# "A COMPARISON OF PREEMPTIVE TRANSVERSUS ABDOMINIS PLANE BLOCK WITH 0.25% BUPIVACAINE AND 0.25% BUPIVACAINE WITH 20MCG FENTANYL FOR POST OPERATIVE ANALGESIA IN LAPAROSCOPIC APPENDICECTOMY - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"

**By**

**REG NO.BA0115002**

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## KLE UNIVERSITY, BELAGAVI, KARNATAKA

# ENDORSEMENT

This is to certify that the dissertation entitled **"A COMPARISON OF PREEMPTIVE TRANSVERSUS ABDOMINIS PLANE BLOCK WITH 0.25% BUPIVACAINE AND 0.25% BUPIVACAINE WITH 20MCG FENTANYL FOR POST OPERATIVE ANALGESIA IN LAPAROSCOPIC APPENDICECTOMY - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"** is a bonafide research work done by **REG NO.BA0115002.**

**Dr. M.G.Dhorigol$_{MD}$**
Professor and Head,
Department of Anaesthesiology,
J.N.MedicalCollege,
Nehru Nagar, Belagavi– 10
Date:
Place: Belagavi

**Dr. N. S. Mahantshetti$_{MD(paed)}$**
Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date:
Place: Belagavi

# LIST OF ABBREVIATIONS USED

| | | |
|---|---|---|
| TAP | - | TransversusAbdominis Plane |
| ASA | - | American society of Anaesthesiologists |
| CNS | - | Central nervous system |
| $CO_2$ | - | Carbon dioxide |
| $O_{2\backslash}$ | - | Oxygen |
| $N_2O$ | - | Nitrous Oxide |
| CVS | - | Cardiovascular system |
| RS | - | Respiratory system |
| DBP | - | Diastolic blood pressure |
| ECG | - | Electrocardiogram |
| GIT | - | Gastrointestinal tract |
| Hb | - | Haemoglobin |
| HR | - | Heart rate |
| Inj. | - | Injection |
| IV | - | Intravenous |
| Kgs | - | Kilograms |
| L | - | Liters |
| Mg | - | Milligrams |
| Mins | - | Minutes |
| Ml | - | Milliliters |

| | | |
|---|---|---|
| µg | - | Micrograms |
| MPG | - | Mallampati Grading |
| PR | - | Pulse rate |
| RBS | - | Randombloodsugar |
| RR | - | Respiratory rate |
| SBP | - | Systolic blood pressure |
| $SPO_2$ | - | Saturation percentage of oxygen |
| Sr | - | Serum |
| Temp | - | Temperature |
| TLC | - | Total Leucocyte count |
| VAS | - | Visual Analogue Scale |
| WDR | - | Wide Dynamic Range |
| DPQ | - | Dartmouth Pain Questionnairre |
| MPQ | - | McGill Pain Questionnairre |
| WHYPQ | - | West Haven – Yale Pain Questionnairre |
| QoR-40 | - | Quality of recovery - 40 |
| α | - | Alpha |
| β | - | Beta |
| NSAIDs | - | Non steroidal anti-inflammatory drugs |

# ABSTRACT

**BACKGROUND:**

In recent years laparoscopic appendicectomy is performed more often than open appendicectomy to reduce postoperative pain, reduced duration of hospital stay, early ambulation and discharge.However laparoscopic surgery is not completely pain free. Several modalities have been tried to treat post operative pain following laparoscopic appendicectomy. Transversus abdominis plane block has been found to be a safe and effective tool to provide postoperative analgesia in a various laparoscopic surgeries.

**OBJECTIVE:**

To compare the efficacy of preemptive Transversus abdominis plane block with 0.25% bupivacaine and 0.25% bupivacaine with fentanyl for duration of postoperative analgesia in patients undergoing laparoscopic appendicectomy.

**METHODOLOGY:**

The present study was conducted at , KLE'S Dr.Prabhakar Kore Hospital and Medical Research Centre, Nehru nagar, Belagavi 590010, on 60 adult patients undergoing elective laparoscopic appendicectomy under General Anaesthesia between January 2016 to December 2016.Patients were divided into 2 groups, Group 1 and Group 2 by computer generated randomisation table. After induction of general anaesthesia Group 1 patients received TAP block with 15ml of 0.25% bupivacaine bilaterally and Group 2 patients received received TAP block with 15ml of 0.25% bupivacaine + 10 mcg of fentanyl bilaterally.Laparoscopic appendicectomy was done according to standard protocol.

In the post operative period patients were assessed for post operative pain at 0, 1,2,3,4,5,6,8,10,12,14,16,18,20,22,24 hours using VAS pain scale. If VAS>3 rescue analgesia in the form of Inj Tramadol 2mg/kg IV was given. Time of first rescue analgesia was noted.

**RESULTS:**

The two groups were comparable with respect to age, mean weight, ASA status and gender distribution. The mean VAS scores were comparable (less than 3) in both the groups at different time intervals post operatively ($p > 0.05$).14 patients in group 1 and 7 patients in group 2 recorded VAS score > 3 and required rescue analgesic in the first 24 hours. This difference was statistically significant ($p=0.029$). The time for requirement of first rescue analgesic was 11.43±4.26 hrs in group 1 and 14.00±1.63 hrs in group 2. Even though the time for first rescue analgesic is longer in group 2, it was not statistically significant ($p=0.142$).

**CONCLUSION:**

Pre-emptive Transversus abdominis plane block with 0.25% bupivacaine or with addition of fentanyl is equally effective in providing postoperative pain relief in patients undergoing elective laparoscopic appendicectomy .

**KEYWORDS:** Transversus abdominis plane block, 0.25% bupivacaine, Fentanyl, laparoscopic appendicectomy, postoperative pain.

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# INTRODUCTION

In recent years laparoscopic appendicectomy is performed more often than open appendicectomy to reduce postoperative pain and duration of hospital stay.[1]However laparoscopic surgery is not completely pain free.[2,3,4] The exact etiology of pain after laparoscopic surgeries is still unclear, however, it appears to be multifactorial and the causes include, abdominal wall trauma by trocar entrances, diaphragmatic irritation secondary to $CO_2$ insufflation and pneumoperitoneum, type and temperature of insufflated gas, residual intraperitoneal gas, intraabdominal trauma, microruptures of the parietal peritoneum due to abdominal distension, chemical irritation of the peritoneum, etc.[2]

Several modalities have been tried to treat post operative pain following laparoscopic appendicectomy like parentral or peroral opioids and NSAIDs, intraperitoneal infiltration of the local anesthetics or opioids, patient-controlled analgesia, injection of local anesthetics into the port sites, rectus sheath block, transverses abdominis plane block etc.[2,5-10]

Many studies have been performed to determine the effectiveness of Transversus Abdominis Plane (TAP) block using ropivacaine (0.5%) or bupivacaine(0.25%) on postoperative quality of recovery and post operative analgesia following laparoscopic cholecystectomy and found it to be highly effective[11,12].

Many studies have shown the efficacy of adding fentanyl to local anaesthetics in regional anesthesia techniques to improve and prolong postoperative analgesia.[13,14,15]

However, no studies have been done to compare the efficacy of adding fentanyl to bupivacaine in TAP block for laparoscopic appendicectomy.

Hence we compared the efficacy of preemptive TAP block with 0.25% bupivacaine and 0.25% bupivacaine with fentanyl for duration of postoperative analgesia in patients undergoing laparoscopic appendicectomy.

# OBJECTIVES

1. To compare the efficacy of preemptive Transversus Abdominis plane block with 0.25% bupivacaine and 0.25% bupivacaine with fentanyl for duration of postoperative analgesia in patients undergoing laparoscopic appendicectomy.
2. To compare the time of first rescue analgesia
3. To compare side effects, if any.

# REVIEW OF LITERATURE

Appendicectomy is one of the most commonly performed surgical procedures.[16]

In 1735, Claudius Amyand performedthe first successful appendicectomy. Later in 1981 Kurt Semm performed the first laparoscopic appendicectomy which became a new gold standard in surgical treatment of appendicitis.[17]

Laparoscopic appendicectomy has advantages over open procedure, such as decreased postoperative pain, better aesthetic result, a shorter time to return to activities, and lower incidence of wound infections or dehiscence. This procedure is cost-effective but may require more operative time and skill as compared with open appendicectomy. In addition, patients who underwent open appendicectomy returned to work later and had more complications.[18]

**Antonio Biondi et al.** conducted a study to compare the laparoscopic approach and the conventional technique in the treatment of acute appendicitis in a retrospective analysis.

Data collected from 593 consecutive patients with acute appendicitis were studied. These comprised 310 patients who underwent open appendectomy and 283 patients treated laparoscopically. They came to the conclusion that laparoscopic approach is a safe and efficient operative procedure in appendectomy and it provides clinically beneficial advantages over open method including shorter hospital stay, decreased need for postoperative analgesia, early food tolerance, earlier return to work, lower rate of wound infection against only marginally higher hospital costs[1].

Although laparoscopic surgeries have several advantages, patients do suffer from postoperative pain especially in the first 24hrs[2,3,4].

Several methods have been tried to alleviate pain in the postoperative period. These include the use of systemic opioids, Non-steroidal anti-inflammatory drugs, NMDA antagonists, Alpha-2 adrenergic agonists. Other methods include port site infiltration of local anaesthetics, intraperitoneal instillation of drugs, Transversus abdominis plane block, rectus sheath block etc[3,5-10].

A meta-analysis by **Gildasio S. De Oliveira Jr, et al.** identified randomized controlled trials which evaluated the effects of the TAP block compared with an placebo group on postoperative pain outcomes in laparoscopic procedures. Primary outcomes included early (0–4 hours) and late (24 hours) postoperative pain at rest and on movement and postoperative opioid consumption (up to 24 hours). Ten randomized clinical trials with 633 subjects were included in the analysis. Postoperative opioid consumption was decreased in the TAP block group compared with control. Preoperative TAP block administration resulted in greater effects on early pain and opioid consumption compared with postoperative administration. The analysis concluded that TAP block is an effective strategy to improve early and late pain at rest and to reduce opioid consumption after laparoscopic surgical procedures[11].

| Authors | Year of publication | Procedures | No. of treatment/ control | Treatment | Postoperative analgesia | Modified Jadad score (1–5) |
|---|---|---|---|---|---|---|
| Albrecht et al. | 2013 | Laparoscopic gastric bypass | 27/30 | Preoperative bilateral TAP blocks using 30 mL of 0.25% bupivacaine with epinephrine | Acetaminophen 1000 mg per os q6h + oxycodone 5–10 mg per os q4h + morphine 2–6 mg IV as needed | 5 |
| Sinha et al. | 2013 | Laparoscopic bariatric surgery | 50/50 | Postoperative bilateral TAP blocks using 20 mL of 0.375% ropivacaine | Tramadol not standardized | 4 |
| Walter et al | 2013 | Laparoscopic colorectal surgery | 33/35 | Preoperative bilateral TAP block using 40 mL of 2 mg/kg bupivacaine | Acetaminophen 1 g IV q6h PCA morphine | 4 |
| Petersen et al | 2012 | Laparoscopic cholecystectomy | 37/37 | Preoperative bilateral TAP block using 20 mL of 0.5% ropivacaine | Acetaminophen 1000 mg per os q6h and ibuprofen 400 mg per os q6h, morphine IV and oral ketobemidone | 5 |
| Kane et al. | 2012 | Laparoscopic hysterectomy | 28/28 | Postoperative bilateral TAP block using 20 mL of 0.5% ropivacaine with epinephrine | Not standardized | 3 |
| Hosgood et al. | 2012 | Laparoscopic nephrectomy | 24/22 | Preoperative bilateral TAP block using 20 mL of 0.375% bupivacaine | PCA morphine + oral tramadol and oral acetaminophen 1 g q6h | 5 |

| | | | | | | |
|---|---|---|---|---|---|---|
| De Oliveira et al. | 2011 | Laparoscopic hysterectomy | 43/23 | Preoperative bilateral TAP blocks using 20 mL of 0.5% ropivacaine or 0.25% ropivacaine | Ketorolac 30 mg IV, hydromorphone and hydrocodone | 5 |
| De Oliveira et al. | 2011 | Laparoscopic outpatient gynecology | 47/23 | Preoperative bilateral TAP blocks using 15 mL of 0.5% ropivacaine or 0.25% ropivacaine | Ketorolac 30 mg IV hydromorphone and hydrocodone | 5 |
| Ra et al. | 2010 | Laparoscopic cholecystectomy | 36/18 | Preoperative bilateral TAP blocks using 15 mL of 0.5% bupivacaine or 0.25% bupivacaine | Ketorolac 30 mg IV q8h, fentanyl | 3 |
| El-Dawlatly et al. | 2009 | Laparoscopic cholecystectomy | 21/21 | Preoperative bilateral TAP blocks using 15 mL of 0.5% bupivacaine | PCA morphine | 4 |

Another study by **Gildasio S. De Oliveira, Jr. et al**.evaluated the dose-dependent effects of a preoperative transverses abdominis plane (TAP) block on patient recovery using the Quality of Recovery 40 (QoR-40) questionnaire after ambulatory gynecological laparoscopic surgery. Global QoR-40 scores range from 40 to 200, representing very poor to outstanding quality of recovery, respectively. 70 healthy women undergoing outpatient gynecological laparoscopy were randomly allocated to receive a preoperative TAP block using saline, ropivacaine 0.25%, or ropivacaine 0.5%. Needle placement for the TAP blocks was performed using

ultrasound guidance and 15 mL of the study solution was injected bilaterally. QoR-40 score and analgesic use were assessed 24 hours postoperatively. The primary outcome was global QoR-40 score at 24 hours after surgery. Data were analyzed and they concluded that TAP blocks with ropivacaine 0.25% and 0.5% reduced pain, decreased opioid consumption, and provided earlier discharge that was associated with better quality of recovery.[19]

A study by **G. Niraj et al.** evaluated the analgesic efficacy of TAP block in patients undergoing open appendicectomy in a randomized controlled double-blinded clinical trial. Fifty-two adult patients undergoing open appendicectomy were randomized to undergo standard care or to undergo a right-sided TAP block with bupivacaine.All patients received patient-controlled IV. morphine analgesia, regular acetaminophen, and non-steroidal anti-inflammatory drug, as required, in the postoperative period. Ultrasound-guided TAP block significantly reduced postoperative morphine consumptionin the first 24 h .Postoperative visual analogue scale pain scores were also reduced in the TAP block group soon after surgery. The study concluded that ultrasound-guided TAP block holds considerable promise as a part of a balanced postoperative analgesic regimen for patients undergoing open appendicectomy[20].

Another study conducted by **John Carney, et al.** evaluated the analgesicefficacy of TAP block over the first 48 postoperative hours after open appendectomy in a randomized, controlled, double-blind clinical trial. Forty children undergoing appendectomy were randomized to undergo unilateral TAP block in addition to standard postoperative analgesia with IV morphine analgesia and regular diclofenac and acetaminophen. All patients received a standard general anesthetic,

and after induction of anesthesia, a TAP block was performed using the landmark technique with 2.5 mg / kg ropivacaine 0.75% or an equal volume (0.3 mL /kg) of saline on the ipsilateral side to the incision. The TAP block with ropivacaine reduced morphine requirements in the first 48 postoperative hours compared with placebo block. The TAP block also reduced postoperative visual analogue scale pain scores at rest and on movement compared with placebo. Interval morphine consumption was reduced over the first 24 postoperative hours.

The study concluded that unilateral TAP block, as a component of a multimodal analgesic regimen, provided superior analgesia compared with placebo in the first 48 postoperative hours after appendectomy in children[21].

**Pernille Lykke Petersen et al.** conducted a randomized, double-blind study in which 80 patients undergoing laparoscopic cholecystectomy were allocated to receive either bilateral ultrasound-guided posterior TAP blocks with 20 mL 0.5% ropivacaine or placebo blocks. They observed that the VAS pain scores while coughing was significantly reduced in the TAP versus the placebo group .VAS pain scores at rest showed no significant difference between groups. They concluded that TAP block after laparoscopic cholecystectomy may have some beneficial effect in reducing pain while coughing and on opioid requirements.[12]

Another study conducted by **Shradha Sinha et al.** evaluated the relative efficacy of bupivacaine versus ropivacaine for post‐operative analgesia using ultrasound‐guidedTAP block in laparoscopic cholecystectomies. Sixty adults undergoing elective laparoscopic cholecystectomy were randomised to receive ultrasound‐guided TAP block at the end of the surgical procedure with either 0.25%

bupivacaine 0.375% ropivacaine. All patients were assessed for post‑operative pain and rescue analgesic consumption at 10 min, 30 min, 1 h, 4 h, 8 h, 12 h and 24 h time points. They observed that patients receiving ultrasound‑guided TAP block with ropivacaine had significantly lower pain scores when compared to patients who received the block with bupivacaine at upto 1 h. But both the drugs were equivalent for post‑operative analgesia and 24 h cumulative rescue analgesic.

The study concluded that ultrasound‑guided TAP block with ropivacaine provides effective analgesia in the immediate post‑operative period up to 1 h as compared to bupivacaine. Both the drugs are similar in terms of 24 h cumulative rescue analgesic requirement[22].

Opioids have been used as adjuvants to local anaesthetics to prolong the duration of action[13,14,15].

**Mostafa Abdel Hamid Abo El Enin et al.** conducted a study to observe the effect of addition of fentanyl to local anaesthetic in peribulbar block.

Forty patients undergoing vitrectomy due to vitreous hemorrhage not associated with retinal detachment were divided into two groups randomly, each group containing 20 patients. In Control group patients received volume of 6- 10 ml (5 ml mepivacaine3% + 1ml hyaluronidase (150mcg)+ 3ml bupivacaine 0.5%+1ml saline) while Fentanyl group received 20 mcg fentanyl added to local anaesthetic, the onset and duration of lid and globe akinesia were assessed at 1,3,5 and 10min. Postoperative VAS was recorded each hour up to 6th hour.

They found statistically significant difference between the two groups in the onset of lid akinesia. Fentanyl group had faster onset of lid akinesia and had significantly longer duration of akinesia (196.5 ± 14.24 min).There was statistically

significant difference between the two groups in the onset of globe akinesia at 3, 5 min. Fentanyl group had faster onset than control group and had longer duration of globe akinesia (294 ± 17.89 min). Fentanyl group had prolonged duration of analgesia 3.25+ 0.67 hr as compared to 1.85+ 0.67 hr in control group, p=0.00 postoperatively. There were statistically significant differences between the two groups as regard the meanVAS in 1,2,3,4 hours, Fentanyl group had lower median pain score than control group. The study concluded that addition of fentanyl to local anaesthetic mixtures causes earlier onset of action and prolongs the duration of akinesia and improve quality of postoperative pain in peribulbar block[15].

A study to evaluate the peripheral effect of fentanyl on postoperative pain was conducted by **Mark Tverskoy et al.** Patients undergoing inguinal herniorrhaphy under spinal anesthesia were randomly assigned to one of two groups . At the end of surgery, the wound was infiltrated with 10 mL of lidocaine 0.5% and fentanyl 0.001% (10 μg) in one group and with 10 mL of lidocaine 0.5% alone (and fentanyl 10 μg IM contralaterally) in the other group. The duration of anesthesia, the duration of analgesia, postoperative meperidine consumption,visual analogue scale of spontaneous and movement-associated pain 24 h after surgery were determined. The addition of fentanyl for wound infiltration enhanced the duration of anesthesia (130 ± 37 vs 197 ± 27 min; $P < 0.001$) and decreased the intensity of spontaneous (50 ± 17 vs 19 ± 18 mm; $P <0.002$) and movement-associated (56 ± 15 vs 26 ± 21 mm; $P < 0.002$) pain 24 h postoperatively.

They concluded that fentanyl can enhance analgesia by a peripheral mechanism. Wound infiltration with mixture of fentanyl and local anaesthetic may have the benefit of relief of postoperative pain[23].

