# COMPARATIVE EVALUATION OF ANALGESIC EFFICACY OF TRANSDERMAL PATCHES OF BUPRENORPHINE AND FENTANYL IN MANAGEMENT OF POSTOPERATIVE PAIN AFTER LOWER LIMB SURGERIES: A RANDOMIZED CONTROLLED STUDY

**BY:**

**Dr. S.P SHRUTHI**

**DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA**

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

**M.D. (ANAESTHESIOLOGY)**

**UNDER THE GUIDANCE OF**

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The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the synopsis entitled **"Comparative evaluation of analgesic efficacy of transdermal patches of buprenorphine and fentanyl in management of postoperative pain after lower limb surgeries: A randomized controlled study"** being investigated by **Dr.S.P.Shruthi** & Dr.Kiran N in the Department of Anaesthesiology at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study.**

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**Place**: Kolar **DR. SP SHRUTHI**

## ABBREVIATIONS

CNS - Central Nervous System

GRS - Graphic Rating Scale

mV - millivolt

Na+ - Sodium Ion

NaV - Voltage-Gated Sodium Channel

NRS - Numerical Rating Scale

PDI - Psychomotor Development Index

TDS - Transdermal Drug Delivery System

VAS - Visual Analogue Scale

VLBW - Very Low Birth Weight

VRS - Verbal Rating Scale

## ABSTRACT

**Background**: “Postoperative pain management remains a significant challenge, as inadequate analgesic relief can delay rehabilitation, prolong hospital stays, and contribute to hemodynamic and psychosocial issues. Transdermal drug delivery systems (TDS) offer a non-invasive alternative to traditional needle injections, providing controlled drug release and enhanced patient compliance. Buprenorphine and fentanyl, two lipophilic opioid analgesics, have shown promise in various clinical settings for postoperative pain management.

**Aim**: This study aimed to compare the analgesic efficacy of buprenorphine and fentanyl transdermal patches in managing postoperative pain following lower limb surgeries.

**Materials and Methods**: A randomized controlled trial was conducted with 58 patients undergoing lower limb orthopedic surgeries under spinal anesthesia. Patients were randomly assigned to either Group A (buprenorphine transdermal patch, 20 μg·h-1, n=28) or Group B (fentanyl transdermal patch, 25 μg·h-1, n=28). Pain scores were measured using the Numerical Rating Scale (NRS) at 1, 2, 4, 8, 12 hours, and every 12 hours up to 72 hours postoperatively. Rescue analgesia was provided with diclofenac and tramadol if NRS >4. Statistical analysis was performed using SPSS v23.0, with a p-value <0.05 considered significant.”

**Results**: The mean age and baseline vital parameters were comparable between the two groups ($p>0.05$). Complete blood picture, random blood sugar levels, and renal parameters showed no significant differences. NRS scores at various time points were similar between the groups ($p>0.05$). The need for rescue analgesia was comparable overall, but at the 4th hour, Group B (fentanyl) required significantly more rescue analgesia (21.4%) compared to Group A (buprenorphine) (3.6%).

**Conclusion**: Both buprenorphine and fentanyl transdermal patches effectively managed postoperative pain with similar efficacy in most measured intervals. However, buprenorphine was associated with a lower requirement for rescue analgesia at the 4th postoperative hour, suggesting a potential advantage in early pain management. Further research with larger sample sizes is necessary to confirm these findings.

**Keywords**: Postoperative pain, Transdermal drug delivery, Buprenorphine, Fentanyl, Analgesic efficacy, Rescue analgesia.

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# INTRODUCTION

# INTRODUCTION

Post operative pain management still remains as a challenging issue.[1] In adequate analgesic relief after surgery will lead to delayed rehabilitation, prolonged hospital stays, deranged hemodynamic variabilities and other psychosocial problems.[2]

Transdermal drug delivery system (TDS) as an alternative to conventional needle injections. TDS is a simple, painless, non-invasive method of drug delivery to the patients.[3,4] Drugs like fentanyl, diclofenac, buprenorphine, scopolamine etc., can be used through transdermal route TDDS, offer a controlled release of the drugs through the skin of the patients, does not involve passage through the gastrointestinal tract thus by reducing the first pass metabolism, without interference drugs can be delivered from potential of hydrogen (pH), enzymes and intestinal bacteria and lesser systemic side effects.[5,6]

TDS improve the dosage efficacy by maintaining steady blood drug profiles throughout the treatment and enhance patient compliance.[7,8] Buprenorphine and fentanyl are low molecular weight lipophilic opioid analgesics. Numerous studies have explored the effectiveness and safety of transdermal buprenorphine and fentanyl patches across various clinical settings, including postoperative pain management. These studies have reported favourable outcomes, including reduced pain intensity, decreased opioid consumption, and improved patient satisfaction. However, comparative studies directly assessing the analgesic efficacy of buprenorphine versus fentanyl transdermal patches specifically in the context of lower limb surgeries are limited. [9–11] Studies were done comparing transdermal buprenorphine and fentanyl patches with non-opioid analgesics using numerical rating scale (NRS) had stated that patients on opiods had enhanced pain relief, decreased pain intensity, and prolonged pain-free sleep, decreased need for rescue analgesia.[12]

The present study aimed to examine the analgesic effectiveness of buprenorphine and fentanyl transdermal patch in management of pain following lower limb surgeries.

# AIMS & OBJECTIVES

# AIMS & OBJECTIVES

- To compare the analgesic efficacy of buprenorphine and fentanyl transdermal patch in postoperative pain management using numerical rating scale (NRS)
- The need for any rescue analgesia

# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

**Nerve anatomy and physiology**[13] Nerve signals move quickly to and from the central nervous system. Due to the action potential jumping between nodes of Ranvier, faster transmission takes place along myelinated fibres. These myelinated A fibres have different functions: Aα fibres control skeletal muscles, Aβ fibres transmit tactile sensations, Aγ fibres innervate muscle spindles, and Aδ fibres transmit nociception and cold sensations. Autonomic pre-ganglionic nerves are carried out by myelinated B fibres, while slower non-myelinated C fibres convey a dull ache from the skin and organs.[14,15]

The depolarization that follows nociceptors' stimulation opens voltage-dependent sodium channels, which are found in the membranes of neuron & cardiac cells. These channels have a complicated structure with one or two β subunits in addition to a big pore-forming α subunit. The α subunit is composed of four domains(I-IV), consisting of six segments(S1-S6) around a central channel shaped like a bell. Segments S5 and S6, together with the brief amino acid loops that link them, constitute the channel. Domains III and IV form a loop that creates the inactivation gate. Each domain's S4 section, which is the voltage-sensitive portion of the sodium channel , is made up of amino acids with positive charge, such as arginine or lysine.[16,17]

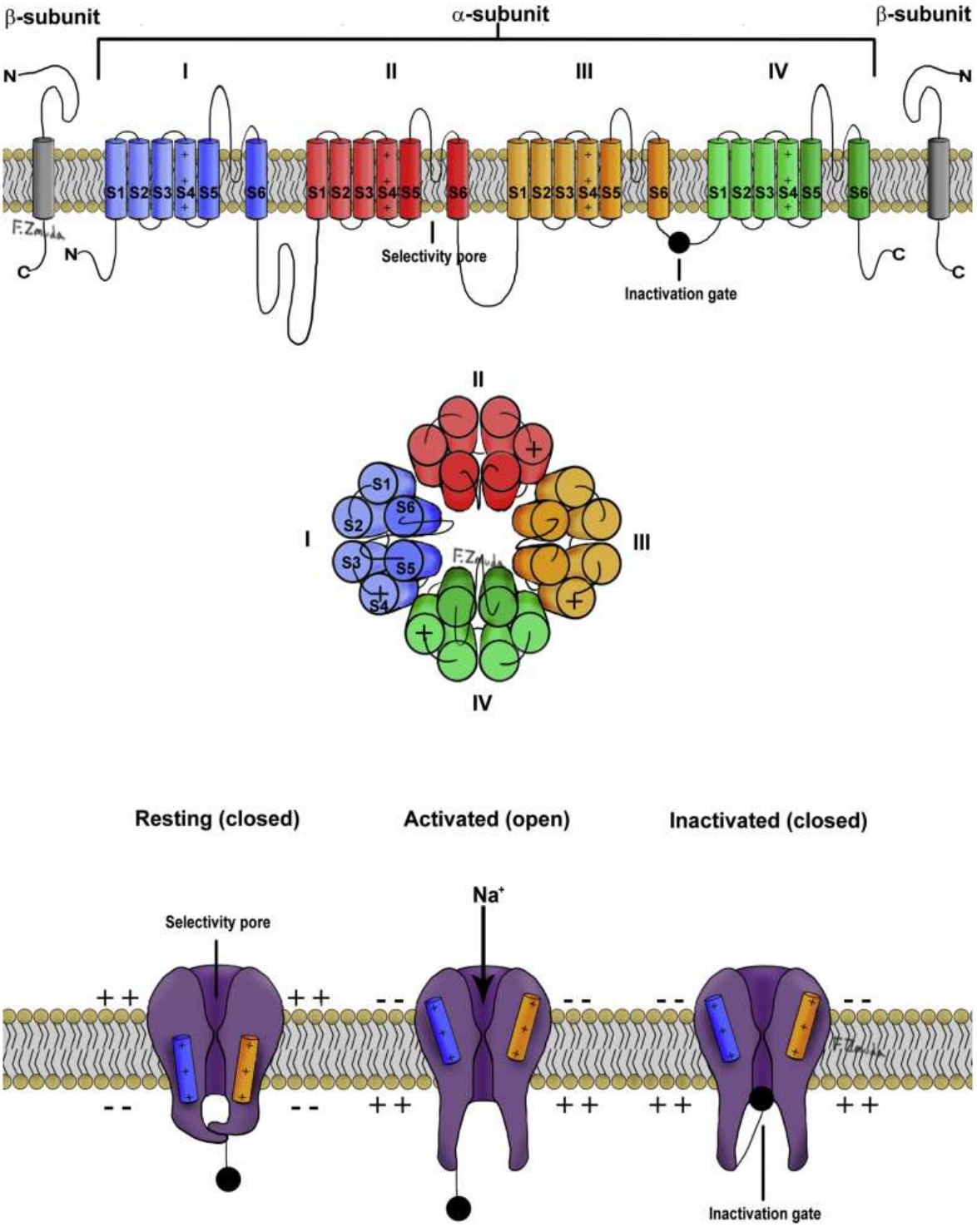


**Figure 1: Structure and configuration of voltage gated Na+ channel**[13]

There are three different structural states for the Na+ channel: open, inactivated, and resting. The membrane potential, which is determined by the outward migration of K+ ions along their concentration gradient, is approximately –70 mV in the resting state. In the meantime, negatively charged anions, mainly proteins, stay inside the cell, creating a transmembrane voltage that is referred to as the resting membrane potential. The S4 segments are oriented downward during this phase, which makes the channel non-conductive.

An outward spiral spin of the S4 segments causes the Na+ channels to open upon depolarization, allowing a fast inflow of Na+ ions along both chemical and electrical gradients. Channel inactivation results from this action's exposure of the inactivation gate's receptor location, which is situated between domains III and IV. To return to the resting state from the inactivated state, the channel must undergo repolarization of the cell membrane.[18]

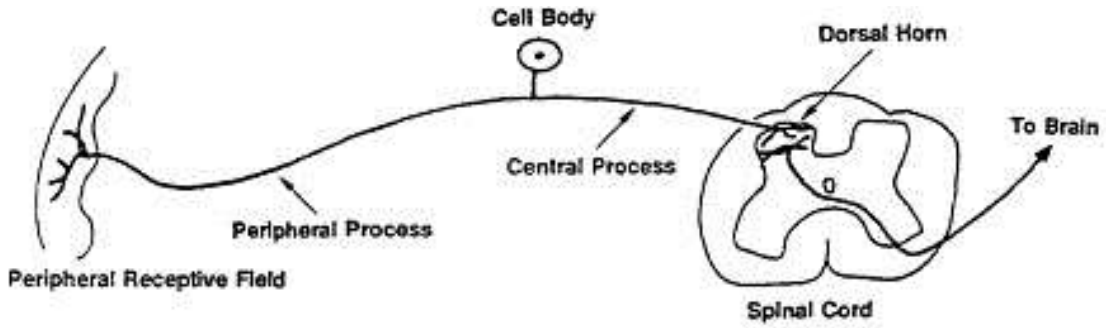


**Figure 2: Primary afferent nociceptors**

Via certain ion channels, “nerve impulse propagation causes fast inward migration of Na+ ions and outward movement of K+ ions. An action potential is triggered by a fast influx of positive Na+ ions through voltage-gated Na+ channels when the membrane potential hits a threshold of -55 mV. This potential peaks at +40 mV. After that, the sodium channel is

inactivated and K+ ions are ejected, causing the neuron to repolarize and go back to resting." Subsequently, the Na+/K+ pump functions to replenish the electrochemical gradients that are necessary to preserve the membrane potential at rest.[18]

There are ten genes responsible for encoding voltage-gated Na+ channels. These channels are all vulnerable to blockade by local anaesthetics. The expression of Na+ channel genes varies across different tissues, indicating differential distribution and function within the body. [18] For instance, NaV1.7 and NaV1.8 Na+ channels exhibit high expression levels in sensory neurons. In contrast, NaV1.5 channels are primarily located in cardiac cells, as well as in metastatic cells of breast and colon cancers.

**PAIN**

"Pain is an unpleasant side effect that is linked to substantial physiological and psychological changes that occur both during and after surgery.[19] This may be resolved with the right medications and methods. There are distinct benefits to using regional anesthetic treatments for both stand-alone anesthesia and as an adjuvant analgesic for postoperative and intraoperative care." The typical method of providing anesthesia for surgeries involving the arms, forearms, and hands is the brachial plexus block. The patient may have paraesthesia in the arm, forearm, hand, or fingers at this point. This is necessary to establish an adequate block. The needle tip should be in touch with or near to a nerve. For upper limb procedures, brachial plexus blocking is a tried-and-true anesthetic approach.[20] The supraclavicular method is thought to be the most straightforward and successful of the brachial plexus block techniques. Kulenkampff carried out the first supraclavicular brachial plexus block in 1912.[21]

**Pathway: "**The four main processes are transduction, transmission, modulation, and perception. Transduction is the process by which tissue-damaging stimuli cause nerve terminals to fire. Transmission refers to the relay systems that move the message from the location of tissue damage to the areas of the brain that support perception. A recently discovered brain function called modulation works specifically to reduce transmission system activity. The subjective awareness that results from sensory input is called perception, and it involves combining many sensory cues to form a coherent and meaningful whole. The process of perception is complex and involves several different processes, including expectation, interpretation, and attention."

