A Randomized Comparative Clinical Trial To Know The Efficacy Of Ultrasound Guided Transversus Abdominis Plane Block Against Multimodal Analgesia For Post-Operative Analgesia Following Caesarean Section

by

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ABBREVIATION

ASA	American Society of Anaesthesiologists
b/l	bilateral
Bpm	Beats per minute
cm	centimeter
DS	Diclofenac Sodium
ECG	Electrocardiography
Fig	Figure
g	Gram
Hg	Mercury
hrs	hours
IM	Intramuscular
IPD No	In-Patient Department number
IV	Intravenous
kg	kilogram
LA	Local Anaesthetic
min	minute
ml	milliliter
NIBP	Non-Invasive Blood Pressure
NRS	Numerical Rating Scale
PACU	Post Anaesthesia Care Unit
PCA	Patient Controlled Analgesia
PONV	Post-Operative Nausea and Vomiting
PR	Pulse rate
SPO_2	Arterial Oxygen Saturation

TAPB	Transversus Abdominis Plane Block
USG	Ultrasonography
VAS	Visual Analogue Scale
VRS	Verbal Rating Scale
yrs	years

ABSTRACT

Introduction:

Transversus abdominis plane (TAP) block as a technique of regional anaesthesia which has been applied as one of the segment of pain control regimen in abdominal surgeries including caesarean sections. In this study we have compared the efficacy of TAP Block against multimodal analgesia.

Key Words:

TAP Block, Caesarean Section, Multimodal analgesia, Bupivacaine.

Aims:

To study

- Reduction of the additional Rescue analgesia 24 hours following caesarean section.
- Duration of analgesia, patient satisfaction, adverse effects like- PONV and sedation.

Methods:

Prospective randomized clinical study was conducted in the department of Anesthesia at _____

_____

Ethical Committee permission- Taken

Informed written consent- Taken

Total of 60 patients scheduled for caesarean section were allotted into two groups.

Group I

USG-guided Bilateral TAP Block with 15ml of 0.25% Bupivacaine was performed on each side following caesarean section.

Group II

Received standard analgesia according to Obstetric department protocol consisting Intramuscular(IM) Diclofenac 75mg, Intravenous(IV) Paracetamol(1000mg) and IV Pentazocine 0.5mg/kg body weight stat at the end of surgery.

Test used were Chi square test, unpaired t test.

Inclusion criteria

- American Society of Anesthesiologists(ASA) status II and III.
- >18 years of age who is pregnant presenting for a caesarean delivery

Exclusion criteria

- Inability to consent.
- Any contraindication to spinal anaesthesia.
- Allergy to local anesthetic agents.
- Local infection.
- Coagulopathy.

Results:

Pain on movement and opioid consumption was found to be lesser in TAP Block (17.2 ±10.4mg vs 28.9±24.2mg), VAS was lower in the TAP block group at the end of 24 hour (0.30±0.75 vs 5.27±0.78). Time for the demand of 1st rescue analgesia was prolonged to 8.9 hours from 3.1 hours. Reduced incidence of PONV and Sedation.

Conclusion:

TAP block is easy to perform under ultrasound guidance and provides effective analgesia with reduced incidence of sedation and PONV.

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INTRODUCTION

Though there are availability of numerous analgesic modalities, management of post-operative pain still continues to be a challenge today. Numerous data has showed that 70% of patients who undergo surgical procedures report to have post-operative pain and it is often inadequately treated in the hospital setting.[1] Untreated or inadequately treated post-operative pain is associated with reduced patient satisfaction, delayed patient recovery, longer hospitalizations and increased medical care costs.[2]

Caesarean section is the most commonly performed surgical procedures in day to day practice by the obstetricians. Pain after cesarean section is commonly defined to be ranging from moderate to severe and failure to the suppress pain may affect the mother-baby bonding, care of baby and also breast feeding[3] and the may result in thromboembolism.[4] These patients require a multimodal post-operative pain treatment regimen that provides high quality analgesia with minimal side effects. The use of opioids for pain management can result in significant adverse effects including sedation, nausea, vomiting and may also be secreted in the breast milk which leads to adverse effects in the neonates making it a necessity to find alternative approaches which reduce the post-operative requirement of strong opioids.

Transversus abdominis plane (TAP) block is a technique of regional anaesthesia which made its appearance in the anaesthesia literature for the first time in the year 2001 and has been applied as one of the segment of pain control regimen in abdominal surgeries including caesarean sections. The injection of local anaesthetic solution in the neuro fascial plane in the anterior abdominal wall has proven itself to be an effective adjunct to central neuraxial narcotic administration. TAP block offers

greater pain relief with lesser side effects and increased patient satisfaction. The duration of TAP block depends on administered local anaesthetic (LA).

The administration of the local anaesthetics centrally (Epidural or Intrathecal) is found effective but, it is associated with hypotension, reduced mobility and also poses a great chance of harm to the patient. Considering the effects of central administration, it is safer to administer local anaesthetic solution into Transversus Abdominis plane, Rectus sheath, Intraperitoneal infiltration. When used for regional blocks the risk of higher plasma levels, cardiac and neurotoxicity of the local anaesthetic solution should always be considered in view of larger amounts of the drug used for blocks. The availability and knowledge of lipid emulsion should be available for the treatment of LA toxicity if occurs.

Since the introduction of Ultrasound(US) in the field of anaesthesiology it has become an indispensable tool for anaesthesiologist and now has become the Gold Standard to perform various peripheral and truncal blocks as recommended by several International guidelines since it permits indirect visualization of the structures like-vessels, muscles and nerves. Though the TAP Block has been popularized for nearly 10 years ago, there has been a growing evidence recently to support the usefulness of the technique. Main principle of TAP Block is to block the sensory motor nerve fibers of the anterior abdominal wall, which is supplied by the anterior rami of the segments T_7-L_1 by injecting the local anaesthetic solution into the plane between the internal oblique and transverse abdominis, which also covers the incision site.[5,6]

Studies have shown that addition of adjuvants like dexamethasone, epinephrine, ketamine, clonidine and fentanyl to the LA solution have resulted in the longer duration of local anaesthetic action, reduced VAS and reduced need for rescue analgesic doses in terms of amount and additional dose requirement.[7-10]

This study aims to compare the efficacy of the Ultrasound guided TAP Block by using 0.25% Bupivacaine versus parenteral analgesics

AIMS AND OBJECTIVES OF THE STUDY

AIMS:

Evaluation of the Transversus Abdominis Plane Block for post-operative analgesia following caesarean section.

OBJECTIVES:

To compare the efficacy of TAP block with multi drug therapy in post-caesarean section with respect to:

1. PRIMARY:

- Reduction of the additional Rescue analgesia 24 hours following caesarean section.

2. SECONDARY:

- To reduce severity of pain.
- To prolong the demand of first analgesic.
- Improve patient satisfaction during post-operative period.
- To reduce the complications following use of analgesics - Sedation, Nausea, Vomiting.

REVIEW OF LITERATURE

TAP blocks have been described as an effective component of multimodal post-operative analgesia for a wide variety of abdominal procedures including large bowel resection, open / laparoscopic appendicectomy, cesarean section, total abdominal hysterectomy, laparoscopic cholecystectomy, open prostatectomy, renal transplant surgery, abdominoplasty with / without flank liposuction and iliac crest bone graft [11]. Most reports demonstrate the efficacy of TAP blocks by highlighting some combination of reduced post-operative opioid requirement, lower pain scores and reduction in opioid-related side effects.

Several studies have revealed that when a TAP block is added to post-operative analgesic regimen, post-operative pain following cesarean delivery is reduced.

In the year 2019, a study conducted by S. Naveen et al. with One hundred and forty patients who were to undergo LSCS were selected and randomly divided into two groups: CONTROL and TAP. CONT group received subarachnoid block (SAB) with hyperbaric bupivacaine and TAP group received similar SAB along with TAP block immediately after surgery under ultrasound guidance with 20 ml of 0.25% bupivacaine with 4 mg dexamethasone on bilaterally. All the patients were monitored for pain in postoperative period, every hour for 1st 4 hrs and 2 hourly for next 4 hrs and then at 12, 18, 24, 36, and 48 hrs with visual analog scale of scale 0 to 10. All the patients received intravenous paracetamol 1000 mg 8 hourly. If VAS score crossed four, they were given intramuscular (IM) diclofenac sodium 75 mg and if pain score persisted above four after an hour, they were given IM pethidine 50 mg. The time to requirement/demand of rescue analgesia was noted and a total amount of opioids given were noted. The results of the study showed that the mean time to first rescue

analgesic was significantly prolonged in Group TAP when compared to CONT group using unpaired t-test. Mean time to rescue analgesia was 88.02 ± 21.62 min and 525.27 ± 114.52 min (P < 0.001) in groups CONT and TAP, respectively. Opioid consumption was found to be 14.29 mg versus 166.95 mg (P < 0.001) respectively in TAP and CONT groups in 48 h. They concluded that TAP block is a very effective modality for postoperative pain relief after LSCS. It helps in reducing opioid consumption and is likely to keep them more alert.[12]

In the year 2018, a study was conducted by Nabanita Das et al. for Comparison of analgesic efficacy between TAP block and local site infiltration post operatively in caesarean section. The study was conducted with 60 patients posted for elective and emergency caesarean section. They were blindly divided into two groups of 30 patients each. Group T received 40ml 0.25% Ropivacaine in Transverses abdominis plane (TAP) block for postoperative analgesia while group I received 40ml 0.25% Ropivacaine as infiltration at incision site for postoperative analgesia. All the Patients were assessed for numeric pain score, analgesic requirements, total analgesic consumption and adverse effects if any for 24hrs postoperatively. The results showed that there was significantly high difference in numeric pain scores at 2^{nd}, 6^{th}, 12^{th} and 24^{th} hours ($p<0.0001$) along with the time for first rescue analgesic and total amount of analgesic consumed were statistically significant($p<0.0001$). They concluded that TAP block in efficient than local wound infiltration.[13]

In the year 2016, Maitreyi Gajanan Mankikar et al. conducted on Ultrasound-guided Transversus Abdominis Plane Block for post-operative analgesia in patients undergoing caesarean section with sixty patients and results showed that TAP Block was associated with reduced VAS and requirement of

rescue analgesia with prolonged duration of demand of first rescue analgesia 4.1 to 9.53 h.

In the year 2015, Uma Srivastava et al. conducted a double blind, randomized trial on Transversus Abdominis Plane Block with 62 patients who underwent caesarean section. Results showed that TAP Block was associated with lower pain scores both on activity and at rest, higher satisfaction, significantly longer time of first rescue analgesia, lesser side effects and rescue analgesia dose was reduced by 50% during 48h post-surgery. [15]

In the year 2013 Lee et al. conducted a randomized double-blind, placebo-controlled study on TAP Block in conjunction with Intrathecal Morphine with 51 women undergoing elective caesarean section. All the patients received spinal anaesthesia with 0.5%hyperbaric Bupivaciane solution with Fentanyl 15mcg, one group received Intrathecal 0.25mg Morphine along with TAP Block with 20ml of 0.9%NS while the other group received b/l TAP Block with 20ml 0.5% Ropivacaine under USG-guidance. Post-operatively all the patients were assessed at 2,24,48 hours for Verbal pain scores at rest, movement and also for colicky pain, Analgesic consumption and any side effects due to opioid. The results showed that the pain scores at initial two hours both at rest and on movement were lesser with ropivacaine group when compared to the saline group (0.5 and 1.9 Vs 2.8 and 4.9) and had no analgesic requirements. There was no difference in pain scores at rest, movement and analgesic consumption at 24 hrs in both the groups. At the end of 48hrs it showed that Ropivacaine group received analgesia for moderate pain (P=0.04) when compared to saline group which received more analgesic for severe pain (P=0.01). They concluded that the TAP Block was found to provide a superior analgesia in conjunction with intrathecal Morphine.[16]

In the year 2013, Onishi et al.conducted a study to know whether addition of TAP Block provided additional analgesic effect when compared to Epidural morphine with 94 patients undergoing elective caesarean sections. All the patients had epidural catheter inserted and caesarean sections were performed after spinal anaesthesia with 0.5% hyperbaric bupivacaine. One group received epidural morphine and other received TAP Block with 0.375% Ropivacaine or Levobupivacaine 0.3% 20ml on either sides of abdomen after the surgery. Both the groups received standard post-op analgesic regimen with PCA with morphine for the next 24 hours. The results showed that time for request of 1st rescue analgesia was significantly higher in TAP Block group(555min) when compared to control group (215min) and also morphine consumption was lower in TAP Block group (5.3mg Vs 7.7mg). They concluded that TAP Block had additional analgesia when compared to epidural morphine alone.[17]

In the year 2012, Tan TT et al. conducted a randomized trial with 40 patients who underwent caesarean section under general anaesthesia. They showed that TAP block with Levobupivacaine was associated with reduced morphine requirement in the 24 h postoperative period [12.3 (2.6) vs. 31.4 mg (3.1), P<0.001)] and higher satisfaction but, there were no differences in VAS score, nausea, vomiting and sedation. [18]

In the year 2012, study conducted by Eslamian L et al. on fifty patients who underwent caesarean section under general anesthesia. Showed that TAP Block was associated with reduced VAS, when assessed at discharge from recovery room, 6, 12 and 24 hrs post-operatively. TAP Block also prolonged the time of first rescue analgesia [210 min (0-300) vs. 30 min (10-180)] along with reduced opioid requirement Tramadol [50 mg (0-150) vs. 250 mg (0-400), P = 0.001].[19]

In the year 2012, Abdallah FW et al. conducted a study on Transversus abdominis plane block for post-operative analgesia after Caesarean delivery performed under spinal anesthesia-A systematic review and meta-analysis. The results showed that the mean consumption of morphine in TAP blocks was reduced by 24 mg, when spinal morphine was not used. TAP also decreased visual analog pain score by 0.8 (10 cm line where 0 cm, no pain, 10 cm worst pain), and decreased the incidence of opioid-related side effects. When using spinal morphine, the differences in primary and secondary outcomes were not significant. In the setting of a multi-mode analgesic regimen that excludes intrathecal morphine, TAP block offers better analgesia than placebo and can decrease the first 24 hour morphine usage. TAP block may offer effective analgesia if there are contraindications for intrathecal use of morphine or not being used.[20]

In the year 2010, Baaj JM et al. conducted a double blind placebo controlled, randomized study on the efficacy of ultrasound guided TAP Block for post caesarean section analgesia with 40 patients undergoing caesarean delivery under spinal anesthesia with Bupivacaine and Fentanyl. At the end of the operation, All patients received a bilateral ultrasound-guided TAP block either with Bupivacaine 0.25% (B group) or saline (S group or placebo group) followed only by IV Morphine as patient controlled analgesia. The results showed that total morphine consumption was reduced by more than 60 percent in the Bupivacaine group; Bupivacaine group reported an improved satisfaction with their pain relief.[21]

In the year 2010 Kanazi et al. conducted a study to know the efficacy of TAP Block for post-operative analgesia in caesarean section with 57 patients undergoing caesarean section under spinal anaesthesia. All the patients received spinal anaesthesia with 0.5% hyperbaric bupivacaine, one group received 0.2mg morphine

intrathecally while other group received b/l TAP Block with 20ml of 0.375% bupivacaine plus epinephrine 5mcg/ml. All the patients were recorded for the time of request of 1st analgesia, pain scores at rest and on movement, analgesic requirement, nausea, vomiting, pruritis, sedation and respiratory depression at 2, 4, 6, 12, 24, 36 and 48hours. The results showed that patients in the TAP group requested pain medication at 4 hours compared to 8 hours in the subarachnoid morphine group. After 12 hours there was no statistically significant difference between the two groups. Post-operative VAS scores at rest at 0, 2 and 4 hours and on movement at 2 and 4 hours were lower in the subarachnoid group than in the TAP group and were not significantly different at all other time points. Nausea scores were higher at 2, 4 and 6 hours in the subarachnoid morphine group with sedation being comparable between the two groups. Higher pruritus scores were recorded in the subarachnoid group at 2, 4, 6 and 12 hours post-operatively versus none in the TAP group. There was no difference in the satisfaction scores between the two groups. The authors concluded that as part of a multimodal analgesia, subarachnoid morphine provided better pain relief than did the TAP block.[22]