# BASIC SCIENCES

## Pain:

Pain is defined by the International association for the study of pain as "an unpleasant sensory and emotional experience associated with actual tissue damage, or described in terms of such damage"[24].

The term nociception is derived from latin word "noci" which means injury. It is used to describe neural responses to traumatic or noxious stimuli. The nociceptive system is highly complex and highly adaptable. Sensitivity of most of its components can be reset by a variety of physiologic and pathologic conditions. Many innovative medications are being developed that target the causes of pain by actions on pain transduction, transmission, interpretation, and modulation in both the peripheral nervous system (PNS) and the central nervous system (CNS) .[25].

There are four physiological processes, namely transduction, transmission, modulation and perception.

***Transduction*** is the process by which a noxious stimulus is converted to an electrical impulse in sensory nerve endings.

***Transmission*** is the conduction of these electrical impulses to the CNS with the major connections for these nerves being in the dorsal horn of the spinal cord and thalamus with projections to the cingulate, insular and somatosensory cortexes.

***Modulation*** of pain is the process of altering pain transmission. It is likely that both inhibitory and excitatory mechanisms modulate pain (nociceptive) impulse transmission in the PNS and CNS.

***Pain perception*** is thought to be mediated through the thalamus acting as the central relay station for incoming pain signals and the primary somatosensory cortex serving for discrimination of specific sensory experiences.

Pain may occur in the absence of the occurrence of these four steps[25].

**Neurophysiology of pain:**

***Nociceptors (pain receptors):***

Nociceptors are free nerve ending receptors present in skin, muscles, joints, viscera, and vasculature. They are responsible for detecting noxious stimuli resulting from chemical, thermal or mechanical changes. In normal tissues, nociceptors are inactive until they are stimulated by sufficient energy to overcome their threshold.

Noxious sensations can often be broken down into two components: a fast, sharp, and well-localized sensation "first pain" which is conducted by Aδ fibers; and a duller, slower onset, and poorly localized sensation "second pain" which is conducted by C fibers. This protopathic pain is transmitted mainly by free nerve endings that sense mechanical or chemical tissue damage.[26-29]

**Several types of pain receptors are recognized**

1. Mechano-nociceptors, which respond to pinprick.

2. Silent nociceptors, which respond only on the presence of inflammation.

3. Polygonal mechano-heat receptors which are more prevalent and respond to excessive pressure, extreme of temperature, and pain producing substances.[26]

Nociceptors are either somatic that include those in skin and deep tissues (muscle, tendons, joints), or visceral nociceptors that include those in internal organs.[26,27,30]

Pain is clinically divided into acute and chronic pain.

**Acute pain:**

Acute pain is caused by noxious stimulation due to injury, a disease process, or the abnormal function of muscle or viscera. It is due to nociception.

Acute pain is associated with a neuroendocrine stress response that is proportional to the intensity of pain. There are different forms of acute pain, commonest forms being post –traumatic, postoperative and obstetric. Other forms are those associated with acute medical illnesses like myocardial infarction, pancreatitis, renal calculi.

Acute pain is usually self- limited or usually resolves with treatment in a few days to weeks. When acute pain fails to resolve due to abnormal healing or inadequate treatment it becomes chronic.[31]

There are two types of acute pain : somatic and visceral.

***Somatic pain:***

Somatic pain is due to nociceptive input arising from skin, subcutaneous tissues, and mucous membranes. It is characterized by being localized and described as sharp, pricking, throbbing or burning sensation.[32]It is further classified into superficial and deep.

Superficial somatic pain is due to nociceptive input arising from skin, subcutaneous tissues, and mucous membranes. It is well localized and described as a sharp, pricking, throbbing, or burning sensation.

Deep somatic pain arises from muscles, tendons, joints, or bones. It usually has a dull, aching quality and is less well localized.[31]

***Visceral pain:***

Visceral pain is due to nociceptive input arising from internal organ or one of its covering. It is dull diffuse pain, which is frequently associated with abnormal sympathetic or parasympathetic activity causing nausea, vomiting, sweating and /or changes in blood pressure or heart rate.

Four subtypes are described: (1) true localized visceral pain, (2) localized parietal pain, (3) referred visceral pain, and (4) referred parietal pain.

Parietal pain is typically sharp and often described as a stabbing sensation that is either localized to the area around the organ or referred to a distant site . The phenomenon of visceral or parietal pain referred to cutaneous areas results from patterns of embryological development and migration of tissues, and the convergence of visceral and somatic afferent input into the central nervous system. Thus, pain

associated with disease processes involving the peritoneum or pleura over the central diaphragm is frequently referred to the neck and shoulder, whereas pain from disease processes affecting the parietal surfaces of the peripheral diaphragm is referred to the chest or upper abdominal wall.[31]

**Chronic Pain:**

Chronic pain is pain that persists beyond the usual course of an acute disease or after a reasonable time for healing to occur, this healing period can vary from 1 to 6 months. Chronic pain may be nociceptive, neuropathic, or mixed. It often has a psychological mechanisms or environmental component. Patients with chronic pain often have attenuated or absent neuroendocrine stress responses and have prominent sleep and mood disturbances.

Pain may also be classified according to pathophysiology as nociceptive or neuropathic pain, etiology as arthritis or cancer pain, or the affected area such as headache or low back pain. Such classifications are useful in the selection of treatment modalities and drug therapy. Nociceptive pain is caused by activation or sensitization of peripheral nociceptors, specialized receptors that transduce noxious stimuli. Neuropathic pain is the result of injury or acquired abnormalities of peripheral or central neural structures.

Many factors influence the occurrence, intensity, quality and duration of postoperative pain like the site, nature and duration of operation, type of incision (thoracic and upper abdominal operations are associated with the most severe pain), the preoperative psychological, physical and pharmacological preparation of the patient, added to this the anaesthetic management and the quality of post operative care.[31]

**Pain pathway:**

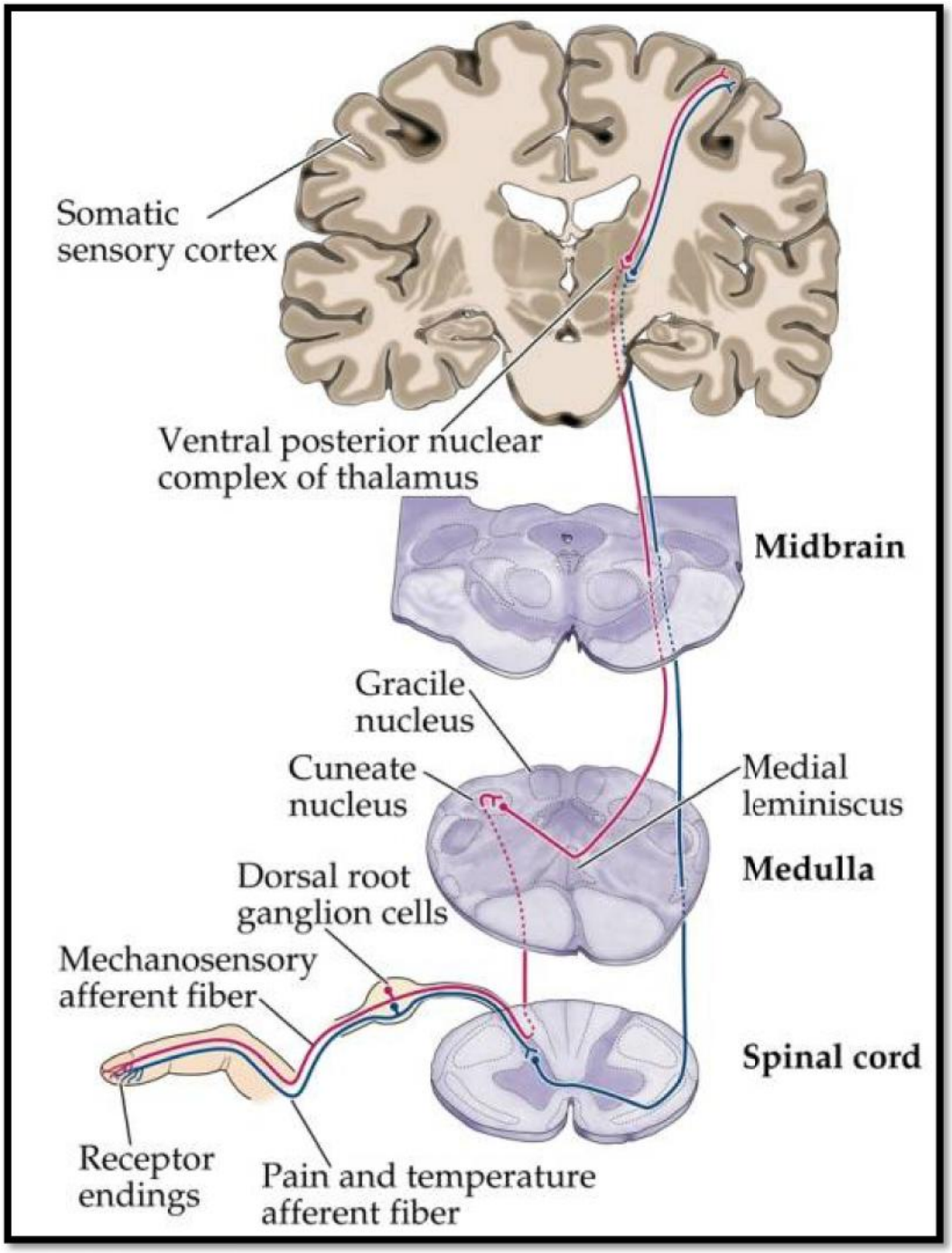



**Figure 1: Pain Pathway**

Pain is conducted along three neuron pathways; from the periphery to the cerebral cortex.[26,27,29,30]

***First order neuron***

Cells of these neurons are located in the dorsal root ganglia (for the body) and specific cranial nerve ganglia (for the head and neck) for example, Gasserian ganglion for trigeminal nerve. The Proximal end of their axons reach spinal cord via the dorsal sensory root of cervical, thoracic, lumbar, and sacral level (for the body) and through the cranial nerves (for head and neck).[26,27,29,30]

***Second order neurons***

Pain fibers may ascend or descend three spinal cord segments in the Lissauer's tract before synapsing with the second order neuron in the gray matter of the ipsilateral dorsal horn, this synapsing may be through interneurons. Second order neurons are either; nociceptive specific which serves only noxious stimuli and are normally silent or wide dynamic range (WDR) neurons that can receive also non-noxious afferent input. WDR neurons are more prevalent in the dorsal horn and are responsible for the increased intensity of firing in response to same stimulus "wind-up". [27,28]

Lamina II of the gray matter of the dorsal horn of the spinal cord, (also called the substantia gelatenosa) contains many interneurons and is believed to play a role in processing and modulating nociceptive input.[27,28]

Axons of most of the second order neurons cross the midline to the contra-lateral side of the spinal cord forming the lateral spinothalamic tract that send its fibers to the thalamus, the reticular formation, nucleus raphe and periaquiductal gray.[27,28]

***Third order neurons***

These are located in the thalamus and send their fibers to the somato-sensory area I and II in the cerebral cortex.[27-29,33]

**Effects of postoperative pain:**

Moderate to severe acute pain, regardless of its site, can affect nearly every organ function and may adversely influence postoperative morbidity and mortality.

Acute pain is typically associated with neuroendocrine stress response that is proportional to pain intensity, and it has been hypothesized that a reduction in surgical stress responses (endocrine, metabolic and inflammatory) will lead to a reduced incidence of postoperative organ dysfunction and thereby lead to an improved outcome. The latter suggests that effective postoperative pain management as a very important aspect of postoperative care.[34]

***a) Cardiovascular effects:***

Cardiac morbidity is a major cause of perioperative death. The realization that, in high risk populations, perioperative myocardial ischemia is most likely to occur after surgery (from day one to day three postoperatively) has led to treatment strategies designed to prevent its development.[35]

Although a variety of factors may contribute to the development of postoperative myocardial ischemia, including hypothermia, anaemia, anxiety, and tracheal intubation / suctioning, responses to poorly controlled pain play a prominent role. In this regard, activation of sympathoadrenal, and neuroendocrine axis may have a major impact on myocardial oxygen supply and demand. Catecholamine-induced

tachycardia, enhanced contractility, increased afterload and increased preload from hypervolemia caused by enhanced release of arginine vasopressin and aldosterone, are well characterized determinants of increased oxygen demand. Increased oxygen demand, with hypervolemia, may precipitate ischemia and acute cardiac failure, especially in patients with poorly compensated coronary artery or valvular heart disease.[36]

Myocardial oxygen supply may be diminished as a result of pulmonary dysfunction, in particular, atelectasis secondary to pain-induced hypoventilation and pulmonary edema resulting from stress-induced hypervolemia. Other causes of reduced oxygen supply include coronary artery constriction secondary to high circulatory levels of catecholamine and increased coronary sympathetic tone, stress-induced increase in plasma viscosity and platelet-induced occlusion; and serotonin induced coronary vasospasm secondary to platelet aggregation.[37]

***b) Pulmonary effects:***

Pulmonary function may be dramatically altered by surgically induced pain. The classical pulmonary response to upper abdominal surgery, include an increase in respiratory rate with decreased tidal volume, vital capacity, forced expiratory volume and functional residual capacity. Those pathophysiologic alterations are characteristic of acute restrictive pulmonary disease and, as such, may be associated with clinically significant hypoxia and hypercarbia.[37]

Pain increases total body oxygen consumption and carbon dioxide production which necessitates an increase in the work of breathing. Patients with poor pain control (specially in upper abdominal and thoracic procedures) breath less deeply and

have inadequate cough which leads to further reduction in the tidal volume and functional residual capacity, which in turn can cause atelectasis, intrapulmonary shunting and hypoxemia.[34]

***c) Gastrointestinal effects:***

Sympathetic hyperactivity induced by pain increases sphincter tone and decrease motility of intestine, causing ileus, pain also increases stress ulceration due to increase in gastric acid secretion.[38]

***d) Endocrinal effects:***

The dominant neuroendocrine responses to pain involve hypothalamic-pituitary-adrenocortical interactions. These interactions result in increased catecholamine and catabolic hormone release. This effects cause sodium and water retention, and increased levels of blood glucose, free fatty acids and lactate. The negative nitrogen balance and protein catabolism may impede patient's convalescence.[39]

***e) Hematological effects:***

The stress response causes decrease in the levels of natural anticoagulants, inhibition of fibrinolysis and increase in platelet reactivity which initiate a postoperative hypercoagulable state. This hypercoagulability causes a series of other events such as deep venous thrombosis and myocardial ischemia.[27]

***f) Immunological effects:***

The stress response potentiate postoperative immunosuppression; the extent of which correlates with the extent of surgery. Stress response has been reported to depress the reticulo-endothelial system which predispose to infection.[40]

***g) Psychogenic effects:***

Intense anxiety, fear, and the loss of control that accompany severe tissue injury may have profound impact on the hypothalamic-pituitary axis. Behavioral responses associated with poorly controlled pain include sleep deprivation and reduced morale.[41]

In many patients, uncontrolled postoperative pain can produce a series of long-term emotional disturbances, which could impair the patient's health, and cause undue fear and anxiety if subsequent surgery is required. Postoperative cognitive dysfunction occurs in up to 20% of patients after major non-cardiac surgery and may persist in about 10% of patients 3 months after surgery.[34]

***h) Development of chronic pain:***

Recently, it is accepted that neuropathic pain can develop after surgery, be persistent, and be the basis for ongoing suffering for the patient. The diagnosis of neuropathic pain can be obtained from the presenting features of burning, stinging or shooting pain, despite apparent tissue healing with a relative lack of response to doses of opioids used in the postoperative period.[42]

Lastly, optimizing treatment of acute postoperative pain can improve health-related quality of life, while poor postoperative pain control may interfere with patient's activities of daily living.

**Measurement of pain:**

Pain measurement is done by two methods;

1. ***Type I methods:***

Those are objective methods, done by the physician as he assigns numbers about the patient condition. It includes the following:

Physiological indices

- Endocrinal (increase in serum cortisol and catecholamine).
- Cardiovascular (increase in blood pressure and heart rate)
- Respiratory (increase in respiratory rate and decrease in tidal volume)

Neuro-pharmacological

- Correlation with beta endorphin (decreased in acute painful conditions)
- Thermography (hypo-emission in chronic pain)

Neurological

- Nerve conduction velocity
- Evoked potentials
- Single positron emission tomography (SPET).

Behavioral

- Sighing, crying, shouting, trembling.

***2. Type II methods:***

It includes either:

Single dimension methods

- Category scale (verbal rating scale)
- Numerical rating scale
- Graphic rating scale

Multi-dimensional methods

- Mc Gill pain Questionnaire, MPQ
- Dartmouth pain Questionnaire, DPQ
- West Haven-Yale pain Questionnaire, WHYPQ.[35]

Measurement of pain in clinical practice depends largely on verbal dialogue between the patient and the doctor or nurse. A rating scale is mandatory in research projects and ideally when clinical data are being collected.

A number of individual differences between patients make comparisons of pain measurements more difficult. For example, the past experiences of the patients influence their present perception of pain. Also, demographic factors such as gender, age, and ethnic background influence the individual's perception of pain. Again,

patients who are clinically depressed and anxious tend to report increased pain intensity.

Although pain is a subjective experience, great attention has been paid to the quantification of this experience. As pain is subjective experience, everyone has different perceptions of that experience. Differences are found in how individuals quantify pain. For example, some individuals would never say that their pain was a (10) on a scale from (0) to (10). On the other hand, other individuals report their pain as a constant (10) despite looking calm and relaxed. Also, all numeric scales used to measure pain have floor and ceiling effects. If the patients describe their pain to be a (10), there is no way to report an increase in pain intensity.

Of the many methods of pain scoring VAS and VRS are the most commonly used in the single dimension method.

***Visual analogue scale (VAS):***

The visual analogue scale uses a straight line with extremities of pain intensity on either end. The line is typically 10 cm long with one end defined as “no pain” and the other end being excruciating unbearable pain”. The line can be either vertical or horizontal. The patients are asked to place a mark on the line to describe the amount of pain that they are currently experiencing. The distance between the end labeled “no pain” and the mark placed by the patient is measured and rounded to the nearest centimeter. To assist in describing the intensity of pain, words can be placed along the scale (for example, mild, moderate, or severe). Such descriptors can help to orient the patient for the degree of pain; this particular variation of the VAS has been known as a graphic rating scale. Explanation to the patient is needed by the clinician when using

the VAS. Occasionally, the patient may be confused about the line, perceiving it to represent time of degree of relief rather than degree of pain intensity.[43]

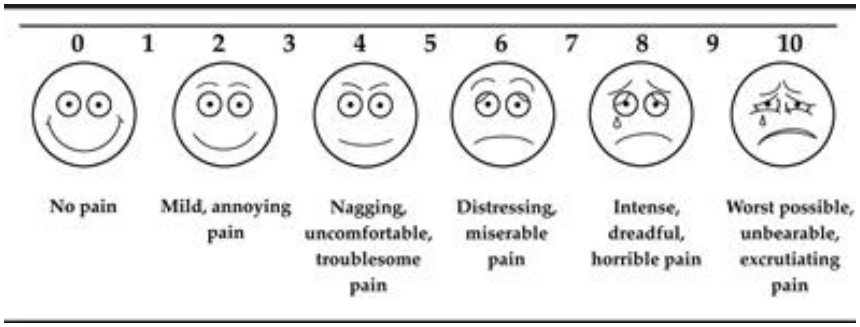



**Figure 2: Visual Analogue Scale**

## MANAGEMENT OF POSTOPERATIVE PAIN

### *Prophylactic measures:*

The incidence, severity, and duration of pain and suffering during the postoperative period can be decreased by proper preoperative and postoperative surgical and psychological care. Although the accepted definition of pain emphasizes the cognitive, emotional response to tissue damage, the role of psychological techniques in the relief of acute pain has been minimized. Psychoeducational care has beneficial effects on recovery, postoperative pain and psychological distress after surgery.