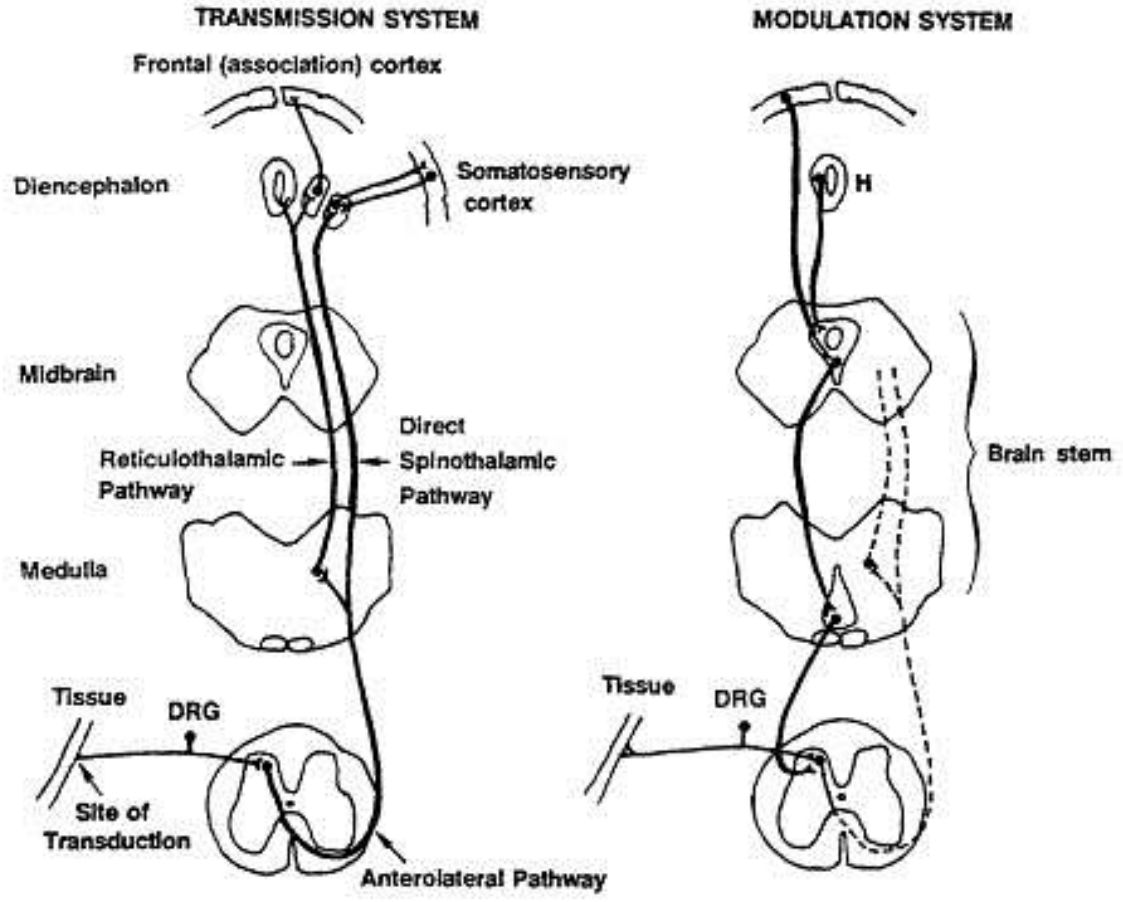


**Figure 3: Pain reflex**

A diagram illustrating the key brain structures involved in the perception of pain. Transduction(bottom left) is the first step in the process that leads to pain perception in the transmission system, where a harmful stimulus triggers nerve impulses in the primary afferent nociceptor. The main afferent nociceptors in the spinal cord connect the central pain-transmission cells with these impulses. Central pain-transmission cells either directly or indirectly, through the spinothalamic tract, the reticular formation, and the reticulothalamic pathway, relay the message to the thalamus. The thalamus sends the message to Cerebral cortex. The pain-modulation system (H) receives information from the hypothalamus and the frontal association cortex. The outflow lowers the intensity of perceived pain by inhibiting pain-transmission cells in the dorsal horn of the spinal cord after passing via the midbrain and medulla.

## PAIN ASSESSMENT[22]

### VISUAL ANALOGUE SCALE OR GRAPHIC RATING SCALE

"The Visual Analogue Scale (VAS) is a straight line with edges that represent extreme limits such as "no pain at all" and "pain at its worst possible level". The patient is asked to draw a line between two points and indicate their level of pain. The patient's suffering is measured by calculating the distance between 'no pain at all' and the given mark. Freyd utilised this method for the first time in psychology in 1923. When descriptive phrases such as "mild", "moderate", or a number scale are added to the VAS, it is referred to as a Graphic Rating Scale (GRS). When compared to the 5- and 20-cm variants, a line-length of 10 or 15 cm demonstrated the smallest measurement error and appears to be the most practical for responders."[23,24]

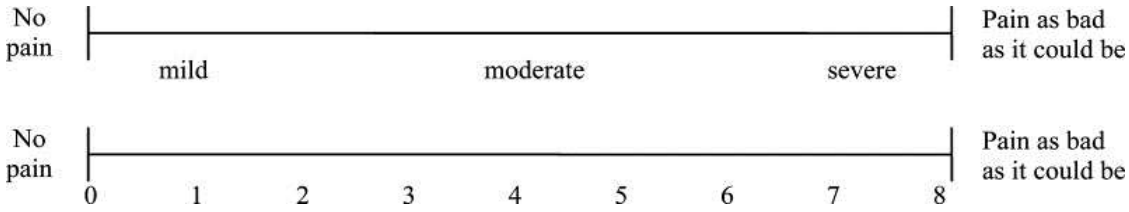


**Figure 4: Graphic rating scale**

The distribution of answers was fairly balanced because "patients with limited experience with a GRS with numbers 1–20 beneath the line favoured the numbers 10 and 15, whereas patients with competence ignored the numbered scale and showed no preferences. To create analogous observations, descriptive language was employed. Numerous experiments have demonstrated that VAS and GRS are sensitive to treatment effects.[25,26] They were found to correlate favourably with other self-reported pain intensity measures.[27] Furthermore, the difference in pain intensity evaluated by VAS at two separate periods in time indicates the true difference in magnitude of pain, which appears to be the main benefit of this instrument over others. This ratio, however, is more reliable at the group level than at the individual level."[23]

**NUMERICAL RATING SCALE**

In a Numerical Rating Scale (NRS), "patients are prompted to select a number from a predetermined range, "typically between 0 and 10, 0 and 20, or 0 and 100, to indicate their pain intensity. Zero typically represents 'no pain at all', while the upper limit signifies 'the worst pain imaginable'." Unlike the Visual Analog Scale (VAS) or Graphic Rating Scale (GRS), where the position along a continuous line is significant, in the NRS, only the numerical values themselves hold importance. This indicates that there are just 11 potential answers for an NRS of 0–10, 21 for an NRS of 0–20, and 101 for an NRS of 0–100. As a

result, the VAS/GRS potentially gives an infinite number of possible answers, whereas the NRS permits a less subtle separation of pain levels."[23]

Numerical rating scales and other pain-assessment tools have demonstrated strong relationships in several studies. Additionally, its compliance and usefulness have been shown. [23] NRS can be used in telephone interviews as it can be given verbally. Findings, unlike VAS/GRS data, cannot always be regarded as ratio data.[27–29]

**VERBAL RATING SCALE**

In this scale (VRS), various adjectives are employed to articulate different degrees of pain intensity. The individual is prompted to select the adjective that most closely aligns with their existing pain level. Like the "Visual Analog Scale (VAS), two endpoints are established, typically 'no pain at all' and 'extremely intense pain'. Between these extremes, a series of adjectives are positioned to represent varying levels of pain severity, arranged in order of increasing intensity. Clinical trials commonly utilize VRS with four to six points. Another variation of the VRS is the behavioural rating scale, where different pain levels are described through sentences containing behavioural cues."[30]

**PHARMACOLOGY OF BURENORPHINE**[31]

The synthetic opioid buprenorphine is used to treat both opioid use disorder and pain. It debuted in the latter part of the 1960s. It is a synthetic version of the alkaloid component called thebaine, which is present in poppy flowers. Because it is a schedule III substance, there is a chance of both significant psychological reliance and moderate to low physical dependence.[32–34]

The FDA has authorized buprenorphine for the treatment of opioid addiction, acute pain, and chronic pain. It is an agent used in agonist substitution therapy, an addiction treatment approach that substitutes a drug (such methadone or buprenorphine) with a stronger full agonist opioid (like heroin). The doctor will then progressively cut back on the alternative, allowing the patient to taper off the opiates with little difficulty. The patient may concentrate on therapy rather than uncomfortable withdrawal symptoms with the help of buprenorphine substitution therapy.

**Indication**

To address the needs of opioid-dependent patients who cannot use methadone due to contraindications or lack of accessibility to methadone facilities or healthcare providers, buprenorphine may be a viable alternative. This option becomes particularly relevant when there is a prolonged waitlist exceeding three months for enrolment in a methadone clinic.

Furthermore, individuals who are intolerant to or have not responded well to methadone treatment may also find relief with buprenorphine therapy.

Moreover, buprenorphine may be advantageous for individuals with a relatively short history of opioid dependence or those requiring lower doses of opioid agonists, potentially offering effective management for their condition.

**Mechanism of action**

Since buprenorphine only partially stimulates opiate receptors, it is only a partial agonist at the mu receptor. "Additionally, it is a little agonist of the delta receptor and antagonist of the kappa receptor. It has effects on the central nervous system and is a potent analgesic

(CNS). One characteristic that sets buprenorphine apart is its partial agonism at the mu receptor. One of its many unique characteristics is that, at higher dosages, its analgesic effects become antagonistic as opposed to plateauing at all." When it comes to agonist replacement treatment for addiction, buprenorphine is safer than methadone since it has a ceiling effect on respiratory depression.

"Buprenorphine exhibits delayed dissociation kinetics and a strong affinity for mu-opioid receptors. This is how it varies from other full-opioid agonists like morphine and fentanyl, enabling the patient to experience less severe and milder withdrawal symptoms."

Because of the first-pass effect, buprenorphine has a limited bioavailability when taken orally. Most of the drug is metabolized in the stomach and liver. Sublingual administration is the method of delivery. The first pass effect is avoided, and the absorption happens quickly. When the tablet is put beneath the tongue, its effects become more pronounced three to four hours after intake. Buprenorphine is changed by cytochrome CYP 34A enzymes into norbuprenorphine, an active metabolite with little intrinsic action. After sublingual administration, average half-life of buprenorphine is 38 hours, ranging from 25 to 70 hours. Higher levels of buprenorphine may be produced by medications that efficiently block the enzyme 3A4, for instance ketoconazole or protease inhibitors, whereas lower levels may be produced by medications that activate this enzyme such as carbamazepine, topiramate, phenytoin, or barbiturates.

**Adverse effects**

Buprenorphine has anticholinergic like actions and may produce central nervous system depression, hypotension, QT prolongation, and reduced seizure threshold. Other adverse effects of buprenorphine include nausea, vomiting, drowsiness, dizziness, headache, memory loss, sweating, dry mouth, miosis, orthostatic hypotension, sexual side effects, and urine retention.

**Contraindication**

Hypersensitivity to buprenorphine is the only real reason not to use it. When used in patients with gastrointestinal obstruction or respiratory depression, it should be utilized carefully.

Additionally, individuals who are currently using full opioid agonists, such heroin or morphine, should not take buprenorphine since this might undermine the purpose of administering buprenorphine by causing a fast withdrawal. It is not necessary to modify the dose of buprenorphine in patients with renal impairment. For those with hepatic impairment, the dosage needs to be lowered in order to prevent toxicity.[35–37]

**Toxicity**

The patient must be evaluated for buprenorphine toxicity on a frequent basis. Vital signs should be taken, and the patient's general physical and mental health state should be assessed. If the patient seems sluggish or drunk, the practitioner should not provide buprenorphine. In rare situations, the pharmacist may be required to withhold the

buprenorphine dosage. Patient safety must be prioritised, hence these measures must be communicated to the healthcare practitioner.

**PHARMACOLOGY OF FENTANYL**[38]

"Fentanyl is a synthetic, lipophilic phenylpiperidine opioid agonist with analgesic and anaesthetic properties. First synthesized by Paul Janssen in 1960 by assaying analogues of the structurally related drug pethidine."[39]

Chemical name: "N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl] propanamide."

Chemical structure:

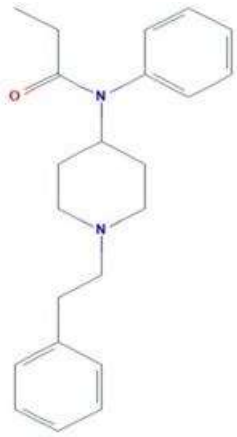


**Figure 5: Fentanyl structure Physio- chemical properties**

- Pka –8.99
- Molecular weight -336.5g/ml
- Molecular formula–C22H28N2O
- Protein binding -80%

Uses

- Premedication
- Patient controlled analgesia

- Pain management
- Adjuvant to regional anaesthesia

Preparations and storage

- Available as 100mcg/2ml and 500mcg/10 ml ampoules
- Transdermal patches
- Lozenges for children

Fentanyl is potent agonist at μ opioid receptors. is a common anaesthetic agent that is around 100 times more effective than morphine. "It causes moderate drowsiness and has a quick onset and short half-life (20–30 minutes) when administered intravenously in modest dosages (1 mcg/Kg). On the other hand, fentanyl has been used as the only anaesthetic drug in cases when large dosages (50–150 mg/kg) result in deep drowsiness and unconsciousness, however awareness has been documented throughout operation." High dosages may cause the chest wall's muscles to become stiff.

Similar to other opioid analgesics, "fentanyl depresses breathing in a way that is dose-dependent. Even at large dosages, the medication causes cardiovascular stability, albeit bradycardia can happen and may need atropine therapy. The stress reaction to surgery is also lessened or eliminated by high dosage fentanyl anaesthesia."