In the year 2010, Owen et al. conducted a study with 34 women undergoing caesarean section. One group received b/l surgical TAP Block with 0.25% bupivacaine after closure of uterus. The other group did not receive TAP Block. Both the groups received IM morphine 10mg at the end of procedure. All the participants were recorded for total morphine consumption and time to request of first morphine rescue analgesia. The results showed that TAP Block patients had significantly longer time to first request of Morphine (P=0.04) and reduced morphine requirement (P=0.011) when compared to the control group. They concluded that morphine

requirement was reduced in the patients receiving TAP Block as a part of multimodal analgesia.[23]

A randomized, double-blind placebo-controlled trial in a tertiary maternity hospital was performed by Belavy D et al in 2009. Fifty women who underwent Caesarean delivery received 0.5% Ropivacaine or saline for bilateral TAP blocks under US-Guidance. The spinal anesthesia with Bupivacaine and Fentanyl was given to all of the participants, accompanied by postoperative acetaminophen, non-steroidal anti-inflammatory drug, IV Morphine, provide as PCA without intrathecal opioids. For morphine usage, average pain score, nausea, vomiting, pruritus and pain relief satisfaction, each patient was evaluated 24 hours after delivery. There were 47 patients-23 separated into the active group and 24 in the placebo group. Active group (median 18.0 mg), compared to placebo (median 31.5 mg, $P<0.05$), had a decreased 24-hour total morphine use compared with the placebo group (average 96 vs 77 mm, P=0,008), the active group recorded an increased degree of pain relief. The anti-emetics required in the active group were reduced (P=0.03). There were no local problems due to TAP, but after Ropivacaine injection one patient experienced an anaphylactoid reaction. They found that, when used as part of a multimodal analgesic regime, the US guided TAP block reduced the morphine demands after Caesarean section.[24]

In the year 2009 Costello et al. conducted a study to know if TAP Block provided superior analgesia when used as a part of multimodal analgesia along with intrathecal morphine with 100 subjects who were to undergo caesarean section. All the patients received spinal anaesthesia with 0.5% hyperbaric bupivacaine with 10mcg fentanyl or 100mcg morphine, one group received TAP Block with 0.375% Ropivacaine and other group received TAP Block with NS. All the patients were

assessed at 6, 12, 24 and 48 hours for VAS pain scores at rest and on movement, total supplemental narcotic consumption, satisfaction with pain management and presence of abdominal pain at 6 weeks duration. The results showed that there was not any statistical difference between Ropivacaine and placebo in the initial 24 hrs, they concluded that the addition of TAP Block as a part of multimodal analgesia with intrathecal morphine conferred no additional analgesia.[26]

In 2008, McDonnell JG et al. conducted a randomized controlled trial to evaluate analgesic effectiveness of the transversus abdominal plane block with fifty patients who underwent elective caesarean section and concluded that TAP Block was associated with lower morphine requirement (66 +/-26 vs. 18+/-14 mg, $p < 0,001$) and had reduced incidences of side effects.[27]

In the year 2007, McDonnell JG et a.l conducted a prospective randomized controlled trial on the analgesic efficacy of transversus abdominis plane block with Thirty-two adults undergoing large bowel resection via a midline abdominal incision and concluded that TAP Block was associated with reduction in the demand of morphine (21.9+/-8.9 mg vs 80.4 +/-19.2 mg, $P < 0.05$), reduced VAS (1 +/-1.4 vs 6.6 +/-2.8, $P < 0.05$) and higher satisfaction with pain management.[28]

PAIN:

DEFINITION:

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience which is primarily associated with tissue damage or describe in terms of such damage or both." This definition recognizes that pain is a perception and not a sensation. One influential model described pain in terms of three hierarchical levels: a sensory-discriminative component (e.g. location, intensity, quality), a motivational–affective component (e.g. depression, anxiety) and a cognitive-evaluative component. [28]

The "pain" system:

The "pain system" ideally be called as the "nociceptive system" because pain is a result subjective perception of nociception. Nociception is the processing and encoding of noxious stimuli that occurs in the nervous system that can be measured with the help of electrophysiological techniques. A schematic representation of the nociceptive system is done in Fig. 1. A noxious stimulus is picked up by the free nerve endings which are formed by the Aδ and C type of peripheral nerve fibers. Nociceptors are usually polymodal, responding to noxious stimulus like- thermal (heat or cold), chemical and mechanical (painful pressure, squeezing or cutting).[29] The sensory molecules at the nerve terminals will transduce these noxious stimulus into a sensory potential and when sufficiently higher potentials are reached leads to action potential and are conducted to the brain stem or spinal cord by the axons of the dorsal horn.

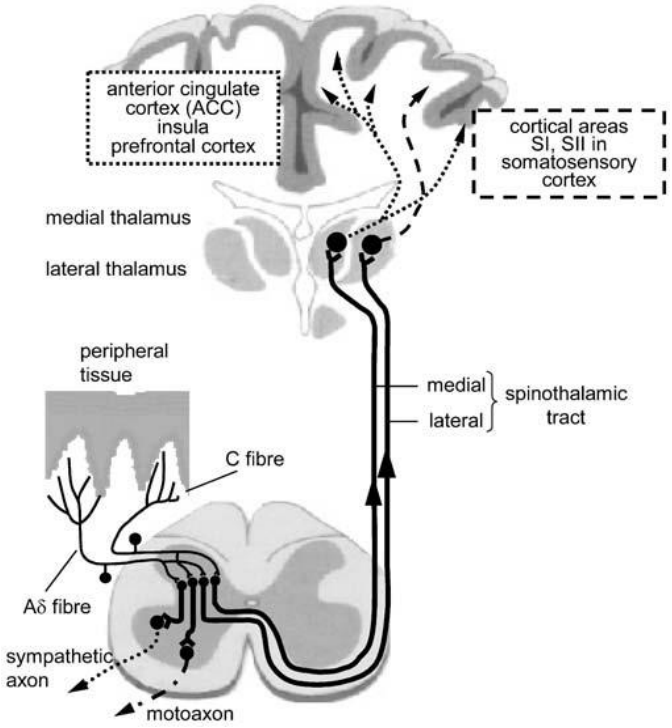


Fig. 1: Schematic representation of the nociceptive system with nociceptive free nerve endings located in the peripheral tissue, afferent nerve fibers and their synapses in the dorsal horn of the spinal cord, also depicting the medial and lateral spinothalamic tracts which ascend to the medial and lateral thalamus and interneurons finally projecting into motor and sympathetic reflex pathways.[30]

Dorsal horn neurons are activated by the nociceptors through their synapses. The dorsal horn contains fibers for ascending tract neurons or interneurons that form a part of either vegetative reflex or segmental motor pathway. The conscious pain sensation is carried by the neurons in the lateral spinothalamic tract which activate the thalamocortical system. The pain sensation has two aspects: A discriminative aspect- in which the noxious stimulus is analysed for its location, intensity and duration which is brought about by the lateral thalamocortical system whose relay nuclei is in the lateral thalamus and Areas SI and SII in the postcentral gyrus. An Affective aspect- which picks up the noxious stimulus as unpleasant and produces aversive

response. This is produced in the Medial thalamocortical system whose relay nuclei is in the medial and central thalamus, prefrontal and insula cortex and in the Anterior Cingulate Gyrus.[30]

Types of Pain:

When a noxious stimulus is applied it elicits acute physiological nociceptive pain in normal tissues. (Fig. 2). This pain elicits withdrawal reflexes which protects the tissues from further damage. When tissues are inflamed or injured leads to pathophysiological nociception.

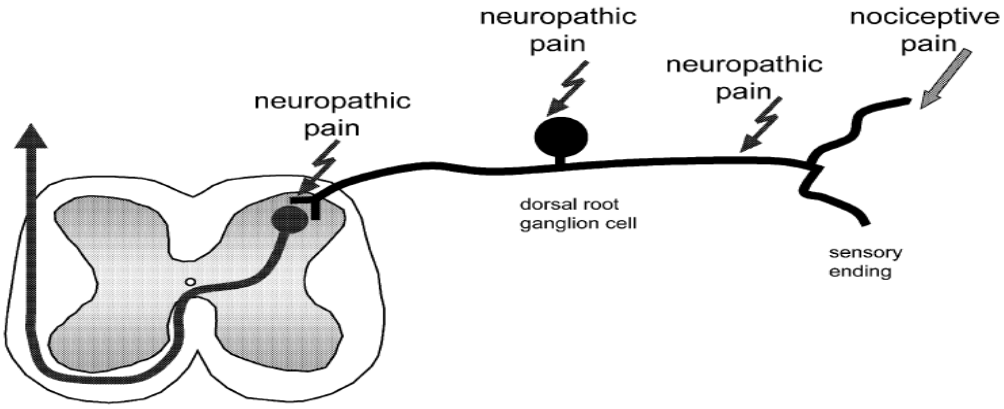


Fig. 2: Sketch of dorsal horn of spinal cord with synapse of nociceptive afferent. Nociceptive pain is caused by the noxious stimulation of nociceptor at its sensory nerve endings. Neuropathic pain is caused by the pathological stimulation of dorsal root ganglion, axon of the neurons of central nervous system. [30]

This pain does primarily signal noxious tissue stimulation and therefore feels abnormal. Pain often has electrical or burning character and can occur in short episodes like in neuralgias or can be persistent. Pain might be associated with allodynia or hyperalgesia.

Acute Pain

Defines as "the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus associated with surgery, trauma and acute illness". Patient's attitudes, beliefs and personalities also strongly affect their immediate experience of acute pain. Acute pain should therefore be viewed as the initiation phase of an extensive, persistent nociceptive and behavioral cascade triggered by tissue injury. [31]

Chronic Pain

The pain is usually called "Chronic" if it lasts for more than 6 months. Recently chronic pain is being defined by its character. There has been no tight relationship between pain and nociception and pain does not depict tissue damage in many chronic pain states. The social and psychological factors appear to play a role in the pain. Chronic disease which stimulates nociceptive processes persistently also result in chronic pain, which may be associated with dysphoria, fatigue, neuroendocrine dysregulation and impaired mental and physical performance.[32]

Assessment of Pain:

Pain assessment can be a simple and straightforward, when dealing with acute pain and pain as a symptom of trauma or disease. In clinical practice, assessment of intensity and location of pain is often sufficient. Evaluation of long-lasting pain and therapy consequences is more difficult in both patients with non-malignant causes of pain and patients with cancer pain. To evaluate qualitative elements of chronic pain and its effect on function, numerous tools have been created for varying types and subtypes of chronic pain situations.

Assessment of pain intensity and Pain Relief in Acute Pain

The location, temporal aspects and intensity of the pain are very important for acute pain triggered by trauma, surgery, childbirth or a serious medical illness to characterize pain, and evaluate the impact of therapy on pain and its underlying cause.

Assessment of Intensity of Acute Pain

The well-known Visual Analogue Scale (VAS) and Numerical Rating Scale (NRS) for the pain intensity evaluation are equally sensitive and agree well in assessing acute pain after surgery and both are superior to categorical four-point Verbal Rating Scale (VRS). They work best for the patient's subjective sense of the present pain intensity.

They can be used for the worst, least, or average pain over the last 24 hours. There are some limitations with this, such as the memory of pain is not precise and often colored by altering context factors. They are also used to evaluate pain unpleasantness and to grade the degree of functional effect of pain. The ranges of the NRS scale categories showed approximately that both patients and individuals at different points of time differ considerably (Figure 3): the superiority of the VAS and NRS over VRS was shown by the simultaneous recordings of VAS, NRS and VRS scales in a large number of patients.[33]

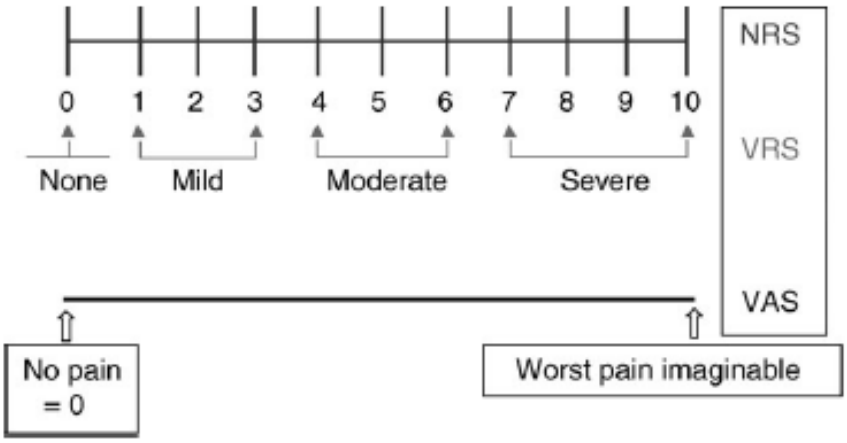
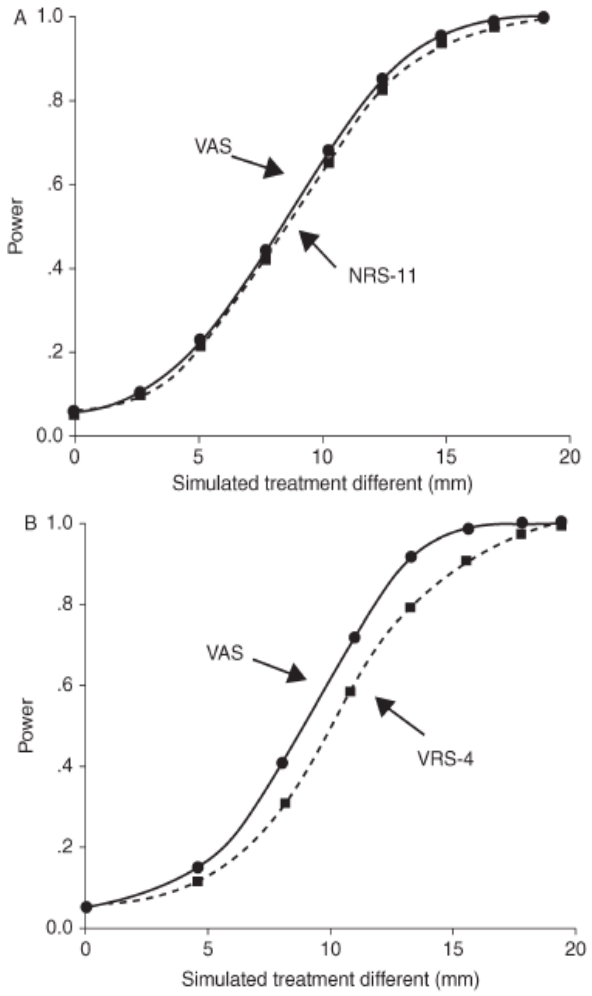


FIG 3: One-Dimensional scales of pain intensity commonly used include: 11-point NRS, no-pain VAS (= 0) to worst imaginable pain [= 10 (or 100)], and categorical four-point verbal rating (VRS).[33]

The power of a trial with high baseline pain intensity to detect a large difference is high compared with a trial where the baseline pain intensity is low and even a very effective treatment will cause only a small change in pain intensity [34] (Graph 1). When comparing a simple, weak analgesic with a potent analgesic drug in patients with only mild baseline pain, they will both relieve the mild pain and appear to be equally effective