Psycho-educational care was classed as health-care information (information in preparation for surgery, timing of procedures, function and roles of health-care providers, self-care actions, and pain and discomfort information); skills teaching (coughing, breathing and bed exercises, relaxation, hypnosis); and psychosocial support (identifying and alleviating concerns, reassurance, problems solving, and encouraging questions).

Optimal surgical care also helps to decrease the severity of postoperative pain. Skillful and gentle handling of tissues while carrying out the operation and observance of other surgical principles assist to minimize trauma. Proper postoperative care help to decrease the magnitude of postoperative pain which involves continuing psychological support, proper care of wounds, early ambulation, and of course good nursing care.[26]

***Active measures***

Postoperative pain can be partially or completely relieved by one of the following methods:

1. *Systemic analgesics and adjuvant*

a) Opioids

b) Non-steroidal anti-inflammatory drugs

c) NMDA antagonists

d) Alpha-2 adrenergic agonists

e) Miscellaneous non-opioid compounds

2. *Local infiltration and field block - Regional analgesia with local anaesthetics*

a) Continuous segmental epidural block

b) Intrapleuralinstillation

c) Intraperitonealinstillation

d) Infiltration of the incision site

3. *Regional analgesia with neuro-axial opioids and local anaesthetics*
4. *Regional analgesia with combined local anaesthetics and opioids*
5. *Electrical analgesia achieved with transcutaneous electrical stimulation or electro-acupuncture.*[26]

**Pain after laparoscopic surgeries:**

Laparoscopic approaches to surgery have increased dramatically over the past several years. However laparoscopic procedures are not pain free and pain occurs after laparoscopy, but is usually less and shorter compared to the same conventional surgical procedure.[44]

***Mechanism of pain in laparoscopic surgeries:***

Early postoperative pain is the most prevalent and dominant complaint that requires strong analgesia including opiates after elective laparoscopic surgeries. For that reason, many efforts have been made to improve postoperative analgesia, but postoperative pain, however, does not completely disappear and several studies have shown that port site incision and visceral pain is the major component. Nonetheless, pain may be moderate or even severe for some patients during the first 24 postoperative hours, and has frequently been treated with nonsteroidal anti-inflammatory drugs (NSAIDs) or opioid treatment.[5,44]

The exact etiology of pain after laparoscopic surgeries is still unclear, however, it appears to be multifactorial and the causes include, abdominal wall trauma by trocar entrances, diaphragmatic irritation secondary to $CO_2$ insufflation and pneumoperitoneum, type and temperature of insufflated gas, residual intraperitoneal gas, intraabdominal trauma, microruptures of the parietal peritoneum due to abdominal distension, chemical irritation of the peritoneum, etc.[5]

Therefore, abdominal distention should be slow with adequate muscle relaxation to ensure suitable abdominal compliance. The prolonged presence of shoulder tip pain suggests irritation of the phrenic nerve that is caused by the

persistence of gas in the abdomen (pneumoperitoneum). There is statistically significant correlation between the width of the gas bubble and pain score, and this pain can be reduced by the aspiration of the gas under the diaphragm.[45]

**Factors associated with gaseous pneumoperitoneum:**

1. ***Neuropraxia of the phrenic nerve***

It has been suggested that distention of the diaphragm during gas insufflations and the resultant phrenic nerve neuropraxia possibly contribute to postoperative pain, which may include the related C4 dermatome.[46]

2. ***The type of insufflated gas and intraabdominalpH***

The phrenic nerves may be damaged by the acid milieu created by the dissolution of $CO_2$. The intraperitoneal pH when $CO_2$ gas is insufflated has been measured to be 6.0, immediate postoperatively. On the first postoperative day, the pH rises to 6.4 to 6.7, and on the second postoperative day to 6.8 to 6.9. Thereafter it normalizes to above 7.0.[47]Similar values were found when argon gas was substituted.

3. ***Residual intraabdominal gas***

Several reports have indicated that residual intraabdominal gas after laparoscopy causes pain. Carbon dioxide dissolution, intraabdominal acidosis, and the consequent peritoneal irritation occur for a longer period if the gas is not evacuated at the end of the laparoscopic procedure. Residual gas also may result in a loss of peritoneal surface tension and support to the abdominal viscera, thus contributing to postoperative pain.[48]

**4. *Temperature of gas***

The effect of gas temperature on postoperative pain after gynaecologic laparoscopic procedures has been investigated in a prospective randomized study of standard insufflation gas ($20^0$ C) versus gas at body temperature. This study found that pain reduction was significantly greater for those patients in whom warmed gas was used, especially with respect to diaphragmatic and shoulder tip pain, with the lasting effect of three days.[46]

***5. Humidity of gas***

A prospective randomized controlled trail was conducted at the Queen Elizabeth Hospital, Adelaide, to investigate the outcome when humidified gas was insufflated during laparoscopic cholecystectomy instead of standard dry gas. This study demonstrated significantly reduced postoperative pain in patients who underwent humidified gas insufflation. The humidified insufflations showed a trend of less post operative analgesic consumption, along with shorter hospital stay and earlier return to work. The exact relation between dry gas and postoperative pain is not yet determined, but other animal studies have observed that dry gas insufflation is implicated in ultrastructural damage to exposed membranes, an effect that was not seen with the use of humidified gas.[49]

**Management of post operative pain after laparoscopic surgeries:**

In order to decrease the postoperative pain after the laparoscopy, some methods such as rectus sheath block, Transversus Abdominis plane block, intraabdominal drain placement in order to throw out $CO_2$ pneumoperitoneum, intraperitoneal infiltration of the local anesthetics or opioids, the use of systemic

opioids, patient-controlled analgesia, and injection of local anesthetics into the port sites are suggested.[5]

**TransversusAbdominis plane block (TAP block):**

***History:***

Transversus abdominis plane (TAP) block is a relatively newer and a novel approach of injecting local anesthesia into the plane between the internal oblique and Transversus abdominis muscle to provide analgesia.[50]

Rafi et al, first described TAP block in 2001, they utilized surface anatomical landmarks to reach Transversus abdominis plane identifying the lumbar triangle of Petit.[51]

In 2004, McDonnell et al,discovered preliminary evidence to support the anatomical basis for TAP block.[52]

Ultrasound-guided technique was subsequently described by Hebbard et al, in 2007.[53]

***Anatomy:***

The musculature of lateral abdomen has 3 layers, superficial to deep, they are the external oblique, the internal oblique and the Transversus abdominis muscles. On its course from medial to lateral, the internal oblique muscle slopes upward and creates a small gap above the iliac crest. It is this sloping edge, above the iliac crest, that defines the medial aspect of the lumbar triangle of Petit.

The posterior edge of the triangle is the latissimus dorsi muscle. The inferior aspect of the triangle is the iliac crest and the peritoneum rests directly deep to the innermost muscle. The Transversus abdominis plane is the fascial layer between the internal oblique and the Transversus abdominis muscles. It exists as a continuous plane located at any point on the abdomen where these two muscle layers exist. Anterior rami of the thoracolumbar nerves that innervate the anterior abdominal wall pass through this plane as small, well defined neurovascular bundles.[54,55]

*Innervation:*

The anterior abdominal wall (skin, muscle, parietal peritoneum ) is innervated by the anterior rami of the lower 6 thoracic nerves ( T7 – T12) and the 1st lumbar nerve (L1). Terminal branches of these somatic nerves course through the lateral abdominal wall within the Transversus abdominis plane (TAP).

Injection of local anaesthetic within the TAP can therefore potentially provide analgesia to the skin, muscles and parietal peritoneum of the anterior abdominal wall from T7 to L1.[54,55]

A cadaveric study of TAP anatomy reveals the following points which are pertinent to performance of the TAP block:

1. There is a fascial sheath between the internal oblique and Transversus abdominis muscles. The nerve lies deep to this fascia.
2. Nerves T6 to T9 enter TAP medial to the anterior axillary line. T6 enters TAP jus lateral to linea alba, and T7 to T9 at progressively increasing distance from linea alba. Nerves running in the TAP lateral to the anterior axillary line

originate from segmental nerves from T9 to L1. This may explain the observation that the TAP block is only suitable for lower abdominal surgeries.

3. There is extensive branching and communication of the segmental nerves in the TAP. In particular the T9 to L1 branches form the TAP plexus, that runs from the deep circumflex iliac artery. This may partly account for the ability of a single injection to cover several segmental levels.[54,55]

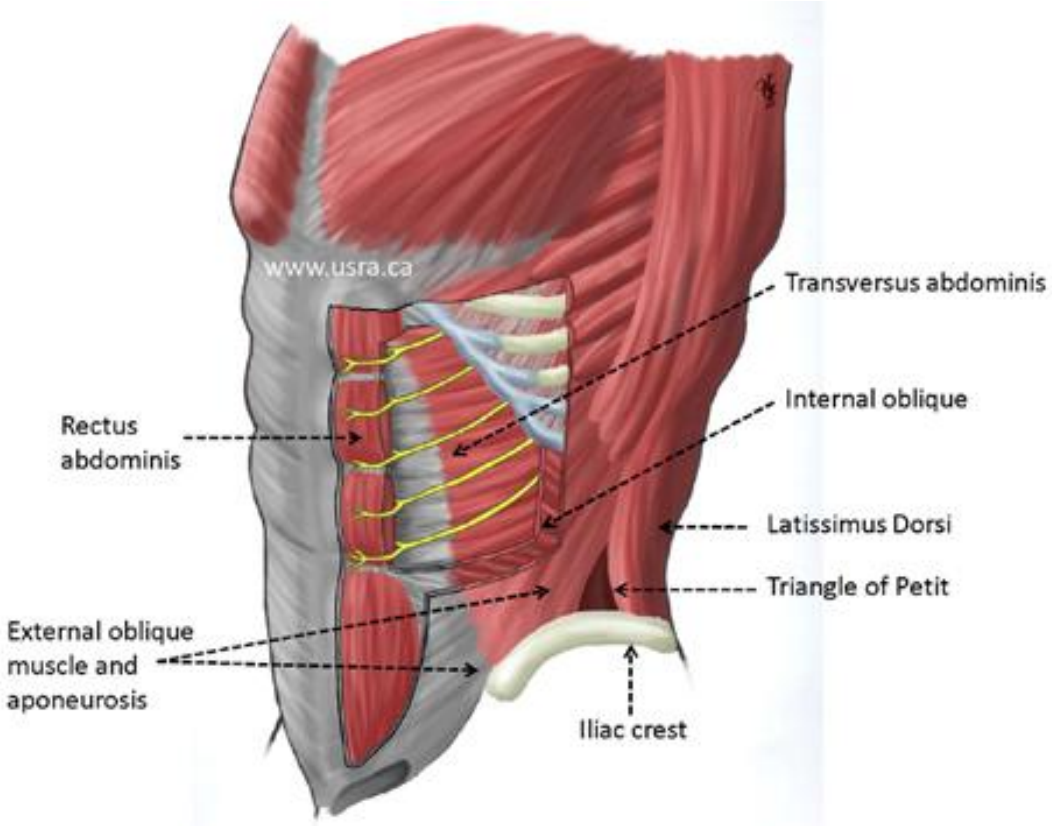



**Figure 3: Transversus Abdominis Plane Anatomy**

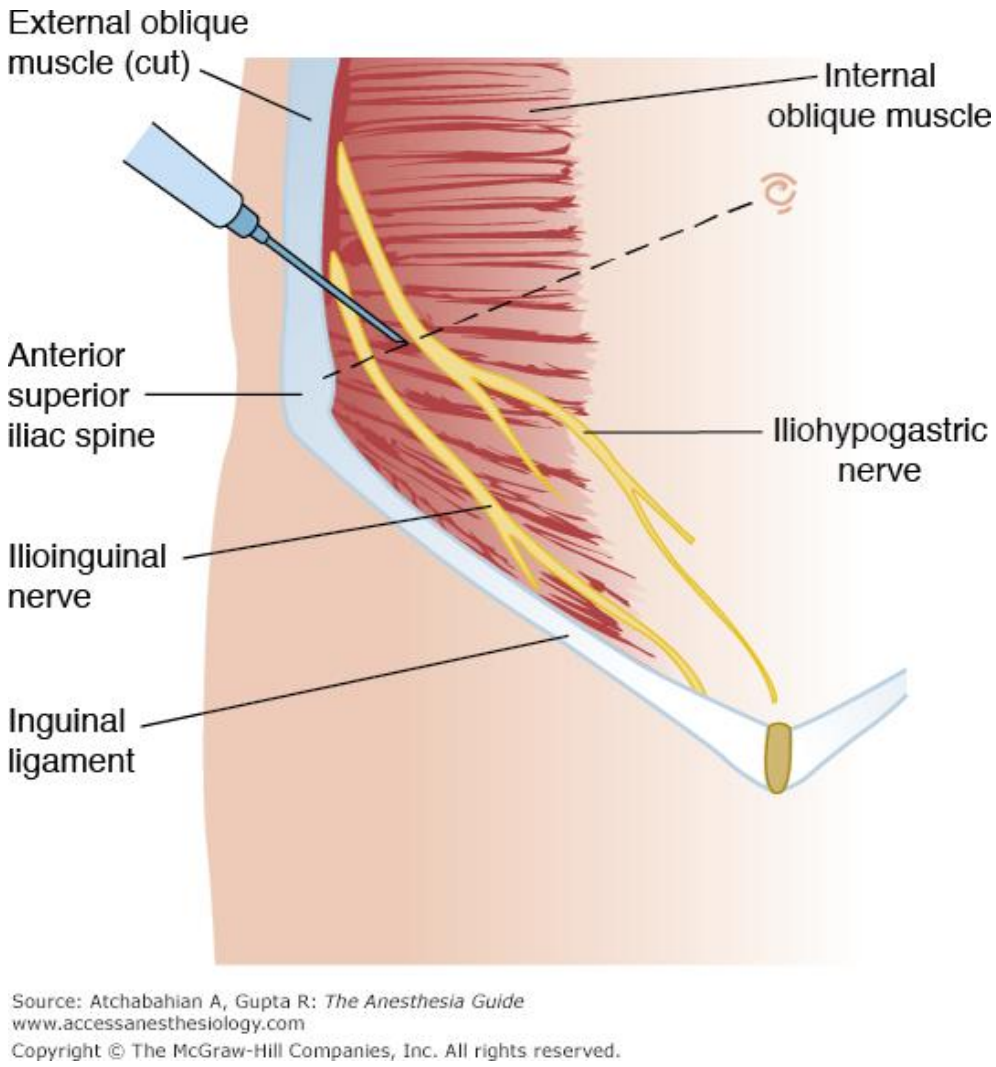



**Figure 4: Site of injection For Transversus Abdominis Plane block( Landmark Method)**

***Technique:***

***Anatomical Landmark-Based Approach:***

In Rafi's classic description of the TAP block, surface anatomic landmarks were used to determine needle insertion site within the lumbar triangle of Petit, and a single "pop" sensation served as an endpoint for appropriate needle depth. Patients were placed in the supine position and a finger was walked from the anterior superior

iliac spine along the top of the iliac crest until it dipped slightly inward. on further posterior movement, the finger tip was felt to slip over the lateral border of the latissimus dorsi, where it is attached to the external lip of the iliac crest. At this location, the skin was first pierced anterior to the fingertip with an 18-gauge cutting needle at the level of the external lip and then followed by a 24- gauge, blunt-tipped, 2-inch needle, which was inserted perpendicular to the skin until it touched the bone of the external lip. The needle was then slowly advanced over the intermediate zone of the iliac crest until the definite "pop" was felt.[51]

This single "pop" method differs from the "double pop" method described by O'Donnel et.al. in which the needle was inserted cephalad to the iliac crest and advanced until two distinct "pops" were appreciated. The authors explained that a "double pop" resulted from the blunt needle passing through the " fascial extensions of the abdominal wall muscles ( external and internal obliques ) within the floor of the triangle of Petit". [52]

All anatomical landmark – based approaches to the TAP make use of blunt-tipped needles to improve tactile sensitivity and appreciation for distinct "pop" sensation.

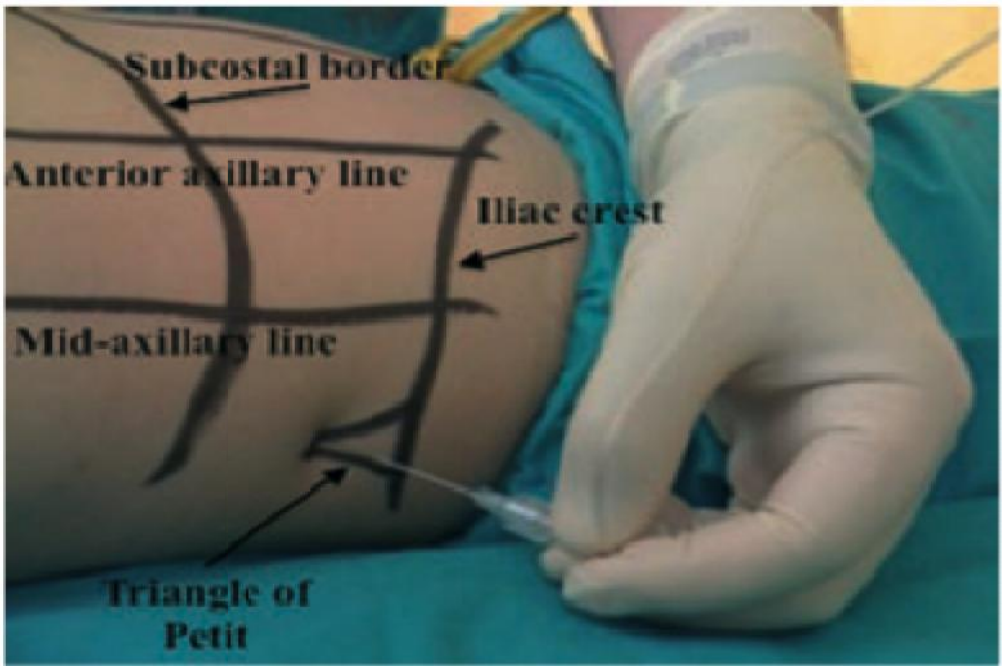



**Figure 5: Landmark method of TAP block showing Triangle of Petit**

***Ultrasound-Guided Approach:***

An ultrasound-guided approach was first described in 2007 by Hebbard et al. The author applied a transversely oriented ultrasound probe to the anterolateral abdominal wall where the three muscle layers are most distinct. After identification of the TAP between the internal oblique and Transversus abdominis muscles, the probe was moved posterolaterally to lie across the midaxillary line just superior to the iliac crest ( over the triangle of Petit ). The block needle was then introduced anteriorly and advanced in an in-plane approach. Real-time ultrasonography facilitates easy needle visualization as it approaches and reaches the target fascial plane. A hypoechoic layer, created by injection of local anaesthetic, is also easily visualized. They also noted that the “pop” sensations in the classic approach could be imprecise due to anatomic variability, especially in patients with large BMI and concluded that real-time visualization of local anaesthetic spread was likely to be a more definitive endpoint,

as it is often the case with other regional block techniques. This ultrasound guided technique is commonly referred to as the posterior approach.[53]