Action duration: Fentanyl passes the blood-brain barrier quickly due to its high lipid solubility, and its concentration in the central nervous system often matches its plasma concentration (with a five-minute delay). Its duration of action is brief at low dosages (1-2 mcg/Kg) because during the distribution phase, plasma and CNS concentrations drop below an effective level. As a result, the effects are recovered from quickly. On the other hand following large or numerous Fentanyl dosages, the distribution phase ends while the Fentanyl plasma concentration remains over the minimally effective threshold. The drug's

duration of action is greatly prolonged, and recovery from its effects is contingent upon its comparatively sluggish clearance from the body. Under these conditions, severe respiratory depression might persist for a few hours after surgery.[40]

**Pharmacokinetics:**

"There is considerable inter-individual variation in the pharmacokinetics of Fentanyl. After an intravenous bolus dose, plasma concentrations decline rapidly (distribution half-life approximately 13 min). Its terminal half life is 3-4 hours in normal subjects, but may be as long as 7-8 hours in some patients. The volume of distribution is relatively large (approximately 4 L/Kg) due to its high lipid solubility and extensive uptake by tissues and clearance is slightly less than hepatic blood flow. Fentanyl is predominantly metabolized by N-dealkylation and hydroxylation in the liver, and metabolites can be detected in blood within 1-2 minutes. Approximately 70% of the drug is excreted in urine as inactive metabolites over severaldays."[41]

**Adverse effects**

- Nausea and vomiting
- Constipation
- Respiratory depression
- Dry mouth
- Retention of urine
- Itching

Univariate and multivariate hierarchical linear analyses identified perinatal risk factors associated with “poor developmental scores (MDI or PDI) in 8517 very low birth weight (VLBW) infants. Factors such as father's education level, teenage pregnancy, multiple pregnancies, infant's gestational age, gender, low birth weight (<999 gm), neonatal intensive care unit stay duration, and presence of various diseases were linked to poor developmental outcomes. Additional risk factors for adverse PDI scores included polyhydramnios, emergency caesarean delivery, birth weight <1250 gm, and periventricular/intraventricular haemorrhage stage I-II. Despite a considerable number of infants showing low MDI or PDI scores below 55 at 24 months, six-month assessments had limited predictive ability for outcomes at 24 months, with sensitivity and positive predictive values below 60% and specificity and negative predictive values exceeding 85%.”

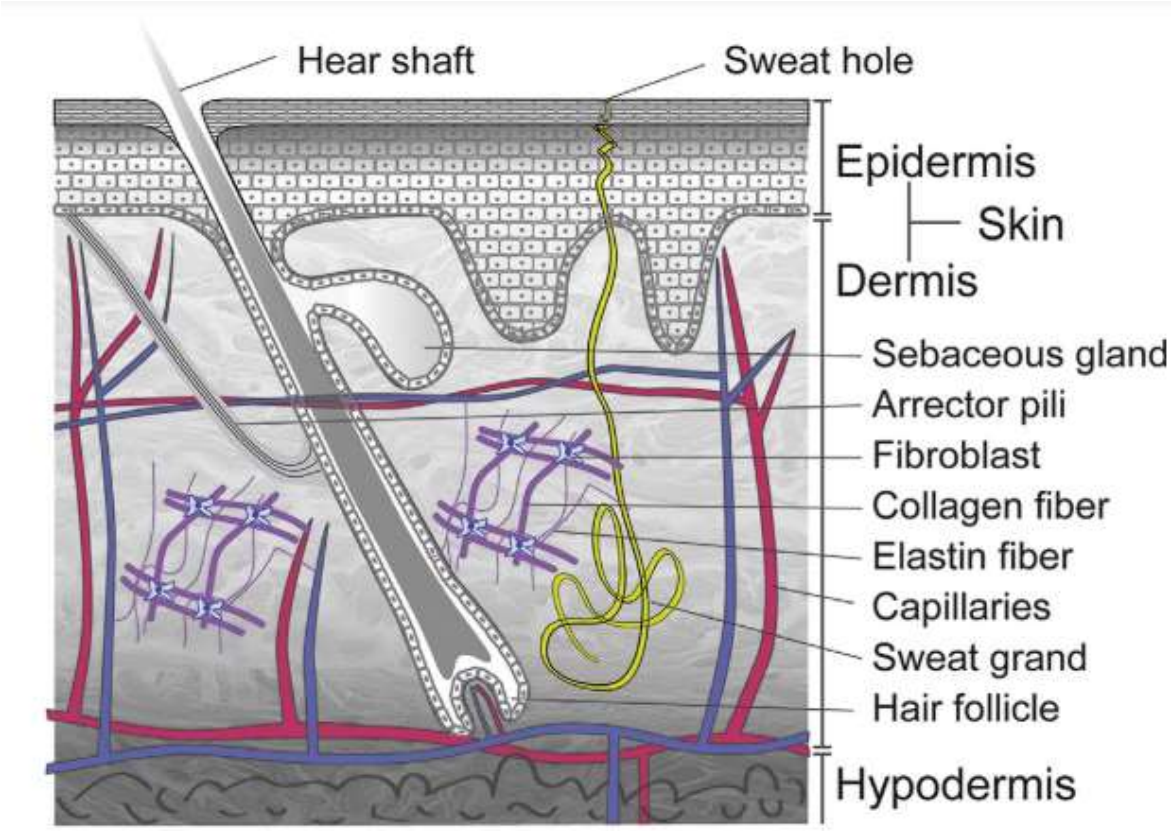


**Figure 6: Anatomical view of skin**

The permeability of drugs through the skin layers can be influenced by factors such as gender and overall health. The stratum corneum, consisting of hardened, flattened, and stacked dead cells with a thickness of 10–20μm, acts as a waterproof barrier. This barrier function poses a significant challenge for the penetration of hydrophilic drugs, as the stratum corneum consists predominantly of proteins (79%–90%) and lipids (5%–15%). Additionally, the stratum corneum restricts the permeation of larger drug molecules into the epidermis, particularly those exceeding 500Da in size. Moreover, the stratum corneum plays a role in regulating natural water loss through skin, maintaining pH levels, and controlling temperature. These functions include water evaporation rates ranging from 5–30 g/m2 h, pH levels between 5.0–5.4, and temperatures of 31–33°C.

In recent times, Transdermal Drug Delivery (TDD) has become increasingly utilized for treating various diseases with transdermal drugs available on the US market. However, the barrier function of the epidermis limits the penetration of transdermal drugs due to their relatively large molecular weight, typically restricting them to molecular weights smaller than 500Da. Since the flux of transdermal drugs is inversely proportional to their molecular size, an ideal molecular size for TDD is typically less than 400. Generally, transdermal drugs exhibit poor absorption via oral medication, resulting in low bioavailability. Consequently, the topical method has been adopted to enhance drug efficacy, even though transdermal drugs may offer higher bioavailability due to other benefits such as long-term healing and self-medication management.

Furthermore, the partition coefficient (Pow) also plays a crucial role in transdermal drug delivery, indicating the drug's solubility or lipophilicity (hydrophobicity). The partition coefficient is defined as follows:

$$\log P_{ow} = \log \frac{C_o}{C_w}$$

In this context, "Co and Cw represent concentrations in oil and water solutions, respectively. The partition coefficient (Pow) of chemicals is determined experimentally using chromatographic instrumentation, such as funnel extraction and high-pressure liquid chromatography. A log Pow of 1.0 indicates that the drug's solubility is 10 times greater in a lipophilic solution (such as octanol) compared to water."

Lipophilic compounds are usually administered transdermal because cell membranes are compatible with oil/water interfaces. Cell membranes consist of phospholipid double layers (lipid bilayers), which preferentially pass lipophilic drugs over hydrophilic ones because of the lipophilic nature of the cells.

***Various articles discussing the transdermal patch of buprenorphine and fentanyl in management of postoperative pain;***

In a study by Prausnitz MR et al in 2008 has stated that "transdermal drug delivery has achieved its potential as an alternative to oral and hypodermic injections. First generation transdermal delivery system is used for delivery of small lipophilic low dose drugs. Second generation uses iontophoresis for control delivery rates. Third generation uses microneedles, thermal ablation, electroporation methods." Using these novel strategies transdermal delivery has increased its impact on medicine.[2]

In a study conducted by Arshad Z et al., (2015) to assess the transdermal buprenorphine and fentanyl for postoperative pain. While none of the patients in Group B needed rescue analgesics, five out of thirty patients (16.7%) in Group A needed a single dosage. Despite this, the necessity for rescue analgesics did not change statistically significantly (p-value 0.0522). The majority of patients (20%) in the fentanyl group and 16.7% in the buprenorphine group reported experiencing adverse effects, with nausea and vomiting accounting for the majority of these cases. In the buprenorphine and fentanyl groups, the incidence of nausea and vomiting was 6.7% and 10%, respectively. Transdermal fentanyl and buprenorphine systems were both generally safe and successful in managing postoperative pain. But fentanyl was discovered to be better in this area than buprenorphine.

In a study by Oh CS et al., (2015) to assess the effect of nefopam versus fentanyl based patients controlled analgesia. "The study involved 94 patients and compared the effects of two patient-controlled analgesia (PCA) regimens: one using nefopam and the other using fentanyl. Results showed that the group using nefopam had significantly lower incidences and severity of postoperative nausea and vomiting (PONV) and Rhodes index scores compared to the fentanyl group across all measured times. Specifically, 24 hours after post-anaesthesia care unit (PACU) discharge, the nefopam group had a lower incidence of PONV and severity, along with lower Rhodes index scores compared to the fentanyl group. There was no significant difference in postoperative pain between the two groups. Dry mouth was more frequent in the nefopam group initially but decreased over time, resulting in a lower incidence after 24 hours". Overall, using a PCA regimen with nefopam provided similar pain control and better PONV outcomes compared to fentanyl, with no adverse events reported. [42]

Study by Gujjar P et al., in 2017 have stated that drug delivery system has been noted newer systems with controlled release, target controlled infusion. Applying pharmacokinetics principles could improve safety and keep the body's drug levels constant.[8]

Desai S et al., (2017) conducted a randomized control trial study to assess the safety of transdermal buprenorphine versus the oral tramadol. "Resting pain scores and pain during movement were consistently lower in the Transdermal Buprenorphine (TDB) Group compared to the Oral Tramadol (OT) Group over the course of seven days, beginning 24 hours after surgery. Additionally, the need for rescue analgesics was significantly lower in the TDB Group compared to the OT Group. While all patients in the OT Group required rescue analgesics, only 68% of patients in the TDB Group needed them. Moreover, the

incidence of vomiting was lower, and satisfaction scores were markedly higher in the TDB Group compared to the OT Group (79% vs. 66%, P < 0.001). These findings suggest that transdermal buprenorphine can be safely used for post-operative pain management and is more effective in reducing post-operative pain after 24 hours, with fewer side effects compared to oral tramadol." [7]

In a randomized control trial study conducted by Oliashirazi A et al., (2017) Fentanyl infusion transdermal system (ITS) significantly enhanced overall patient mobility, as well as each aspect of mobility (with a p-value less than 0.0001) across various patient demographics (such as gender, age, BMI categories), and types of surgeries. This improvement was consistent across assessments conducted by both nurses and physical therapists. The incidence of treatment-emergent adverse events (TEAEs) was generally comparable between the two treatment groups. In contrast to fentanyl intravenous PCA, a greater percentage of patients had TEAEs associated with opioids when receiving intravenous morphine patient-controlled analgesia (PCA) (p-value: 0.003). In conclusion, fentanyl ITS's increased mobility indicates that problems are probably less common than with intravenous and epidural PCA. By include this strategy in postoperative pain treatment guidelines, hospital expenses and length of stay (LOS) might be decreased. [43]

In a systemic review conducted by Machado FC et al., (2020) to assess the role of transdermal buprenorphine for acute postoperative pain. Studies examining the use of transdermal buprenorphine in the perioperative setting typically commence administration 6 to 48 hours before surgery, continuing for 1 to 28 days post-procedure. Although the frequency of side effects varies throughout research, most suggest that using buprenorphine does not significantly increase the risk of drug-related adverse effects, with the exception

of comparisons with transdermal fentanyl and oral tramadol. It's crucial to remember, though, that a large number of these conclusions are predicated on data that has a high or ambiguous risk of bias overall. In summary, preliminary data indicate that transdermal buprenorphine may be a feasible and secure opioid treatment alternative for immediate postoperative pain, even if more investigation is necessary. [44]

In a study by Khandelwal H et al., (2021) to assess the analgesic efficacy of buprenorphine transdermal patch and fentanyl patch. "A final analysis was performed on 150 of the 175 patients who were originally tested; baseline characteristics were similar for all three groups. At different times after surgery, Group 3's median Numeric Rating Scale (NRS) score was found to be considerably lower than the other groups (the Kruskal-Wallis test yielded a p-value < 0.05). Furthermore, without a discernible rise in adverse events, Group 3 demonstrated the lowest overall intake of the postoperative rescue analgesic diclofenac. In conclusion, applying a 20 μg·h-1 buprenorphine patch 12 hours before to arthroscopic lower limb surgery has been shown to be an effective postoperative analgesic with no appreciable side effects." [45]

In a study conducted by Kauser D et al., (2022) to assess the transdermal buprenorphine patch versus transdermal fentanyl patch for postoperative analgesia. With a p-value of 0.0005, the results showed significant VAS values at the fourth hour for Group B and the eighth hour for Group F. With six patients in Group F and two in Group B, pruritus was more common in Group F than in Group B—a statistically significant difference. Additionally, although this difference was not statistically significant, Group F needed more antiemetic medicine and experienced a greater incidence of nausea and vomiting. In summary, the buprenorphine patch outperformed the fentanyl patch for managing

postoperative pain following lower limb arthroscopic surgeries, and no increase in hemodynamic instability or adverse effects was noted. [46]

In a study by Mythili N et al., (2022) to study the efficacy of transdermal buprenorphine patch in postoperative pain. The study found that the "mean Visual Analogue Scale (VAS) score was higher in females (4.4) compared to males (3.9), indicating potentially greater effectiveness of the patch in males. Trauma patients had a mean VAS score of 3.9, while pathology patients had a mean VAS score of 4.1. About 36% of patients required additional analgesics due to VAS scores exceeding 5, with varying percentages across age groups: 20% in the 20–30 age group, 66.7% in the 31–40 age group, no patients in the 41–50 age group, and 13.3% in the 51–60 age group. Furthermore, 24% of female patients required additional analgesics compared to 12% of male patients, and 21.6% of pathology patients required additional analgesics compared to 8.2% of trauma patients.

The study demonstrated a sensitivity of 94.1% and specificity of 33.3%. In conclusion, buprenorphine displayed high analgesic potential, a favourable safety profile, ease of opioid switching, and reversibility by μ-antagonists. Its transdermal administration was cost-effective and associated with increased patient compliance and ease of handling, with fewer adverse effects, indicating good efficacy in postoperative pain management." [47]

# MATERIAL & METHOD

# MATERIAL & METHOD

**Source of data** This study was conducted among patients undergoing lower limb surgeries done under spinal anaesthesia without any adjunct at R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar during the period from September 2022 –December 2023

**Study Design**: Randomized control trial.

**Sample Size**: 56

**Duration of study**: 16 months

**Sampling Method**: Computerized random sampling

**Sample size estimation**: According to previous studies P=16.7 Q = (100-P) = 83.3 Sample size = 4PQ/L2 = 4x16x83.3/100 = 55.64 n = 55.64 /56

FORMULA: n = 2sp 2 [z1-ά/2+z1-ß] 2 µd 2 sp 2 = s1 2 + s2 2 2

Where, s1 2= Standard deviation in the first group

s2 2= Standard deviation in the second group

µd 2= Mean difference between the samples

ά = Significance level 1-ß = Power

**Inclusion Criteria**

- Age 18 to 60 years
- Individuals receiving spinal anaesthesia for orthopaedic procedures for lower limbs.
- ASA 1 and 2

**Exclusion Criteria**

- Chronic alcoholics
- Hepatic disease and renal disease
- Taking opioids, NSAIDS or any pain medication for more than 3 months
- Chronic pain syndrome
- On antiepileptics or antidepressants
- Undergoing emergency operation, pregnancy, malignancy.