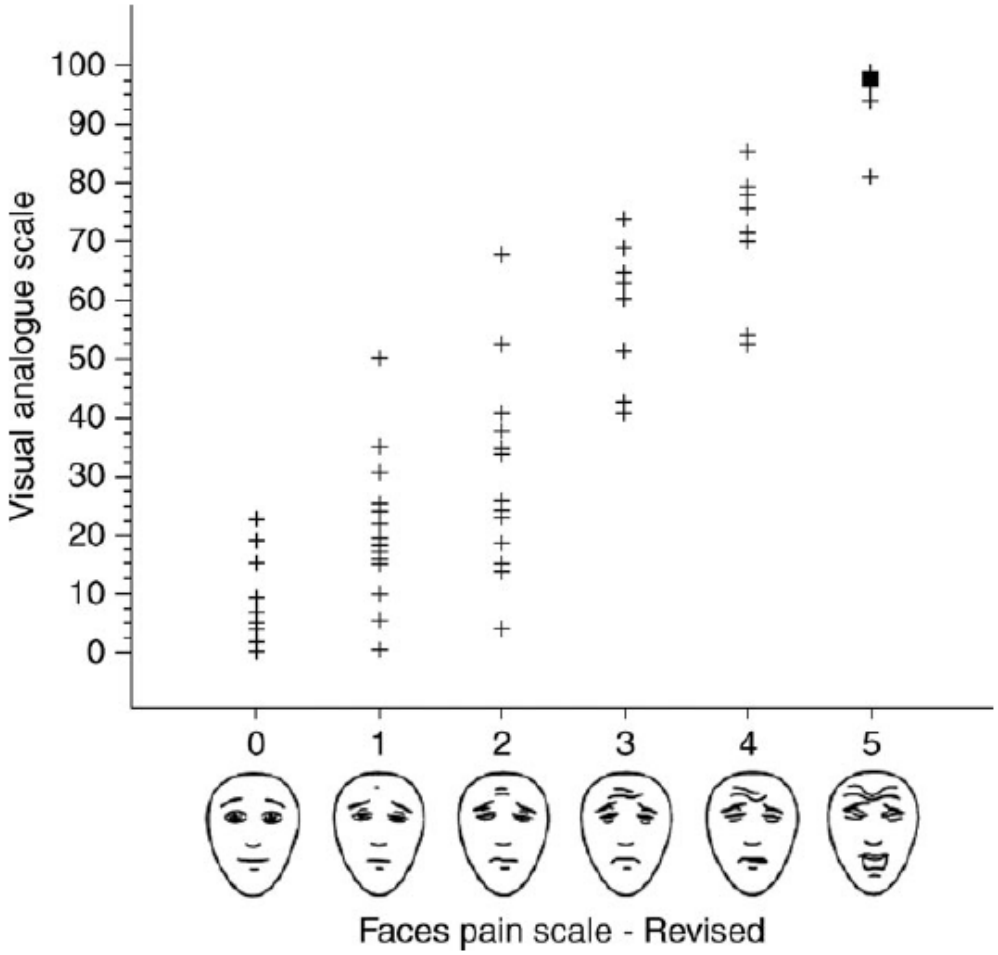


Graph 1:(A) the power of the pain-intensity difference seen in the VAS relative to NRS values observed concurrently. Computer simulation results of samples

with 10 000 NRS and VAS pain intensity scores concurrently noted. With the extent of the difference of pain intensities before and after pain therapy the strength to detect a difference rises. There is also clinically less significant difference when difference between (0-100) VAS score is less than 15 and 1.5 (0–10 NRS). (B) The power to detect a pain intensity difference observed with the VAS is greater than the 4-point categorical VRS values observed simultaneously. Computer simulation of results of samples from VRS noted simultaneously.[33]

For the same patient on several occasions, the verbal categories mild, moderate, and severe pains may correspond to different VAS values but, the NRS and VAS values usually agreed well.[33] The categorical scale of pain should therefore be used only as a gross screening device and for more precise evaluation of pain intensity VAS or NRS are relyed upon which is also applicable in routine clinical practice.

Pain-scales with happy and unhappy faces for younger kids, eg:faces pain scale, from about 3 years of age are well validated[35] (Graph 2).



Graph 2: Agreement between VAS and six-point Faces pain scale on pain intensity that is simultaneously recorded: experimental pain: earlobe pinching in kids aged between 4 and 12 years.[35]

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

Evaluating the intensity of acute rest pain following the surgery is essential to make the patient comfortable in bed. But appropriate relief of dynamic pain is more essential during mobilization, coughing and deep breathing, as it reduces the risk of thromboembolic and cardiopulmonary complications following surgery. The recognized risk factor for chronic hyperalgesic pain is immobilization, which is a major health issue is approximately 1% and in another 10% a troubling but not insignificant issue. Effective dynamic pain relief promotes mobilization and can thus

increase long-term surgical outcomes.[36] Evaluation of pain only at rest will not show distinctions between less efficient epidurals or systemic opioid analysis and more powerful pain relieving techniques such as optimal thoracic epidural analgesia. Even after significant surgery, systemic opioids may make the patient comfortable when resting. However, the systemically administered strong opioids cannot alleviate severe dynamic pain resulting from movements needed in order to get the patient out of bed and mobilization of bronchial secretions through strong cough without unacceptable negative consequences.

Assessment of Neuropathic Components in Acute Pain after Surgery

Awareness of changes in the central nervous system pain-modulation processes following surgical trauma, has increased recently. It is essential for us to evaluate and treat symptoms of central sensitizing in acute pain that such a sensitization of the spinal cord may evolve into chronic neuropathic pain after surgery in many patients.[36] Mechanical Allodynia assessment with von Frey filaments showed that a low-dose ketamine, a glutamate receptor antagonist, can suppress central sensitization of pain transmission mechanisms. The same impact is observed with glucocorticoid administration, which may be the cause of a 60% to 30% reduction in dysesthesia discomfort in patients 1 year after breast augmentation surgery when methylprednisolone was given before the skin incision.

Post-operative Pain

Postoperative pain is regarded to be acute type of pain owing to an inflammatory reaction and initiation of afferent neuronal barrage following surgical trauma. This is a mixed constellation of a number of unpleasant sensory, psychological and emotional experiences precipitated by the operative trauma and linked to autonomic, metabolic, physiological and behavioral reactions.[35] The sufferer

only perceives pain as it is a subjective phenomenon. The patients are not incompatible and unreliable in any way as they describe pain.[37] Even in a given person, the intensity of pain may not be constant, but it waxes and wanes in a cyclical pattern. Women need less analgesia than males likely because of the difference in neuroendocrine pain relief mechanism. The postoperative pain is higher in neurotic patients than in non-neurotic patients. Smokers metabolize analgesics much quicker than non-smokers and need more analgesics.

Post-operative Pain Management

The pain after surgery is both distressing and harmful. Postoperative pain management consists- evaluation of pain intensity and related pain with activity, treatment with pharmacological and non-pharmacological therapy and monitoring side effects. The pain is associated with different physiological impacts involving increased perioperative stress reaction, apart from being physically and mentally disabling. Poor postoperative pain control may be due to a number of factors including uniform prescription of drugs without taking into account the physical condition of the individual patient, surgery or the site and intensity of the pain. Furthermore, the poor adherence to prescribed analgesic orders and the absence of the aim of ideal pain relief can also lead to insufficient post-operative pain management. Thus, in the majority of patients, pain relief is still insufficient despite all attempts. The introduction of multimodal analgesia including opioids or non-opioids, the use of local anaethetics alone, or in conjunction with other drugs for neuronal blocks and anti-hyperalgesics have significantly enhanced pain control effectiveness, while reducing the side-effects of any one modality. The recently launched suggestion to plan and implement Acute Pain Services (APS) in an organized way has proved to be helpful and rewarding.

Problems Associated with Post-operative Pain

Severe post-operative pain may have physiological implications that increase the surgical stress reaction seen as a cascade of endocrinous-metabolic events, increased hospital stay, morbidity, mortality and inflammatory events that may eventually add to organ dysfunction. The pain often makes the patient to stay immobile, thus becoming susceptible to deep venous thrombosis, lung atelectasis, muscle wasting and urinary retention. It may lead to postoperative hypoxemia in addition to restlessness. Some patients may continue to experience a chronic pain due to peripheral neural activation together with central neuroplastic modifications associated with postoperative pain.[37] The chances of chronic pain are higher for patients with moderate to severe pain after surgery and for those who undergo nerve damage during procedure. Preemptive analgesic treatment of acute pain can help to avoid this complication.

Pharmacological Measures:

Include administration of drugs like opioids and non-opioids by various routes including intra-muscular, intra-venous, oral, per-rectal, intrathecal, epidural, sublingual, subcutaneous, intra-articular etc.[37]

The use of opioids for post-operative pain relief has been well known. Different factors can influence opioid absorption and the clinical response that results. These include route of administration, presence of hepatic or renal disease, age of the patient, concomitant administration of other drugs, hypotension, hypovolemia, hypothyroidism, hypothermia, etc.

Patient **Controlled Analgesia (PCA)**

PCA was introduced in 1966 and was used for both pain treatment and analgesic deficiency quantification. It has been shown that PCA is much better than

standard intramuscular analgesia and that there is reduced post-operative morbidity, quicker recovery of minute ventilation, fast ambulation and early patient discharge. In the postoperative period, appropriate pain relief without significant respiratory depression has been shown to be provided. [38]

The patient can use a tiny microprocessor-controlled pump-to administer his own analgesia and therefore titrate the dose to his own pain relief point. Theoretically, the analgesic plasma level is comparatively steady and side effects induced by plasma level changes are eliminated. Some parameters must be determined such as- the bolus dose size, the minimum time between the doses (lockout period) and the maximum allowable dose. Some systems allow continuous infusion in the background. Morphine is the most frequently used medicine with a lockout period of 5-10 minutes at 1-1.5 mg dose. In every case, however, periodic check-up is required to guarantee an appropriate relief for pain. PCA may also be provided by subcutaneous and epidural routes, in addition to intravenous administration.

Intrathecal and Epidural Analgesia

This can be achieved either by separately or by combining opioids and local anaesthetics. Intrathecal opioids are simple to administer without demonstrable motor, sensory or autonomous deficits and are efficient in generating analgesia.

The epidural route may be used as a continuous infusion or as a single bolus. It has shown beneficial physiological impacts such as effective activity-dependent pain relief, improved economy, decrease in ileus and improving postoperative lung function and a reduction in cardiac demand.[39] An opioid alone or combined with a local anesthetic may be used. The latter has demonstrated better outcomes in postoperative pain relief.

Opioid Analgesic Agents

Opioids act as agonists on those stereospecific opioid receptors that occur in the CNS and peripheral tissues at presynaptic and post-synaptic locations. These receptors of opioids are categorized as μ, δ and κ. Opioids simulate the action of endogenous ligands through binding with opioid receptors, which leads to pain modulation system activation. Neuraxial route-administered opioids work by diffusion through the dura to obtain access to opioid μ-receptors in the substansia gelatinosa of the spinal cord and systemic absorption to generate impacts that are comparable to those that follow intravenous administration of the opiate. Opioid analgesic products include: Morphine, Pethidine, Fentanyl, Sufentanil, Alfentanil, Pentazocine, Nalbuphene, Butorphanol And Buprenorphin.[40]

Non-opioid analgesics: Diclofenac sodium and Paracetamol.

TRANSVERSUS ABDOMINIS PLANE BLOCK

After abdominal operation, the anterior abdominal wall is an important source of pain. The Gold standard for pain management after significant abdominal surgery is traditionally epidural analgesia. However, the analgesic alternatives are scarce if epidural analgesia is contraindicated or not feasible. Large-dose intravenous opiates that can be poorly tolerated may be necessary. In the search for alternative ways of delivering efficient analgesia, the Transversus Abdominis (TAP) block was developed.[27,41,43]

TAP block is a relatively new method used after abdominal surgery to provide somatic analgesia. TAP is a regional analgesic technique for the parietal peritoneum, skin, muscles of the anterior abdominal wall.[43] It was first defined ten years ago, and subsequently investigated by cadaveric research and underwent several changes that have highlighted its potential usefulness for increasing array of surgeries. [44,45] TAP blocks remain overwhelmingly under-utilized despite the relatively low risk of complications and high success rates using the latest technologies.[46] The introduction of an ultrasound has revived interest in this block, since the layers of muscles on the abdomen are easily traced using ultrasound and can be performed with improved success.

TAP block only relieves the somatic part of postoperative pain, just like other field blocks. In order to manage the visceral component, oral and parenteral analgesics should be adhered as usual. This block offers excellent somatic analgesia for most abdominal operations when done properly and decreases opioid need.[47]

History

The TAP block was first described by Rafi in 2001. It was depicted as a sophisticated abdominal field block, with a focused single shot of anaesthetic delivery

to the Transversus Abdominis Plane. This was an important advancement compared to previous therapies, which needed multiple injections. In this procedure the TAP was first identified, using surface anatomical landmarks, by the lumbar triangle of Petit (Fig 4), an area medially enclosed by the internal oblique, latissimus dorsi posteriorly and the iliac crest inferiorly. Then a 24-gauge, blunt-tipped 2 inch needle was inserted perpendicular to the skin, until a single confirmatory "pop" was appreciated. This feeling was meant to show anesthetic needle depth. [48,49]

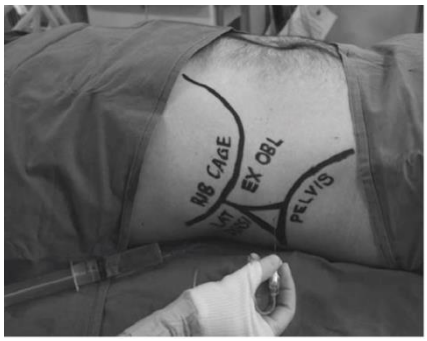


Fig 4: Surface anatomical landmarks can be utilized to identify the triangle of Petit.

During the American Society of Anaesthesiologists science conference, McDonnell et al. provided preliminary research on TAP blocks in cadavers and healthy volunteers in 2007.[44] The writers presented preliminary proof to support the anatomic basis of the TAP blocks, while the method of regional abdominal field infiltration (RAFI), demonstrated a sensory loss from xiphoid to pubic symphysis following the local anaesthetic delivery into the TAP via triangle of Petit.[45]

By the time the research had been finished in 2007, McDonnell and his colleagues already had adopted the word TAP block and shown its analgesic utility in open retropubic prostatectomy patients.

Anatomy

The sensory nerve supply to the anterior abdominal wall comes in large part from the lower divisions of the thoracic nerves (T7-T11), also known as Thoraco-abdominal nerves), the subcostal nerve (T12) and as well as the first lumbar nerve.

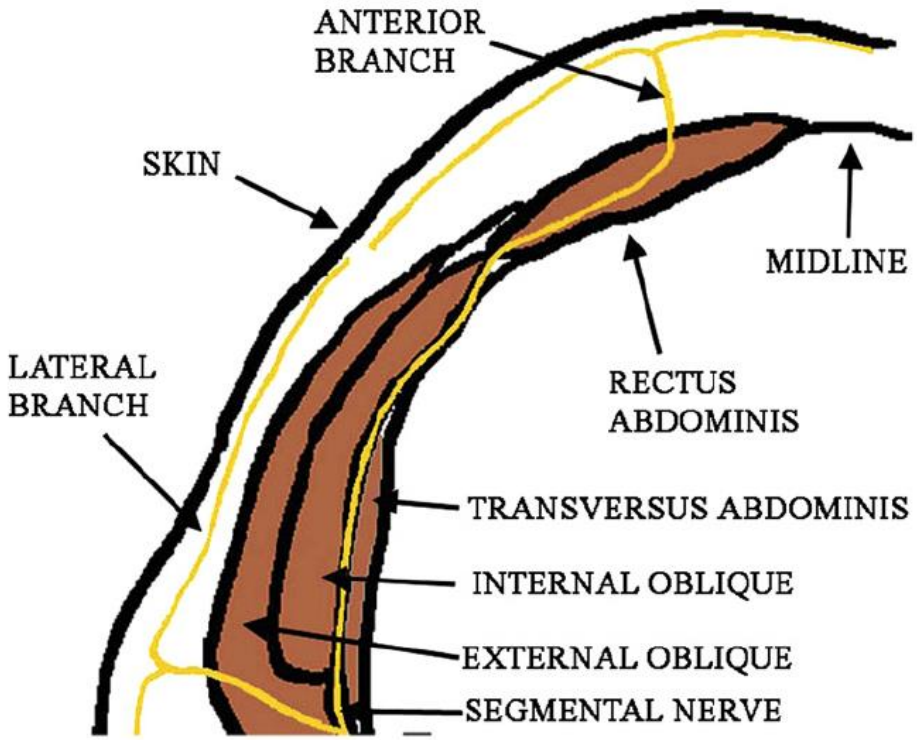


Fig. 5: Cross sectional anatomy illustrating the anterior abdominal wall nerves and muscles

T6 supplies a small area close to the xiphoid process. The thoracic nerves split into anterior and posterior divisions after leaving intervertebral foraminas.