In 2008, Hebbard described another ultrasound guided TAP block technique designed for upper abdominal surgery referred to as the oblique subcostal approach. In this variation, the needle entered the skin in an area near the xiphoid and was advanced inferolaterally such that local anaesthetic is delivered to the TAP along the costal margin. Importantly, the lateral abdominal muscle layers give way to an aponeurosis medially so that the TAP is defined by different muscle layers in this region. In some patients, the Transversus abdominis muscle extended medially, and the roof of the TAP was formed by the rectus abdominis muscle. In other patients, the transversus abdominis muscle did not extend to the site of local injection ,so the plane between the rectus abdominis and the rectus sheath was targeted.[56] Borglum et al. have described an ultrasound-guided, four point, single-shot technique that combines the posterior and oblique sub costal techniques in an effort to provide a wider bilateral analgesic coverage. The subcostal TAP block was performed in a manner similar to that described by Hebbard when the Transversus abdominis extended medially beneath the rectus abdominis. This method was referred to as the medial intercostals TAP block. When the transversus abdominis terminated laterally at the linea semilunaris, the subcostal block was instead performed within the TAP at the lateral most extent of the transversus abdominis. This method was referred to as the lateral intercostal TAP block. In addition, the posterior TAP block was performed between the costal margin and the iliac crest at the anterior axillary line. [57]

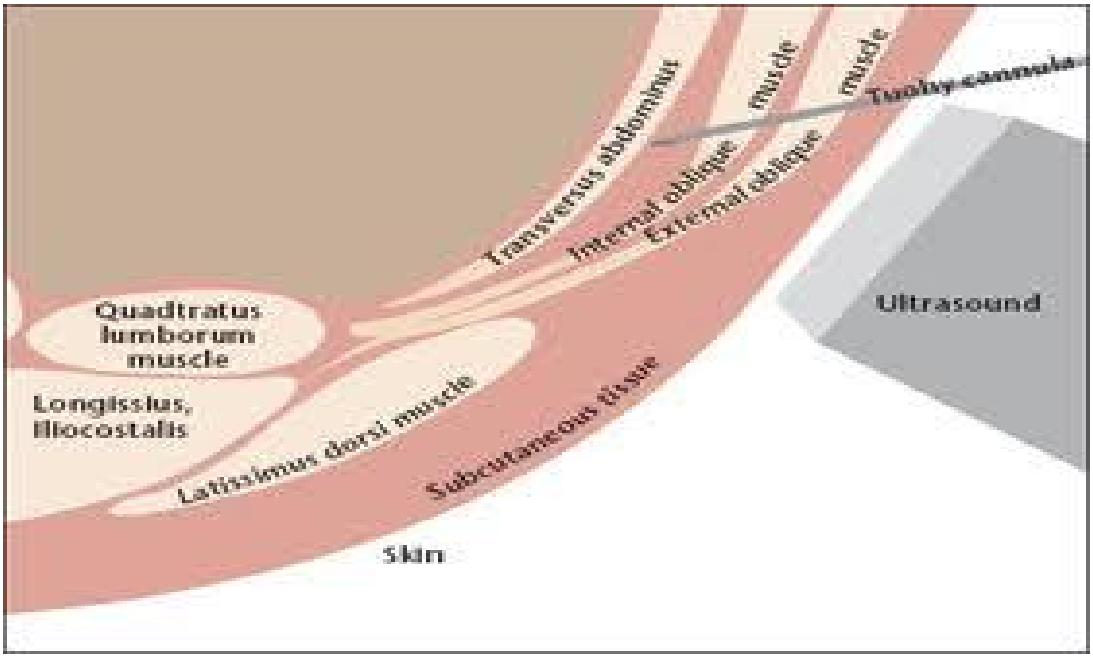



**Figure 6: Ultrasound guided TAP block**

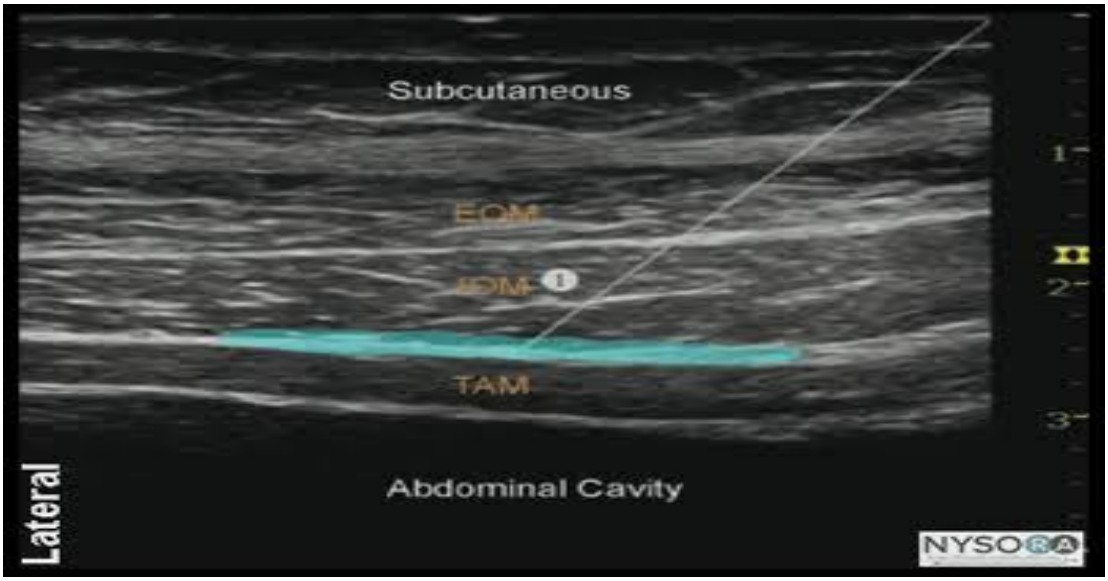



**Figure 7: Ultrasound image of needle at the Transversus abdominis plane**


**Figure 8: Local anaesthetic spread in the Transversus abdominis plane**

***Surgeon- Assisted Approach:***

Although majority of published literature on TAP blocks is purely from the perspective of the anaesthesiologists, a growing number of reports have demonstrated that surgeons can help to facilitate these blocks.

Chetwood et al. described a laparoscopic-assisted technique wherin a classic TAP block was performed while the injection area is observed with an intra-abdominal laparoscopic camera . A peritoneal bulge at the area of injection was seen after local anaesthetic was delivered within the TAP, and this visual served as the desired endpoint. Such direct visualization may help to avoid intraperitoneal injection, one of the major potential risks of TAP block. Recently a surgical TAP block utilizing transperitoneal approach was also described. Intraoperatively, a blunt-tipped block needle was advanced from inside the abdominal wall through the parietal peritoneum, and the transversus abdominis muscle ,in to the TAP as indicated by a single “pop” sensation.[58] In addition, Araco et al. described a surgical TAP block in which blunt dissection through the external and internal oblique muscles leads to injection of local anaesthetic into the TAP under direct visualization.[59]

**PHARMACOLOGY:**

**Bupivacaine:**[60-62]

Bupivacaine hydrochloride is a local anaesthetic agent belonging to amide group. It was synthesized in Sweden by A.F.Ekenstam and his colleagues in 1957. It was used clinically by L.J. Televuo in 1963.

**Structure:** It is anilide compound. Its chemical name is 1-n-butyl-DL-piperidine-2-carboxylic acid-2,6dimethylanilide hydrochloride.

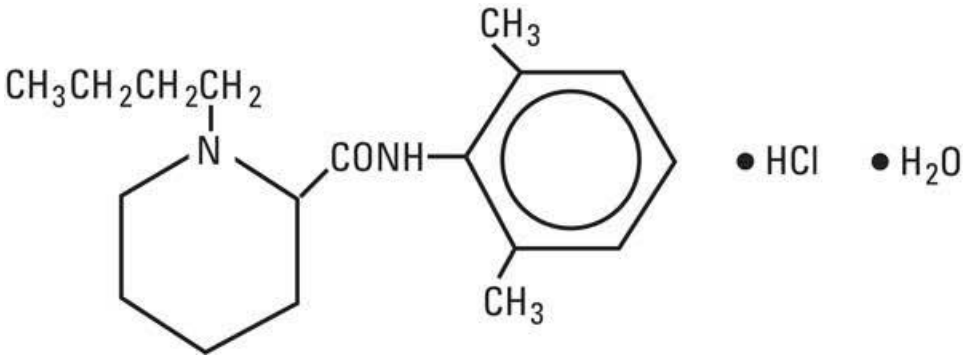



**Figure 9: Chemical structure of Bupivacaine**

**Molecular formula:** $C_{18}H_{28}N_2O$

**Molecular weight:** 288.435 g/mol

**pKa :** 8.1

**Melting point:** $258^0$ C

It is available in vials of 20ml containing clear colourless solution of 0.25% / 0.5% Bupivacaine hydrochloride. 20ml vials of 0.25% / 0.5% Bupivacaine without preservative are also available.

Ampoules containing 4ml of 0.5% ( Heavy) solution with 8% dextrose available for spinal anaesthesia.

**Physicochemical properties:**

It is sparingly soluble in the base form, but the hydrochloride is readily soluble in water.

**Anaesthetic properties:**

Bupivacaine is 3-4 times more potent than lidocaine or mepivacaine. It is 8times more potent than procaine.

The duration of action is 2-3times longer than lidocaine and 20-25% longer than tetracaine.

**Pharmacokinetics:**

Bupivacaine is highly lipid soluble drug and therefore uptake into fat is rapid and it has direct vasodilator effect. A linear relationship exists between the total dose and peak blood concentration achieved. In the plasma, drug is 95% bound to plasma proteins ( α 1 acid glycoprotein).

Peak plasma concentration of 0.14 – 1.8 μg/ml occurs within 5mins to 2 hours after administration and gradually decline by 4 hours. Bupivacaine is metabolized in the liver by N-dealkylation and is conjugated with glucuronic acid to 2,6,pipecolyloxylidine. N-desbutyl bupivacaine and 4 hydroxy bupivacaine are also formed. Hepatic disease potentiates its toxicity. About 10% of the drugs is excreted unchanged in urine within 24hrs. The elimination half life of bupivacaine is 4-5 hours.

**$V_d$ :** 73L

**Onset of action:** 5-20mins

**$T_{1/2}$ :**2.7 hrs

**Duration:** 1.5-3 hrs

**Clearance:** 0.58L/min

**Mechanism of Action:**

Bupivacaine diffuses in its unchanged base form through the neural sheaths and the axonal membrane to the internal surface of cell membrane sodium ion channels where it combines with hydrogen ions to form a cationic species which enters the internal opening of the sodium ion channel and combines with a receptor. This produces blockade of the sodium ion channel, thereby decreasing sodium ion conductance and preventing depolarization of the cell membrane. In this way it blocks the generation and conduction of nerve impulses by increasing the threshold of electrical excitation in the nerve by slowing the propagation of nerve impulse. At blood levels of 1-2 µg /ml achieved with therapeutic doses, no significant side effects are seen.

**Routes of Administration and Dosages:**

Bupivacaine can be administered topically, by infiltration, intrathecally or by epidural routes.

Toxic dose is above 3mg/kg

**Spinal anaesthesia :** 0.5% , duration of 75-150mins. Available as isobaric or hyperbaric solution.

**Epidural:** 0.5% to 0.375%. onset – 10-20mins, duration 180-350mins.

**Infiltration:** 0.5% - 0.25%, rapid onset, duration 180-240mins

**Peripheral nerve blocks:** 0.25% to 0.5%, onset 10-20mins, duration 400mins

**Obstetric analgesia:** concentration as less as 0.0625% to 0.25%

At concentrations of 0.125% to 0.0625% sensory blockade predominates and at concentrations above 0.25% motor blockade is seen.

It should not be used in IVRA.

Average duration of action for epidural bupivacaine is 120-180mins and for nerve blocks its 5-6hrs.

**Systemic effects:**

***Cardivascular system:***

When the theraepeutic dose of bupivacaine is injected, it causes minimal change in cardiac excitability, conduction,contractility and peripheral resistance.

If toxic levels are achieved bupivacaine may depress cardiac conduction and excitability which may lead to atrioventricular block, ventricular arrhythmia and cardiac arrest. It causes peripheral vasodilation which will lead to decrease in cardiac output and arterial blood pressure.

***Central nervous system:***

The principle effect of Bupivacaine is reversible neural blockade which leads to a characteristically biphasic effect in the CNS.

Initially, excitation ( light headedness, dizziness, fits ,visual and auditory disturbances), occur due to blockade of inhibitory pathways in the cortex.With increasing doses, depression of both facilitatory and inhibitory pathways occur leading to CNS depression ( drowsiness, disorientation and coma).

***Autonomic nervous system:***

Bupivacaine is a weak cholinergic and ß-adrenergic blocking drug.

***Antithrombin activity:***

Local anaesthetic inhibits platelet aggregation and prostacyclin synthesis.

***Bactericidal activity:***

Bupivacaine without preservative is bactericidal at clinical concentrations

**Side effects:**

Bupivacaine toxicity is seen with plasma levels of more than 4 µg/kg. The toxicity is increased by hypoxia, hypercarbia and pregnancy.

Allergic reactions to amide type local anaesthetic agents are extremely rare.

CVS effects are more prominent. There is depression of contractility and blockade of His- purkinje conduction system. Accidental IV injection of bupivacaine

may result in precipituous hypotension, cardiac dysrhythmias and atrioventricular heart blocks. Plasma level of bupivacaine to cause cardiac toxicity is 8-10µg/kg.

CNS effects: Low plasma levels produce circum oral numbness and twitching. A toxic level initially stimulates and later depresses the CNS. The plasma concentration of bupivacaine associated with seizures is 4.5 to 5.5µ/kg. Seizures are followed by CNS depression which may be accompanied by hypotension and apnoea.

**Fentanyl:**[60-63]

Fentanyl was first synthesized in 1960 by Dr.Paul Jannsen, a chemist working for a Belgian pharmaceutical company. It came into clinical practice in 1963. It is a synthetic opioid and a tertiary amine. Chemically it is a phenyl piperidine derivative of Mepiridine( a reversed ester of Pethidine ).It primarily acts on µ opioid receptors in CNS to cause analgesia.

**Structure:** it is a phenylpiperidine derivative. It is N-( 1- ( 2- phenethyl)-4-piperidinyl-N-phenyl-propanamide.

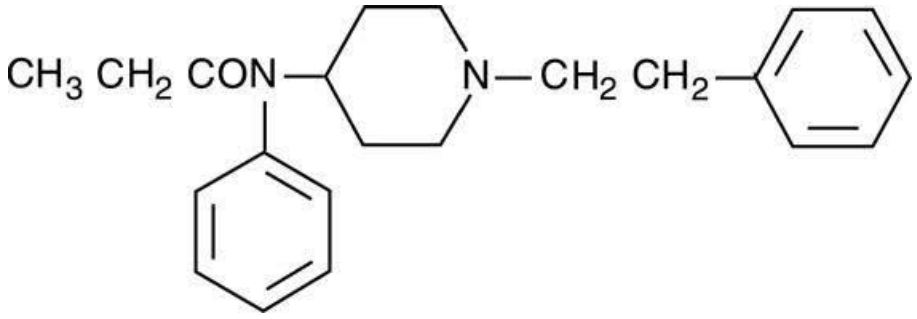



**Figure 10: Chemical structure of Fentanyl**

**Molecular formula:** $C_{22}H_{28}N_{20}C_6H_8O_7$

**Molecular weight:** 528.6 g/mol

Fentanyl is available as a clear, colourless solution .Fentanyl is available as a citrate salt .

## PHYSIOCHEMICAL PROPERTIES :

Fentanyl occurs as a white , crystalline powder . It has a very high lipid solubility as compared to its sparing water solubility . In fact due to its much higher lipid solubility as compared to morphine , it crosses the blood brain barrier more easily. This is the cause for Fentanyl having an analgesic property 75 – 125 times that of morphine.

pH of the commercial preparations ranges between 7 to 7.5 while the pKa value is 8.4. At physiologic pH of 7.4 less than 10% is unionized. It is highly plasma protein bound ( 84%). Solution should be protected from light and stored at 15 to 30° C. It is also available as intrabuccal, transdermal and aerosolized preparations.

## PHARMACOKINETICS :

### *Absorption :*

After I.V administration the onset of action is much more rapid with shorter duration of action. A single I V dose of Fentanyl has a more rapid onset than morphine ( around 30 seconds ) . This can be explained on the basis of higher lipid solubility of the former. Similarly for the same reason Fentanyl has a much lesser duration of action as it gets redistributed quickly .

***Distribution :***

Fentanyl has high lipid solubility, so distributes widely throughout the body to inactive sites. Initially it distributes to vascular organs such as heart, lungs and brain, then to skeletal muscles and fat. Lungs also serve as inactive storage site with estimated 75% of initial dose undergoing first pass pulmonary uptake. Volume of distribution for Fentanyl after administration is $4 \pm 0.4$ liters/kg.

***Metabolism and Excretion :***

The main seat for metabolism is liver where it undergoes N – de methylation and hydroxylation to produce Norfentanyl and 4-N amilinonopiperidine& propionic acid respectively.

Fentanyl undergoes significant first pass metabolism in lungs which transiently take up 75% of injected dose of Fentanyl. 80% of Fentanyl is bound to plasma proteins (approximately 50% to α – acid glycoprotein).

Fentanyl is excreted mainly in the urine as metabolite and less than 8% is excreted as unchanged drug. The mean clearance after i/v administration is between the range of 34-53 liters/hour or approximately 13 ml $min^{-1}$ $kg^{-1}$. Mean terminal half lives are between 2.5 and 8 hours.

**MECHANISM OF ACTION :**

Fentanyl is primarily a μ receptor agonist and these μ receptors are present in the brain, (periaqueductal gray matter of brain stem, amygdala, corpus striatum and hypothalamus), spinal cord (substantia gelatinosa) and peripheral nerves. These

receptors are involved with pain perception, integration of pain impulses and responses to pain.

At cellular level it binds to its specific binding site on μreceptors , increasing potassium conductance across the cell membrane causing hyper polarisation or inactivation of calcium channels or both. This causes the depression of adenylcyclase activity thus decreasing intracellular cAMP levels.

Opioids act as agonists at stereospecific opioid receptors at presynaptic and postsynapatic sites. The most likely mechanism of these peripheral actions appears to be activation of opioid receptors on primary afferent neurons, Fentanyl mimics the actions of endogenous ligands by binding to receptors resulting in activation of pain modulating system. Opioid receptor activation leads to decrease in neurotransmission. This decrease occurs largely by presynaptic inhibition of neurotransmitter (acetylcholine, dopamine, norepinephrine, substance P) release.

To a lesser extent , Fentanyl also binds to the κ - opioid receptors mediating sedation and miosis.

**DOSE :**

1) I.V. : 1 – 2 mcg/ kg body weight
2) Intrathecal : 25-40 mcg (adults)
3) Epidural : 25-50 mcg (adults)

## PHARMACODYNAMICS:

***Central Nervous System*** :

In the absence of hypoventilation, fentanyl decreases cerebral blood flow and in turn decreases intracranial pressure. Myoclonus during administration may resemble grand mal seizures. It can produce thoracic and abdominal skeletal muscle rigidity. Miosis can also occur as most of μ and κ agonists causes constriction of pupil by an excitatory action on the parasympathetic nerve innervating the pupils.

It causes pruritus when administered for central neuraxial blockade. . Pruritus produced by neuraxial opioids is likely due to cephalad migration of opioids in cerebrospinal fluid and subsequent interaction with opioid receptors in trigeminal nucleus.

***Cardio Vascular System :***

Fentanyl can cause a depression of cardiovascular system leading to hypotension, syncope and drug induced bradycardia.Hypotension after fentanyl is due to decrease in systemic vascular resistence and bradycardia . Bradycardia due to the drug can be explained due to central sympathetic soutflowblockade .

Fentanyl causes enhanced entry of calcium ions during plateau phase of action potential and decrease in outward potassium movement thus slowing A-V conduction. This can cause prolonged Q-T interval ,asystole and bradycardia.

***Respiratory System*** :

Fentanyl causes dose dependent depression of ventilation and this effect can be more prolonged than the analgesic action and can even continue in the post operative period. Such patients may require treatment with opioid antagonists ( Naloxone ) or respiratory stimulants ( Doxapram ).