**Sampling procedure**

- Patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia were randomly selected.
- Informed consent was taken from the patients.
- Result values were recorded using a proforma.
- The patient's complete medical history was obtained
- A comprehensive physical assessment was conducted.
- Routine investigations were checked.
- Intravenous line was secured and IV fluids was connected.

- Patients were divided into two groups randomly, 28 in Group-A and 28 in Group-B
- Group A: Buprenorphine transdermal patch of 20 μg·h-1 was applied on prepared areas of the right upper arm.
- Group B: Fentanyl transdermal patch of 25 μg·h-1 was applied on prepared areas of the right upper arm.
- All the patients received subarachnoid block in sitting or lateral position using 0.5% bupivacaine heavy without any adjunct.
- Intraoperative monitoring and fluids are given as per the ASA protocol to maintain heart rate and mean arterial pressure within +/-20% of baseline.
- All patients were analyzed for post operative pain (using NRS), after surgery in postoperative room at 1,2,4,8 and 12 hrs. After 12 hrs. the patients were assessed at 12 hourly intervals up to 72 hrs. The patients who had NRS >4 was given diclofenac 75 mg slow intravenous as rescue analgesia. If the pain persisted or NRS >4 within 6 hrs. of last dose of diclofenac then the patients were given tramadol 50 mg intravenous. Ondansetron 4 mg intravenous was given to the patients who complained of nausea and vomiting.

**Parameters to be observed**

- Pain scores was measured and compared using Numerical analogue scale (NRS) which was recorded at 1hr, 2 hr, 4 hr, 8 hr, 12 hr and after 12 hourly the patient was assessed up to 72 hrs
- Postoperative 1st rescue analgesia dose and time, hemodynamic variability like heart rate and mean arterial pressures was noted

Does the study require any investigation or intervention to be conducted on patients or other humans or animals? If so, please describe briefly. No intervention on animals required. Routine investigations will be done. No special investigations required.

# STATISTICAL ANALYSIS

# STATISTICAL ANALYSIS

"All the collected data were entered in excel sheet and analysed using SPSS v23.0. the data were summarised as mean, standard deviation, frequency and percentage. The summarised data were compared using unpaired t-test for continuous data and for categorical data using chi-square test. The data were represented with help of tables, figures and bar diagram. For all statistical purpose a p-value of <0.05 was considered statistically significant."

# RESULTS

# RESULTS

Present study included total of 56 patients, divided into two group with 28 in group A and 28 patients in group B.

**Table 1: Comparison of the mean age among the groups**

| | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Age | 30.4 | 11.7 | 28.8 | 10.0 | 0.574 |

The mean age of patients in both the groups were comparable with no significant difference noted. (p>0.05)

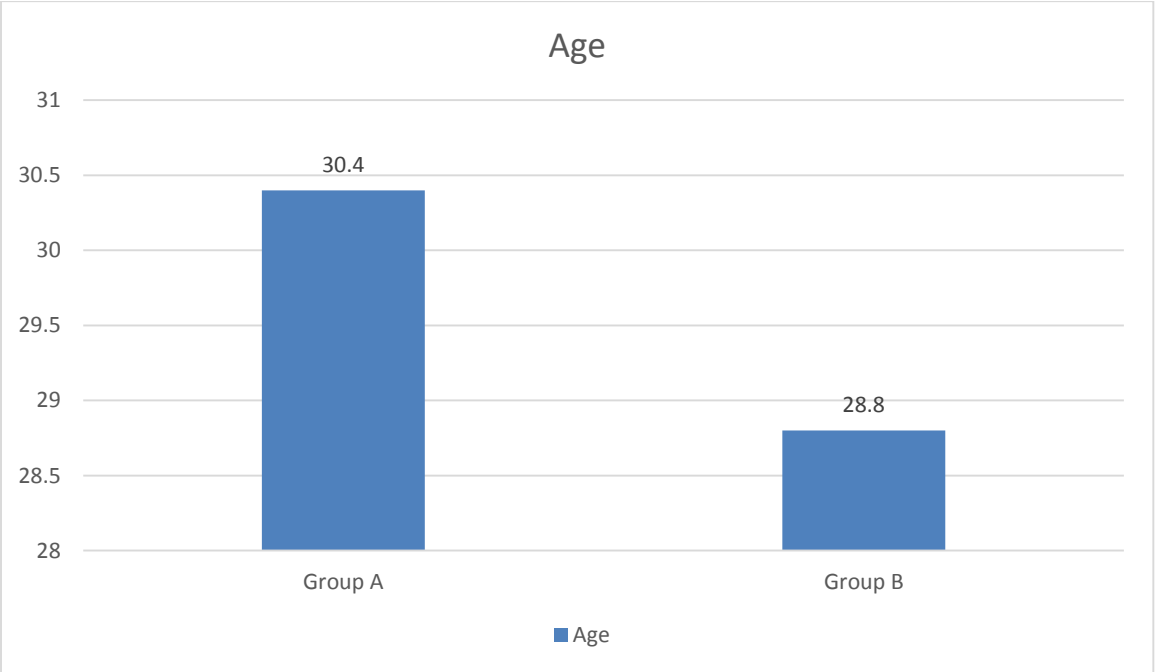


**Figure 7: Comparison of the mean age among the groups**

**Table 2: Comparison of the vital parameters among the groups**

| | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| PR | 92.3 | 8.5 | 94.7 | 8.5 | 0.29 |
| RR | 16.2 | 1.7 | 16.2 | 1.8 | 0.98 |
| SBP | 125.1 | 8.9 | 126.2 | 9.6 | 0.66 |
| DBP | 79.7 | 6.8 | 79.6 | 7.2 | 0.93 |

On assessment of the baseline vital parameters, there is no noticeable difference among the groups. (p>0.05)

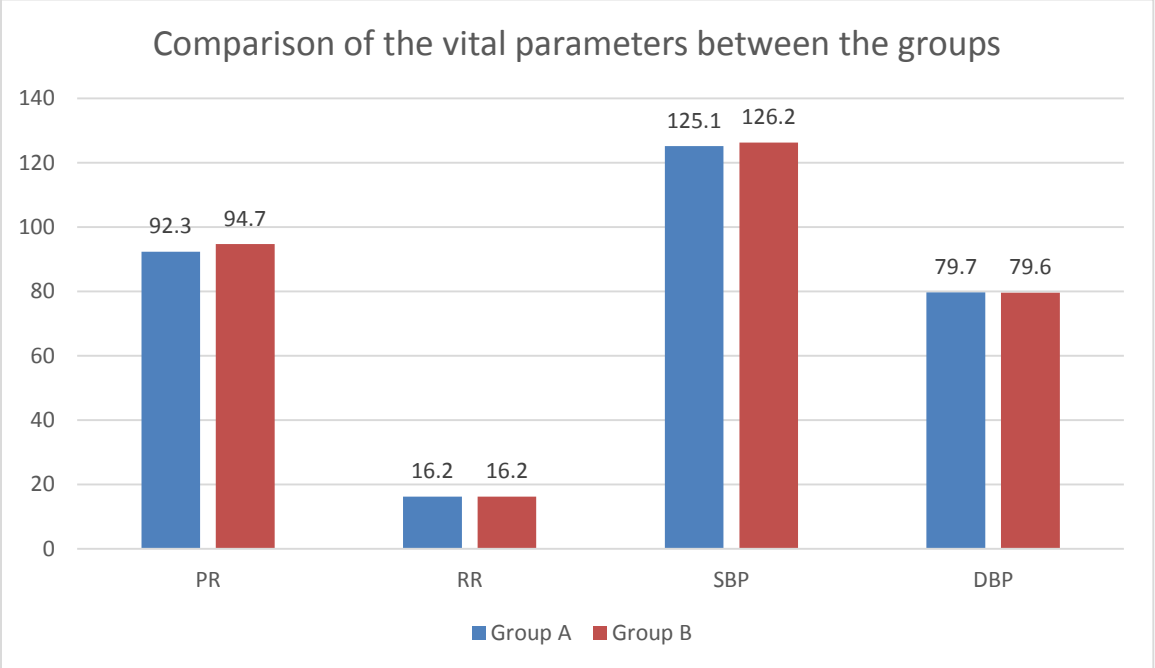


**Figure 8: Comparison of the vital parameters between the groups**

**Table 3: Comparison of the general physical examination findings among the groups**

| | | Group A | | Group B | | p-value |
|---|---|---|---|---|---|---|
| | | Count | N % | Count | N % | |
| General examination findings | Normal | 27 | 96.4% | 27 | 96.4% | 1.1 (0.99) |
| | Pallor | 1 | 3.6% | 1 | 3.6% | |

On general physical examination, pallor was seen in 1 patient in both the groups.

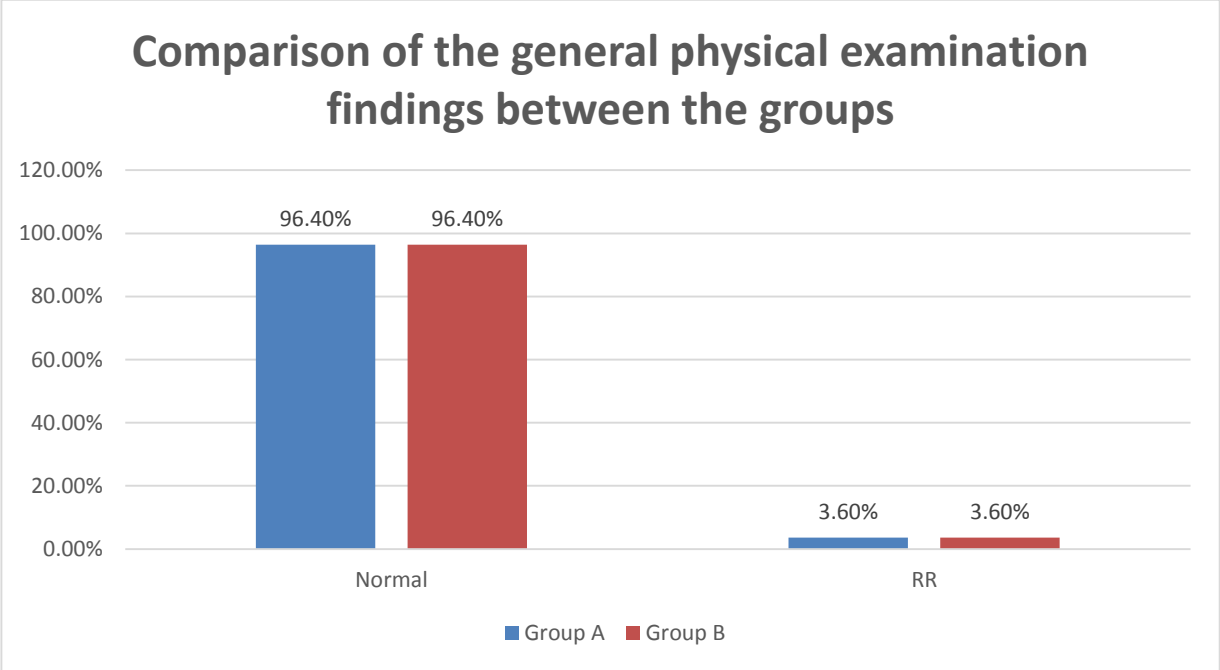


**Figure 9: Comparison of the general physical examination findings among the groups**

**Table 4: Comparison of the blood count, RBS and renal profile among the groups**

| | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| HB | 13.5 | 4.6 | 13.7 | 3.6 | 0.83 |
| WBC | 13.29 | 24.62 | 8.95 | 17.99 | 0.45 |
| Platelet | 99.0 | 76.3 | 87.8 | 63.6 | 0.55 |
| RBS | 107.6 | 17.8 | 115.3 | 24.2 | 0.18 |
| Blood urea | 14.9 | 2.7 | 15.1 | 3.0 | 0.85 |
| S Creatinine | .9 | .2 | 1.0 | .2 | 0.15 |
| Sodium | 139 | 3 | 139 | 3 | 0.82 |
| Potassium | 4.06 | .59 | 4.22 | .81 | 0.37 |

The complete blood picture parameters such as hemoglobin level, WBC, platelet were found to be comparable among the groups.

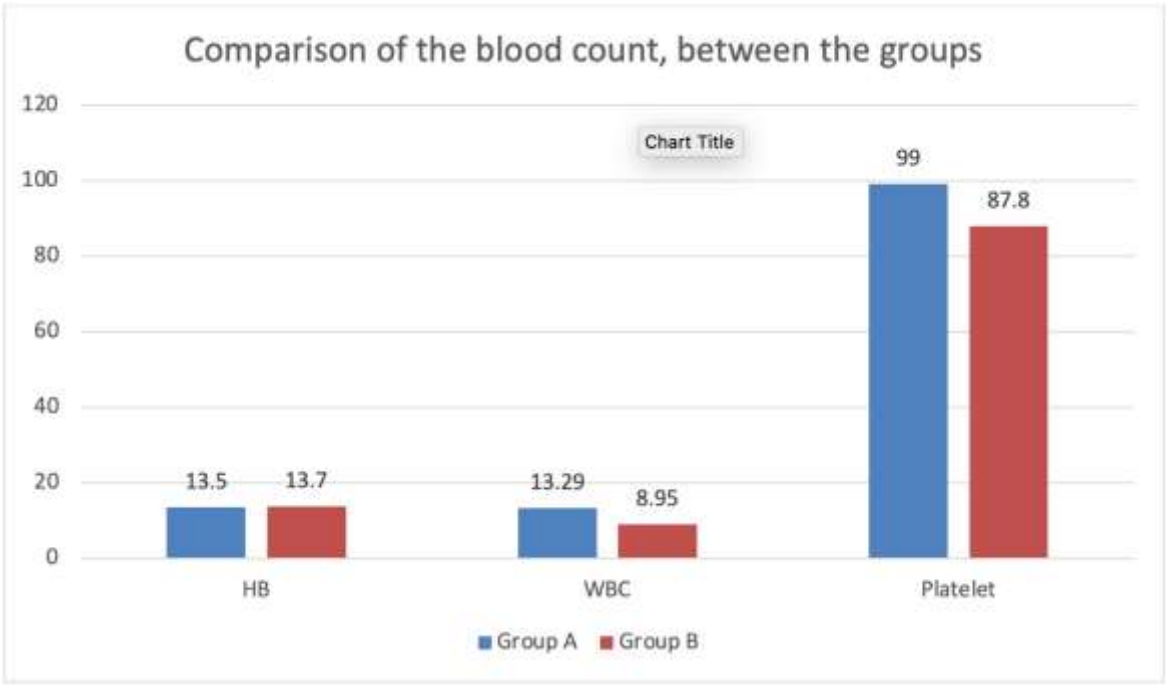


**Figure 10: Comparison of the blood count, between the**

The random blood sugar level was found to be comparable between two groups.