The posterior division further splits into medial and lateral branches and supplies the posterior trunk. Along the intercostal space, the anterior division traverses the intercostal groove along with the intercostal vessels (Fig. 5).

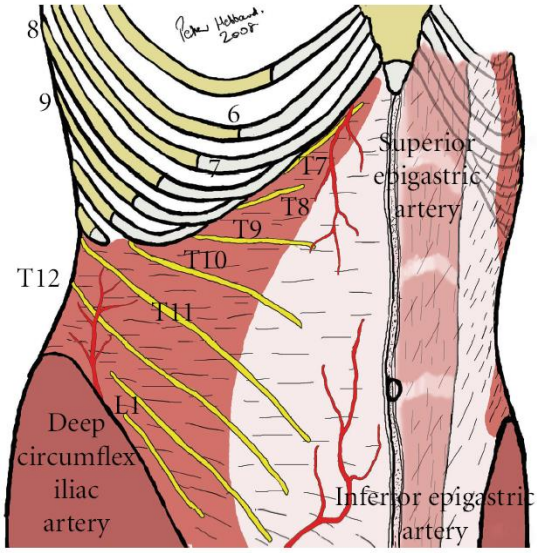


Fig. 6: Typical distribution of nerves in the TAP

Throughout its course, the anterior divisions of the thoracic nerves give lateral branches close to the mid-axillary line and proceed forward. In the end, the thoracic nerve anterior divisions penetrate the rectus sheath and terminate as the cutaneous nerves of anterior abdominal wall.[49] The skin of the whole antero-lateral abdominal wall, including groin is supplied by the thoracic-abdominal nerves, first lumbar nerve (also referred as iliohypogastric and ilio-inguinal nerves) and sub-costal nerve.

The anterior division of thoracoabdominal nerves in the abdominal wall runs through the plane between internal oblique and transversus abdominis muscle.[49] There is extensive cross-branching and branching between the nerves in this plane. This plane is known as the Transversus Abdominis Plane (TAP). The shape of this plane is roughly triangular. The linea semilunaris, formed by the aponeurosis of the internal oblique muscle forms the anterior border which is further strengthened by external oblique aponeurosis anteriorly and by transverse abdominis aponeurosis posteriorly. The linea semilunaris reaches to the pubic tubercle from the tip of the 9th cartilage. Superior border of TAP is formed by is the sub-costal margin, which extends from the 9th to 12th ribs to the anterior edge of the Latissimus dorsi muscle and inferiorly to

lumbar triangle of Petit. The inguinal ligament and the iliac crest forms the inferior boundary. The local anesthetic deposited in this plane blocks the first lumbar and lower thoracic nerves, thus providing useful analgesia to the anterior abdominal wall.[50]

TAP block methods/techniques

The landmark technique

Rafi's (2001) initial abdominal field block description was a landmark technique through the inferior lumbar triangle of Petit.[46,50] Petit's triangle is bounded by external oblique muscle anteriorly, latissimus dorsi muscle posteriorly and iliac crest inferiorly. This triangle is felt like a dip when the finger palpates posteriorly over iliac crest from the anterior superior iliac spine.

Sometimes in a slender individual the anterior edge of the latissimus dorsi is easily palpated. The bed of the triangle is formed by external and internal oblique fascia. This inferior triangle of Petit provides simple access to the TAP as the inserted needle passes through the two fasciaes, providing two unique palpable pops before reaching the plane.

A' flank bulge' sign may be noted if a local anesthetic is placed in the correct plane. in thin patients. This is a sign of local anesthetic in the TAP that leads to muscle weakness, thereby creating a unique bulge over the iliac crests.[45]

The landmark technique has many disadvantages though it is simple to perform. Not all persons have the inferior lumbar triangle of Petit and its anatomical place may be inconsistent.[50] Ultrasound picture has also disclosed a possibility of overlap between external oblique and latissimus dorsi muscles leading to four layers of muscles in this region.[51] This could explain a block failure in the use of the

anatomical landmark method. Ultrasound guidance is therefore suggested to improve the rate of success.

Ultrasound-guided posterior TAP block

Walter and colleagues emphasized the anatomical inconsistency of Pettit's triangle,[54] which proposed the use of ultrasound to view the transverse abdominal plane. The 3 muscle layers of the abdominal wall are shown by a high-frequency ultrasound probe positioned transversely between the crest and the costal margin.[51] (Figure 7).

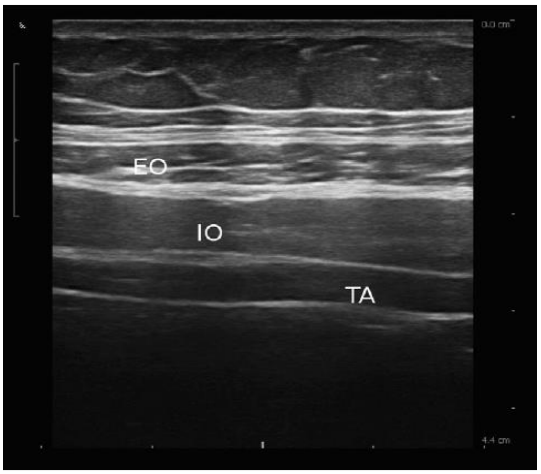


Fig. 7: Picture showing the sonoanatomy of the posterior TAP block EO – External Oblique; IO - Internal Oblique; TA - Transversus abdominis.

An epidural or regional block needle can then be inserted from the anterior abdominal wall slightly away from probe and carefully advanced to reach the plane. The needle and its tip are visualized by in-plan method (Fig. 8). As needle pierce underneath the internal oblique muscle into the transversus plane, small amount of local anaesthetic is then injected to confirm the needle's position before injecting full dose. The distribution of the local anaesthetic solution (Fig. 9) is displayed as a 'tear drop expansion'. If necessary, further hydrodissection can be performed or catheter can be inserted to instill local anesthesia continuously. By means of this procedure, the operator on one side of the patient can block both sides,

thereby alleviating the operator's need to move from one side of the patient to the other.

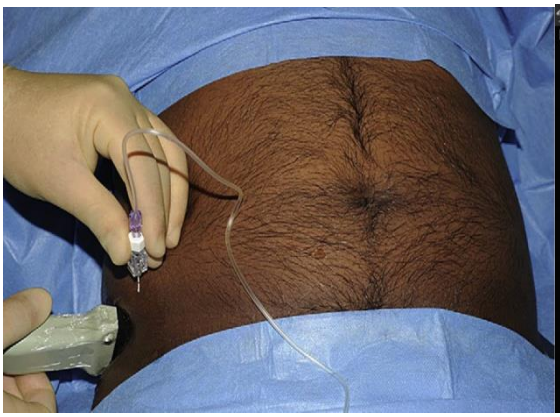


Fig. 8: Image displaying the needle position in "in-plane" technique in relation to the ultrasound probe.

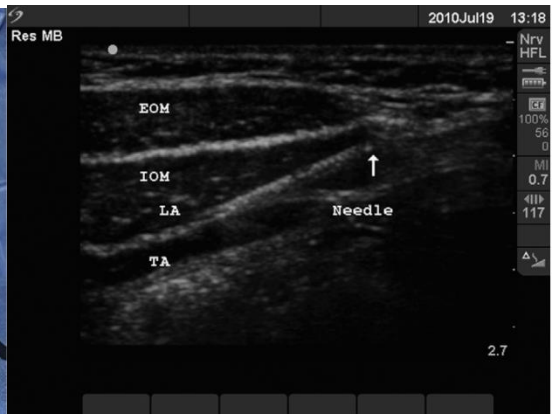


Fig. 9: Local anesthetic injection causing a drop in tear spreading within TAP; EOM — External oblique muscle ; IOM — internal oblique muscle ; TA — Transverse Abdominis; LA- Local anesthetic solution ;

Ultrasound-guided sub-costal TAP block

This block was originally defined by Hebbard et al. (2008) and being frequently used for analgesia after upper abdominal surgeries. The ultrasound probe is located close and parallel to the costal margin in this approach.[53] The rectus abdominis and tranversus muscles can be visualized in this location. The transversus abdominis muscle is seen from the back side of the rectus muscle and in this field the TAP is well defined.

This block commonly spares the lumbar segment (L1).[53] A new technique, called the oblique sub-costal block, has recently been defined by certain writers. They state in a short technical report that the oblique subcostal TAP block generates a sensory blockage far larger than the previous sub-costal block.[54]

TAP catheters

A single-shot TAP block can generate analgesia for up to 24 hours after the procedure. A catheter must be inserted in the transversus plane to achieve effective analgesia for long periods of time and local anaesthetics should be infused

continuously or injected at regular intervals (e.g. every 12 h).[54] The insertion of catheters is normally conducted under the guidance of ultrasound.

Surgeon-Assisted Approaches:

While most published TAP blocks literature is from anaesthesiologists point of view, increasing amount of studies have shown that surgeons can help facilitate these blocks. Chetwood et al. described a laparoscopic-assisted technique, using an intraabdominal laparoscopic camera, which was used to observe injection area when a classic TAP block is being performed using landmark technique.[55] After local anaesthetic was injected within the TAP, a peritoneal bulge was seen at the injection site and this visual was the required target for this method. This direct visualization can prevent intraperitoneal injection, which is one of the greatest potential risk of the TAP block. A Transperitoneal approach surgical TAP block was also recently defined. A blunt tipped block needle was inserted through the parietal peritoneum from inside the abdominal wall intraoperatively, then through transversus abdominis muscle of the abdominal wall then into the TAP, which was demonstrated by a simple pop sensation. [23,43] Araco et al. also defined the surgical TAP block in which local anesthetic was injected into the TAP under direct visualization, with the blunt dissection through the external and internal Oblique muscles. [56]

Extent of analgesia:

Earlier trials by McDonnell et al. (2007)[44] have shown that LA injected into the TAP resulted in sensory block from T7 to L1. Many case reports and research showed a block between T10 and L1, with TAP Block. If the subcostal method is used, the block extends from T7 to T12. The block height distinction has been made by Hebbard et al. (2007)[53] following coventional and subcostal TAP Block. A subcostal TAP block is more appropriate for lower abdominal incisions. A

posterior TAP block provides appropriate post-operative analgesia for all lower abdominal procedure.

While the quantity, concentration and technique of delivery of local anaesthetics vary between research, these methods have still not been compared. There is therefore not enough proof to support any specific combination instead of another. There is excellent proof to support TAP catheters when the time of analgesia is a problem.

Indications:

Lower abdominal surgery

1. Open appendicectomy.
2. Inguinal herniorrhaphy.
3. Total abdominal hysterectomy.
4. Open retropubic prostatectomy.
5. Iliac crest bone harvest.

Obstetric patients

Caesarean section.

Laparoscopic surgery

1. Appendicectomy.
2. Cholecystectomy.
3. Hernia repair.
4. LAVH.

Pediatric and neonatal surgery

Examphalos repair.

Intensive care unit

Analgesia.

Others

1. Open nephrectomy.
2. Thoraco-Abdominal injuries.
3. Renal transplantation.

PHARMACOLOGY OF BUPIVACAINE

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

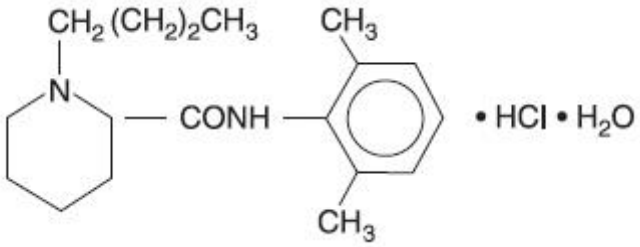


Fig.10: Structural formula of bupivacaine.

Molecular weight of its chloride salt is 325. melting point is 108℃. Bupivacaine hydrochloride is related chemically and pharmacologically to aminoacyl local anaesthetics. It is a homologue of mepivacaine and is chemically related to lidocaine. All three of these anaesthetics contain an amide linkage between the aromatic nucleus and amino or piperidine group. They differ in this respect from the procaine- type local anaesthetics, which have ester linkage.

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

Mechanism of Action:

Like all local anaesthetics, Bupivacaine causes a reversible nerve conduction blockade by decreasing nerve membrane permeability of sodium. The binding of local anaesthetic to sites on voltage gated Na^+ channel prevents opening of channels by inhibition of conformational changes. This causes decrease in the rate of membrane

depolarization, thereby increasing the threshold for electrical excitability. The blockade affects all nerves in the following sequence: autonomic, sensory and motor with effects diminishing in reverse order. Loss of nerve function clinically is as follows- pain, temperature, touch, proprioception and skeletal muscle tone. Direct nerve membrane penetration is essential for effective anaesthesia. During onset and recovery from local anaesthesia, impulse blockade is incomplete and partially blocked fibres are further inhibited by repetitive stimulation, which produces an additional use dependent binding to Na^+ channels.

Pharmacokinetics:

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

The ultimate plasma concentration of local anaesthetic is determined by the rate of tissue absorption, distribution and rate of clearance of the drug. The tissue distribution of a drug in turn depends upon the tissue blood flow and lipid solubility of drug. The patient related factors such as age, cardiovascular status and hepatic function also influence the absorption and resultant plasma concentration. Lungs are capable of extracting bupivacaine from circulation. This limits the concentration of the drug that reaches the systemic circulation. This first pass pulmonary extraction is dose dependent and can be blocked by propranolol. Propranolol reduces plasma clearance of the drug presumably by decreasing hepatic blood flow and competitive blockade at receptor site. After injection for peripheral nerve blocks, peak blood levels are achieved in 30-40 minutes. Bupivacaine's onset of action is rapid (1-10 minutes) and significantly longer than other local anaesthetics (3-9 hours).

Bupivacaine is distributed to all tissues, with a high concentration in well perfused organs such as liver, lung, heart and brain.

Table 1: Pharmacokinetic properties of bupivacaine

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

Metabolism:

Local amide anaesthetics undergo varying rates of metabolism by the microsomal enzymes in the liver. Initial step is conversion of amide base to amino carboxylic and a cyclic aniline derivative. For complete metabolism additional steps such as dealkylation and hydroxylation are required. Possible pathways for metabolism of bupivacaine include aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation. Only the N-dealkylated metabolite N-desbutyl-bupivacaine has been measured in urine or blood after epidural or spinal anaesthesia. The mean total urinary excretion of bupivacaine and its metabolite accounts for >40 % of total anaesthetic dose. Alpha 1 glycoprotein the most important protein binding for bupivacaine and its concentration is increased in many clinical situations, including post-operative trauma.

Side Effects:

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

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

CNS Toxicity:

At low concentrations- numbness of the tongue and circumoral tissues. On further increase in plasma concentration there is vertigo, tinnitus, restlessness and difficulty focussing. Further increase in concentration leads to slurred speech and skeletal muscle twitching followed by seizures (tonic clonic) at a concentration of 1 mcg/ml. The seizures are classically followed by central nervous system depression accompanied by hypotension and apnea. The explanation for the local anaesthetic seizures is as follows:

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

There is an inverse relationship between PaCO2 levels and seizure threshold. This is due to increased cerebral blood flow and increased delivery of drug to brain. A

decrease in arterial pH also decreases the seizure threshold probably due to ion trapping and subsequent decrease of drug in the brain. Treatment includes mechanical ventilation and benzodiazepines for supressing seizures.