Rigidity of respiratory muscles ( chest wall ) may require treatment with muscle relaxants.

***Gastrointestinal system :***

Fentanyl decreases tone of lower oesophageal sphincter and increases gastric emptying time.

***Hepatobiliarysystem*** :

Causes a spasm of sphincter of oddi, increasing the biliary pressure .

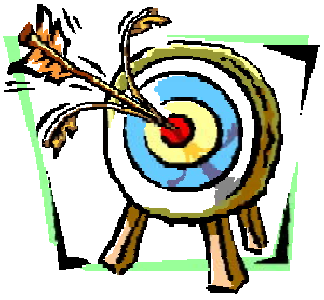
***Tolerance and physical dependence***:

Tolerance can occur without physical dependence but the reverse does not seem to occur. Cross tolerance develops between all the opioids.

**ADVERSE EFFECTS :**

1. Persistent and recurrent depression of ventilation
2. Hypotension and bradycardia
3. Muscle rigidity
4. Rarely can cause laryngospasm .

# *Introduction*



# *Objectives*

# *Review of Literature*


# *Basic Sciences*

# *Methodology*

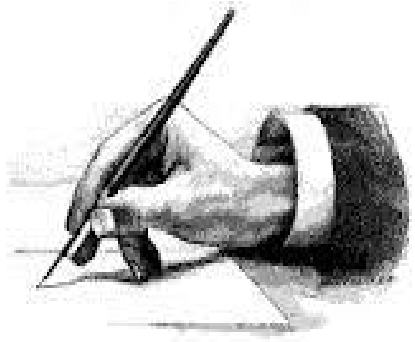
# Results

# *Discussion*

# Conclusion

# Summary

# Bibliography



# *Annexure-I*

# *Annexure-II*

# *Annexure-III*

# *Annexure-IV*

# Annexure-V

# MATERIALS AND METHODS

The present study was conducted at, KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Nehru nagar, Belagavi 590010, on patients undergoing laparoscopic appendicectomy under General Anaesthesia between January 2016 to December 2016.

**Study design**: A one year double blind randomized controlled trial.

**Study Period:** One year from January 2016 to December 2016.

**Sample size**: A total sample size of 60 cases.

**Sample size calculation**

Using the formula,

$$\text{Sample Size (n)} = \frac{(Z\alpha + Z\beta)^2(p_1+p_2)}{(p_1 - p_2)^2}$$

Level of significance was taken as 5% where Zα is 1.96

Power of the test used was taken as 80% where Zβ is 3.84

type I error rate α = 0.05 and

type II error rate β = 0.2

$$n = \frac{(1.96 + 3.84)^2 ( 0.166666667 + 0.533333333 )}{( 0.166666667 - 0.533333333 )^2}$$

$$n = 27$$

As the sample size calculated is less than the minimum number required, the sample size is taken as 30 in each group.

**Selection criteria:**

**Inclusion criteria:**

- Patients undergoing laparoscopic appendicectomy ↓GA.
- Age: 18 to 60 years group
- ASA Grade I and Grade II patients

**Exclusion criteria:**

- Age below 18yrs and above 60yrs.
- ASA Grade III and IV
- Patients allergic to local anaesthetic and opioids
- Patient on long term opioids
- Patient with coagulation abnormality

**Methodology:**

After obtaining the approval of ethical committee and written informed consent, a total of 60 patients undergoing laparoscopic appendicectomy were included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients were randomized based on computer generated randomization table into one of the two groups.

Group 1- Patient received TAP block with 15ml of 0.25% bupivacaine bilaterally

Group 2- Patient receivedTAP block with 15ml of 0.25% bupivacaine + 10 mcg of fentanyl bilaterally

The total dose of Bupivacaine was maintained within the safe limit (3mg/kg).[60]

A thorough Pre-Anaesthetic Evaluation was done.Routine investigations such as Complete blood picture, Random Blood Sugar, Serum Creatinine, Blood Urea were done. Chest X-ray, Electrocardiography were carried out in patients above 40yrs of age. Patientwas advised overnight fasting.

On the previous day, Visual analogue score was shown to the patient and explained its use for the postoperative pain assessment.

In the operation theatre patients was monitored by pulse oximetry, non invasive blood pressure measurement and electrocardiography. Following preoxygenation, patient was premedicated with Inj Glycopyrrolate 0.005mg/kg IV, Inj Midazolam 0.05mg/kg IV and Inj Pentazocin 0.5mg/kg IV. Induction of anaesthesia was done with Inj Thiopentone sodium 5mg/kg IV, sufficient to obtund the eye-lash reflex, followed by Inj Vecuronium 0.1mg/kg IV to facilitate orotracheal intubation. After confirming bilateral equal air entry general anesthesia was maintained with $O_2$:$N_2O$ in the ratio of 50:50 and 0.4% isoflurane with intermittent top ups of vecuronium.

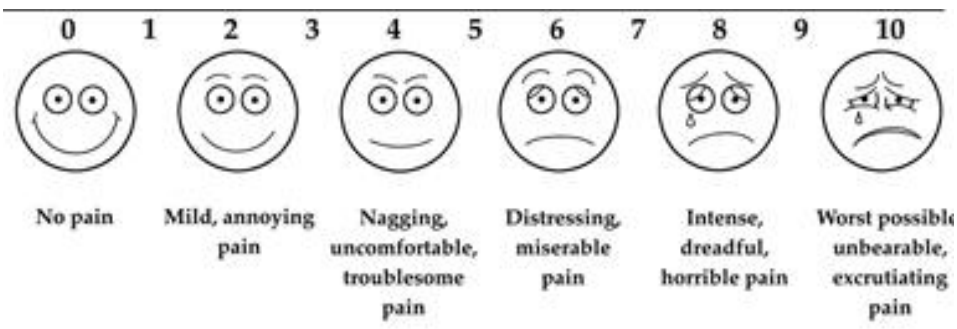
After instituting general anaesthesia but before starting the surgical procedure, bilateral Transversus abdominis plane block was performed in all subjects using ultrasound guidance with a portable ultrasound device.

The ultrasound probe was placed transversely on the anterolateral abdominal wall between the iliac crest and the subcostal margin. The external oblique, the internal oblique and the transversus abdominis muscles were visualized. Under strict aseptic precautions a 23-gauge needle was introduced anteriorly in the plane of the ultrasound beam. The needle was directed to approach the transversus abdominis plane and on entering the fascial plane, and after negative aspiration of blood, either15ml of 0.25% bupivacaine or 0.25% bupivacaine with 10µg fentanyl was administered.

The injectate was seen spreading in the transversus abdominis plane as a dark oval shape. A contralateral block was performed in the same manner.[20]Laparoscopic appendicectomy was performed. Patient was extubated after thorough suctioning and adequate reversal with Inj Glycopyrrolate IV(0.01mg/kg) and Inj Neostigmine IV(0.05mg/kg).

Patient was shifted to recovery and assessed for postoperative pain using VAS, at hourly intervals for the first 1-6hrs, 2 hourly upto 24hrs postoperatively. Patients with VAS 3 or more was given Inj Tramadol 2mg/kg IV. The time of request of 1st dose of Tramadol was noted. Side effects if any were noted. Incidence of failed block (patient with VAS score >3 in the immediate postoperative period) was also noted.

**VAS Pain scale:**



**Statistical Analysis**

The data was entered into the Microsoft Excel Spreadsheet. The data was analyzed using SPSS statistical software version 20.0. Student's unpaired't' test was used to compare quantitative variables in both groups and the qualitative variables was compared using student's paired 't' test for each group independently. The categorical data are compared using Chi square test. Non- parametric data was analyzed by using Mann Whitney Test All data were expressed as mean ± standard deviation. A probability ('p' value) of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant

# RESULTS

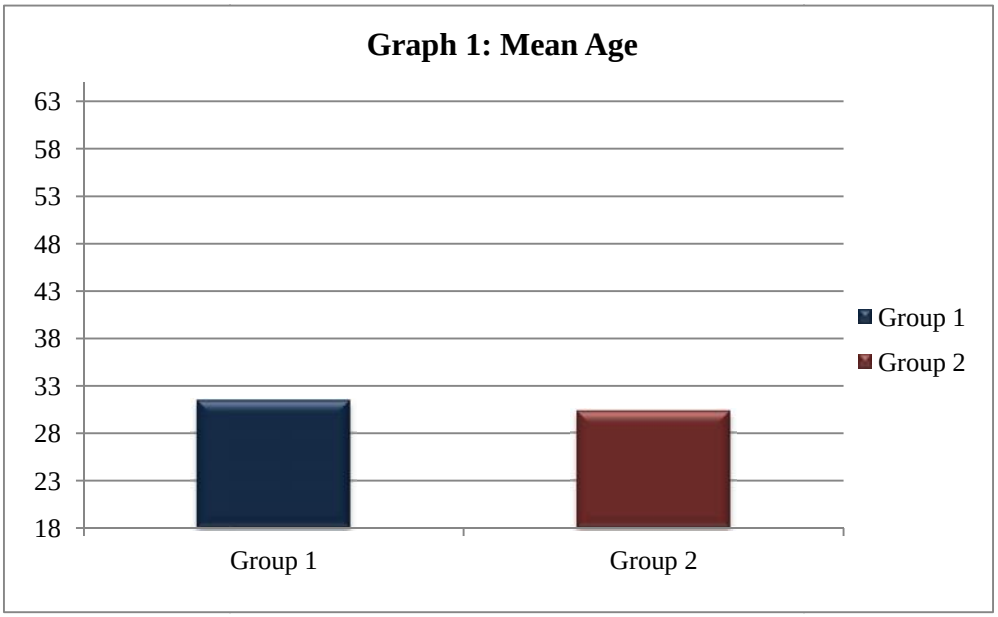
The present study was conducted to compare duration of postoperative analgesia by TAP block using 0.25% bupivacaine or 0.25% bupivacaine with fentanyl in patients undergoing laparoscopic appendicectomy.

60 patients were enrolled for the study, keeping in mind the inclusion and the exclusion criteria. 30 patients in Group 1 (0.25% bupivacaine) and 30 patients in Group2 (0.25% bupivacaine+ fentanyl).

## DEMOGRAPHIC DATA

**Table 1: Mean Age**

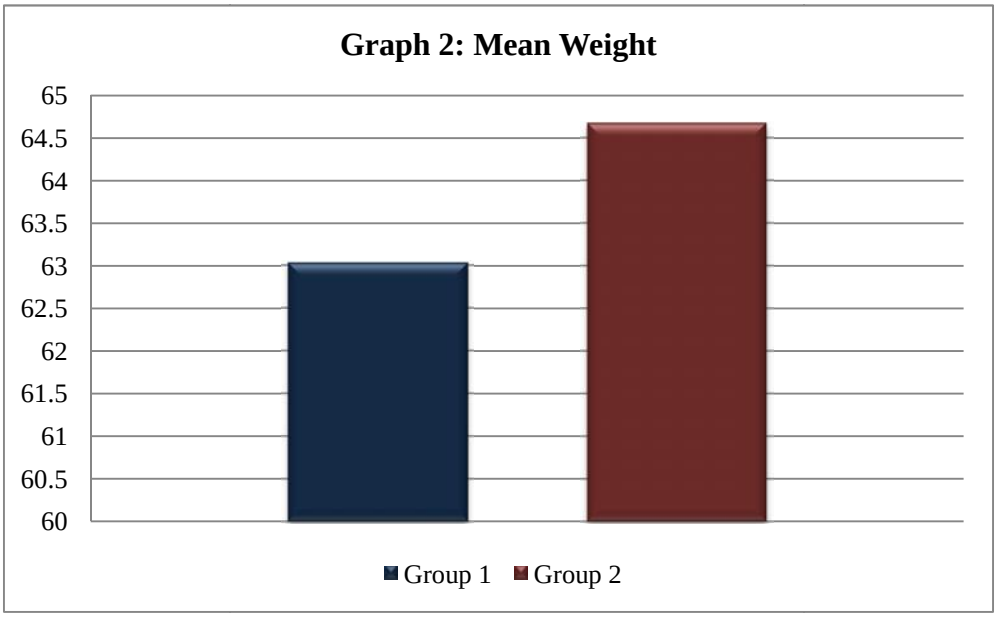
| | Group 1 | | Group 2 | | p value |
|---|---|---|---|---|---|
| | Mean | Standard Deviation | Mean | Standard Deviation | |
| Age( years ) | 31.47 | 11.72 | 30.30 | 11.26 | 0.6957 |




In our study we found no statistically significant difference between group 1and group 2 with regards to mean age (31.47±11.72 years, 30.30±11.26 years respectively; p =0.6957),

**Table 2: Mean Weight**

| Group 1 | | Group 2 | | p value |
|---|---|---|---|---|
| Mean | S.D | Mean | S.D | |
| 63.03 | 9.10 | 64.67 | 7.61 | 0.4536 |



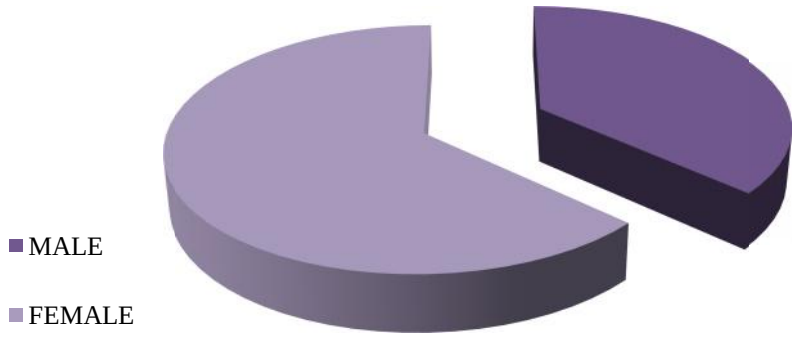

In our study we found no statistically significant difference between group 1and group 2 with regards to mean weight (63.03±9.10 years,64.67±7.61years respectively; p =0.4536)

**Table 3: Percentage of male and female**

| | Group 1 | | Group 2 | | P value |
|---|---|---|---|---|---|
| | Number | Percent | Number | Percent | |
| Male | 11 | 36.66 | 11 | 36.66 | 1.00 |
| Female | 19 | 63.33 | 19 | 63.33 | 1.00 |
| Total | 30 | 100 | 30 | 100 | 1.00 |

**Graph 3: Percentage of male and female Group 1**

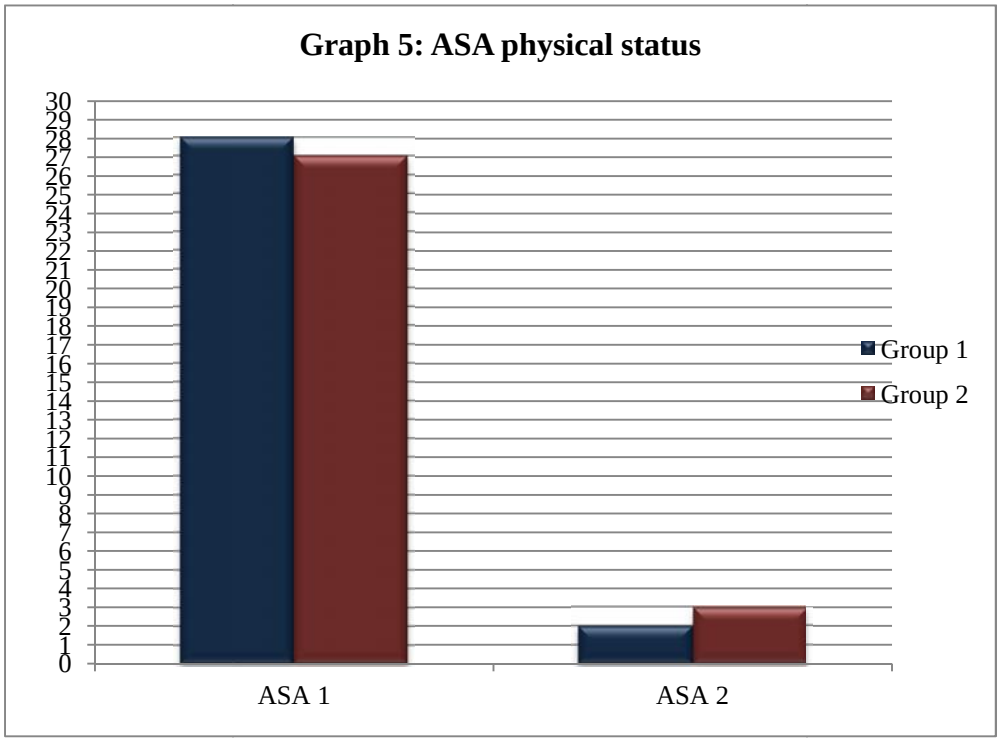
**Graph 4: Percentage of male and female Group 2**




Of the total 30 patients in Group 1, 19 (63.33%) were female & 11 (36.66%) were male. Of the total 30 patients in Group 2, 19 (63.33%) were female & 11 (36.66%) were males. When compared the difference between the two groups was not found to be statistically significant (p=1).

**Table 4: ASA physical status**

| | Group 1 | | Group 2 | | P value |
|---|---|---|---|---|---|
| | Number | Percent | Number | Percent | |
| ASA Grade I | 28 | 93.33 | 27 | 90 | 0.6404 |
| ASA Grade II | 2 | 6.66 | 3 | 10 | |
| Total | 30 | 100 | 30 | 100 | |



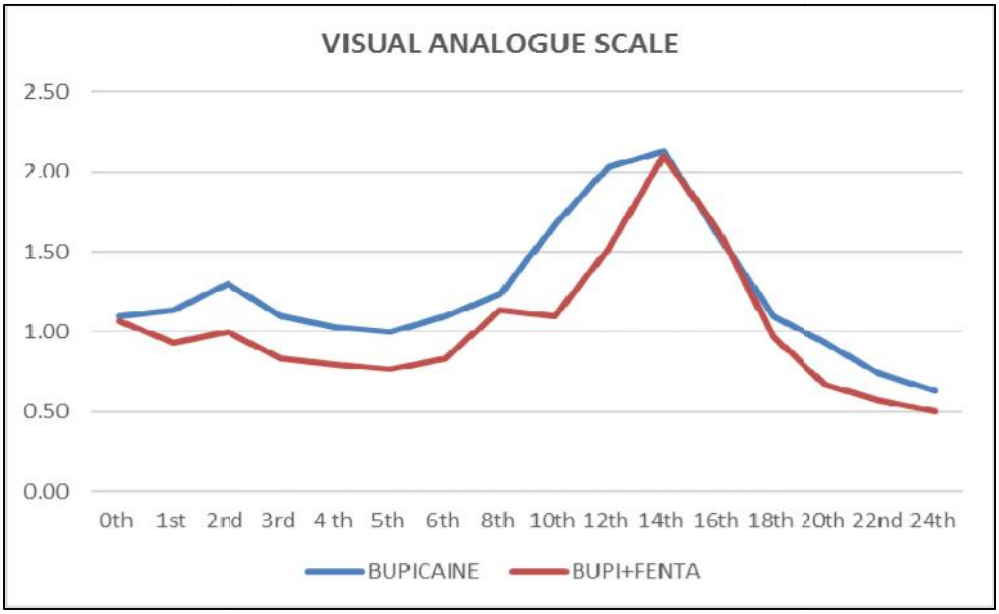

In group 1, 93.33% patients were ASA grade I and 6.66 % were ASA grade II. In group 2, 90 % patients were ASA grade I while 10 % were ASA grade II.

The data was comparable in both groups (p=0.6404).