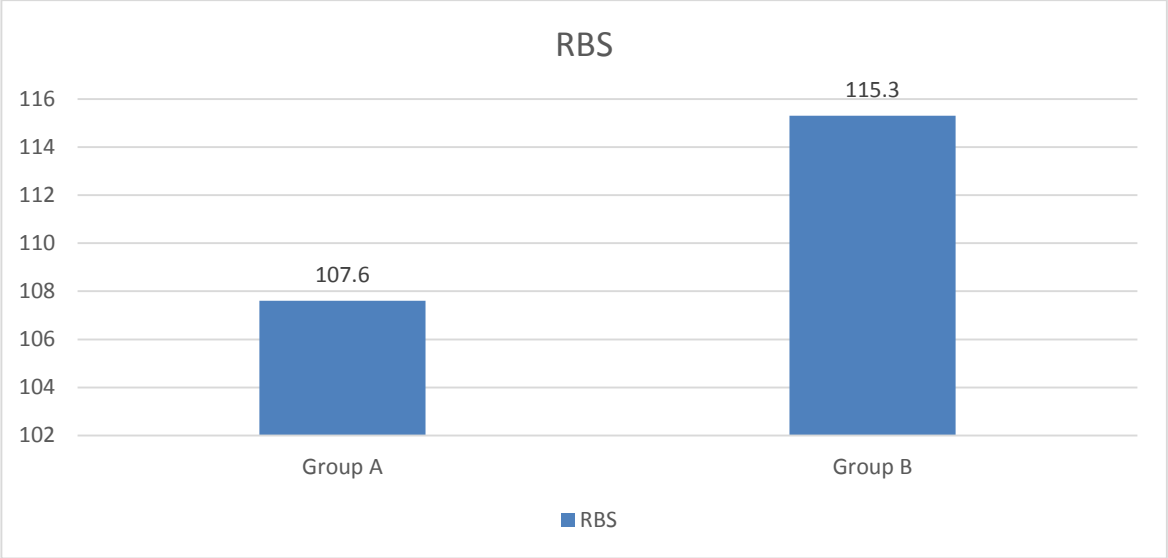


**Figure 11 : Comparison of the RBS among the groups**

The renal parameters such as urea, creatinine and electrolytes were found to be comparable with no noticeable difference noted among the groups.(p>0.05)

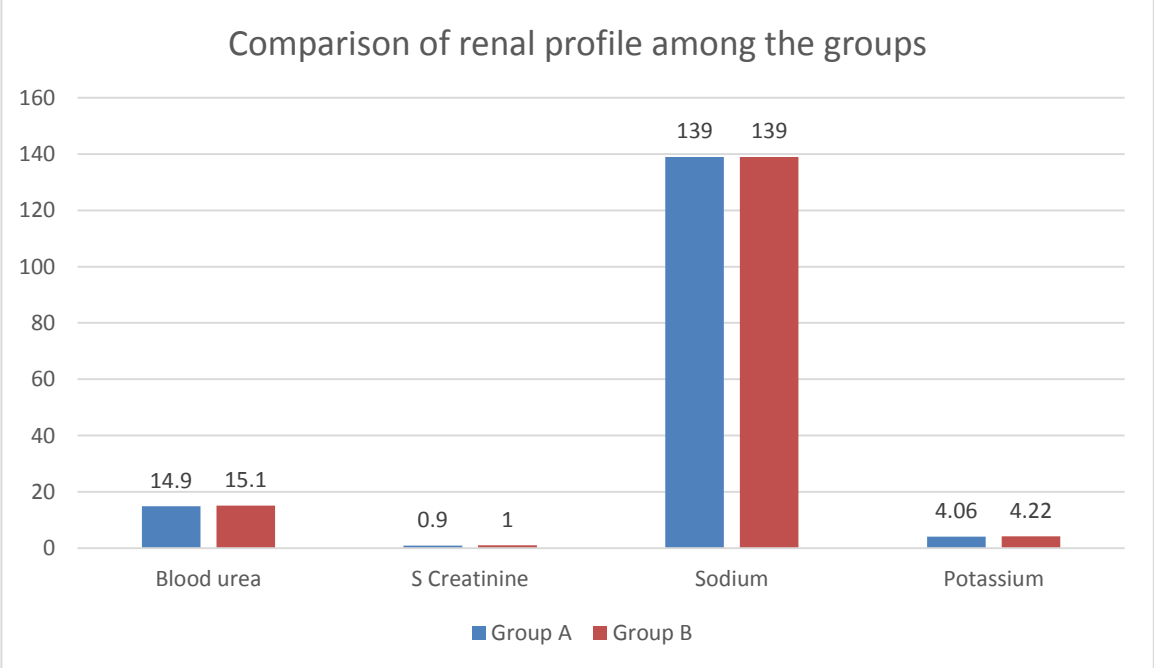


**Figure 12: Comparison of renal profile among the groups**

### Table 5: Comparison of the NRS score among the groups

| NRS | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Immediate | 8.2 | .4 | 8.2 | .4 | 0.74 |
| 1hr | 8.2 | .4 | 8.2 | .4 | 0.74 |
| 2hr | 6.6 | .5 | 6.6 | .5 | 0.99 |
| 4hr | 4.6 | .5 | 4.6 | .5 | 0.59 |
| 8hr | 4.5 | .5 | 4.6 | .5 | 0.59 |
| 12hr | 4.5 | .5 | 4.6 | .5 | 0.61 |
| 24hr | 4.5 | .6 | 4.6 | .6 | 0.64 |
| 36hr | 2.2 | .4 | 2.2 | .4 | 0.74 |
| 48hr | 2.7 | .5 | 2.8 | .4 | 0.56 |
| 60hr | 2.7 | .4 | 2.8 | .4 | 0.51 |
| 72hr | 1.9 | .6 | 1.9 | .5 | 0.9 |

On assessment of the NRS scoring at different point of time, there is no noticeable difference noted among the groups at varied time interval of measurements. ($p>0.05$)

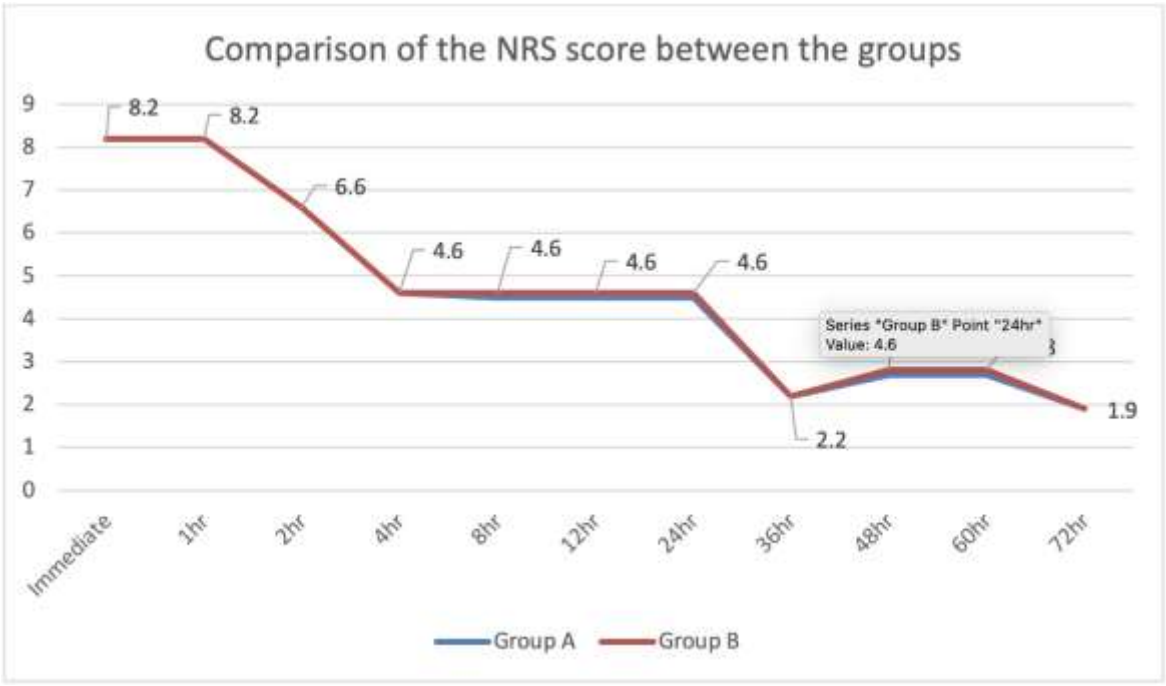


**Figure 13: Comparison of the NRS core among the groups**

**Table 6: Comparison of the rescue analgesia among the groups**

| Rescue analgesia | | Group A | | Group B | | Chi-square (p-value) |
|---|---|---|---|---|---|---|
| | | Count | N % | Count | N % | |
| Immediate | No | 17 | 60.7% | 23 | 82.1% | 3.15 (0.07) |
| | Yes | 11 | 39.3% | 5 | 17.9% | |
| 1hr | No | 21 | 75.0% | 24 | 85.7% | 2.8 (0.24) |
| | Yes | 7 | 25.0% | 4 | 14.3% | |
| 2hr | No | 12 | 42.9% | 14 | 50.0% | 0.28 (0.59) |
| | Yes | 16 | 57.1% | 14 | 50.0% | |
| 4hr | No | 27 | 96.4% | 22 | 78.6% | 4.08 (0.04)* |
| | Yes | 1 | 3.6% | 6 | 21.4% | |
| 8hr | No | 21 | 75.0% | 24 | 85.7% | 2.8 (0.24) |
| | Yes | 7 | 25.0% | 4 | 14.3% | |
| 12hr | No | 12 | 42.9% | 15 | 53.6% | 0.64 (0.44) |
| | Yes | 16 | 57.1% | 13 | 46.4% | |
| 24hr | No | 27 | 96.4% | 28 | 100.0% | 1.01 (0.313) |
| | Yes | 1 | 3.6% | 0 | 0.0% | |
| 36hr | No | 12 | 42.9% | 15 | 53.6% | 0.64 (0.422) |
| | Yes | 16 | 57.1% | 13 | 46.4% | |
| 48hr | No | 27 | 96.4% | 28 | 100.0% | 1.01 (0.313) |
| | Yes | 1 | 3.6% | 0 | 0.0% | |
| 60hr | No | 28 | 100.0% | 27 | 96.4% | 1.01 (0.31) |
| | Yes | 0 | 0.0% | 1 | 3.6% | |
| 72hr | No | 28 | 100.0% | 28 | 100.0% | - |

The requirement of the rescue analgesia was found to be comparable between the groups at various time interval of measurements. At 4th hr, the requirement of rescue analgesia was seen to be substantially greater in patients in group B (21.4%) as opposed to those in group A (3.6%).

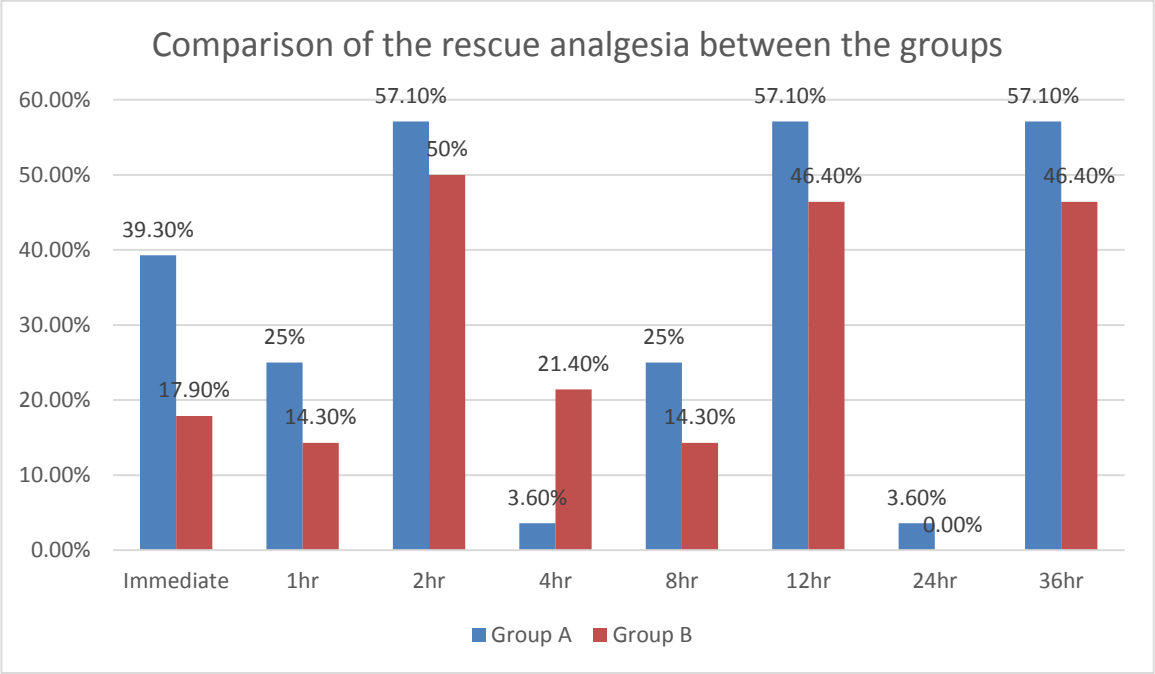


**Figure 14 : Comparison of the rescue analgesia between the groups**

# DISCUSSION

# DISCUSSION

Effective postoperative pain management is critical for enhancing recovery and improving patient outcomes following lower limb surgeries. Opioid analgesics remain a cornerstone for managing moderate to severe postoperative pain, with transdermal systems offering significant advantages in terms of sustained delivery and patient compliance. Among the options available, buprenorphine and fentanyl transdermal patches are widely utilized due to their unique pharmacological profiles and efficacy in controlling pain.

Buprenorphine, a semi-synthetic opioid, is a partial agonist at the mu opioid receptor, providing potent analgesic effects without a ceiling effect within its therapeutic range. This characteristic allows buprenorphine to be used alongside full mu-agonists without the risk of antagonism, making it a versatile option in multimodal pain management strategies. Additionally, buprenorphine is notable for its lack of immunosuppressive activity at therapeutic doses, differentiating it from other opioids such as fentanyl and morphine. The transdermal delivery system (TDS) for buprenorphine is designed to provide continuous pain relief over an extended period, typically up to one week, enhancing convenience and compliance.