CVS Toxicity:

Local anaesthetics may produce profound hypotension due to relaxation of arteriolar vascular smooth muscle and direct myocardial depression. Hypotension reflects both decreased systemic vascular resistance and cardiac output. Part of cardiac toxicity that results from high plasma concentrations of local anaesthetic occur because these drugs also block cardiac sodium channels. Cardio toxic plasma concentration of bupivacaine is 8-10 mcg/ml. When the plasma levels are excessive, sufficient cardiac sodium channels are blocked so that conduction and automaticity is adversely depressed manifesting as prolongation of P-R interval and wide QRS complex on ECG. Effects on the calcium ion and potassium ion channels and inhibition of cyclic adenosine monophosphate (cAMP) production may also contribute to cardiac toxicity. Accidental IV injection of bupivacaine may result in precipitous fall in blood pressure, cardiac arrhythmias and atrioventricular heart block. After accidental IV administration, the protein binding sites for bupivacaine are quickly saturated, leaving a significant amount of unbound drug available for diffusion into conducting tissues of the heart. Pregnancy may increase sensitivity to cardio toxic effects of bupivacaine. Threshold of cardiac toxicity produced by bupivacaine may be decreased in patients treated with drugs which inhibit myocardial impulse propagation (beta blocker, digitalis and calcium channel blocker). In presence of propranolol, cardiac arrhythmias can occur at plasma concentration of 2-3 mcg/ml. Epinephrine and phenylephrine increases bupivacaine induced toxicity. Dissociation of highly lipid soluble bupivacaine from sodium channel receptor sites is slow,

accounting for the drug's persistent depressant effect on cardiac action potential and subsequent toxicity. R enantiomer of bupivacaine is more toxic than S enantiomer. Tachycardia can enhance frequency dependent blockade of cardiac sodium channels by bupivacaine. Cardiac resuscitation is difficult in bupivacaine induced cardio vascular collapse.

Indications:

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

Dosages:

The dose of local anaesthetics differ with the anaesthetic procedure, area to be anaesthetized, vascularity of tissues, number of segments to be blocked, duration of anaesthesia and individual tolerance.

Maximum dosage limit: 2-3 mg/kg body weight.

Fig 11: Standard 0.5% vial used in our hospital.

PHARMACOLOGY OF PENTAZOCINE

Chemistry: Pentazocine is a benzmorphan compound which is related chemically to Morphine. It is a crystalline powder, which is white or cream, odorless. It is a racemic mixture containing dextro-(d) and laevo-(l) isomers, which is soluble in acidic aqueous solutions. For oral uses are pentazocine hydrochloride, and for parenteral and rectal administration lactate form is used.

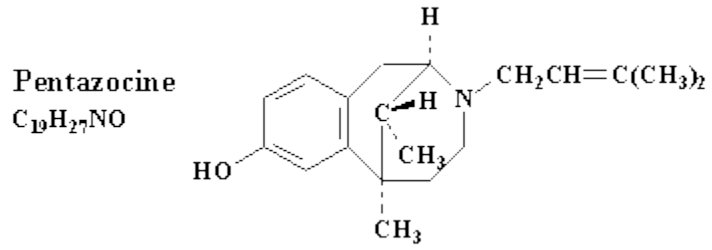


Fig 12: Chemical structure of Pentazocine.

Molecular weight (free base)-321.9

pKa -8.7

Solubility in water -1 in 30

Chemical structure -C19H27NO.HCl

PHARMACODYNAMICS:

The effect of analgesia is due to its agonistic action on OP2 (κ) receptors and weak antagonist action at OP3 (μ) receptors. It also has an agonist action on other receptors that can lead to dysphoroic side-effetcts.

30-40mg of Pentazocine has actions similar to 10mg of Morphine.

Other actions: Cough suppression, decreased gastric emptying, Miosis, Respiratory depression, constipation and increased smooth muscle tone in the uterus and bladder.

PHARMACOKINETICS:

Absorption-Pentazocine is completely absorbed after oral administration with peak plasma concentration at about 1-3 hours and a mean plasma half-life of about 2 hours. Action lasts for 2- hours.

Oral bioavailability ranges from 11% to 32% due to variable hepatic (first pass) metabolism which determines the peak plasma levels.

50% plasma protein bound. Placental transfer occurs with mean cord blood concentration of 60-70% of maternal blood levels.[57]

TABLE 2: Route of administration with time to peak concentration of Pentazocine.[57]

Route of administration	Time to peak Plasma Concentration (minutes)
IV	2-3
IM/ Subcutaneous(S/C)	15-30
Per Oral(PO)	60-90

Metabolism and Elimination: In urine, 10 percent is cleared unchanged, with 1-2% being excreted by enterohepatic circulation. The rest is subjected to extensive hepatic metabolism, such as conjugation with glucuronic acid and oxidation in the dimethylallyl side chain terminal methyl groups. The two main metabolites in the blood are the metabolite of trans-carboxylic acid (40%) and cis-alcohol (11%). Both of them are inactive.

Pharmaceutical preparations of pentazocine:

a) Parenteral forms:

1. Talwin injection (USA): 30mg/ml in 1 or 2ml ampoules, sterile cartridge needle units,10 ml multiple dose vials. Mixed in an aqueous solution of pH4-5 as pentazocine lactate. For IV, IM and subcutaneous injection.

2. Fortral injection (UK): 30mg/ml in 1 or 2 ml ampoules for IV, IM or subcutaneous use.

b) Oral forms:

1. Talwin-Nx (USA) 50mg pentazocine with 500mcg naloxone
2. Fortral tablets (UK) 25mg and 50mg pentazocine hydrochloride tablets
3. Talwin Compound12.5mg pentazocine with 325mg aspirin (2 tablets three-four times daily)
4. Talacen (acetaminophen) 25mg pentazocine with 650mg paracetamol (1 tablet four hourly).

c) Rectal forms: 1. Fortral suppositories 50mg Pentazocine lactate

TABLE 3: Dosing of Pentazocine[58]

Route of administration	Dose	Interval	Total dose in 24 hour
Intravenous - inject undiluted by slow bolus	0.5mg/kg or 30 to 40mg	4 hourly	Not exceeding 360mg
Intramuscular - inject deep into well developed tissue	10mg/kg or 30 to 60mg	3-4 hourly	Not exceeding 360mg
Oral (CHILDREN)	25mg	3-4 hourly	Not exceeding 150mg
Oral (ADULTS)	50-100mg	3-4 hourly	Not exceeding 600mg

In Pregnancy: In females who have taken 50-300 mg per day during pregnancy, neonatal dependence has been recorded.

It is not proved that pentazocine passes into breast milk but it is advised to monitor when higher doses are prescribed.

Therapeutic Uses[58]:

1. Postoperative pain- moderate to severe pain 30-60mg IM or SC.
2. Chronic pain- limited by its weak and unpredictable analgesic effect.
3. Obstetrics- Pentazocine appears to be an effective analgesic during labour. There is some evidence that uterine activity may be increased and, compared with pethidine.
4. Renal and biliary colic- in acute conditions.
5. Myocardial Infarction.

Contraindications:

1. Respiratory depression
2. Raised intracranial pressure
3. Arterial or pulmonary hypertension
4. Pre-existing opioid dependency
5. Porphyria.

Adverse reactions:

1. Respiratory depression.
2. Agranulocytosis.
3. Epileptic seizures.
4. Pruritis.
5. Addiction.
6. Psychotomimentic effects in 20% of patients.

7. Sedation, light headedness, vertigo.
8. Nausea and vomiting
9. Other opioid side-effects include sweating, hot flushes, dry mouth, urinary retention, Blurred vision, nystagmus, diplopia, miosis, Headaches, chills and fever.

PHARMACOLOGY OF DICLOFENAC:

Diclofenac is the most frequently used NSAID. COX-2 selective inhibitor, Lumiracoxib is a diclofenac analog.

The structure of diclofenac is:

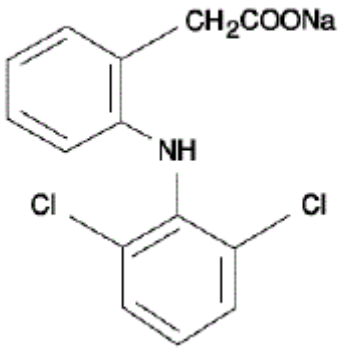


Fig 13: CHEMICAL STRUCTURE OF DICLOFENAC SODIUM

Pharmacological properties:

Diclofenac has analgesic, antipyretic and anti-inflammatory actions. Its COX-2 inhibitor potency is significantly higher than that of other NSAIDS.

Pharmacokinetics:

Diclofenac is metabolized to 4-hydroxydiclofenac, the main metabolite and other hydroxylated forms in the liver by a member of the CYP2C subfamily ; metabolites are excreted in urine (65%) and bile (35%) after glucuronidation and sulfation.

Peak plasma concentration: 2-3 hours.

Half-life: 1-2 hours.

Therapeutic uses:

a) long-term symptomatic treatment of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis.

b) short-term treatment of acute musculoskeletal pain, postoperative pain, and dysmenorrhea.

c) Postoperative inflammation following cataract extraction in ophthalmology.

Dosage and routes of administration:

1. Oral- 50mg, 3-4times daily, not exceeding 200mg per day.
2. Parenteral (IM/IV)- 75mg twice daily, not exceeding 150mg per day.
3. Transdermal patch- 100mg, applied over the chest at the beginning of the surgery.
4. Topical application as 1.5%/ 3% gels or ointments.
5. Ophthalmic solution- 1 drop to the affected eye, starting 24 hours after cataract surgery and continue for 2 weeks.

Adverse effects:

1. Gastrointestinal-Abdominal pain, nausea, anorexia, gastric erosion / ulcers, anemia, GI hemorrhage, perforation, diarrhea.
2. Platelets-Inhibited platelet activity, bruising propensity, hemorrhage risk increased.
3. Uterus-gestation prolongation, labor inhibition.
4. Hypersensitivity-Vasomotor rhinitis, asthma, urticaria, flushing, hypotension, shock, angioneurotic edema.
5. Renal -salt and water reabsorption, edema, worsening renal function in people with renal / cardiac and cirrhosis, decreased efficacy of antihypertensive drugs, decreased efficacy of diuretic drugs, hyperkalemia.

PHARMACOLOGY OF PARACETAMOL:

The chemical name is N – Acetyl- p- amino phenol. Also known as Acetaminophen or 4'-OH acetanilide.

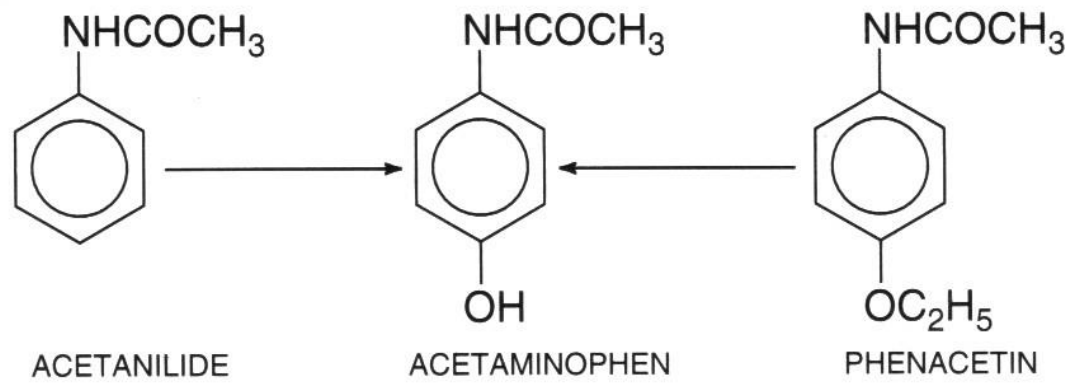


Fig 14: Chemical structure of Paracetamol.

It is a mild analgesic and antipyretic. Studies have demonstrated opioid sparing effect. It has weak anti-inflammatory action.

Mechanism of action:

It reduces the production of prostaglandins in brain and spinal cord. It inhibits COX 3 in the hypothalamus.[59]

Routes of administration:

Oral- Peak blood levels after 30-60.

Rectal- Peak blood levels after 1-2 hours.

Intramuscular.

Intravenous- Infusion of 1g over 15minutes.[59]

Dose:

IV: 10-15mg/kg, Maximum 3g/day

Rectal: Loading dose 40 mg/kg followed by 20mg/kg 6th hourly upto a maximum daily dose of 100mg/kg.

Oral: 15 – 20mg/kg 4th hourly.

Pharmacokinetics:

Readily absorbed from the GIT. It is distributed into most body tissues, crosses placenta and is present in breast milk.

Elimination half -life 2-4 hours. 25% of the drug is protein bound.

Metabolism-in the liver and excreted as glucoronide conjugate in urine. Conjugation also occurs with glutathione . < 5% is excreted unchanged.

Adverse effects:

Hepatotoxicity- >150mg/kg/day.

Nephropathy.

Hypersensitivity reactions like-urticaria, hypotension, rashes.

MATERIALS AND METHODS.

SOURCE OF DATA:

This study was carried out in the Department of Anaesthesiology, _____

METHOD OF COLLECTION OF DATA

Study Design: A prospective randomized clinical study.

Study Period: One and half year from December 2017 to August 2019

Sample size calculation: With Anticipated Mean Difference of VAS score between study groups as 2.5 and Anticipated SD as 2.7, the minimum sample size per group is 30 with 90% power and 5% level of significance.

Total is 60

By using the formula:

$$n = \frac{(z_\alpha + z_\beta)^2 \, 2 \, SD^2}{MD^2}$$

Where Z= Z statistic at a level of significance

MD= Anticipated mean difference.

SD= Anticipated Standard deviation.

Statistical analysis:

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value.

The difference of the means of analysis variables between two independent groups was tested by unpaired t test. The t statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

where $\bar{x}_1$ = mean of sample 1

$\bar{x}_2$ = mean of sample 2

n_1 = number of subjects in sample 1

n_2 = number of subjects in sample 2

s_1^2 = variance of sample 1 = $\frac{\Sigma(x_1 - \bar{x}_1)^2}{n_1}$

s_2^2 = variance of sample 2 = $\frac{\Sigma(x_2 - \bar{x}_2)^2}{n_2}$

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

RANDOMIZATION:

The study population of patients matched age, undergoing caesarean section were randomly selected and divided by chit system into two groups with 30 patients in each group.

Group I – USG-guided Bilateral TAP Block with 15ml of 0.25% Bupivacaine was performed on each side following caesarean section.

Group II –Received standard analgesia according to Obstetric department protocol consisting Intramuscular(IM) Diclofenac 75mg, Intravenous(IV) Paracetamol 1g and IV Pentazocine 0.5mg/kg body weight stat at the end of surgery.

Rescue analgesia in both the groups was given with IV Pentazocine 0.5mg/kg body weight.

INCLUSION CRITERIA:

- American Society of Anesthesiologists (ASA) status II and III.
- >18 years of age who is pregnant presenting for a caesarean delivery via Pfannensteil incision elective or non-urgent caesarean.

EXCLUSION CRITERIA:

- Inability to consent.
- Any contraindication to spinal anaesthesia.
- Allergy to local anesthetic agents.
- Local infection.
- Coagulopathy.

INVESTIGATIONS REQUIRED:

- Complete Blood Count (CBC), BT, CT.
- Urine analysis.
- RBS, Blood urea and Serum Creatinine.
- ECG.
- HBsAg, HIV (Universal precautions).
- 2d ECHO if required.

PRELIMINARIES:

- Written consent.
- Intravenous access with a 20G I.V cannula was established in the upper limb under aseptic precautions.

EQUIPMENTS:

A Sonosite M Turbo Ultrasound Machine

a) For the procedure:

A portable tray covered with sterile towels containing:

- Sterile syringes - one 20ml and one 10ml.
- Hypodermic needles of 5cm length, 22G.
- Bowl containing povidone iodine and spirit.
- Sponge holding forceps.
- Towel and Towel clips.
- Sterile gauze pieces.

b) For emergency resuscitation:

- The anaesthesia machine, emergency oxygen source (E type cylinders), pipeline O2 supply, working laryngoscopes, appropriate size endotracheal tubes and connectors.
- Working suction apparatus with suction catheter.
- Oropharyngeal airways.
- Intravenous fluids.
- Drugs:

  Thiopentone,Succinylcholine,Hydrocortisone,Atropine,Adrenaline,Aminophylline,Mephenteramine,Calcium gluconate and Sodium bicarbonate.

c) Monitors:

- Pulse oximeter.
- ECG.
- NIBP monitor.