**Table 5 : Comparison of mean VAS score**

| | Group 1 | | Group 2 | | | |
|---|---|---|---|---|---|---|
| **TIME** | **MEAN** | **S.D.** | **MEAN** | **S.D.** | **p VALUE** | **INFERENCE** |
| **0th hour** | 1.10 | 0.71 | 1.07 | 0.64 | 0.8494 | NS |
| **1st hour** | 1.13 | 0.68 | 0.93 | 0.58 | 0.2269 | NS |
| **2nd hour** | 1.30 | 1.42 | 1.00 | 0.59 | 0.2887 | NS |
| **3rd hour** | 1.10 | 0.71 | 0.83 | 0.65 | 0.1346 | NS |
| **4th hour** | 1.03 | 0.67 | 0.80 | 0.61 | 0.1634 | NS |
| **5th hour** | 1.00 | 0.74 | 0.77 | 0.57 | 0.1771 | NS |
| **6th hour** | 1.10 | 0.71 | 0.83 | 0.65 | 0.1346 | NS |
| **8th hour** | 1.23 | 0.77 | 1.13 | 0.78 | 0.6191 | NS |
| **10th hour** | 1.67 | 1.12 | 1.10 | 0.88 | 0.0342 | NS |
| **12th hour** | 2.03 | 1.59 | 1.52 | 1.30 | 0.1777 | NS |
| **14th hour** | 2.13 | 1.33 | 2.10 | 2.37 | 0.9467 | NS |
| **16th hour** | 1.60 | 0.89 | 1.63 | 1.16 | 0.9012 | NS |
| **18th hour** | 1.10 | 0.55 | 0.97 | 0.56 | 0.3533 | NS |
| **20th hour** | 0.93 | 0.64 | 0.67 | 0.61 | 0.1029 | NS |
| **22nd hour** | 0.73 | 0.74 | 0.57 | 0.68 | 0.3670 | NS |
| **24th hour** | 0.63 | 0.72 | 0.50 | 0.68 | 0.4640 | NS |

**Graph 6: Comparison of mean VAS score**



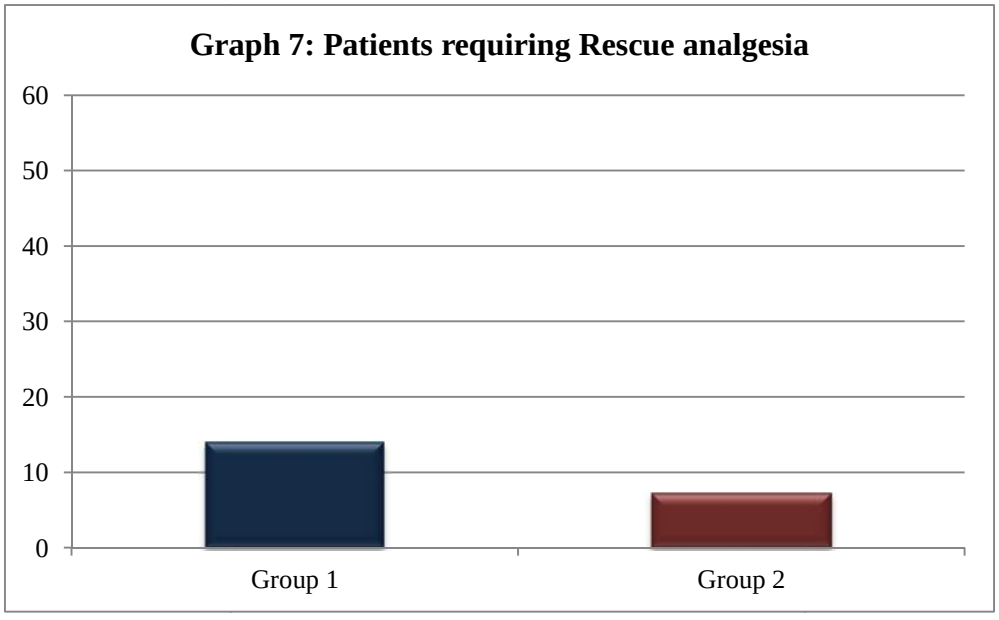

In our study the mean VAS score at 0$^{th}$ hour post operatively was 1.10±0.71 in group 1 and 1.07±0.64 in group 2 and was comparable ( p=0.849). the VAS score consistently decreses in both the groups upto 6$^{th}$ hour.

The mean VAS score at 6$^{th}$ hour post operatively is1.10±0.71 in group 1 and 0.83±0.65 in group 2 and was comparable ( p=0.134). The mean VAS score was higherat 12$^{th}$ hour postoperatively and was 2.03±1.59 in group 1 and 1.52±1.30 in group 2 and both the groups were comparable (p=0.177). VAS scoreat 24$^{th}$ hour post operatively was 0.63±0.72 in group 1 and 0.50±0.68 in group 2 and was comparable ( p=0.464).

Hence the mean VAS scores were comparable in both the groups .

**Table 6: Total number of patients requiring rescue analgesia**

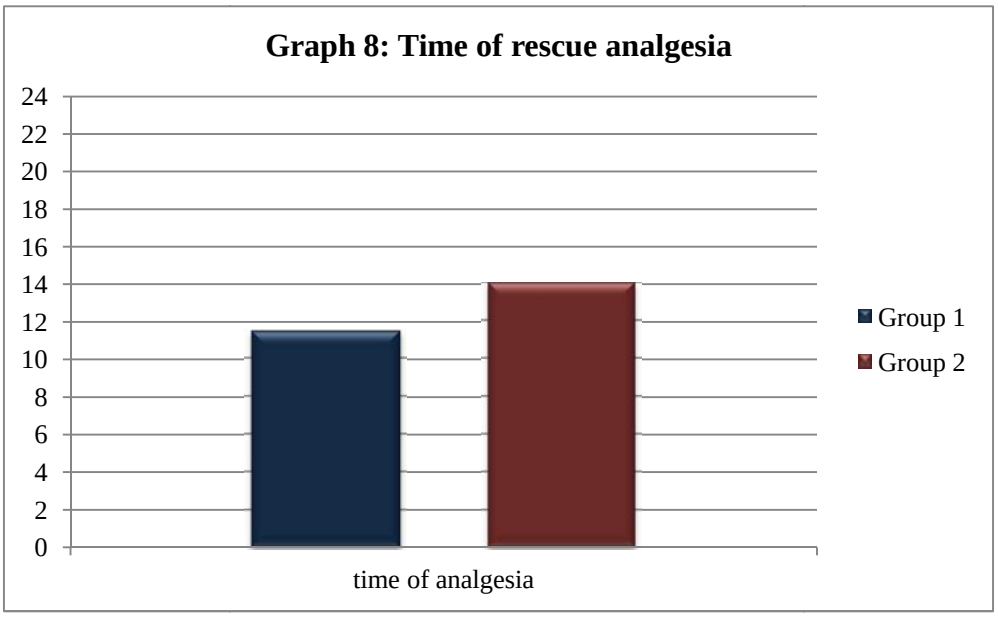
| Rescue analgesia | Group 1 | Group 2 | P Value |
|---|---|---|---|
| | Number | Number | |
| Number of patients | 14 | 7 | 0.0291 |
| Total | 30 | 30 | |
| Percentage | 46.66 | 23.33 | |




In our study 14 patients out of 30 in group 1and 7 patients out of 30 in group 2 required rescue analgesia. The number of patients who required rescue analgesia was more in group 1 (p =0.0291) and was statistically significant

**Table 7: Time of rescue analgesia**

| | Group 1 | | Group 2 | | p value |
|---|---|---|---|---|---|
| Time | MEAN | S.D | MEAN | S.D | 0.1432 |
| | 11.43 | 4.26 | 14.00 | 1.63 | |




In Group 1 the mean time for rescue analgesic was 11.43±4.26 hours postoperatively and that in Group 2 was 14.00±1.63 hours. The difference between the groups was not statistically significant (p = 0.1432).

# DISCUSSION

Acute appendicitis is a common gastrointestinal emergency. As compared to open techniques, the emergence of laparoscopic surgeries results in less postoperative pain, faster recovery and early discharge from the hospital which will enable the patient to resume their routine activities early.[1]

However laparoscopic surgeries are not pain free.[2-4]The post operative pain remains a prevalent problem and may delay discharge from the hospital.[1] Pain intensity usually peaks during the first few postoperative hours and declines. Pain after laparoscopic surgeries results from port site incision, stretching of the parietal peritoneum, peritoneal inflammation, and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity.[2]

Various modalities have been tried to achieve post operative pain relief following laparoscopic surgery. These include parenteral opioids, NSAID's ,port site infiltration with local anaesthetics, intraperitoneal instillation of local anaesthetics, etc.[2,5-10]

Opioid analgesics are frequently used to treat post surgical pain, but opioid-related side effects like respiratory depression, sedation, nausea, vomiting etc can prevent rapid functional recovery.[64]

NSAIDs are associated with complications such as gastric ulcers, anaphylaxis, bleeding , decreased hemostasis, renal dysfunction, gastrointestinal hemorrhage etc .[61,64]

Infiltration of trocar site with local anaesthetics in patients undergoing laparoscopic surgeries has been found to be advantageous in improving postoperative analgesia to only a limited extent.[19]

Local anaesthetic irrigation of peritoneum has not shown consistently beneficial effects in management of postoperative pain.[19]

TAP block is a new and novel regional block technique which was first described by Rafi in 2001. TAP block inhibits abdominal neural afferents by introducing local anaesthetic into neurofascial plane between internal oblique and transversus abdominis muscles.[20]

The neurofascial plane present between internal oblique and trasversus abdominal muscle is traversed by intercostal nerves (T7-12) , ilioinguinal and iliohypogastric nerves (L1). These nerves supply part of parietal peritoneum and skin and muscles of the anterior abdominal wall.[65]

Over the last few years, TAP blockade has been shown to improve patient comfort, reducing postoperative pain and decrease systemic opioid requirements postoperatively.[66]

TAP block has shown consistent beneficial results in providing postoperative analgesia in laparoscopic procedures.[11,12]

Various local anaesthetic agents have been used for providing postoperative analgesia with ultrasound guided TAP block such as bupivacaine, ropivacaine, levobupivacaine.[11,20,67,68]

Bupivacaine is a long acting amide linked local anaesthetic which is widely used for TAP block.[22]

Sinha.S et al in their study in 2016 to evaluate the relative efficacy of 0.25% bupivacaine and 0.375% ropivacaine for postoperative analgesia in laparoscopic cholecystectectomy using TAP block. Their study concluded that both the drugs were equivalent for postoperative analgesia and 24hr cumulative rescue analgesic requirement. Therefore in our study we have used 0.25% bupivacaine.[22]

De Oliveira et al. in 2011 conducted a study in women undergoing outpatient gynecological laparoscopy to evaluate the dose-dependent effects of a preoperative TAP on patient recovery. TAP block was given using saline, ropivacaine 0.25%, or ropivacaine 0.5% 15ml bilaterally. They concluded that TAP blocks with ropivacaine 0.25% and 0.5% reduced pain, decreased opioid consumption, and provided earlier discharge readiness that was associated with better quality of recovery.[19] Various other studies have also used 15ml of local anaesthetic agent for TAP block.[69,70] Hence in our study we have used 15ml of the local anaesthetic agent on each side.

Concept of preemptive analgesia is based on the hypothesis that the most effective way to eliminate or reduce post operative pain is to prevent nociceptive input from afferent stimuli to the CNS hence, preventing CNS hyperexcitability.[71]

In the previously mentioned study by De Oliveira et al. TAP block was performed preemptively.[19]

In a meta-analysis conducted by Gildasio S. De Oliveira et al. in 2014, Ten randomized controlled trials with 633 subjects were included in the analysis. They

evaluated the effects of TAP block compared with control group on postoperative pain outcomes in laparoscopic surgical procedures. They observed a greater effect on early pain at rest when TAP block was performed preoperatively. [11]

Therefore we have given TAP block preemptively to prevent CNS hyperexcitability.

Various adjuvants like opioids ,$\alpha_2$ adrenergic agonists, epinephrine, neostigmine have been used with bupivacaine to prolong its action and improve the quality of analgesia but are associated with undesirable side effects.[11,64]

The major side effects of $\alpha_2$ adrenergic agonists are haemodynamic changes like bradycardia and hypotension.[64]

The addition of epinephrine to bupivacaine prolongs the duration of conduction blockade and decreases systemic absorption but this action is less compared to addition of epinephrine to lidocaine. Whenever local anesthetic solutions containing epinephrine are administered in the presence of inhaled anesthetics, there may be the possibility of enhanced cardiac irritability. Systemic absorption of epinephrine may accentuate systemic hypertension in vulnerable patients.[62]

Neostigmine stimulates muscarinic receptors in the bronchial smooth muscles and leads to bronchospasm.it also causes sedation, nausea and vomiting.[64]

Fentanyl is a phenylpiperidine-derivative synthetic opioid agonist that is structurally related to meperidine. As an analgesic, fentanyl is 75 to 125 times more potent than morphine.[61-63]

Fentanyl is used as an adjuvant to local anaesthetics in both neuraxial and peripheral blocks.[13,15,72]

In our study we have added 20μg of fentanyl (10 μg on each side) to 0.25% bupivacaine as done by Mostafa Abdel Hamid Abo El Eninet in their study to examine the effect of adding fentanyl to local anaesthetic in peribulbar block. The results showed that addition of fentanyl to local anaesthetic fastens the onset of block, prolongs duration of lid akinesia and improves quality of postoperative pain in peribulbar block.[15]

The present one year randomized clinical study was conducted on 60 ASA grade I and II patients aged between 18 to 60 years of either gender who were divided into 2 groups by computer generated randomization table. Group 1 received 15ml of 0.25% bupivacaine bilaterally Group 2 received 15ml of 0.25% bupivacaine + 10 mcg of fentanyl bilaterally in patients undergoing laparoscopic appendicectomy under general anaesthesia at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Nehru nagar, Belagavi. Post operatively pain was assessed using VAS score at 0,1,2,3,4,5,6,8,10,12,14,16,18,20,22 and 24 hours post operatively. Rescue analgesia was provided if VAS score recorded was > 3.

In our study we found no statistically significant difference between group 1 and group 2 with regards to mean age (31.47±11.72 and 30.30±11.26 years respectively; p value = 0.6957) and mean weight (63.03±9.10 and 64.67±7.61kgs respectively; p value =0.4536).

Of the total 30 patients in group 1, 19 (63.33%) were female & 11 (36.66%) were male. Of the total 30 patients in group 2, 19 (63.33%) were female & 11 (36.66%) were males. When compared the difference between the two groups was not found to be statistically significant (p=0.782). In group 1 93.33% patients were ASA grade I and 6.67 % were ASA grade II. In group 2 90% patients were ASA grade I while 10 % were ASA grade II. The data was comparable in both groups ( p = 0.6404). Therefore both the groups had similar demographic characteristics.

In the present study we found that the mean VAS score at $0^{th}$ hour post operatively was 1.10 $\pm$ 0.71 in group 1 and 1.07 $\pm$ 0.64 in group 2 and was comparable in both the groups ( p=0.849).The mean VAS score at $1^{st}$ hour post operatively was 1.13$\pm$ 0.68 in group 1 and 0.93 $\pm$ 0.58 in group 2.Though group 1 recorded higher mean VAS score compared to group 2 it was statistically insignificant ( p=0.226). At $2^{nd}$ hour post operatively the mean VAS score was 1.30$\pm$ 1.42 in group 1 and 1.00 $\pm$ 0.59 in group 2 .Though group 1 recorded higher mean VAS score compared to group 2 it was statistically insignificant ( p=0.288). At $3^{rd}$ hour post operatively the mean VAS score decreased to 1.10$\pm$ 0.71 in group 1 and 0.83 $\pm$ 0.65 in group 2 and was comparable in both the groups ( p=0.134). Further at $4^{th}$ hour post operatively the mean VAS scores were further reduced to 1.03$\pm$ 0.67 in group 1 and 0.80 $\pm$ 0.61 in group 2 and were comparable ( p=0.163). The mean VAS score at $5^{th}$ hour post operatively was further reduced to 1.00$\pm$ 0.74 in group 1 and 0.77 $\pm$ 0.57 in group 2 and was comparable ( p=0.177).

At $6^{th}$ hour post operatively the mean VAS score was 1.10$\pm$ 0.71 in group 1 and 0.83 $\pm$ 0.65 in group 2 and was comparable ( p=0.134). At $8^{th}$ hour post operatively the mean VAS score was 1.23$\pm$ 0.77 in group 1 and 1.13 $\pm$ 0.78 in group 2

and was comparable in both the groups ( p=0.619). The mean VAS score increased at $10^{th}$ hour post operatively to 1.67± 1.12 in group 1 and 1.10± 0.88 in group 2 and was comparable ( p=0.034). At $12^{th}$ hour post operatively the mean VAS score further increased to 2.03± 1.59 in group 1 and 1.52 ± 1.30 in group 2 and was comparable in both the groups ( p=0.177). The mean VAS score at $14^{th}$ hour post operatively was 2.13± 1.33 in group 1 and 2.10 ± 2.37 in group 2 and was comparable ( p=0.946). At $16^{th}$ hour postoperatively the mean VAS score decreased to 1.60±0.89 in group 1 and 1.63±1.16 in group 2 and was comparable( p= 0.901). The mean VAS score at $18^{th}$ hour was 1.10±0.55 in group 1 and 0.97±0.56 in group 2 and were comparable in both groups(p=0.353).The mean VAS score at $20^{th}$ hour was 0.93±0.64 in group 1 and 0.67±0.61 in group 2 which were comparable (p=0.102).

The mean VAS score at $22^{nd}$ hour decreased to 0.73±0.72 in group 1 and 0.57±0.68 in group 2 and was comparable (p= 0.367). the mean VAS score at $24^{th}$ hour postoperatively was 0.63±0,72 in the $1^{st}$ group and 0.50±0.68 in group 2. Even though the mean score was low in group 2 it was not statistically significant (p= 0.464).

In both the groups, the mean VAS score was less than 3 and was comparable (p >0.05) at all the recorded time intervals. Hence bupivacaine 0.25% was found to be equally effective given alone or with fentanyl in providing post operative analgesia following laparoscopic appendicectomy.

A study in 2013 by Parmer et al, evaluated the analgesic efficacy of Surgeon-assisted Transversus abdominis Plane Block in reducing pain score in patients undergoing open cholecystectomy. 40 patients undergoing cholecystectomy were randomly allocated into 2 groups.. Group A received routine analgesic which included

Diclofenac sodium 75 mg intravenously (IV) at 8 hourly and group B received routine analgesic &Transversus abdominis Plane Block with 15 ml of bupivacaine 0.25%. The study concluded that Transversus abdominis Plane block reduced visual analogue scale for pain on emergence and at all postoperative time points up to 12 hours ($p < 0.0009$).[69] These results are comparable to our study.

In the previously mentioned meta- analysis by Gildasio S. De Oliveira.Jr in 2014, they observed TAP block is an effective strategy to improve early and late pain at rest over control.[11] This is comparable to our study as both the groups had low mean VAS scores at rest.

A study by G. Niraj et al. in 2009 evaluated the analgesic efficacy of TAP block in patients undergoing open appendicectomy. Fifty-two adult patients undergoing open appendicectomy were randomized to undergo standard care or to undergo a right-sided TAP block with bupivacaine. All patients received standard anaesthetic, and after induction of anaesthesia, the TAP group received an ultrasound-guided unilateral TAP block. They observed that postoperative visual analogue scale pain scores were reduced in the TAP block group soon after surgery and at 24 h.[20] The results of our study are consistent with the above study.

John Carney et al. conducted a study in 2010 to evaluate the analgesic efficacy of unilateral TAP block over the first 48 postoperative hours after open appendectomy in children. Forty children undergoing appendectomy were randomized to undergo unilateral TAP block with 2.5 mg /kg 0.75% ropivacaine versus placebo. They came to the conclusion that TAP block reduced postoperative visual analog scale pain scores at rest significantly compared with placebo.[21] These results are comparable to ours.