Synthetic opioids like fentanyl are known for their strong effects and quick start. It is really well suited for transdermal administration as they are more lipid soluble in nature along with less molecular weight which enables a constant release of the medication at rates between 25 to 100 mg/hr. By keeping plasma concentration constant, the fentanyl patches affectively control acute postoperative pain by lowering variations and the need of

changing dosage frequently. So, fentanyl shows immunosuppressive effects at analgesic dosages unlike buprenorphine.

The effectiveness of transdermal systems in managing the pain after lower limb surgery is an area of significant clinical interest. Buprenorphine and Fentanyl patches provide sustained analgesia, their various side effect profiles and receptor affinity may affect how beneficial they are in comparison and how appropriate they are for the postoperative environment. The aim of this discuss is to compare and inspect the analgesic efficacy, side effects, and the overall impact of the buprenorphine and fentanyl transdermal patches in pain management post limb surgery. By understanding these factors in detail, final goal is to provide judgement that could suggest better analgesic strategies and improve patient result in postoperative care.

Present study included total of 58 patients, divided into two group with 28 in group A and 28 patients in group B. The mean age of patients in both the groups were comparable with no significant difference noted. ($p>0.05$) On assessment of the baseline vital parameters, there is no significant difference noted between the groups.($p>0.05$) On general physical examination, pallor was seen in 1 patient in both the groups.

In similar to presents study Arshad Z et al., documented comparable mean age of the patients between the groups, with mean age of 39.87 in buprenorphine group and 38.8yrs in fentanyl group. Overall they also documented with male preponderance in both the group. The vitals were comparable with stable blood pressure and heart rate between the groups. [12] In concordance another study by Khandelwal et al., documented male

preponderance in study with mean age of patients 46.65yr. The physical characteristics such as height, weight BMI were comparable between the groups.[45]

The synthetic opioid fentanyl has strong analgesic effects. Its exceptional lipid solubility and less molecular weight make it a very good candidate for transdermal therapeutic systems delivery. The medication is reliably delivered by these devices at rates between 25 and 100 micrograms per hour. As a partial agonist at the mu opioid receptor, buprenorphine is a semi-synthetic opioid analgesic. Prescription buprenorphine transdermal delivery systems (TDS) relieve pain for a maximum of seven days. There is no evidence of a ceiling impact on analgesia within its therapeutic dosage range. Complete mu-agonists can be used with buprenorphine without running the risk of antagonistic effects. Unlike fentanyl and morphine, buprenorphine does not exhibit immunosuppressive activity at therapeutic analgesic concentrations. On assessment of the NRS scoring at different point of time, there is no significant difference noted between the group at various time interval of measurements.($p>0.05$)

In study by Kauser D et al., found that the VAS score at $4^{th}$ hour in buprenorphine group and $8^{th}$ hr fentanyl group were significant difference. Additionally, the fentanyl group had a greater frequency of nausea or vomiting and needed antiemetics. For the purpose of managing pain during lower limb arthroscopic operations, the buprenorphine patch outperformed the fentanyl patch, with no discernible increase in hemodynamic instability or adverse effects. [46]

Another study by Khandelwal H et al., found that application of a 20 μg·h-1 buprenorphine patch 12 hours before the procedure proves to be an effective postoperative analgesic with no significant associated adverse effects. [45] in concordance to present study Arshad Z et al., documented significant lower mean VAS score in fentanyl group compared to the buprenorphine and also lower incidence of requirement of rescue analgesia in fentanyl group. Also, found overall, both fentanyl and buprenorphine transdermal systems were effective and safe in controlling postoperative pain. However, fentanyl was found to be superior to buprenorphine in this regard. [12]

Mythili N et al., documented buprenorphine displayed strong analgesic potency, a good safety record, ease of switching between opioids, and reversibility when combined with μ-antagonists. Its transdermal delivery was economical, linked to better patient compliance, convenience of use, and fewer side effects, suggesting that it was useful in managing pain following surgery. [47]

The requirement of the rescue analgesia was found to be comparable between the groups at various time interval of measurements. At $4^{th}$ hr, the requirement of rescue analgesia was found to be significantly higher in group B patients (21.4%) compared to group A patients (3.6%).

In study by Desai S et al., the requirement of the additional rescue analgesia was significantly reduced. These findings suggest that transdermal buprenorphine is more effective at lowering post-operative pain after 24 hours and has fewer adverse effects when used carefully for pain management following surgery. [7]

# SUMMARY

# SUMMARY

- Present study included total of 58 patients, divided into two group with 28 in group A and 28 patients in group B.
- The mean age of patients in both the groups were comparable with no significant difference noted. ($p>0.05$)
- On assessment of the baseline vital parameters, there is no significant difference noted between the groups.($p>0.05$)
- On general physical examination, pallor was seen in 1 patient in both the groups.
- The complete blood picture parameters such as haemoglobin level, WBC, platelet were found to be comparable between the groups.
- The random blood sugar level was found to be comparable between two groups.
- The renal parameters such as urea, creatinine and electrolytes were found to be comparable with no significant difference noted between the groups.($p>0.05$)
- On assessment of the NRS scoring at different point of time, there is no significant difference noted between the group at various time interval of measurements.($p>0.05$)
- The requirement of the rescue analgesia was found to be comparable between the groups at various time interval of measurements. At $4^{th}$ hr, the requirement of rescue analgesia was found to be significantly higher in group B patients (21.4%) compared to group A patients (3.6%).

# CONCLUSION

# CONCLUSION

Overall, both buprenorphine and fentanyl transdermal patches were effective in managing postoperative pain, with similar efficacy in most time points measured. The notable difference in rescue analgesia requirement at the 4th hour suggests a potential advantage of fentanyl over buprenorphine in the immediate postoperative period.

These findings support the use of both agents for pain management but indicate that fentanyl may provide more consistent pain relief without the need for additional analgesia early in the postoperative phase. Further studies with larger sample sizes are warranted to validate these results.

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# ANNEXURE

**PROFORMA**

STUDY**: COMPARATIVE EVALUATION OF ANALGESIC EFFICACY OF TRANSDERMAL PATCHES OF BUPRENORPHINE AND FENTANYL IN MANAGEMENT OF POSTOPERATIVE PAIN AFTER LOWER LIMB SURGERIES**

**Investigators:** Dr S P Shruthi / Dr Kiran.N

**Name of the patient:** **Age/Sex:** **Ward:**

**IP No:** **ASA grade:**

- **General physical examination:**

| | | | |
|---|---|---|---|
| Height: | | Weight: | |
| Pulse rate: | | Blood pressure: | |

Pallor/icterus/cyanosis/clubbing/lymphadenopathy/edema

- **Systemic examination:**

| | | | |
|---|---|---|---|
| RS: | | CVS: | |
| CNS: | | P/A: | |

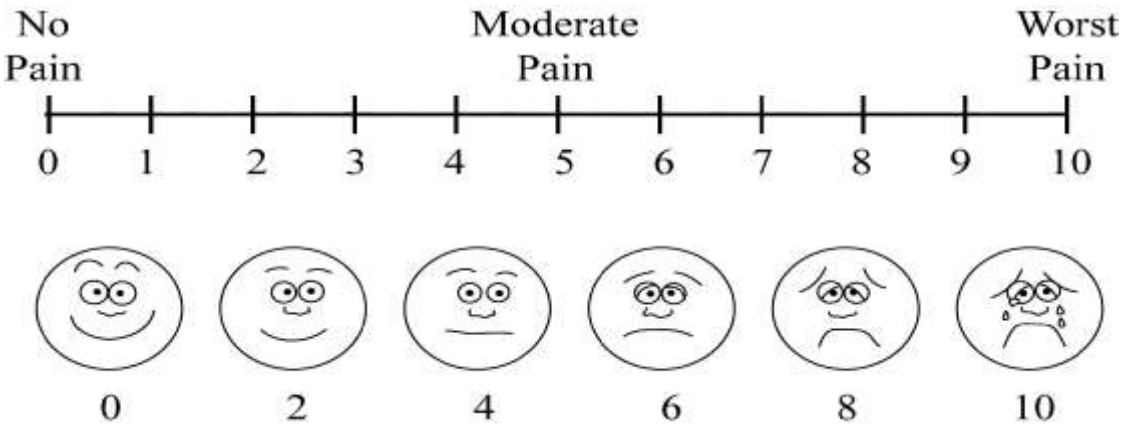
- **Investigations:**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Blood Grp: | | Hb: | | WBC: | | Platelets: | |
| RBS Potassium: | | Blood Urea: | | Sr. Creatinine: | | Sodium: | |

| | |
|---|---|
| ECG: | |

- **Diagnosis:**
- **Surgery:**
- **Group A:** Patient will be applied buprenorphine patch 20 µg·h-1
- **Group B:** Patient will be applied fentanyl patch 25 µg·h-1
- **NUMERICAL RATING SCALE (NRS)** (for pain)

0 - No pain
1-3 - mild pain
4-6 - moderate pain
7-10 – severe pain



| TIME | Numerical rating scale | Group 1 (BUPRENORPHINE PATCH 20 µg·h-1) | Group 2 (FENTANYL PATCH 25 µg·h-1 | RESCUE ANALGESIA (DICLOFENAC 75 MG OR TRAMADOL 50 MG) |
|---|---|---|---|---|
| Immediate post op | | | | |
| 1hr | | | | |
| 2hr | | | | |
| 4hr | | | | |
| 8hr | | | | |
| 12hr | | | | |
| 24hr | | | | |
| 36hr | | | | |
| 48hr | | | | |
| 60hr | | | | |
| 72hr | | | | |

| TIME | HEART RATE | MAP |
|---|---|---|
| Immediate post op | | |
| 1hr | | |
| 2hr | | |
| 4hr | | |
| 8hr | | |
| 12hr | | |
| 24hr | | |
| 36hr | | |
| 48hr | | |
| 60hr | | |
| 72hr | | |

## PATIENT INFORMATION SHEET

**Study: Comparative evaluation of analgesic efficacy of transdermal patches of buprenorphine and fentanyl in management of postoperative pain after lower limb surgeries**

**Investigators: Dr S P Shruthi/ Dr Kiran.N**

**Study location:** R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

**Details -**Patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia.

This study aims is to compare the efficacy of buprenorphine transdermal patch (20 μg·h-1) and fentanyl transdermal patch (25 μg·h-1) in managing acute postoperative pain in lower limb surgeries. Patient and the attenders will be completely explained about the procedure being done .All the patients were analyzed for postoperative pain (using NRS),mean arterial pressure ,heart rate after surgery in postoperative room at 1,2,4,8 and 12 hr after 12 hr the patients are assessed up to 72 hr .

Trandermal patches will be avoided in the patients associated with test drug, known hypersensitivity to the drug, chronic alcoholic, renal impairment and psychiatric patients.

Please read the information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study, then relevant information and history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. There will not be any monetary benefits/incentives for taking part in this study. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

| | |
|---|---|
| Dr S P Shruthi<br><br>Post graduate in Anaesthesiology, SDUMC Kolar<br>Mobile no: 7416952767 | Dr Kiran N<br><br>Professor in Anaesthesiology, SDUMC Kolar<br>Mobile no: 9740468460 |

# ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

**ಅಧ್ಯಯನ: ಬುಪ್ರೆನಾರ್ಫಿನ್ ಟ್ರಾನ್ಸ್‌ಡರ್ಮಲ್ ಪ್ಯಾಚ್ ಮತ್ತು ಫೆಂಟನಿಲ್ ಪ್ಯಾಚ್‌ನ ನೋವು ನಿವಾರಕ ಪರಿಣಾಮಕಾರಿತ್ವದ ತುಲನಾತ್ಮಕ ಮೌಲ್ಯಮಾಪನವು ಕೆಳ ಅಂಗಗಳ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ನೋವಿನ ನಿರ್ವಹಣೆಯಲ್ಲಿ**

**ತನಿಖಾಧಿಕಾರಿಗಳು: ಡಾ ಎಸ್ ಪಿ ಶೃತಿ/ ಡಾ ಕಿರಣ್.ಎನ್**

**ಅಧ್ಯಯನ ಸ್ಥಳ**: ಆರ್.ಎಲ್.ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರವು ಶ್ರೀ ದೇವರಾಜ್ ಅರ್ಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜು, ಟಮಕ, ಕೋಲಾರ.

**ವಿವರಗಳು** - ಸಂಯೋಜಿತ ಬೆನ್ನುಮೂಳೆಯ ಅರಿವಳಿಕೆ ಅಡಿಯಲ್ಲಿ ಕಡಿಮೆ ಅಂಗ ಮೂಳೆ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಗೆ ಒಳಗಾಗುವ ರೋಗಿಗಳು.

ಈ ಅಧ್ಯಯನವು ಬುಪ್ರೆನಾರ್ಫಿನ್ ಟ್ರಾನ್ಸ್‌ಡರ್ಮಲ್ ಪ್ಯಾಚ್ (20ಮೈಕ್ರೊಮ್/ಗಂ) ಮತ್ತು ಫೆಂಟಾನಿಲ್ ಟ್ರಾನ್ಸ್‌ಡರ್ಮಲ್ ಪ್ಯಾಚ್ (25ಮೈಕ್ರೊಗ್ರಿ/ಗಂ) ಯ ಪರಿಣಾಮಕಾರಿತ್ವವನ್ನು ಕಡಿಮೆ ಅಂಗಗಳ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಗಳಲ್ಲಿ ತೀವ್ರವಾದ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ನೋವನ್ನು ನಿರ್ವಹಿಸುವ ಗುರಿಯನ್ನು ಹೊಂದಿದೆ. ರೋಗಿಯು ಮತ್ತು ಹಾಜರಾದವರಿಗೆ ಮಾಡಲಾದ ಕಾರ್ಯವಿಧಾನದ ಬಗ್ಗೆ ಸಂಪೂರ್ಣವಾಗಿ ವಿವರಿಸಲಾಗುವುದು .ಎಲ್ಲಾ ರೋಗಿಗಳಿಗೆ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ನೋವು (ಎನ್‌ಆರ್‌ಎಸ್ ಬಳಸಿ), ಸರಾಸರಿ ಅಪಧಮನಿಯ ಒತ್ತಡ, ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರ ಹೃದಯ ಬಡಿತವನ್ನು 1,2,4,8 ಮತ್ತು 12 ಗಂಟೆಗಳ ನಂತರ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ಕೋಣೆಯಲ್ಲಿ ವಿಶ್ಲೇಷಿಸಲಾಗಿದೆ. 12 ಗಂಟೆ ರೋಗಿಗಳನ್ನು 72 ಗಂಟೆಗಳವರೆಗೆ ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುತ್ತದೆ.

ಪರೀಕ್ಷಾ ಔಷಧಿ, ಔಷಧಿಗೆ ತಿಳಿದಿರುವ ಅತಿಸೂಕ್ಷ್ಮತೆ, ದೀರ್ಘಕಾಲದ ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ, ಮೂತ್ರಪಿಂಡದ ದುರ್ಬಲತೆ ಮತ್ತು ಮನೋವೈದ್ಯಕಯ ರೋಗಿಗಳಿಗೆ ಸಂಬಂಧಿಸಿದ ರೋಗಿಗಳಲ್ಲಿ ಟ್ರಾಂಡರ್ಮಲ್ ಪ್ಯಾಚ್‌ಗಳನ್ನು ತಪ್ಪಿಸಲಾಗುತ್ತದೆ.