Methodology:

Pre-anaesthetic evaluation included the following:

History:

History of underlying medical illness.

Past history- Previous history of surgery and anaesthetic exposure.

Previous hospitalization.

Personal history

Family history.

Physical examination:

- General condition of the patient.
- Vital signs- heart rate, blood pressure, respiratory rate.
- Height and weight

Systemic examination:

- Cardiovascular system.
- Respiratory system.
- Central nervous system.
- Vertebral system.

Airway assessment by Mallampati grading.

Procedure will be explained to the patient

Procedure:

Baseline investigations like- complete blood count, urine routine and ECG were done.

- Informed written consent was taken from the patient.
- Patients were kept nil by mouth at least six hours prior to surgery.
- Pre-operative vital parameters in the form of baseline pulse rate, blood pressure and saturation were recorded.
- On the day of surgery, patients were given Non-Particulate Antacid(NPA) 30 minutes(min) before being taken to Operation Theater. Standard monitoring devices including ECG leads, sphygmomanometer cuff and pulse oximeter were connected and baseline values were recorded.
- IV line will be secured with 20G cannula, Ringer Lactate infusion was started and patients were premedicated with IV Ranitidine 50mg and IV Metoclopramide 10mg, 20-30 min before surgery.
- Patients were positioned in left lateral positon and Spinal anaesthesia was given with 2-2.2ml(10-12mg) of 0.5% Bupivaciane Heavy.
- After the surgery, The block site was painted with povodine iodine solution, spirit and draped with a sterile towel. Sterile gel was applied to ultrasound probe and probe covered by sterile cover.
- The USG probe (SonoSite M-Turbo machine) was placed in the midway between iliac crest and subcostal margin.
- Group I received Bilateral TAP Block with 15ml of 0.25% Bupivacaine slowly with 5 ml increments after careful negative aspiration using 22G 5 cm long blunt tip regional anaesthesia needle. The block was given on the other side using the same method. Abdominal wound was covered with a pressure

dressing that covered even the puncture sites of the TAP Block and patients were shifted to PACU.

- Group II received standard analgesia according to Obstetric department protocol consisting IM Diclofenac 75mg, IV Paracetamol 1g and IV Pentazocine 0.5mg/kg body weight stat at the end of surgery.
- Rescue analgesia in both the groups was given with IV Pentazocine 0.5mg/kg body weight on demand from the patient.
- The assessment of presence and intensity of pain (both at rest and on passive flexion of hip and knee), vomiting, nausea and sedation,1st demand of Rescue analgesia with Pentazocine was done immediately after transfer to PACU at 0hr, 4,8,12,24hr after surgery.
- The intensity of pain was assessed on VISUAL ANALOGUE PAIN SCALE:

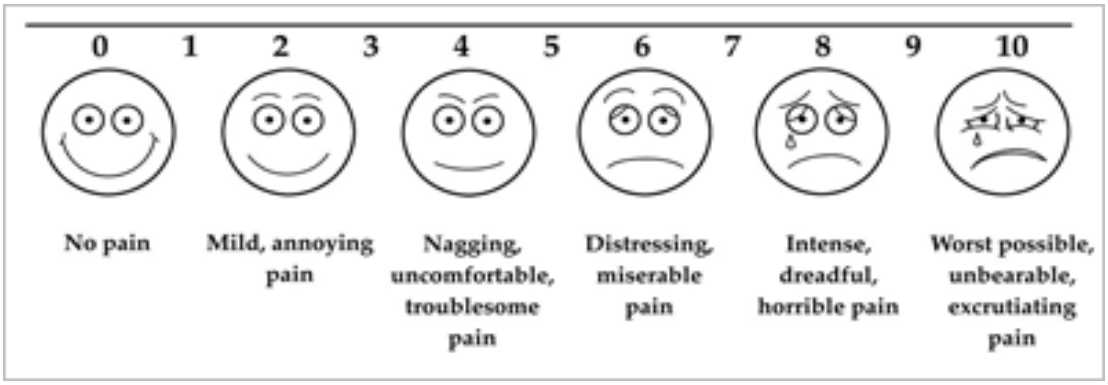


Fig 15: VAS

- Nausea and vomiting were assessed on categorical scale (0=no symptoms,1=only nausea,2=nausea and /vomiting)
- Level of sedation was assessed based on Ramsay sedation score. (0=awake and alert,1=quietly awake,2=asleep but, easily arousable,3=deep sleep, responding to painful stimulus).

- The patients were interviewed after 24 hour of surgery regarding satisfaction with their pain management on scale of 0-10 (0=very unsatisfied, 10=highly satisfied).

OBSERVATION AND RESULTS

Results

60 patients were included in the study and were randomly allocated in two groups. In group I patients were to receive TAP block with 0.25% Bupivacaine and in group II were to receive multidrug therapy for postoperative analgesia.

Demographic Profile

The mean age (mean ± S.D.) in Group I was 24.43 ± 3.35 yrs and in group II was 24.50 ± 3.92 yrs. The groups were comparable in terms of age (p =0.94).

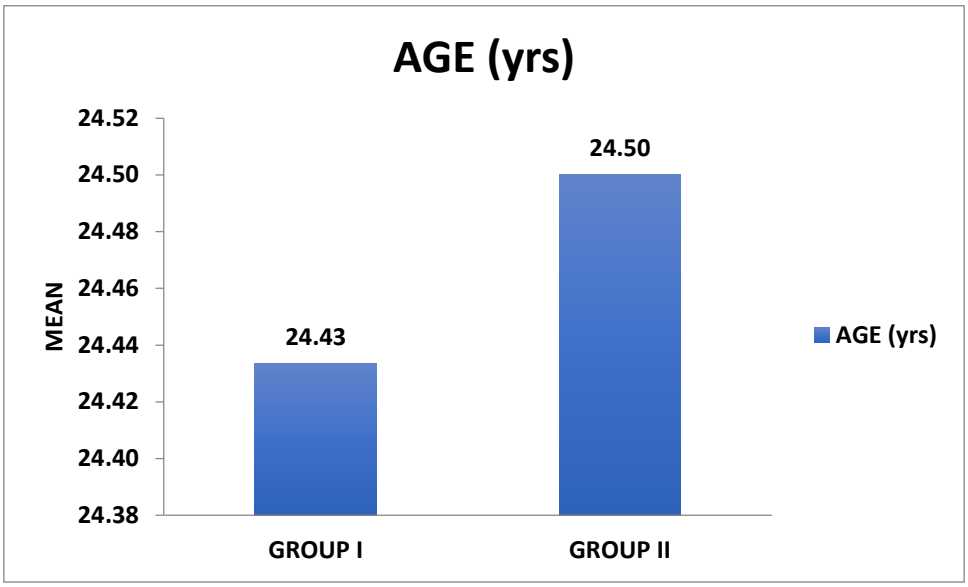
The mean height was 158.33 ± 5.01 cm in group I and 157.60 ± 5.51 cm in group II. The groups were comparable in terms of height. (p=0.591).

The mean weight was 62.40 ± 5.15 kg and 61.80 ± 4.96 kg respectively in group I and group II which was not statistically significant (p=0.842)

Therefore, both groups were comparable in terms of their demographic profile.

TABLE 4: MEAN AGE BETWEEN STUDY GROUPS

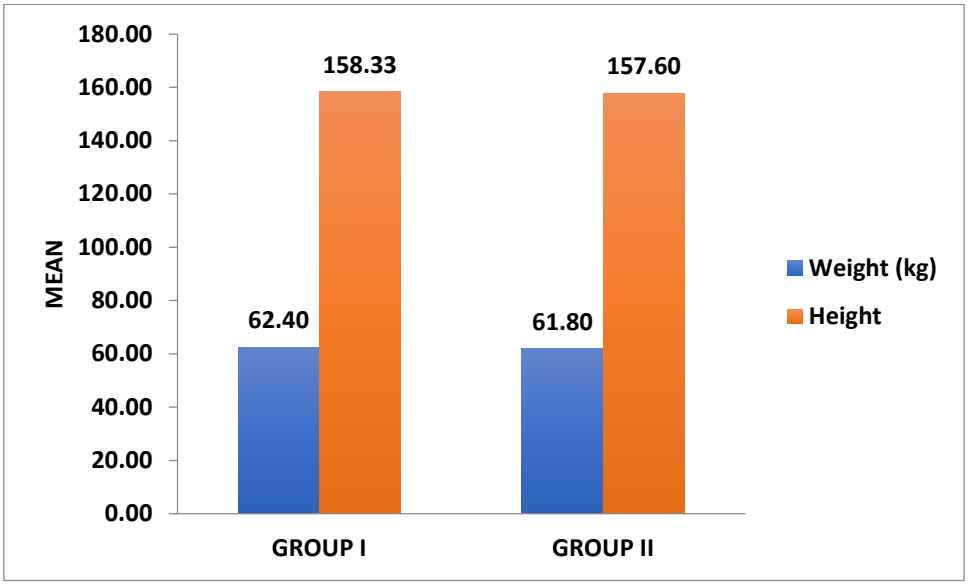
Parameter	GROUP I		GROUP II		p value
	Mean	SD	Mean	SD	
AGE (yrs)	24.43	3.35	24.50	3.92	0.944



GRAPH 3: MEAN AGE BETWEEN STUDY GROUPS

TABLE 5: MEAN WEIGHT & HEIGHT BETWEEN STUDY GROUPS

Parameters	GROUP I		GROUP II		p value
	Mean	SD	Mean	SD	
Weight (kg)	62.40	5.15	61.80	4.96	0.648
Height	158.33	5.01	157.60	5.51	0.591



GRAPH 4: MEAN WEIGHT & HEIGHT BETWEEN STUDY GROUPS

Postoperative Pain

The mean VAS score in group I at 0, 4, 8, 12 and 24 hours were 0.00±0.00, 0.87±1.28, 1.1±1.47, 0.93±1.31 and 0.3±0.75 respectively.

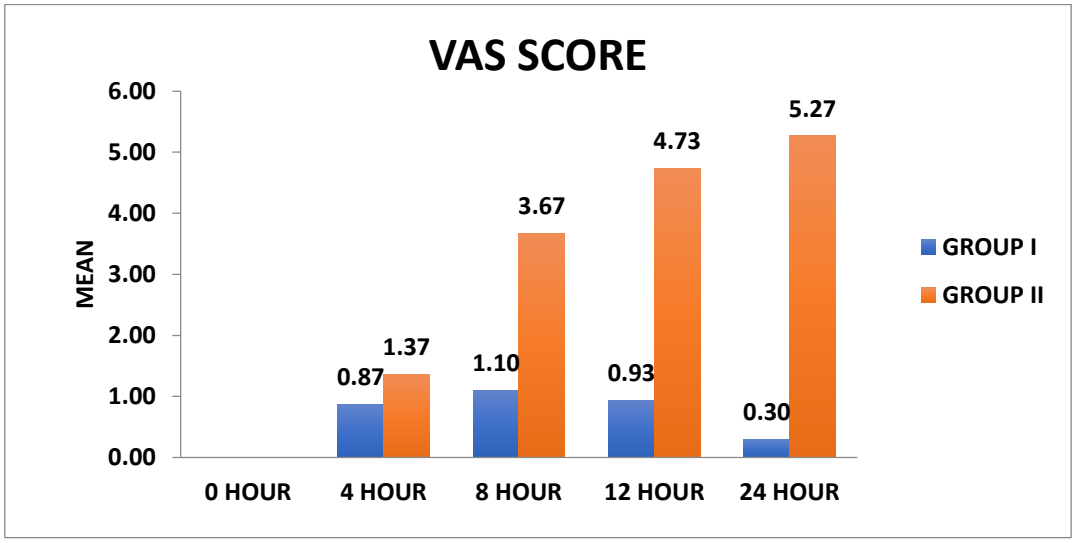
The mean VAS score in group II at 0, 4, 8, 12 and 24 hours were 0.00±0.00, 1.37±1.43, 3.67±1.06 , 4.73±0.94 and 5.27±0.78 respectively .

The difference in mean VAS score was less at 0 and 4 hour interval in group I and group II but significant difference was found at and after 8 hour interval.

TABLE 6: CHANGE IN VAS BETWEEN STUDY GROUPS

VAS AT	GROUP I		GROUP II		p value
	Mean	SD	Mean	SD	
0 HOUR	0.0	0.0	0.00	0.00	-
4 HOUR	0.87	1.28	1.37	1.43	0.158
8 HOUR	1.10	1.47	3.67	1.06	<0.001*
12 HOUR	0.93	1.31	4.73	0.94	<0.001*
24 HOUR	0.30	0.75	5.27	0.78	<0.001*

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



GRAPH 5: CHANGE IN VAS BETWEEN STUDY GROUPS

The comparison of VAS scores at different time interval in both groups showed that TAP block provided better analgesia when compared to multidrug therapy.

In the first 12 hours, 9 patients in TAP group received rescue analgesia, out of which 4 received twice and 24 patients in Multimodal group required rescue analgesia, out of which 6 patients received twice.

Mean Dose of Rescue analgesia

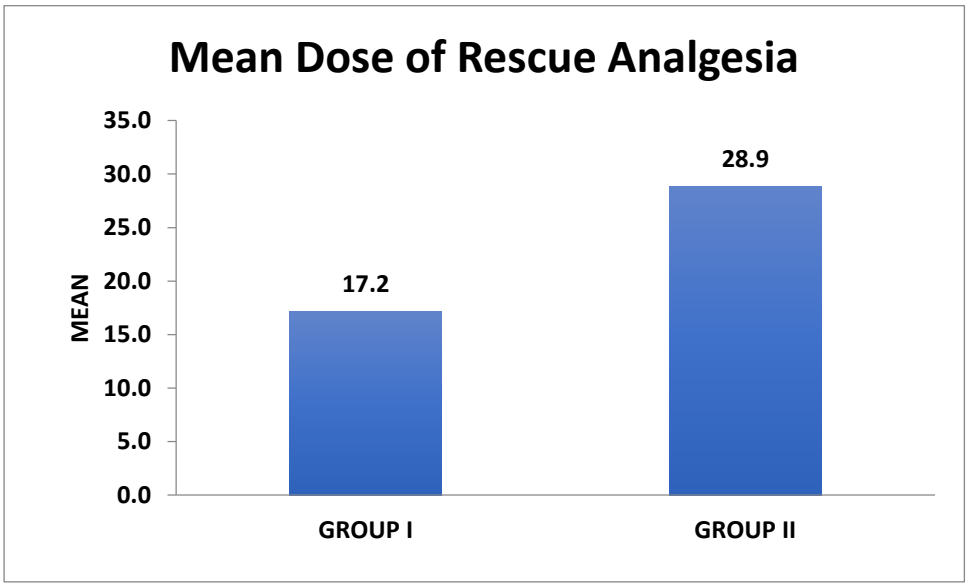
In group I mean requirement was found to be 17.2±10.4mg and in group II it was found to be 28.9±24.2 mg which was statistically significant and recorded reduction in the requirement of rescue analgesia by 40%.

