 | 71 | 76 | 74 | 76 | 82 | 88 | 89 | 90 | 88 | 90 | 86 | 140 | 110 | 118 | 128 | 130 | 120 | 130 | 120 | 110 | 120 | 140 | 120 | 130 | 140 | 140 | 128 | 130 | 140 | 90 | 88 | 80 | 78 | 78 | 80 | 70 | 76 | 74 | 78 | 70 | 80 | 90 | 80 | 88 | 90 | 90 | 80 | 3 | N | N | N | N | Y | N |
| 72 | 72 | 80 | 76 | 78 | 76 | 78 | 76 | 76 | 79 | 76 | 87 | 88 | 80 | 82 | 84 | 84 | 85 | 118 | 120 | 120 | 120 | 118 | 112 | 110 | 120 | 120 | 120 | 120 | 118 | 120 | 114 | 120 | 120 | 110 | 120 | 80 | 70 | 68 | 64 | 70 | 72 | 70 | 70 | 70 | 72 | 70 | 74 | 70 | 70 | 76 | 70 | 70 | 70 | 6 | N | N | N | N | N | N |
| 88 | 88 | 86 | 85 | 81 | 78 | 84 | 88 | 82 | 85 | 86 | 80 | 68 | 73 | 91 | 101 | 94 | 80 | 150 | 150 | 150 | 110 | 110 | 130 | 120 | 130 | 112 | 120 | 130 | 140 | 120 | 120 | 140 | 136 | 140 | 130 | 100 | 90 | 70 | 72 | 80 | 70 | 76 | 72 | 70 | 72 | 76 | 70 | 76 | 78 | 80 | 86 | 90 | 80 | 4 | N | N | Y | N | N | N |
| 85 | 85 | 86 | 76 | 78 | 70 | 75 | 80 | 83 | 80 | 78 | 94 | 94 | 80 | 82 | 82 | 87 | 85 | 140 | 130 | 120 | 120 | 118 | 116 | 112 | 120 | 140 | 120 | 118 | 130 | 112 | 130 | 120 | 130 | 120 | 120 | 80 | 82 | 80 | 76 | 70 | 72 | 70 | 80 | 88 | 80 | 86 | 80 | 78 | 78 | 80 | 80 | 76 | 80 | 4.5 | N | N | N | N | N | N |
| 78 | 78 | 76 | 74 | 78 | 80 | 82 | 80 | 76 | 74 | 70 | 90 | 92 | 88 | 75 | 76 | 90 | 88 | 130 | 130 | 130 | 130 | 110 | 110 | 120 | 120 | 130 | 120 | 130 | 120 | 130 | 120 | 120 | 110 | 120 | 130 | 90 | 90 | 80 | 78 | 72 | 70 | 76 | 70 | 70 | 76 | 78 | 70 | 80 | 84 | 80 | 70 | 78 | 80 | 3.5 | Y | N | N | N | N | N |
| 99 | 97 | 92 | 88 | 86 | 83 | 84 | 86 | 80 | 82 | 97 | 98 | 80 | 82 | 84 | 82 | 86 | 84 | 114 | 110 | 100 | 110 | 112 | 110 | 112 | 110 | 120 | 110 | 120 | 120 | 110 | 120 | 130 | 120 | 110 | 110 | 60 | 64 | 68 | 70 | 60 | 70 | 72 | 80 | 70 | 76 | 72 | 70 | 80 | 78 | 80 | 78 | 66 | 70 | 3 | N | N | N | N | N | N |
| 78 | 78 | 82 | 76 | 72 | 74 | 86 | 83 | 88 | 86 | 85 | 90 | 68 | 73 | 70 | 76 | 78 | 80 | 124 | 128 | 120 | 112 | 110 | 110 | 118 | 120 | 120 | 120 | 130 | 120 | 120 | 120 | 130 | 120 | 120 | 118 | 80 | 90 | 88 | 80 | 70 | 76 | 78 | 70 | 78 | 82 | 80 | 80 | 90 | 88 | 80 | 86 | 78 | 72 | 5 | N | N | N | N | N | N |
| 88 | 88 | 80 | 78 | 82 | 84 | 82 | 76 | 88 | 78 | 76 | 80 | 82 | 80 | 82 | 84 | 82 | 80 | 130 | 140 | 130 | 120 | 120 | 110 | 120 | 130 | 120 | 120 | 130 | 130 | 128 | 112 | 120 | 130 | 120 | 118 | 90 | 80 | 80 | 78 | 70 | 72 | 74 | 70 | 78 | 76 | 80 | 88 | 82 | 80 | 78 | 76 | 70 | 80 | 2 | N | N | N | N | N | N |
| 83 | 81 | 74 | 77 | 72 | 82 | 76 | 80 | 82 | 68 | 73 | 81 | 84 | 68 | 73 | 76 | 78 | 76 | 130 | 120 | 120 | 110 | 100 | 110 | 118 | 120 | 112 | 110 | 100 | 120 | 128 | 120 | 120 | 130 | 130 | 130 | 80 | 78 | 76 | 70 | 64 | 68 | 70 | 72 | 72 | 70 | 80 | 78 | 80 | 70 | 70 | 78 | 76 | 80 | 4 | N | N | N | N | N | N |
| 78 | 78 | 80 | 70 | 72 | 71 | 82 | 71 | 74 | 77 | 80 | 80 | 78 | 75 | 80 | 78 | 80 | 82 | 116 | 110 | 100 | 100 | 110 | 100 | 120 | 118 | 110 | 130 | 120 | 128 | 120 | 120 | 130 | 130 | 120 | 110 | 80 | 70 | 64 | 68 | 70 | 68 | 74 | 70 | 78 | 80 | 76 | 70 | 80 | 82 | 80 | 80 | 80 | 70 | 3 | N | N | N | N | N | N |