ದಯವಿಟ್ಟು ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿದರೆ, ನಂತರ ಸಂಬಂಧಿತ ಮಾಹಿತಿ ಮತ್ತು ಇತಿಹಾಸವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುತ್ತದೆ. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವನ್ನು ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಒತ್ತಾಯವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿಯು ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಯಾವುದೇ ವಿತ್ತೀಯ ಪ್ರಯೋಜನಗಳು/ಪ್ರೋತ್ಸಾಹಗಳು ಇರುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸಿದರೆ ಮಾತ್ರ ನೀವು ಸಹಿ/ಹೆಬ್ಬೆರಳಿನ ಗುರುತನ್ನು ಒದಗಿಸಬೇಕಾಗುತ್ತದೆ.

**ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ ಸಂಪರ್ಕಿಸಿ**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|---|---|
| ಡಾ ಎಸ್ ಪಿ ಶೃತಿ<br>ಅರಿವಳಿಕೆ ಶಾಸ್ತ್ರದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ಪದವಿ,<br>SDUMC ಕೋಲಾರ<br>ಮೊಬೈಲ್ ಸಂಖ್ಯೆ: 7416952767 | ಡಾ ಕಿರಣ್.ಎನ್<br>ಅರಿವಳಿಕೆ ಶಾಸ್ತ್ರದ ಪ್ರಾಧ್ಯಾಪಕ<br>ಅರಿವಳಿಕೆ ವಿಭಾಗ, SDUMC ಕೋಲಾರ<br>ಮೊಬೈಲ್ ಸಂಖ್ಯೆ: 9740468460 |

## INFORMED CONSENT FORM

**Name of the institution:** SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH.

**Name of the principal investigator:** Dr. S P Shruthi
**Name of the guide:** Dr. Kiran.N
**Name of the subject/participant:**

STUDY: Comparative evaluation of analgesic efficacy of transdermal patches of buprenorphine and fentanyl in management of postoperative pain after lower limb surgeries

Date:

I, _____ aged _____ ,after being explained in my own vernacular language about the purpose of the study and the risks and complications of the procedure, hereby give my valid written informed consent without any force or prejudice for using analgesic efficacy of buprenorphine transdermal patch and fentanyl patch in management of postoperative pain after lower limb orthopaedic surgeries under spinal anaesthesia. The nature and risks involved have been explained to me to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research. I hereby give consent to provide my history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc. to the doctor / institute etc. For academic and scientific purpose, the operation / procedure, etc. may be video graphed or photographed. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc. responsible for any untoward consequences during the procedure / study. I am aware that there wont be any monetary benefits for taking part in this study.
A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

_____ _____

(Signature & Name of Pt. Attendant)

(Relation With Patient) :

(Signature/Thumb Impression & Name of Patient/Guardian

Witness 1:
Witness 2:

Name of Doctor: DR. SP SHRUTHI
(Principal Investigator)

# ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ ನಮೂನೆ

**ಸಂಸ್ಥೆಯ ಹೆಸರು:** ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಅಕಾಡೆಮಿ ಆಫ್ ಹೈಯರ್ ಎಜುಕೇಶನ್ ಅಂಡ್ ರಿಸರ್ಚ್.

**ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು:** ಡಾ. ಎಸ್ ಪಿ ಶೃತಿ

**ಮಾರ್ಗದರ್ಶಕರ ಹೆಸರು:** ಡಾ. ಕಿರಣ್.ಎನ್

**ವಿಷಯ/ಭಾಗವಹಿಸುವವರ ಹೆಸರು:**

**ಅಧ್ಯಯನ:** ಬುಪ್ರೆನಾರ್ಫಿನ್ ಟ್ರಾನ್ಸ್ಡರ್ಮಲ್ ಪ್ಯಾಚ್ ಮತ್ತು ಫೆಂಟನಿಲ್ ಪ್ಯಾಚ್‌ನ ನೋವು ನಿವಾರಕ ಪರಿಣಾಮಕಾರಿತ್ವದ ತುಲನಾತ್ಮಕ ಮೌಲ್ಯಮಾಪನವು ಕೆಳ ಅಂಗಗಳ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ನೋವಿನ ನಿರ್ವಹಣೆಯಲ್ಲಿ

ದಿನಾಂಕ:

ನಾನು, _____ ವಯಸ್ಸಿನ _____, ಅಧ್ಯಯನದ ಉದ್ದೇಶ ಮತ್ತು ಕಾರ್ಯವಿಧಾನದ ಅಪಾಯಗಳು ಮತ್ತು ತೊಡಕುಗಳ ಬಗ್ಗೆ ನನ್ನದೇ ಆದ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಿದ ನಂತರ, ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರದ ನಿರ್ವಹಣೆಯಲ್ಲಿ ಬಪ್ರೆನಾರ್ಫಿನ್ ಟ್ರಾನ್ಸ್ಡರ್ಮಲ್ ಪ್ಯಾಚ್ ಮತ್ತು ಫೆಂಟನಿಲ್ ಪ್ಯಾಚ್‌ನ ನೋವು ನಿವಾರಕ ಪರಿಣಾಮಕಾರಿತ್ವವನ್ನು ಬಳಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನನ್ನ ಮಾನ್ಯ ಲಿಖಿತ ತಿಳುವಳಿಕೆಯನ್ನು ನೀಡುತ್ತೇನೆ. ಬೆನ್ನುಮೂಳೆಯ ಅರಿವಳಿಕೆ ಅಡಿಯಲ್ಲಿ ಕಡಿಮೆ ಅಂಗ ಮೂಳೆ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ನಂತರ ನೋವು. ಒಳಗೊಂಡಿರುವ ಸ್ವಭಾವ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನಗೆ ತೃಪ್ತಿಪಡಿಸಲು ವಿವರಿಸಲಾಗಿದೆ. ನಡೆಸುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವವರಾಗಿ ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸುತ್ತೇನೆ. ನನ್ನ ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ಇತ್ಯಾದಿಗಳನ್ನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳಿಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಶೈಕ್ಷಣಿಕ ಮತ್ತು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ, ಕಾರ್ಯಾಚರಣೆ / ಕಾರ್ಯವಿಧಾನ, ಇತ್ಯಾದಿ. ಗ್ರಾಫ್ ಅಥವಾ ಛಾಯಾಚಿತ್ರ. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಅಹಿತಕರ ಪರಿಣಾಮಗಳಿಗೆ ನಾನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳನ್ನು ಹೊಣೆಗಾರರನ್ನಾಗಿ ಮಾಡುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದರಿಂದ ಯಾವುದೇ ಹಣಕಾಸಿನ ಪ್ರಯೋಜನಗಳು ಇರುವುದಿಲ್ಲ ಎಂದು ನನಗೆ ತಿಳಿದಿದೆ.

ಈ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ನಮೂನೆಯ ಪ್ರತಿಯನ್ನು ಮತ್ತು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಭಾಗವಹಿಸುವವರಿಗೆ ಒದಗಿಸಲಾಗಿದೆ

_____

(ರೋಗಿಯ ಪರಚಾರಕ ಹಸರು ಮತ್ತು ಸಹ )

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

ಸಾಕ್ಷಿ 1:

ಸಾಕ್ಷಿ 2:

_____

(ರೋಗಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ/ಹೆಬ್ಬೆರಳ ಅನಿಸಿಕೆ)

ವೈದ್ಯರ ಹೆಸರು: DR. ಎಸ್ಪಿ ಶೃತಿ

(ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ)