TABLE 7: MEAN DOSE OF RESCUE ANALGESIA BETWEEN STUDY GROUPS

Mean Dose of Rescue Analgesia (mg)	GROUP I		GROUP II		p value
	Mean	SD	Mean	SD	
	17.2	10.4	28.9	24.2	0.047*

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

GRAPH 6: MEAN DOSE OF RESCUE ANALGESIA BETWEEN STUDY GROUPS



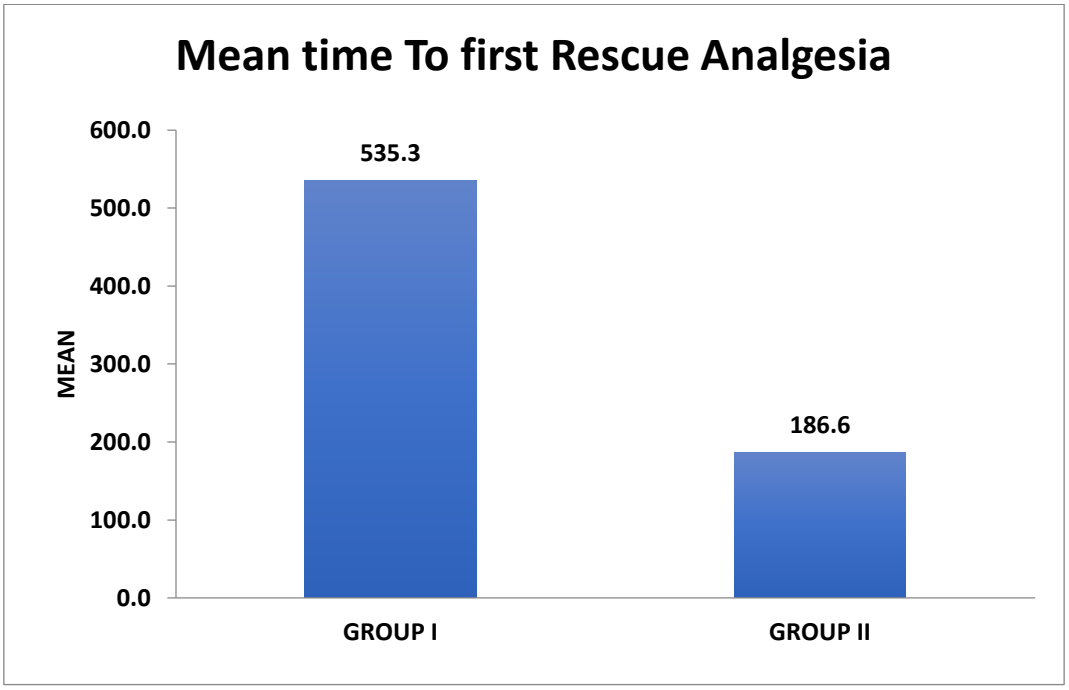
Mean Time to First Rescue Analgesia

The mean time to first rescue analgesia in Group I was 535.27 ± 118.542 min and in Group II it was 186.6 ± 67.6 min which was significant statistically (p<0.05).

TABLE 8: MEAN TIME TO FIRST RESCUE ANALGESIA BETWEEN STUDY GROUPS

Mean time To First Rescue Analgesia (min)	GROUP I		GROUP II		p value
	Mean	SD	Mean	SD	
	535.3	118.5	186.6	67.6	<0.001*

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



GRAPH 7: MEAN TIME TO FIRST RESCUE ANALGESIA BETWEEN STUDY GROUPS

Postoperative Nausea and Vomiting

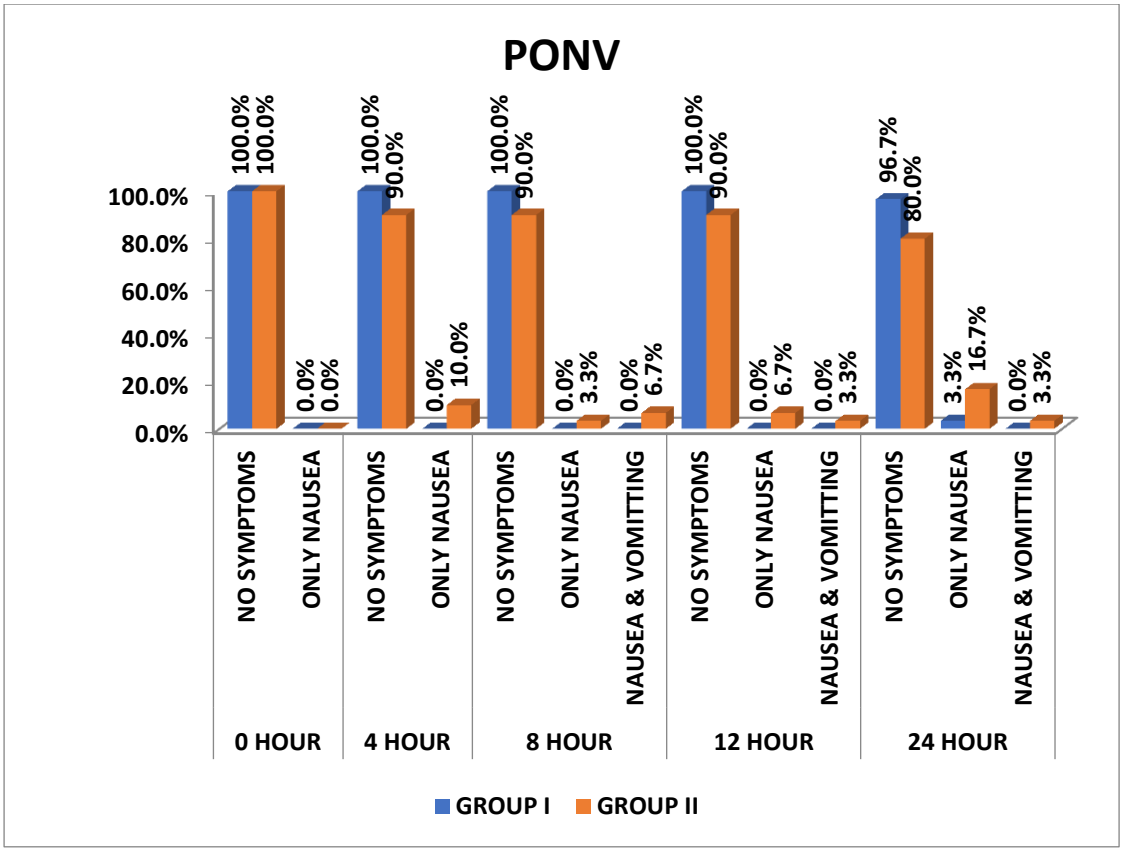
The incidence of nausea in group I was found to be 0 at 0, 4, 8 and 12 hour and 3% at 24 hours. In Group II it was found to be 0%, 10%, 3.3%, 6.7% and 16.7% at 0, 4, 8, 12 and 24 hours, respectively.

There were no incidences of vomiting recorded in Group I but, 6.7%, 3.3% and 3.3% at 8, 12 and 24 hours in Group II. The results indicating that incidence of PONV was lesser in TAP block when compared to multidrug therapy group.

The results were not significant statistically.

TABLE 9: DISTRIBUTION OF PONV BETWEEN STUDY GROUPS

PONV		GROUP I		GROUP II		p value
		N	%	N	%	
0 HOUR	NO SYMPTOMS	30	100.0%	30	100.0%	-
	ONLY NAUSEA	0	0.0%	0	0.0%	
4 HOUR	NO SYMPTOMS	30	100.0%	27	90.0%	0.076
	ONLY NAUSEA	0	0.0%	3	10.0%	
8 HOUR	NO SYMPTOMS	30	100.0%	27	90.0%	0.206
	ONLY NAUSEA	0	0.0%	1	3.3%	
	NAUSEA & VOMITING	0	0.0%	2	6.7%	
12 HOUR	NO SYMPTOMS	30	100.0%	27	90.0%	0.206
	ONLY NAUSEA	0	0.0%	2	6.7%	
	NAUSEA & VOMITING	0	0.0%	1	3.3%	
24 HOUR	NO SYMPTOMS	29	96.7%	24	80.0%	0.126
	ONLY NAUSEA	1	3.3%	5	16.7%	
	NAUSEA & VOMITING	0	0.0%	1	3.3%	
Total		30	100.0%	30	100.0%	



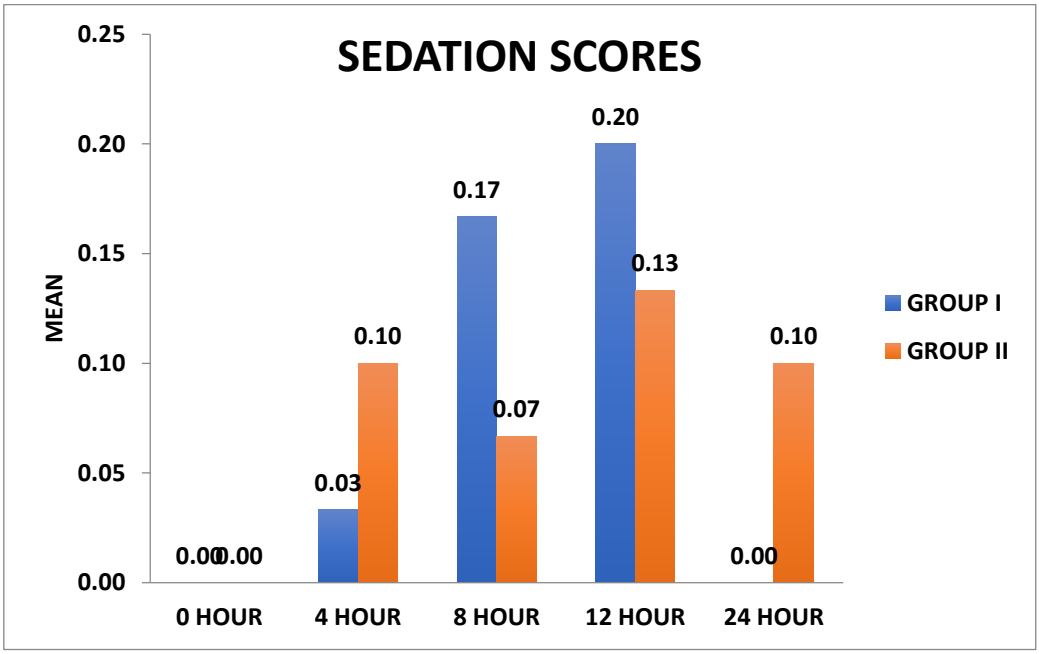
GRAPH 8: DISTRIBUTION OF PONV BETWEEN STUDY GROUPS

Sedation scores

Sedation scores in both the group were comparable and did not show any significance with respect to incidence.

TABLE 10: DISTRIBUTION OF SEDATION SCORES BETWEEN STUDY GROUPS

SEDATION SCORES AT	GROUP I		GROUP II		p value
	Mean	SD	Mean	SD	
0 HOUR	0.00	0.00	0.00	0.00	-
4 HOUR	0.03	0.18	0.10	0.40	0.412
8 HOUR	0.17	0.46	0.07	0.37	0.356
12 HOUR	0.20	0.48	0.13	0.35	0.542
24 HOUR	0.00	0.00	0.10	0.31	0.078



GRAPH 9: DISTRIBUTION OF SEDATION SCORES BETWEEN STUDY GROUPS

DISCUSSION

Adequate post-operative analgesia clearly benefits by reducing postoperative stress, postoperative morbidity and improving operative outcomes in certain kinds of surgery. Effective pain control also promotes recovery and accelerates surgical recovery. Other advantages of efficient regional analgesics include decreased pain intensity, lower incidence of analgesic adverse reactions and increased patient convenience.

TAPB is a straightforward efficient analgesic method, suitable for surgeries where, parietal pain is a major component of postoperative suffering. In patients undergoing surgery of the colon with a midline abdominal wall incision, caesarean patients and radical prostatectomy TAP Blocks were demonstrated to provide excellent analgesia of the musculature and skin of the anterior abdominal wall.

In the present study we investigated the use of the TAP block for post-operative analgesia with Bupivacaine 0.25% when compared to multidrug therapy with Diclofenac sodium, Paracetamol and Pentazocine.

The principal finding of our study is that TAP block with 0.25% bupivacaine provides effective postoperative analgesia in patients undergoing Lower Segment Caesarean Section.

We have found the superiority of TAP block in providing immediate postoperative analgesia reflected by a lower VAS score. The current literature on TAP block is unanimous in the matter that it improves postoperative pain score.

In our study patients were assessed for pain post-operatively by VAS at regular time intervals. Rescue analgesia was administered when VAS was more than or equal to 4 at any given time and the time of administration was noted. VAS score in TAP Block patients was found to be 0.30 Vs 5.27 which was comparable with

study conducted by Lee et al.[16] in 2013, with values of 0.5 and 4.9. Similarly, study conducted by Sharma et al.[60] for lower abdominal surgeries and McDonnell et al.[26] in 2008, showed reduced VAS scores.

The time to demand of first rescue analgesia was prolonged in our study to 8.9 hours compared to multimodal analgesia which was 3.1 hour, which was similar to the study conducted by Mankikar MG et al.[14] in the year 2016, which had results of 9.5 hour and 4.1 hour.

Total dose of opioid requirement in our study was found to be 40% lesser in the patients receiving TAP Block compared to non-TAP patients (17.2±10.4mg vs 28.9±24.2 mg) which was comparable to Baaj JM et al.[21] who found 60% reduction in the Morphine requirement in the TAP group. Similarly, in the study conducted by Mankikar MG et,.[14] total Tramadol requirement was reduced from 246.6mg to 140 mg in the TAP block patients. Similar study conducted by McDonnell JG et al.[26] in the year 2008 showed a reduction in the Morphine requirement in the TAP Block patients when compared to conventional group. All these demonstrated the opioid sparing effect of TAP block which was observed in our study too. In the first 12 hours, 9 patients in TAP group received rescue analgesia, out of which 4 received twice and 24 patients in Multimodal group required rescue analgesia, out of which 6 received twice.

There were reduced incidence of PONV and sedation observed in our study which was similar to the findings of Uma Srivastava et al.[15], Baaj JM et al.[21] and Elsamian et al.[19] They also demonstrated higher satisfaction of pain management in the patients who had received TAP Block and the findings were similar in our study.

The reason why the analgesic effect is long after a single shot TAP block is not fully known. The fact that the TAP is relatively poorly vascularized and that the

slower metabolism of drugs can explain this.[43] Inadequate analgesia may be due to technical failure or the visceral pain component, which is not addressed by the TAP block. As such, all local anesthetic techniques still have unsuccessful rate of 5-20% depending on the operator's ability. The main clinical implication of our results are the significant opioid sparing effect of TAP block during the postoperative period. Opioids may be associated with nausea, pruritus and respiratory depression, although they are very efficient in peri-operative pain management. In addition, some people with morbid obesity or obstructive sleep apnea will benefit from the TAP block, as it significantly reduces the requirement of opioids. For patients with coagulopathy, intra-operative and post-operative analgesia can be provided by TAP Block which is a relatively safer alternative to neuraxial block.

SUMMARY

This randomized controlled study was conducted in the department of anaesthesiology, After obtaining approval by the Institutional Ethical Committee and written informed patient consent from sixty patients of ASA II and III scheduled for caesarean section under spinal anaesthesia were randomized into two groups comprising thirty each.

Group I --USG-guided Bilateral TAP Block with 15ml of 0.25% Bupivacaine was performed on each side following caesarean section.

Group II --Received standard analgesia according to Obstetric department protocol consisting Intramuscular(IM) Diclofenac 75mg, IV Paracetamol 1g and Pentazocine 0.5mg/kg body weight stat at the end of surgery.

Rescue analgesia in both the groups was given with IV Pentazocine 0.5mg/kg on requirement.

Demographic profile: Both the groups were similar in terms of age, ASA grading, height and weight and undergone same surgical procedure.

VAS Scores: at 0, 4, 8, 12, 24 hours respectively are-

Group I- 0.00±0.00, 0.87±1.28, 1.1±1.47, 0.93±1.31 and 0.3±0.75

Group II- 0.00±0.00, 1.37±1.43, 3.67±1.06, 4.73±0.94 and 5.27±0.78.

Time for first rescue analgesia:

Group I was 535.27 ± 118.542 min

Group II it was 186.6 ± 67.6 min

Rescue analgesia dose:

Group I-17.2±10.4mg

Group II-28.9±24.2mg

PONV score: at 0, 4, 8, 12 and 24 hours are respectively

Group I-0, 0, 0, 0 and 3.3% for nausea,0% for vomiting.

Group II-0%, 10%, 3.3%, 6.7% and 16.7% for nausea.

0%, 0%, 6.7%, 3.3% and 3.3% for vomiting.

Sedation score was found to be statistically insignificant.

From reduced VAS, Prolonged duration for rescue analgesia and total dose of rescue analgesia consumed, it was observed that TAPB had better profile than multimodal analgesia.

CONCLUSION

On the basis of the present comparative trial, we conclude that TAP block is easy to perform under ultrasound guidance. It provides effective analgesia with reduced rescue analgesic requirement 24 hours following surgery, with prolonging the duration of analgesia and reduced incidence of PONV and sedation along with higher patient satisfaction.

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ANNEXURE – I

ETHICAL CLEARANCE CERTIFICATE

ANNEXURE – II

INFORMED CONSENT FORM:

TITLE OF THE PROJECT: **“A RANDOMIZED COMPARATIVE CLINICAL TRIAL TO KNOW THE EFFICACY OF ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK AGAINST MULTIMODAL ANALGESIA FOR POST-OPERATIVE ANALGESIA FOLLOWING CAESAREAN SECTION”**

PRINCIPAL INVESTIGATOR:

PG GUIDE :

PURPOSE OF RESEARCH:

I have been informed that this study is**: "A RANDOMIZED COMPARATIVE CLINICAL TRIAL TO KNOW THE EFFICACY OF ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK AGAINST MULTIMODAL ANALGESIA FOR POST-OPERATIVE ANALGESIA FOLLOWING CAESAREAN SECTION ".**

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: "**A RANDOMIZED COMPARATIVE CLINICAL TRIAL TO KNOW THE EFFICACY OF ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK AGAINST MULTIMODAL ANALGESIA FOR POST-OPERATIVE ANALGESIA FOLLOWING CAESAREAN SECTION ".**

RISKS AND DISCOMFORTS:

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

BENEFITS:

I understand that my wards participation in this study will help in finding out: **"A RANDOMIZED COMPARATIVE CLINICAL TRIAL TO KNOW THE EFFICACY OF ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK AGAINST MULTIMODAL ANALGESIA FOR POST-OPERATIVE ANALGESIA FOLLOWING CAESAREAN SECTION ".**

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. _____ 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 _____ will terminate my participation in this study at any time after 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:

(Investigator)

Patient's signature Witness

STUDY SUBJECT CONSENT STATEMENT:

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

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

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

ANNEXURE – III

10. SCHEME OF CASE TAKING:

PROFORMA

STUDY: **"A RANDOMIZED COMPARATIVE CLINICAL TRIAL TO KNOW THE EFFICACY OF ULTRASOUND TRANSVERSUS ABDOMINIS PLANE BLOCK AGAINST MULTIMODAL ANAGLGESIA FOR POST-OPERATIVE ANALGESIA FOLLOWING CAESAREAN SECTION".**

PATIENT DETAIL: **DATE OF SURGERY:**

- Name: Age: I.P No: Wt: Ward:
- Group allotted by randomization: Group I / Group II
- Date of Admission:
- Indication:
- Significant History:
- Obstetric History:
- General Physical Examination:

  Pallor Icterus Cyanosis Clubbing Koilonychia

  Lymphadenopathy Oedema
- Teeth Dentures
- Vital Parameters

  Pulse Blood Pressure

  Respiratory Rate Temperature
- Systemic Examination
  - Cardiovascular system
  - Respiratory system
  - Central nervous system

- Per abdomen

- Airway Assessment:

  Mallampatti Grade: Cervical Spine:

  Mouth Opening: Neck Movement:

- Investigation

  Haemoglobin(gm%): TLC:

  Platelet count: Differential count:

  BT: CT:

  B. Urea: S. Creatinine:

  LFT(If required): Urine routine:

  ECG(If required):

  Any other Investigation(If required):

- ASA grade:

- Baseline readings: Pulse rate- Blood Pressure-

  Respiratory rate- SPO_2-

- **Procedure**

- Thorough monitoring will be carried out and complications will be looked for post-operatively at 0,4,8,12 & 24hrs.

X. Parameters

Block Performance Data					
Parameters	0 HR	4HR	8HR	12HR	24HR
Pain at rest and on movement on visual analog scale(VAS)					
Time of 1st demand of Rescue analgesia					
Sedation score					
Satisfaction with pain management					
Side effects if any					

DATE

SIGNATURE

KEY TO MASTER

1. VAS
2. Rescue analgesia.
3. Duration of Analgesia.
4. PONV.
5. Sedation score.

MASTER CHART

SR NO.	IPD NO	AGE (YEARS)	Weight (kg)	Height (cm)	DIAGNOSIS	Group	ASA Grade	VAS AT					Rescue Analgesia	Duration Of Analgesia (mins)	PONV AT					SEDATION SCORES AT				
								0 HOUR	4 HOUR	8 HOUR	12 HOUR	24 HOUR			0 HOUR	4 HOUR	8 HOUR	12 HOUR	24 HOUR	0 HOUR	4 HOUR	8 HOUR	12 HOUR	24 HOUR
1	42600	21	64	154	G3P2L2 D2 with 37weeks 2 day POG with severe pe	I	3	1	1	0	2	2	0	1450	1	0	0	0	0	0	0	0	0	0
2	42255	27	58	158	G4P2L2A1 with 40wk pog with previous lscs	I	2	2	0	0	2	0	0	1440	0	0	0	0	0	0	0	0	0	0
3	42268	24	62	162	G2P1L1 WITH 39 WEEKS WITH PREVIOUS LSCS with oligohydromnios	I	2	3	3	4	1	0	1	480	0	1	0	0	0	O	O	2	O	O
4	42248	25	56	163	Primi with41wk pog for safe confinement	I	2	0	0	0	0	0	0	1500	0	0	0	0	0	0	0	0	0	0
5	25827	22	57	158	G2P1L1 with 40wk 2d pog with previous lscs	I	2	0	2	3	3	3	0	1525	1	1	0	0	0	0	0	0	0	0
6	25686	22	68	155	G2P2L1 with 41WK POG WITH PREVIOUS LSCS	I	2	0	0	0	0	0	0	1550	0	0	0	0	0	0	0	0	0	0
7	21281	20	72	166	PRIMI WITH 37WK POG WITH OLIGOHYDROMNIOS	I	2	0	2	2	3	0	0	1505	0	0	0	0	0	0	0	0	0	0
8	21138	23	56	162	PRMI WITH 37 WK POG	I	2	0	0	0	0	0	0	1580	0	0	0	0	0	0	0	0	0	0
9	21592	29	66	149	G3P2L1A1 WITH 37WK POG WITH PREVIOUS LSCS	I	2	2	2	2	0	0	1	565	0	0	0	0	0	0	0	0	0	0
10	19060	28	67	150	PRIMI WITH 36WK WITH PROM	I	2	0	0	2	2	2	2	540	1	1	0	0	0	0	0	0	0	0
11	20583	23	64	153	G3A2 WITH 36 WK WITH TWIN GESTATION IN LATENT LABOUR	I	2	2	3	3	4	0	1	780	0	0	0	0	0	0	0	0	2	0
12	14096	23	58	159	G2P1D1 WITH 40WK 2D POG WITH PREVIOUS LSCS	I	2	0	0	0	0	0	0	1450	0	0	0	0	0	0	0	0	0	0
13	13985	35	61	148	PRIMI WITH 37WK 3D POG	I	2	2	1	2	0	0	0	1530	0	0	0	0	0	0	0	0	0	0
14	13542	24	59	154	PRIMI WITH 40WK 6D POG WITH GHTN	I	3	0	0	0	0	0	0	1460	0	0	0	0	0	0	0	0	0	0
15	26106	24	60	158	PRIMI WITH 37WK POG	I	2	2	3	3	4	0	1	690	0	0	0	0	0	0	0	0	1	0
16	16907	20	58	154	PRIMI WITH 39WK 3D POG WITH GHTN	I	3	0	0	0	0	0	0	1550	1	0	0	0	0					
17	16974	25	55	162	PRIMI WITH 40WK 3D POG WITH BREECH PRESENTATION	I	2	0	0	0	0	0	2	780	0	0	0	0	0	0	0	0	0	0
18	43074	23	65	164	G3P2L2 WITH 38WK POG WITH PREVIOUS LSCS	I	2	0	0	0	0	0	0	1480	0	0	0	0	0	0	0	0	0	0
19	43103	23	66	158	PRIMI WITH 38WK 4D POG WITH	I	2	3	3	4	1	0	2	480	0	0	0	0	0	0	0	1	1	0
20	25069	25	70	158	G2P1L1 WITH 38WK 5D POG WITH PREV LSCS WITH OLIGOHYDROMNIOS	I	2	0	0	0	0	0	0	1500	0	0	0	0	0	0	0	0	0	0
21	25097	25	68	164	PRIMI WITH 38WK 4D POG	I	2	0	0	2	2	0	0	1480	0	0	0	0	1	0	0	0	0	0
22	22029	30	63	162	G2P1L1A1 WITH 37 WK 4D WITH PREVIOUS LSCS	I	2	0	0	0	0	0	0	1440	0	0	0	0	0	0	0	0	0	0
23	22331	28	72	168	PRIMI WITH 38WK 3D POG WITH OLIGOHYDROMNIOS	I	2	0	0	0	0	0	0	1440	1	0	0	0	0	0	0	0	0	0
24	1416	23	61	157	G2D1L1 WITH 39WK 1D POG WITH PREVIOUS LSCS	I	2	3	4	2	2	1	2	240	0	0	0	0	0	0	1	1	0	0
25	913	24	64	158	G2P1L1 WITH 39 WK 4 D WITH PREVIOUS LSCS	I	2	0	0	0	0	0	0	1550	0	0	0	0	0	0	0	0	0	0
26	172	28	57	156	G2P1L1 WITH 34WK 5D POG	I	2	0	0	0	0	0	0	1500	0	0	0	0	0	0	0	0	0	0
27	6209	26	54	154	G2P1L1 WITH 40 WK WITH PREVIOUS LSCS	I	2	0	0	0	0	0	0	1600	0	0	0	0	0	0	0	0	0	0
28	7574	22	58	160	PRIMI WITH 38WK 2D POG	I	2	0	0	0	0	0	0	1500	0	0	0	0	0	0	0	0	0	0
29	8211	21	65	162	PRIMI WITH 42WK 1D POG	I	2	0	0	0	0	0	0	1560	0	0	0	0	0	0	0	0	0	0
30	10894	20	68	164	G2P1L1 WITH 39WK 3D POG	I	2	0	2	4	2	1	2	340	0	0	0	0	0	0	0	1	1	0

SR NO.	IPD NO	AGE (YEARS)	Weight (kg)	Height (cm)	DIAGNOSIS	Group	ASA Grade	VAS AT					Rescue Analgesia	Duration Of Analgesia (mins)	PONV AT					SEDATION SCORES AT				
								0 HOUR	4 HOUR	8 HOUR	12 HOUR	24 HOUR			0 HOUR	4 HOUR	8 HOUR	12 HOUR	24 HOUR	0 HOUR	4 HOUR	8 HOUR	12 HOUR	24 HOUR
1	22738	21	58	154	G3P2L1D1 WITH 38WK POG WITH PREVIOUS LSCS	II	2	0	2	3	5	6	2	350	0	0	1	0	0	0	0	0	0	0
2	22840	22	55	152	G2P1L1 WITH 40 WK 1D POG WITH PREVIOUS LSCS	II	2	0	0	2	3	5	1	375	0	0	0	0	0	0	0	0	0	1
3	22617	22	65	164	G2P1L1 WITH 37WK WITH PREVIOUS LSCS	II	2	0	0	3	5	6	1	300	0	0	0	0	1	0	0	0	1	0
4	1850	25	66	158	PRIMI WITH 39WK POG	II	2	0	0	3	3	5	1	365	0	0	0	0	0	0	0	0	0	0
5	381	20	60	158	PRIMI WITH 41WK POG	II	2	0	0	3	5	5	1	390	0	0	0	2	0	0	0	0	0	1
6	12720	20	68	164	PRIMI WITH 34WK 2D POG	II	2	0	2	3	3	5	0	370	0	0	0	0	0	0	0	0	0	0
7	4282	25	63	162	G3P1L1A1 WITH 40WK 5D POG	II	22	0	0	3	5	6	1	370	0	0	0	0	0	0	0	0	0	0
8	5174	24	72	168	G3P2L1D1 WITH 39WK 5D POG WITH BREECCH PRESENTATION.	II	2	0	2	3	3	5	0	345	0	0	0	0	1	0	0	0	0	0
9	5760	28	63	157	G2P1L1 WITH 38 WK 1D POG WITH PREVIOUS LSCS	II	2	0	3	5	5	6	0	300	0	0	0	1	0	0	0	0	0	0
10	6919	25	64	158	G2P1L1 WITH 39WK 2 D POG WITH PREVIOUS LSCS	II	2	0	3	3	5	5	1	355	0	0	2	0	0	0	0	0	0	0
11	9417	20	57	156	PRIMI WITH 40WK POG	II	2	0	0	3	3	6	1	400	0	0	0	0	0	0	0	0	0	0
12	9497	22	67	154	G2P1L1 WITH 33WK POG WITH OLIGOHYDROMNIOS	II	2	0	0	3	5	5	1	360	0	0	0	0	0	0	0	0	0	0
13	13095	25	58	160	G3P1L1A1 WITH35WK 6D POG WITH PREVIOUS LSCS	II	2	0	2	3	5	5	1	480	0	0	0	0	0	0	0	0	0	0
14	14609	24	65	162	G5P2L1D1 WITH 5 WK POG WITH OLIGOHYDROMNIOS	II	2	0	0	3	5	6	1	480	0	0	0	0	1	0	0	0	0	0
15	14709	25	55	164	G3P2L2 WITH 37 WK 5D POG WITH PREVIOUS LSCS	II	2	0	3	5	5	6	2	360	0	0	0	0	0	0	0	0	0	0
16	15156	20	64	154	PRIMI WITH 39WK 5D POG	II	2	0	3	5	6	6	2	310	0	0	0	0	0	0	0	0	1	0
17	15170	26	58	152	G3P2L2 WITH 40WK POG WITH PREVIOUS LSCS	II	2	0	0	3	5	6	2	375	0	0	0	0	0	0	0	0	0	0
18	15255	25	54	148	G5P2L2A2 WITH 39WK POG WITH PREVIOUS LSCS	II	2	0	0	3	5	5	2	380	0	0	0	0	0	0	0	0	0	0
19	16037	22	56	158	PRIMI WITH 42WK POG	II	2	0	0	3	5	6	1	330	0	0	0	0	0	0	0	0	0	0
20	16090	27	57	156	PRIMI WITH 37WK POG	II	2	0	3	5	5	5	1	315	0	0	0	0	0	0	0	0	0	0
21	16362	32	68	159	G4P2D1 WITH 5WK WITH PREVIOUS LSCS	II	2	0	0	3	5	5	1	390	0	0	0	0	1	0	0	0	1	0
22	16742	21	70	166	PRIMI WITH 37 WK 5D POG	II	2	0	0	3	5	5	1	420	0	0	0	0	0	0	0	0	0	0
23	16713	22	56	148	PRIMI WITH 40WK POG	II	2	0	3	5	5	4	0	320	0	0	0	0	0	0	0	0	O	1
24	16907	20	66	168	PRIMI WITH 9WK POG	II	2	0	0	3	3	4	0	430	0	0	0	0	2	0	0	0	1	0
25	3859	29	67	156	G3P2L1D1 WITH 37WK 4D POG	II	2	0	3	5	5	5	1	300	0	0	0	0	0	0	0	0	0	0
26	7921	29	64	153	G2P1L1 WITH 38 WK WITH PREVIOUS LSCS	II	2	0	3	5	6	6	1	310	0	0	0	0	1	0	2	0	0	0
27	12121	25	58	159	G2P1L1 WITH 34 WK POG	II	2	0	3	5	5	4	`1	340	0	0	0	1	0	0	0	2	0	0
28	10756	22	61	148	G2P1L1 WITH 36WK POG WITH BREECH PRESENTATION	II	2	0	3	5	6	3	1	315	0	0	0	0	0	0	0	0	0	0
29	12007	34	59	154	G4P2L2A1 WITH 39WK POG WITH PREVIOUS LSCS	II	2	0	3	6	6	6	2	300	0	0	0	0	0	0	1	0	0	0
30	10250	33	60	158	PRIMI 37WK POG	II	2	0	0	3	5	6	1	420	0	0	2	0	0	0	0	0	0	0