# MASTERCHART

## MASTERCHART

| Sl No | Group | Age | Gender | ASA Grade | PR | RR | SBP | DBP | General examination findings | RS | CVS | CNS | Abdomen | Blood group | HB | WBC* 10 3 cumm | Platelet * 10 3 cumm | RBS | Blood urea | S. Creatinine | Sodium | Potassium | ECG | Surgery |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | A | 23 | M | 1 | 86 | 18 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | A + | 12.4 | 5.2 | 114 | 96 | 13 | 0.8 | 137 | 4.5 | Normal | Lowerlimb surgery |
| 2 | A | 24 | M | 2 | 84 | 16 | 128 | 80 | Normal | Normal | Normal | Normal | Normal | AB - | 14.1 | 6.4 | 54 | 94 | 15 | 0.9 | 142 | 4.4 | Normal | Lowerlimb surgery |
| 3 | A | 30 | M | 2 | 78 | 14 | 124 | 78 | Normal | Normal | Normal | Normal | Normal | O + | 12.1 | 3.1 | 309 | 99 | 11 | 1.1 | 140 | 5.1 | Normal | Lowerlimb surgery |
| 4 | A | 20 | M | 1 | 96 | 15 | 130 | 90 | Normal | Normal | Normal | Normal | Normal | O + | 27.5 | 2.4 | 155 | 123 | 12 | 0.9 | 140 | 3.01 | Normal | Lowerlimb surgery |
| 5 | A | 60 | M | 2 | 96 | 16 | 134 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 11 | 4.7 | 52 | 96 | 20 | 0.7 | 136 | 3.8 | Normal | Lowerlimb surgery |
| 6 | A | 30 | F | 1 | 98 | 14 | 142 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 12 | 34 | 178 | 81 | 18 | 0.7 | 136 | 3.8 | Normal | Lowerlimb surgery |
| 7 | A | 45 | M | 1 | 100 | 15 | 130 | 84 | Pallor | Normal | Normal | Normal | Normal | O + | 7 | 96 | 39.8 | 93 | 19 | 0.9 | 140 | 3.01 | Normal | Lowerlimb surgery |
| 8 | A | 22 | F | 2 | 110 | 16 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 13.9 | 4.5 | 26 | 101 | 17 | 1.1 | 136 | 4.6 | Normal | Lowerlimb surgery |
| 9 | A | 46 | M | 1 | 100 | 18 | 110 | 78 | Normal | Normal | Normal | Normal | Normal | O + | 8.8 | 5.3 | 83 | 98 | 12 | 1.4 | 141 | 3.9 | Normal | Lowerlimb surgery |
| 10 | A | 32 | M | 2 | 90 | 17 | 132 | 92 | Normal | Normal | Normal | Normal | Normal | O + | 10.9 | 6.59 | 39 | 142 | 14 | 1 | 134 | 3.6 | Normal | Lowerlimb surgery |
| 11 | A | 34 | F | 2 | 90 | 20 | 126 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 14 | 2.8 | 44 | 98 | 15 | 1.4 | 141 | 3.9 | Normal | Lowerlimb surgery |
| 12 | A | 20 | M | 1 | 92 | 16 | 110 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 13.9 | 6.8 | 79 | 128 | 13 | 0.9 | 141 | 4.1 | Normal | Lowerlimb surgery |
| 13 | A | 23 | M | 2 | 86 | 18 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 12.2 | 5.46 | 105 | 128 | 16 | 0.9 | 141 | 4.1 | Normal | Lowerlimb surgery |
| 14 | A | 18 | M | 1 | 84 | 16 | 128 | 80 | Normal | Normal | Normal | Normal | Normal | B + | 13.3 | 3.6 | 41 | 126 | 13 | 0.9 | 138 | 4.1 | Normal | Lowerlimb surgery |
| 15 | A | 30 | M | 2 | 78 | 14 | 124 | 78 | Normal | Normal | Normal | Normal | Normal | AB + | 14.9 | 5.14 | 144 | 100 | 15 | 1 | 139 | 4.4 | Normal | Lowerlimb surgery |
| 16 | A | 22 | M | 1 | 96 | 15 | 130 | 90 | Normal | Normal | Normal | Normal | Normal | A + | 14.9 | 5.14 | 144 | 112 | 11 | 1 | 136 | 4.4 | Normal | Lowerlimb surgery |
| 17 | A | 24 | M | 2 | 96 | 16 | 134 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 13.4 | 2.29 | 47 | 132 | 12 | 0.9 | 132 | 4.4 | Normal | Lowerlimb surgery |
| 18 | A | 19 | M | 1 | 98 | 14 | 142 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 13.1 | 7 | 82 | 140 | 20 | 0.8 | 142 | 4 | Normal | Lowerlimb surgery |
| 19 | A | 27 | M | 2 | 100 | 15 | 130 | 84 | Normal | Normal | Normal | Normal | Normal | O + | 18.4 | 4.09 | 24 | 94 | 18 | 0.9 | 147 | 5 | Normal | Lowerlimb surgery |
| 20 | A | 40 | M | 1 | 110 | 16 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 12.4 | 5.2 | 114 | 132 | 19 | 1.1 | 140 | 4 | Normal | Lowerlimb surgery |
| 21 | A | 35 | M | 2 | 100 | 18 | 110 | 78 | Normal | Normal | Normal | Normal | Normal | O + | 14.1 | 6.4 | 54 | 118 | 17 | 1.1 | 139 | 3.8 | Normal | Lowerlimb surgery |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 22 | A | 19 | M | 1 | 90 | 17 | 132 | 92 | Normal | Normal | Normal | Normal | Normal | B + | 12.1 | 3.1 | 309 | 96 | 12 | 0.8 | 137 | 4.5 | Normal | Lowerlimb surgery |
| 23 | A | 24 | M | 2 | 90 | 20 | 126 | 80 | Normal | Normal | Normal | Normal | Normal | AB + | 27.5 | 2.4 | 155 | 94 | 14 | 0.9 | 142 | 4.4 | Normal | Lowerlimb surgery |
| 24 | A | 30 | M | 1 | 92 | 16 | 110 | 70 | Normal | Normal | Normal | Normal | Normal | A + | 11 | 4.7 | 52 | 99 | 15 | 1.1 | 140 | 5.1 | Normal | Lowerlimb surgery |
| 25 | A | 20 | M | 1 | 86 | 18 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 12 | 34 | 178 | 123 | 13 | 0.9 | 140 | 3.01 | Normal | Lowerlimb surgery |
| 26 | A | 60 | M | 2 | 84 | 16 | 128 | 80 | Normal | Normal | Normal | Normal | Normal | B + | 7 | 96 | 39.8 | 96 | 16 | 0.7 | 136 | 3.8 | Normal | Lowerlimb surgery |
| 27 | A | 30 | F | 1 | 78 | 14 | 124 | 78 | Normal | Normal | Normal | Normal | Normal | AB + | 13.9 | 4.5 | 26 | 81 | 13 | 0.7 | 136 | 3.8 | Normal | Lowerlimb surgery |
| 28 | A | 45 | M | 1 | 96 | 15 | 130 | 90 | Normal | Normal | Normal | Normal | Normal | A + | 8.8 | 5.3 | 83 | 93 | 15 | 0.9 | 140 | 3.01 | Normal | Lowerlimb surgery |
| 29 | B | 22 | F | 1 | 96 | 16 | 134 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 10.9 | 6.59 | 39 | 101 | 11 | 1.1 | 136 | 4.6 | Normal | Lowerlimb surgery |
| 30 | B | 46 | M | 2 | 98 | 14 | 142 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 14 | 2.8 | 44 | 98 | 12 | 1.4 | 141 | 3.9 | Normal | Lowerlimb surgery |
| 31 | B | 32 | M | 2 | 100 | 15 | 130 | 84 | Normal | Normal | Normal | Normal | Normal | O + | 13.9 | 6.8 | 79 | 142 | 20 | 1 | 134 | 3.6 | Normal | Lowerlimb surgery |
| 32 | B | 34 | F | 1 | 110 | 16 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 12.2 | 5.46 | 105 | 98 | 18 | 1.4 | 141 | 3.9 | Normal | Lowerlimb surgery |
| 33 | B | 20 | M | 2 | 100 | 18 | 110 | 78 | Normal | Normal | Normal | Normal | Normal | O + | 13.3 | 3.6 | 41 | 128 | 19 | 0.9 | 141 | 4.1 | Normal | Lowerlimb surgery |
| 34 | B | 23 | M | 1 | 90 | 17 | 132 | 92 | Normal | Normal | Normal | Normal | Normal | O + | 14.9 | 5.14 | 144 | 128 | 17 | 0.9 | 141 | 4.1 | Normal | Lowerlimb surgery |
| 35 | B | 18 | M | 1 | 90 | 20 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 14.9 | 5.14 | 144 | 126 | 12 | 0.9 | 138 | 4.1 | Normal | Lowerlimb surgery |
| 36 | B | 30 | M | 1 | 86 | 18 | 128 | 80 | Normal | Normal | Normal | Normal | Normal | B + | 13.4 | 2.29 | 47 | 100 | 14 | 1 | 139 | 4.4 | Normal | Lowerlimb surgery |
| 37 | B | 22 | M | 2 | 84 | 16 | 124 | 78 | Normal | Normal | Normal | Normal | Normal | AB + | 18.4 | 4.09 | 24 | 112 | 15 | 1 | 136 | 4.4 | Normal | Lowerlimb surgery |
| 38 | B | 24 | M | 2 | 78 | 14 | 130 | 90 | Normal | Normal | Normal | Normal | Normal | A + | 12.4 | 5.2 | 114 | 99 | 13 | 0.8 | 147 | 7.5 | Normal | Lowerlimb surgery |
| 39 | B | 27 | M | 1 | 96 | 15 | 134 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 14.1 | 6.4 | 54 | 180 | 16 | 1.4 | 143 | 5.1 | Normal | Lowerlimb surgery |
| 40 | B | 29 | F | 2 | 96 | 16 | 142 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 12.1 | 3.1 | 309 | 123 | 13 | 1.1 | 139 | 3.8 | Normal | Lowerlimb surgery |
| 41 | B | 23 | M | 1 | 98 | 14 | 130 | 84 | Normal | Normal | Normal | Normal | Normal | O + | 27.5 | 2.4 | 155 | 96 | 15 | 0.8 | 137 | 4.5 | Normal | Lowerlimb surgery |
| 42 | B | 24 | M | 1 | 100 | 15 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 11 | 4.7 | 52 | 81 | 11 | 0.9 | 142 | 4.4 | Normal | Lowerlimb surgery |
| 43 | B | 30 | M | 2 | 110 | 16 | 110 | 78 | Normal | Normal | Normal | Normal | Normal | O + | 12 | 34 | 178 | 93 | 12 | 1.1 | 140 | 5.1 | Normal | Lowerlimb surgery |
| 44 | B | 20 | M | 1 | 100 | 18 | 132 | 92 | Pallor | Normal | Normal | Normal | Normal | B + | 7 | 96 | 39.8 | 101 | 20 | 0.9 | 140 | 3.01 | Normal | Lowerlimb surgery |
| 45 | B | 60 | M | 2 | 90 | 17 | 126 | 80 | Normal | Normal | Normal | Normal | Normal | AB + | 13.9 | 4.5 | 26 | 98 | 18 | 0.7 | 136 | 3.8 | Normal | Lowerlimb surgery |
| 46 | B | 30 | F | 2 | 90 | 20 | 110 | 70 | Normal | Normal | Normal | Normal | Normal | A + | 8.8 | 5.3 | 83 | 142 | 19 | 0.7 | 136 | 3.8 | Normal | Lowerlimb surgery |
| 47 | B | 45 | M | 1 | 92 | 16 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | O + | 10.9 | 6.59 | 39 | 98 | 17 | 0.9 | 140 | 3.01 | Normal | Lowerlimb surgery |
| 48 | B | 22 | F | 2 | 86 | 18 | 128 | 80 | Normal | Normal | Normal | Normal | Normal | B + | 14 | 2.8 | 44 | 128 | 12 | 1.1 | 136 | 4.6 | Normal | Lowerlimb surgery |
| 49 | B | 46 | M | 1 | 84 | 16 | 124 | 78 | Normal | Normal | Normal | Normal | Normal | AB + | 13.9 | 6.8 | 79 | 128 | 14 | 1.4 | 141 | 3.9 | Normal | Lowerlimb surgery |
| 50 | B | 32 | M | 2 | 78 | 14 | 130 | 90 | Normal | Normal | Normal | Normal | Normal | A + | 12.2 | 5.46 | 105 | 126 | 15 | 1 | 134 | 3.6 | Normal | Lowerlimb surgery |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 51 | B | 34 | F | 1 | 96 | 15 | 134 | 70 | Normal | Normal | Normal | Normal | Normal | O + | 13.3 | 3.6 | 41 | 100 | 13 | 1.4 | 141 | 3.9 | Normal | Lowerlimb surgery |
| 52 | B | 20 | M | 2 | 96 | 16 | 142 | 70 | Normal | Normal | Normal | Normal | Normal | A- | 14.9 | 5.14 | 144 | 112 | 16 | 0.9 | 141 | 4.1 | Normal | Lowerlimb surgery |
| 53 | B | 23 | M | 1 | 98 | 14 | 130 | 84 | Normal | Normal | Normal | Normal | Normal | O + | 14.9 | 5.14 | 144 | 99 | 18 | 0.9 | 141 | 4.1 | Normal | Lowerlimb surgery |
| 54 | B | 18 | M | 2 | 100 | 15 | 118 | 80 | Normal | Normal | Normal | Normal | Normal | A + | 13.4 | 2.29 | 47 | 180 | 12 | 0.9 | 138 | 4.1 | Normal | Lowerlimb surgery |
| 55 | B | 30 | M | 1 | 110 | 16 | 110 | 78 | Normal | Normal | Normal | Normal | Normal | B + | 18.4 | 4.09 | 24 | 96 | 19 | 1 | 139 | 4.4 | Normal | Lowerlimb surgery |
| 56 | B | 22 | M | 2 | 100 | 18 | 132 | 92 | Normal | Normal | Normal | Normal | Normal | AB + | 12.4 | 5.2 | 114 | 115 | 11 | 1 | 136 | 4.4 | Normal | Lowerlimb surgery |

| Sl No | Group | Immediate_NRS | 1 hr_NRS | 2 hr_NRS | 4 hr_NRS | 8 hr_NRS | 12 hr_NRS | 24 hr_NRS | 36 hr_NRS | 48 hr_NRS | 60 hr_NRS | 72 hr_NRS | Immediate_Rescue analgesia | 1 hr_Rescue analgesia | 2 hr_Rescue | 4 hr_Rescue | 8 hr_Rescue | 12 hr_Rescue | 24 hr_Rescue | 36 hr_Rescue | 48 hr_Rescue | 60 hr_Rescue | 72 hr_Rescue |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | A | 8 | 8 | 7 | 5 | 4 | 4 | 3 | 2 | 3 | 3 | 2 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 2 | A | 8 | 8 | 7 | 4 | 4 | 4 | 5 | 2 | 2 | 2 | 2 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 3 | A | 8 | 8 | 6 | 4 | 5 | 5 | 4 | 2 | 3 | 3 | 3 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 4 | A | 9 | 9 | 7 | 5 | 5 | 5 | 4 | 3 | 3 | 3 | 2 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 5 | A | 8 | 8 | 6 | 5 | 4 | 4 | 5 | 2 | 3 | 3 | 2 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 6 | A | 8 | 8 | 7 | 4 | 5 | 5 | 5 | 2 | 2 | 2 | 1 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 7 | A | 8 | 8 | 6 | 5 | 4 | 4 | 4 | 2 | 3 | 3 | 2 | Yes | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 8 | A | 9 | 9 | 7 | 4 | 5 | 5 | 5 | 3 | 2 | 2 | 2 | Yes | No | No | No | No | No | No | No | No | No | No |
| 9 | A | 8 | 8 | 6 | 5 | 5 | 5 | 4 | 2 | 3 | 3 | 1 | Yes | No | No | No | No | No | No | No | No | No | No |
| 10 | A | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | Yes | No | No | Yes | No | No | No | No | No | No |
| 11 | A | 8 | 8 | 7 | 5 | 4 | 4 | 5 | 2 | 3 | 3 | 2 | No | Yes | No | No | Yes | No | No | No | No | No | No |
| 12 | A | 8 | 8 | 7 | 4 | 4 | 4 | 5 | 2 | 2 | 2 | 2 | No | Yes | No | No | Yes | No | No | No | No | No | No |
| 13 | A | 8 | 8 | 6 | 4 | 5 | 5 | 4 | 2 | 3 | 3 | 3 | No | Yes | No | No | Yes | No | No | No | No | No | No |
| 14 | A | 9 | 9 | 7 | 5 | 5 | 5 | 4 | 3 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 15 | A | 8 | 8 | 6 | 5 | 4 | 4 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 16 | A | 8 | 8 | 7 | 4 | 5 | 5 | 5 | 2 | 2 | 2 | 1 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 17 | A | 8 | 8 | 6 | 5 | 4 | 4 | 4 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 18 | A | 9 | 9 | 7 | 4 | 5 | 5 | 4 | 3 | 2 | 2 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 19 | A | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 1 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 20 | A | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 21 | A | 8 | 8 | 7 | 5 | 4 | 4 | 5 | 2 | 3 | 3 | 2 | No | Yes | No | No | Yes | No | No | No | No | No | No |
| 22 | A | 8 | 8 | 7 | 4 | 4 | 4 | 4 | 2 | 2 | 2 | 2 | Yes | No | No | No | No | No | No | No | No | No | No |
| 23 | A | 8 | 8 | 6 | 4 | 4 | 4 | 4 | 2 | 3 | 3 | 3 | Yes | No | No | No | No | No | No | No | No | No | No |
| 24 | A | 9 | 9 | 7 | 5 | 5 | 5 | 5 | 3 | 3 | 3 | 2 | No | Yes | No | Yes | Yes | No | Yes | No | Yes | No | No |
| 25 | A | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | Yes | No | No | Yes | No | No | No | No | No | No |

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 26 | A | 8 | 8 | 7 | 4 | 4 | 4 | 4 | 2 | 2 | 2 | 1 | No | No | No | No | No | No | No | No | No | No |
| 27 | A | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 28 | A | 9 | 9 | 7 | 4 | 4 | 4 | 4 | 3 | 2 | 2 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 29 | B | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 1 | Yes | No | Yes | No | No | Yes | No | Yes | No | No |
| 30 | B | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 31 | B | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | Yes |
| 32 | B | 8 | 8 | 7 | 4 | 4 | 4 | 4 | 2 | 2 | 2 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 33 | B | 8 | 8 | 6 | 4 | 4 | 4 | 4 | 2 | 3 | 3 | 3 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 34 | B | 9 | 9 | 7 | 5 | 5 | 5 | 5 | 3 | 3 | 3 | 2 | Yes | No | No | No | No | No | No | No | No | No |
| 35 | B | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | yes | No | No | yes | No | No | No | No | No |
| 36 | B | 8 | 8 | 7 | 5 | 4 | 4 | 3 | 2 | 3 | 3 | 2 | No | Yes | No | No | Yes | No | No | No | No | No |
| 37 | B | 8 | 8 | 7 | 4 | 5 | 5 | 5 | 2 | 2 | 2 | 2 | No | No | Yes | No | No | No | No | No | No | No |
| 38 | B | 8 | 8 | 6 | 4 | 4 | 4 | 4 | 2 | 3 | 3 | 3 | No | No | No | Yes | No | No | No | No | No | No |
| 39 | B | 9 | 9 | 7 | 5 | 5 | 5 | 4 | 3 | 3 | 3 | 2 | Yes | No | No | No | No | No | No | No | No | No |
| 40 | B | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 41 | B | 8 | 8 | 7 | 4 | 5 | 5 | 5 | 2 | 2 | 2 | 1 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 42 | B | 8 | 8 | 6 | 5 | 4 | 4 | 4 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 43 | B | 9 | 9 | 7 | 4 | 4 | 4 | 5 | 3 | 2 | 2 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 44 | B | 8 | 8 | 6 | 5 | 4 | 4 | 4 | 2 | 3 | 3 | 1 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 45 | B | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | Yes | No | Yes | No | No | Yes | No | Yes | No | No |
| 46 | B | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 47 | B | 8 | 8 | 7 | 4 | 4 | 4 | 5 | 2 | 2 | 2 | 2 | No | No | No | Yes | No | No | No | No | No | No |
| 48 | B | 8 | 8 | 6 | 4 | 5 | 5 | 4 | 2 | 3 | 3 | 3 | No | No | No | Yes | No | No | No | No | No | No |
| 49 | B | 9 | 9 | 7 | 5 | 4 | 4 | 4 | 3 | 3 | 3 | 2 | No | No | No | Yes | No | No | No | No | No | No |
| 50 | B | 8 | 8 | 6 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | No | Yes | No | No | No | No | No | No |
| 51 | B | 8 | 8 | 7 | 4 | 5 | 5 | 5 | 2 | 2 | 2 | 1 | No | No | No | Yes | No | No | No | No | No | No |
| 52 | B | 8 | 8 | 6 | 5 | 5 | 5 | 4 | 2 | 3 | 3 | 2 | No | No | Yes | No | No | Yes | No | Yes | No | No |
| 53 | B | 9 | 9 | 7 | 4 | 4 | 4 | 4 | 3 | 2 | 2 | 2 | No | Yes | No | No | Yes | No | No | No | No | No |
| 54 | B | 8 | 8 | 6 | 5 | 4 | 4 | 5 | 2 | 3 | 3 | 1 | Yes | No | No | No | No | No | No | No | No | No |

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 55 | B | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | Yes | No | No | Yes | No | No | No | No | No | No |
| 56 | B | 8 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 3 | 2 | No | No | No | No | No | No | No | No | No | No | No |