In 2015, Alireza Saliminia et al, conducted a study to evaluate the efficacy of TAP block on the post laparoscopic cholecystectomy pain intensity and analgesic consumption.Fifty-four patients were enrolled in the study.TAP block with saline or with 0.5% bupivacaine was given. Postoperative pain intensity at 30 minutes, 1 hour, 6 hours, 12 hours, and 24 hours following discharge for recovery were measured and recorded. They found that there was significant difference in pain scores between the bupivacaine and the saline group with the saline group having higher scores. They concluded that TAP block with bupivacaine provides better postoperative analgesia than the control group.[73]These results were comparable with our study.

In a study conducted by John G. McDonnell et al, in 2007, they evaluated the analgesic efficacy of TAP block in patients during the first 24 postoperative hours after abdominal surgery. Thirty-two adults undergoing large bowel resection via a midline abdominal incision were randomized to receive standard care or to undergo TAP block in addition to standard care .After induction of anesthesia, 20 mL of 0.375% levobupivacaine was deposited into the transversus abdominis neuro-fascial plane via the bilateral lumbar triangles of Petit. They found that the group with TAP block had significantly lower VAS scores as compared to the control group in the first 24hrs.[67] These results were comparable to ours.

Out of 30 patients in each group, 14 patients in group 1 and 7 patients in group 2 recorded VAS score > 3 and required rescue analgesic in the first 24 hours. This difference is statistically significant (p=0.029).

We could not compare this to any studies however as there are no studies done where fentanyl is added to bupivacaine to achieve TAP block.

The time for requirement of first rescue analgesic was 11.43±4.26hrs in group 1 and 14.00±1.63hrs in group 2. Even though the time for first rescue analgesic is longer in group 2, it is not statistically significant (p=0.142).

We could not find a study done to compare the time of first analgesic requirement in laparoscopic surgeries. Therefore we could not make a comparison with our study.

Hence in our study pre-emptive Transversus abdominis plane block with 0.25% bupivacaine alone or with fentanyl was found to be equally effective in most patients in preventing post-operative pain following laparoscopic appendicectomy.

In the previously mentioned meta-analysis by Gildasio S. De Oliveira et al, the study found that the effect of TAP block on time to first analgesic administration was significant. This is dissimilar to our study. Our study compares the addition of fentanyl to bupivacaine to TAP block. As TAP block is given in both the groups the time for rescue analgesia is comparable in our study.

There were no block failures in our study.No adverse effects or complications like local anaesthetic toxicity, post-operative nausea and vomiting, pruritis were observed in our study which is consistent with the results of Sinha.S et al.

Our study has certain limitations. In our study we have observed the VAS score for rest. However the VAS score at movement have not been taken into account.

Although our study did not show any significant advantage in adding fentanyl, addition of higher dose of fentanyl to bupivacaine in TAP block may be useful and further studies to evaluate the effect of higher doses of bupivacaine may be done. Addition of higher dose of fentanyl may significantly prolong the time to first rescue analgesic.

# CONCLUSION

Pre-emptive Transversus abdominis plane block with 0.25% bupivacaine or with addition of fentanyl is equally effective in providing postoperative pain relief in patients undergoing elective laparoscopic appendicectomy .

# SUMMARY

The present study was conducted in the Department of Anaesthesiology, KLES Dr.Prabhakar Kore Hospital and MRC, Nehru nagar, Belagavi after obtaining an approval from institutional ethics committee and written informed consent.

The study was conducted on 60 ASA grade I and IIpatients aged between 18 to 60 yearsof either gender, undergoing elective laparoscopic appendicectomy under general anaesthesia. Thorough Pre Anaesthetic Evaluation was done. Computer generated randomization table was used to allocate the patients into 2 groups, Group 1 (TAP block with 15ml of 0.25% bupivacaine) and Group 2 (TAP block with 15ml of 0.25% bupivacaine + 10 mcg of fentanyl ). After induction of general anaesthesia, group 1 received TAP block with 15ml of 0.25% bupivacaine bilaterally and group 2 received TAP block with 15ml of 0.25% bupivacaine + 10 mcg of fentanyl bilaterally. Laparoscopic appendicectomy was done according to standard protocol.

Post operatively pain was assessed using VAS score at 0,1,2,3,4,5,6,8,10,12, 14,16,18,20,22 and 24 hours post operatively. Inj Tramadol 2mg/kg IV, was given as rescue analgesic if VAS score recorded was > 3. The time of request of 1$^{st}$ dose of Tramadol was noted. Side effects if any were noted. Incidence of failed block (patient with VAS score >3 in the immediate postoperative period) was also noted.

The mean VAS score was less than 3 and was comparable in both the groups at different time intervals post operatively ($p > 0.05$). The time for requirement of first rescue analgesic was 11.43±4.26hrs in group 1 and 14.00±1.63hrs in group 2 and was comparable($p=0.142$).14 patients in group 1 and 7 patients in group 2 recorded VAS score > 3 and required rescue analgesic in the first 24 hours. This difference was

statistically significant (p=0.029). There were no block failures. No complications or side effects were noted in our study.

Thus based on the results we conclude that Pre-emptive Transversus Abdominis plane block with 0.25% bupivacaine or with addition of fentanyl is equally effective in providing postoperative pain relief in patients undergoing elective laparoscopic appendicectomy.

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# ANNEXURE – I - CONSENT FORM

Mr/Mrs/Miss. _____ we are requesting you to enroll yourself in study titled **"A COMPARISON OF PREEMPTIVE TRANSVERSUS ABDOMINIS PLANE BLOCK WITH 0.25% BUPIVACAINE AND 0.25% BUPIVACAINE WITH 20MCG FENTANYL FOR POST OPERATIVE ANALGESIA IN LAPAROSCOPIC APPENDICECTOMY - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"** conducted by J.N. Medical College, Belagavi under KLE university, Belagavi.

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

**Purpose of the study:**

The purpose of research is to compare the efficacy of preemptive Transversus abdominis plane block with 0.25% bupivacaine and 0.25% bupivacaine with fentanyl for duration of postoperative analgesia in patients undergoing laparoscopic appendicectomy

**Procedure Involved:**

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail and investigated accordingly. You will be randomly allocated in either of the two study groups by computer generated randomisation table. You will receive Transversus abdominis plane block with 0.25% bupivacaine or 0.25% bupivacaine with fentanyl and under general anaesthesia you will undergo laparoscopic appendicectomy as per standard guidelines,there is no change in the anaesthesia or surgical procedure.

**Benefits and Risks**

The benefits of taking part in this research are that we can avoid adverse effects of opoids, NSAIDS and prolonged hospitalization with good quality of analgesia and early ambulation. There are no observable risks associated with the study.

**Voluntary participation / Withdrawal**

Taking part in the study is voluntary; you may choose not to enroll in this study. Your decision will not change present or future health care services offered to you at Dr. Prabhakar Kore Hospital.

**Alternatives**

Even if you decline the participation in the study, you will get the routine line of management.

**Confidentiality**

All information collected about you during the course of the study will be kept confidential. The code numbers will identify you in this study records and the information from this study may be published but your identity will be confidential in any publication. The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

- In emergency to protect your rights and welfare.
- If required by law.

**Authorization to Publish Results:**

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

**Financial Incentives for participation**

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

**Compensation**

In the event of injury, related to the study, treatment will be made available at Dr. Prabhakar Kore Hospital and MRC, Belagavi. No reimbursement, compensation or free medical care will be given by law.

**Queries/ Contact details**

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Prof. & Head of Pathology as Chairman of J. N. Medical College Institutional Ethics Committee on Human Subjects Research, Phone No.9480275601or Extension-4052 at J. N. Medical College, Belagavi.

**Consent for participation in research trial**

I, _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read form in my own vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject :_____

Date: _____

Place : _____

Witness Name : _____ Signature: _____

Investigators Name: _____ Signature: _____

Date:

Place : _____

# ANNEXURE - II – PROFORMA

## "A COMPARISON OF PREEMPTIVE TRANSVERSUS ABDOMINIS PLANE BLOCK WITH 0.25% BUPIVACAINE AND 0.25% BUPIVACAINE WITH 20MCG FENTANYL FOR POST OPERATIVE ANALGESIA IN LAPAROSCOPIC APPENDICECTOMY- A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"

| | |
|---|---|
| Patient Name: | IP No.: |
| Age: | Gender: |
| Height: | Weight: |
| Date of Operation: | Occupation: |
| Address: | Anaesthesiologist: |

**Preanesthetic Evaluation:**

Chief Complaints:

Past History includes

a. HTN / DM / Asthma / Epilepsy / Drug allergy

b. Drug therapy

c. Previous exposure to Anesthesia

d. H/o allergy to opioids or local anaesthetics

e. H/o coagulation abnormality

f. H/o long term opioid consumption

Family history :

**General physical examination**

Pallor / Icterus / Clubbing / Cyanosis / Lymphadenopathy / Edema

PR : BP :

RR : Temp :

Musculoskeletal examination

Jaw movements : Teeth :

Airway assessment : Spine :

**Systemic Examination**

RS : CNS :

CVS : Abdominal :

**Investigations**

Hb : Total Leukocyte Count :

S.urea : Platelet Count:

S.creatinine: Urine routine:

ECG : Chest X-Ray:

RBS: BT/CT/PT,INR

**Preoperative physical status:** ASA Grade I, II, III, IV, V

Diagnosis :

Proposed Surgery :Laparoscopic appendicectomy

**Preoperative baseline values**

HR: BP:

**Monitors attached**

Pulse oximetry : NIBP : ECG :

**Selection criteria:**

**Inclusion criteria:**

- Patients undergoing laparoscopic appendicectomy ↓GA.
- Age: 18 to 60 years group
- ASA Grade I and Grade II patients

**Exclusion criteria:**

- Age below 18yrs and above 60yrs.
- ASA Grade III and IV
- Patients allergic to local anaesthetic and opioids
- Patient on long term opioids
- Patient with coagulation abnormality

**Methodology:**

After obtaining the approval of ethical committee and written informed consent, a total of 60 patients undergoing laparoscopic appendicectomy were included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients were randomized based on computer generated randomization table into one of the two groups.

Group 1- Patient received TAP block with 15ml of 0.25% bupivacaine bilaterally

Group 2- Patient receivedTAP block with 15ml of 0.25% bupivacaine + 10 mcg of fentanyl bilaterally

The total dose of Bupivacaine was maintained within the safe limit (3mg/kg)[60]

A thorough Pre-Anaesthetic Evaluation was done.Routine investigations such as Complete blood picture, Random Blood Sugar, Serum Creatinine, Blood Urea were done. Chest X-ray, Electrocardiography were carried out in patients above 40yrs of age. Patientwas advised overnight fasting.

On the previous day, Visual analogue score was shown to the patient and explained its use for the postoperative pain assessment

In the operation theatre patients was monitored by pulse oximetry, non invasive blood pressure measurement and electrocardiography. Following preoxygenation, patient was premedicated with Inj Glycopyrrolate 0.005mg/kg IV, Inj Midazolam 0.05mg/kg IV and Inj Pentazocin 0.5mg/kg IV. Induction of anaesthesia was done with Inj Thiopentone sodium 5mg/kg IV sufficient to obtund the eye-lash reflex, followed by Inj Vecuronium 0.1mg/kg IV to facilitate orotracheal intubation. After confirming bilateral equal air entry general anesthesia was maintained with $O_2$:$N_2O$ in the ratio of 50:50 and 0.4% isoflurane with intermittent top ups of vecuronium.

After instituting general anaesthesia but before starting the surgical procedure, bilateral Transversus abdominis plane block was performed in all subjects using ultrasound guidance with a portable ultrasound device.

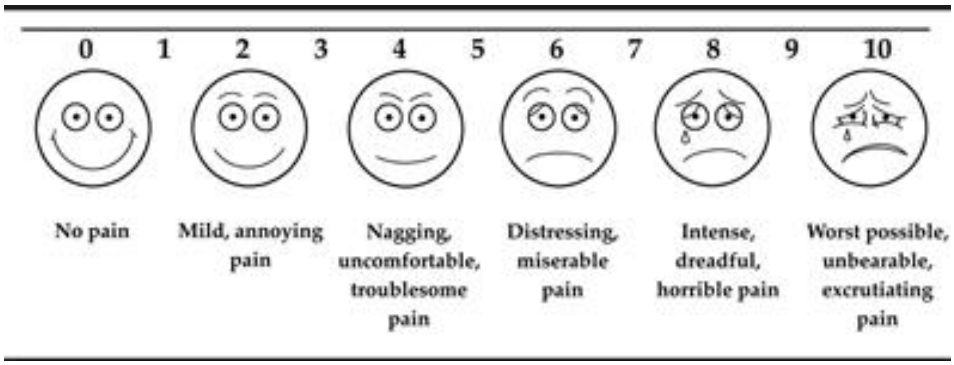
The ultrasound probe was placed transversely on the anterolateral abdominal wall between the iliac crest and the subcostal margin. The external oblique, the internal oblique and the transversus abdominis muscles were visualized. Under strict aseptic precautions a 23-gauge needle was introduced anteriorly in the plane of the ultrasound beam. The needle was directed to approach the transversus abdominis plane and on entering the fascial plane, and after negative aspiration of blood, either15ml of 0.25% bupivacaine or 0.25% bupivacaine with 10µg fentanyl was administered.

The injectate was seen spreading in the transversus abdominis plane as a dark oval shape. A contralateral block was performed in the same manner.[20]Laparoscopic appendicectomy was

performed. Patient was extubated after thorough suctioning and adequate reversal with Inj Glycopyrrolate IV(0.01mg/kg) and Inj Neostigmine IV(0.05mg/kg).

Patient was shifted to recovery and assessed for postoperative pain using VAS, at hourly intervals for the first 1-6hrs, 2 hourly upto 24hrs postoperatively. Patients with VAS 3 or more was given Inj Tramadol 2mg/kg IV. The time of request of 1st dose of Tramadol was noted. Side effects if any were noted. Incidence of failed block (patient with VAS score >3 in the immediate postoperative period) was also noted.

**VAS pain scale:**




**Postoperative Pain Assessement:**

| **TIME(hrs)** | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| **VAS** | | | | | | | |

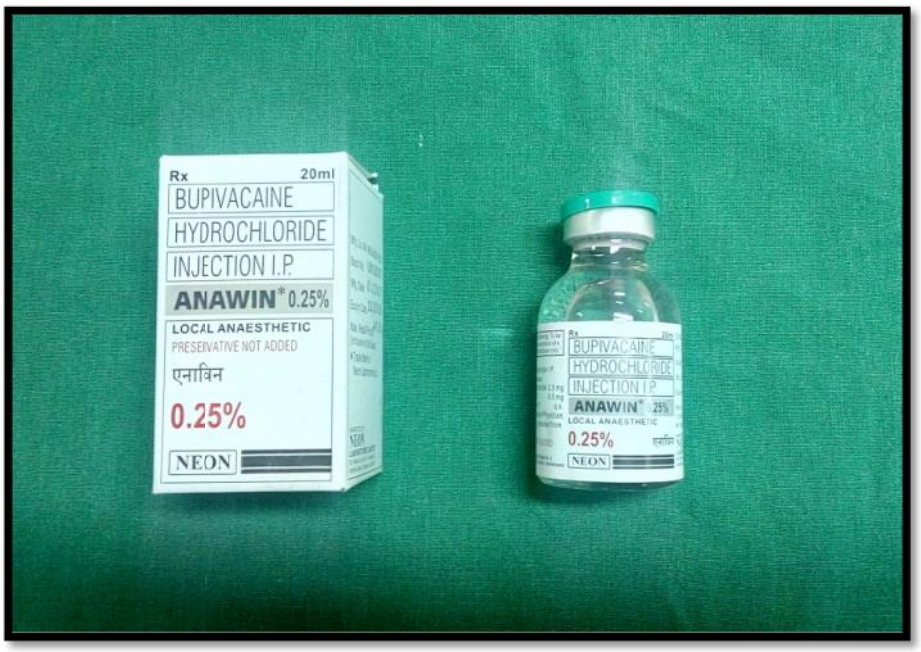
| TIME(hrs) | 8 | 10 | 12 | 14 | 16 | 18 | 20 | 22 | 24 |
|---|---|---|---|---|---|---|---|---|---|
| VAS | | | | | | | | | |

**Time for first rescue analgesia :**

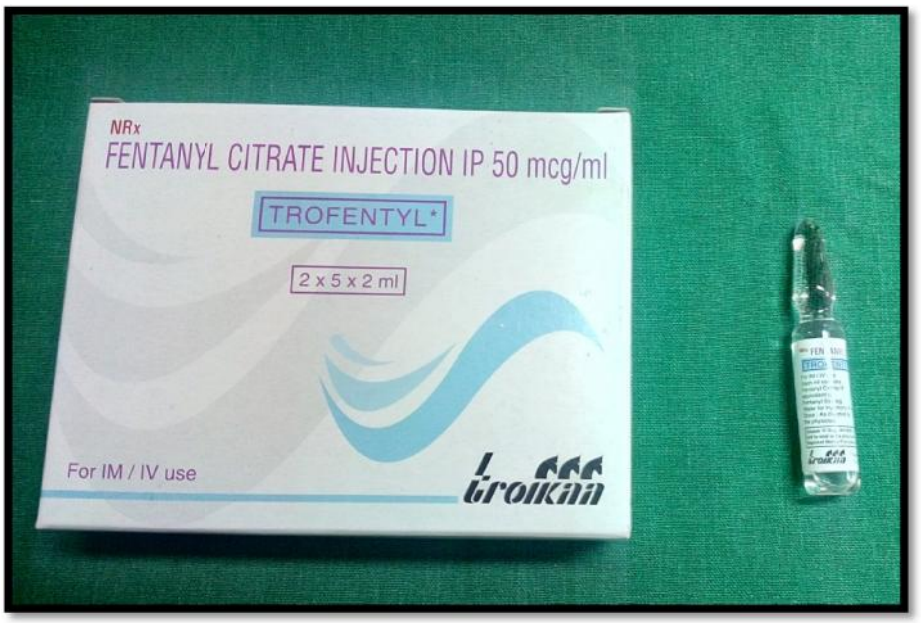
**Adverse effects (**if any**)**:

## ANNEXURE III – PHOTOGRAPHS

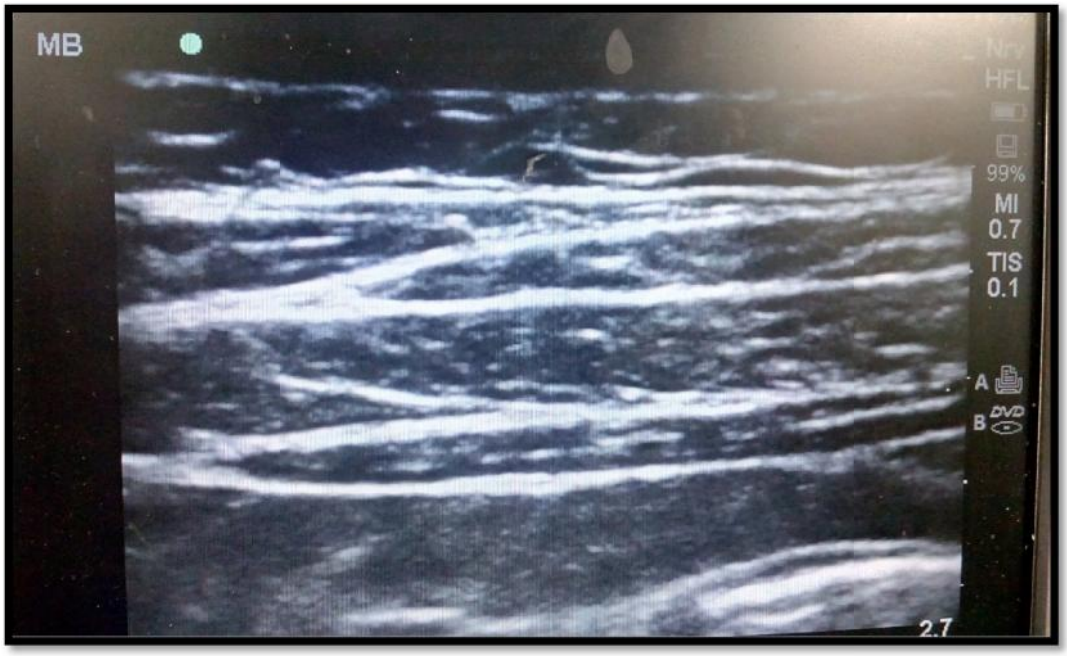
## DRUGS USED FOR TRANSVERSUS ABDOMINUS PLANE BLOCK



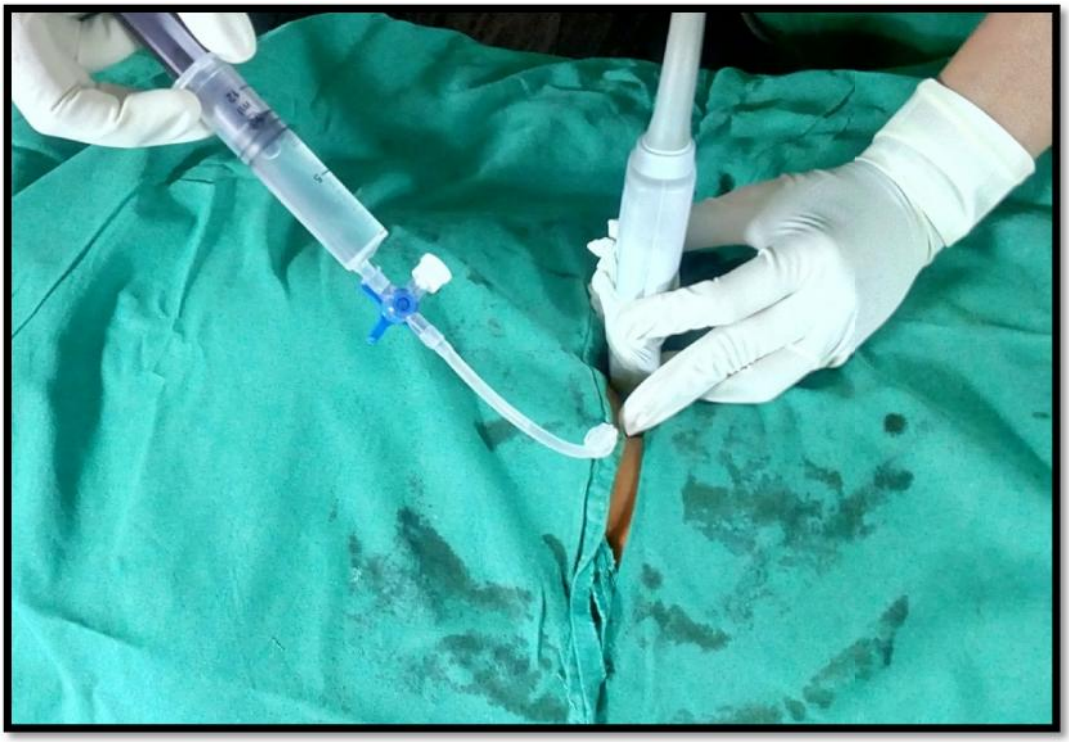

**PHOTOGRAPH 1 –- Showing 0.25% Bupivacaine**



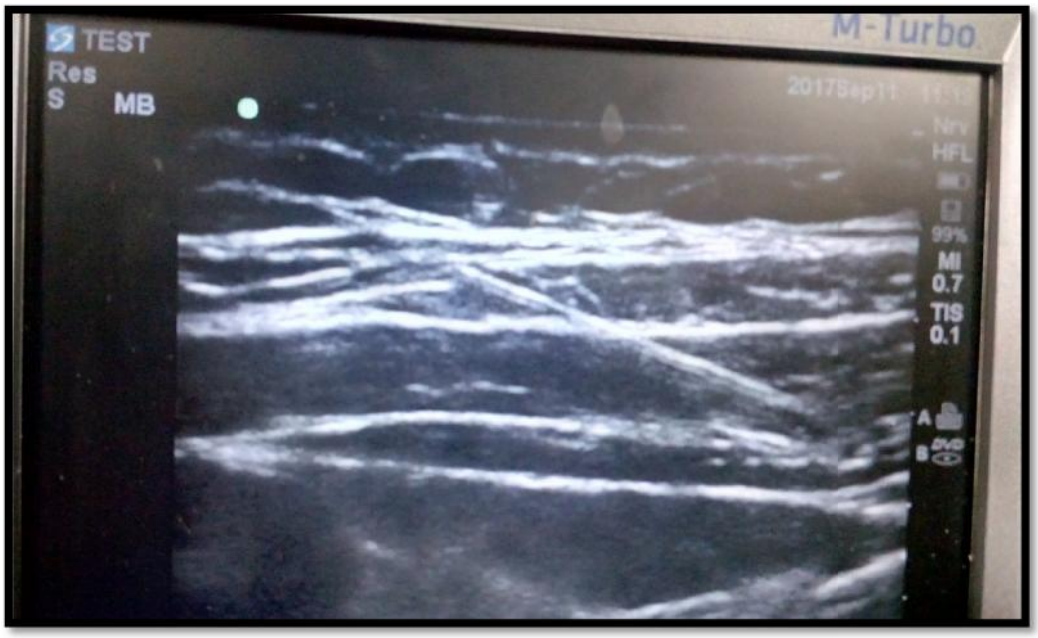

**PHOTOGRAPH 2 –- Showing Fentanyl**



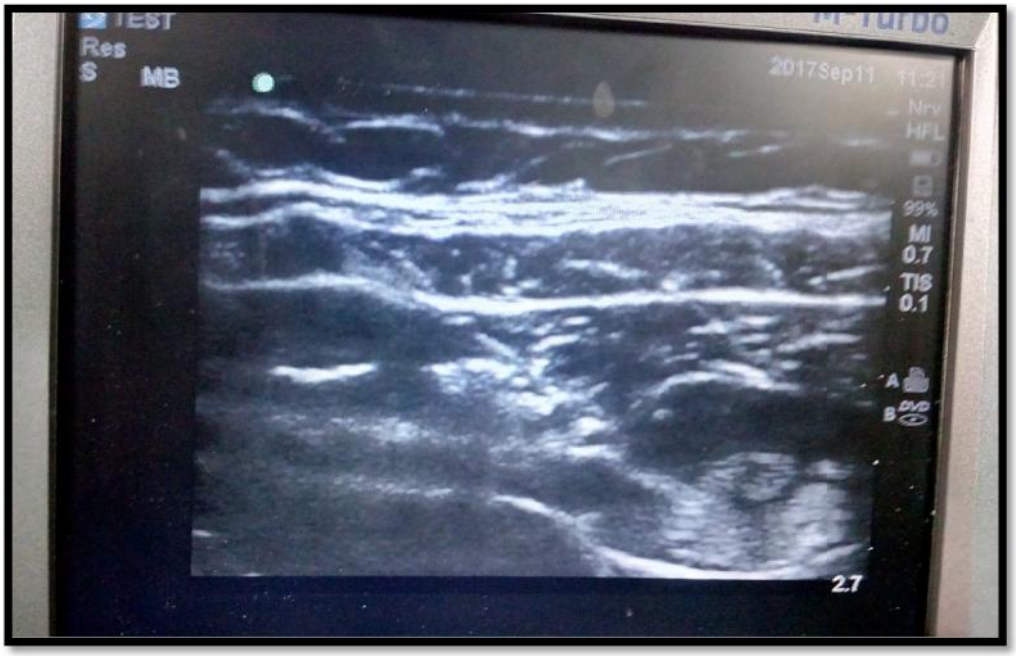

**PHOTOGRAPH 3 –- Ultrasound image showing abdominal muscles and Transversus Abdominus plane**



**PHOTOGRAPH 4–- TAP block under Ultrasound guidance**




**PHOTOGRAPH 5–- Ultrasound image of needle in Transversus Abdominus Plane**




**PHOTOGRAPH 6-- Ultrasound image of spread of local anaesthetic in Transversus abdominus plane**

| Group -1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Baseline | | | | VISUAL ANALOGUE SCALE(VAS) | | | | | | | | | | | | | | | | | | |
| Serial number | Randomisation Number | In patient number | Age (Yrs) | Sex | ASA Grade | Weight(kgs) | HR (bpm) | SBP (mm Hg) | DBP (mm Hg) | Respiratory rate(BPM) | 0 th hour | 1 st hour | 2 nd hour | 3rd hour | 4 th hour | 5 th hour | 6 th hour | 8 th hour | 10 th hour | 12 th hour | 14 th hour | 16th hour | 18th hour | 20th hour | 22nd hour | 24th hour | Time for first rescue analgesia in hrs | Total analgesic consumed in 24 hrs in mg |
| 1 | 1 | 705785 | 22 | Female | 1 | 52 | 86 | 120 | 70 | 12 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 4 | 1 | 1 | 1 | 1 | 2 | 2 | 12 | 100 |
| 2 | 1 | 706747 | 44 | Female | 1 | 68 | 70 | 130 | 80 | 14 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 3 | 5 | 2 | 2 | 1 | 2 | 2 | 14 | 100 |
| 3 | 1 | 721274 | 21 | Male | 1 | 65 | 71 | 120 | 70 | 12 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 6 | 2 | 2 | 2 | 2 | 2 | 1 | 12 | 100 |
| 4 | 1 | 721685 | 33 | Female | 1 | 75 | 75 | 130 | 84 | 13 | 3 | 3 | 6 | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 100 |
| 5 | 1 | 723488 | 25 | Female | 1 | 58 | 76 | 120 | 68 | 14 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 4 | 1 | 1 | 1 | 1 | 1 | 14 | 100 |
| 6 | 1 | 726948 | 25 | Female | 1 | 65 | 90 | 120 | 70 | 14 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 4 | 2 | 1 | 1 | 1 | 1 | 14 | 100 |
| 7 | 1 | 727079 | 25 | Female | 1 | 50 | 90 | 120 | 76 | 12 | 2 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 3 | 5 | 2 | 1 | 1 | 1 | 1 | 1 | 12 | 100 |
| 8 | 1 | 727954 | 18 | Male | 1 | 70 | 100 | 120 | 86 | 14 | 2 | 3 | 6 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 100 |
| 9 | 1 | 730543 | 18 | Female | 1 | 40 | 88 | 116 | 80 | 14 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 5 | 2 | 2 | 1 | 2 | 1 | 1 | 12 | 100 |
| 10 | 1 | 735766 | 26 | Female | 1 | 58 | 80 | 126 | 80 | 14 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 4 | 2 | 2 | 1 | 1 | 1 | 1 | 12 | 100 |
| 11 | 1 | 736075 | 50 | Female | 1 | 60 | 88 | 130 | 80 | 14 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 2 | 3 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 12 | 1 | 749972 | 48 | Male | 1 | 75 | 74 | 130 | 80 | 12 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 1 | 1 | 0 | 0 | NA | 0 |
| 13 | 1 | 748282 | 48 | Male | 1 | 69 | 60 | 124 | 90 | 12 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 2 | 1 | 1 | 1 | NA | 0 |
| 14 | 1 | 755862 | 27 | Male | 1 | 70 | 68 | 126 | 80 | 14 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 2 | 1 | 0 | NA | 0 |
| 15 | 1 | 756213 | 35 | Female | 1 | 70 | 80 | 130 | 78 | 14 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 16 | 1 | 758056 | 18 | Male | 1 | 65 | 70 | 124 | 80 | 14 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 1 | 1 | 1 | 0 | NA | 0 |
| 17 | 1 | 757532 | 25 | Female | 1 | 65 | 80 | 124 | 86 | 12 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 2 | 2 | 2 | 3 | 2 | 1 | 1 | 0 | 0 | NA | 0 |
| 18 | 1 | 760019 | 55 | Female | 1 | 55 | 80 | 130 | 80 | 15 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 2 | 1 | 1 | 1 | 1 | NA | 0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | 1 | 760381 | 33 | Male | 1 | 70 | 78 | 124 | 80 | 12 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 20 | 1 | 761785 | 21 | Female | 1 | 55 | 75 | 120 | 70 | 12 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 2 | 3 | 2 | 1 | 0 | 0 | NA | 0 |
| 21 | 1 | 761976 | 30 | Female | 1 | 60 | 74 | 128 | 80 | 12 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | NA | 0 |
| 22 | 1 | 761912 | 23 | Female | 1 | 66 | 86 | 130 | 80 | 13 | 1 | 1 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | NA | 0 |
| 23 | 1 | 764517 | 38 | Male | 2 | 75 | 90 | 140 | 94 | 12 | 2 | 2 | 2 | 2 | 1 | 2 | 1 | 1 | 2 | 2 | 4 | 1 | 1 | 1 | 1 | 1 | 14 | 100 |
| 24 | 1 | 764739 | 32 | Female | 1 | 70 | 80 | 136 | 80 | 14 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 25 | 1 | 769320 | 35 | Male | 2 | 75 | 76 | 134 | 80 | 12 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 4 | 1 | 1 | 1 | 1 | 16 | 100 |
| 26 | 1 | 773224 | 19 | Male | 1 | 50 | 68 | 114 | 60 | 12 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 5 | 1 | 1 | 0 | 0 | 0 | 14 | 100 |
| 27 | 1 | 776231 | 26 | Female | 1 | 66 | 78 | 120 | 70 | 13 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | NA | 0 |
| 28 | 1 | 774736 | 54 | Female | 1 | 54 | 70 | 118 | 70 | 11 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | NA | 0 |
| 29 | 1 | 767722 | 50 | Female | 1 | 50 | 90 | 118 | 76 | 12 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 5 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 10 | 100 |
| 30 | 1 | 771664 | 20 | Male | 1 | 70 | 84 | 124 | 60 | 11 | 1 | 1 | 1 | 2 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | NA | 0 |

| Group -2 | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Serial number | Randomisation Number | In patient number | Age (Yrs) | Sex | ASA Grade | Baseline | | | | | VISUAL ANALOGUE SCALE(VAS) | | | | | | | | | | | | | | | Time for first rescue analgesia in hrs | Total analgesic consumed in 24 hrs in mg |
| | | | | | | Weight(kgs) | HR (bpm) | SBP (mm Hg) | DBP (mm Hg) | Respiratory rate(BPM) | 0 th hour | 1 st hour | 2 nd hour | 3rd hour | 4 th hour | 5 th hour | 6 th hour | 8 th hour | 10 th hour | 12 th hour | 14 th hour | 16th hour | 18th hour | 20th hour | 22nd hour | 24th hour | | |
| 1 | 2 | 722291 | 33 | Female | 1 | 65 | 84 | 116 | 70 | 12 | 2 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 3 | 5 | 2 | 2 | 1 | 1 | 1 | 1 | 12 | 100 |
| 2 | 2 | 722106 | 28 | Female | 1 | 75 | 80 | 128 | 76 | 14 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 | 5 | 2 | 2 | 2 | 2 | 16 | 100 |
| 3 | 2 | 724624 | 30 | Female | 1 | 68 | 90 | 136 | 80 | 12 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 4 | 2 | 2 | 1 | 1 | 1 | 1 | 12 | 100 |
| 4 | 2 | 727373 | 24 | Male | 1 | 70 | 90 | 118 | 70 | 12 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | NA | 0 |
| 5 | 2 | 727816 | 18 | Female | 1 | 50 | 80 | 124 | 80 | 13 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 | 4 | 2 | 1 | 1 | 1 | 1 | 14 | 100 |
| 8 | 2 | 730441 | 22 | Male | 1 | 66 | 96 | 120 | 80 | 12 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 3 | 2 | 2 | 1 | 2 | 2 | NA | 0 |
| 7 | 2 | 735932 | 52 | Female | 2 | 58 | 70 | 140 | 90 | 14 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | NA | 0 |
| 8 | 2 | 737459 | 31 | Female | 1 | 68 | 76 | 124 | 80 | 12 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 9 | 2 | 737732 | 25 | Female | 1 | 58 | 72 | 120 | 80 | 14 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 1 | 0 | 0 | NA | 0 |
| 10 | 2 | 737977 | 25 | Female | 1 | 58 | 90 | 116 | 80 | 14 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 11 | 2 | 745003 | 53 | Female | 1 | 75 | 90 | 140 | 80 | 13 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 1 | 1 | 1 | 0 | 0 | NA | 0 |
| 12 | 2 | 743944 | 35 | Male | 1 | 75 | 76 | 128 | 70 | 12 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 3 | 2 | 1 | 1 | 1 | 0 | NA | 0 |
| 13 | 2 | 745671 | 45 | Female | 1 | 60 | 68 | 124 | 80 | 11 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | NA | 0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 14 | 2 | 750008 | 60 | Female | 2 | 70 | 65 | 146 | 80 | 14 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 15 | 2 | 751332 | 27 | Female | 1 | 58 | 80 | 120 | 80 | 11 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 1 | 1 | 1 | 1 | 0 | NA | 0 |
| 16 | 2 | 752036 | 22 | Male | 1 | 60 | 80 | 116 | 80 | 14 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 2 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | NA | 0 |
| 17 | 2 | 752298 | 24 | Female | 1 | 55 | 70 | 110 | 74 | 14 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 4 | 2 | 1 | 1 | 1 | 1 | 14 | 100 |
| 18 | 2 | 752270 | 18 | Female | 1 | 53 | 80 | 116 | 70 | 15 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 1 | 1 | 5 | 2 | 2 | 2 | 2 | 16 | 100 |
| 19 | 2 | 756616 | 21 | Male | 1 | 70 | 76 | 120 | 76 | 12 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | NA | 0 |
| 20 | 2 | 756840 | 40 | Female | 2 | 70 | 84 | 134 | 90 | 14 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 21 | 2 | 760156 | 23 | Male | 1 | 68 | 68 | 120 | 70 | 12 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 2 | 3 | 2 | 1 | 1 | 1 | 1 | NA | 0 |
| 22 | 2 | 765313 | 26 | Male | 1 | 74 | 78 | 132 | 80 | 15 | 1 | 1 | 1 | 2 | 2 | 2 | 1 | 1 | 0 | 0 | 1 | 2 | 1 | 1 | 0 | 0 | NA | 0 |
| 23 | 2 | 770235 | 29 | Female | 1 | 58 | 85 | 126 | 80 | 12 | 1 | 1 | 2 | 1 | 1 | 0 | 0 | 0 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | NA | 0 |
| 24 | 2 | 770559 | 19 | Male | 1 | 54 | 70 | 118 | 70 | 13 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 25 | 2 | 772857 | 19 | Male | 1 | 70 | 68 | 120 | 76 | 12 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 26 | 2 | 773395 | 42 | Male | 1 | 76 | 74 | 130 | 90 | 11 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | 1 | 2 | 4 | 1 | 1 | 1 | 0 | 0 | 14 | 100 |
| 27 | 2 | 773633 | 42 | Female | 1 | 65 | 88 | 140 | 82 | 14 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | NA | 0 |
| 28 | 2 | 774681 | 20 | Female | 1 | 59 | 90 | 140 | 74 | 16 | 2 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | NA | 0 |
| 29 | 2 | 775353 | 22 | Female | 1 | 60 | 76 | 140 | 60 | 13 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 3 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | NA | 0 |
| 30 | 2 | 778938 | 34 | Male | 1 | 74 | 87 | 140 | 76 | 12 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | NA | 0 |

# ANNEXURE V – MASTER CHART

| | | |
|---|---|---|
| ASA | - | American Society of Anaesthesiologist |
| bpm | - | Beats per minute |
| BPM | - | Breaths per minute |
| Kgs | - | Kilograms |
| VAS | - | Visual analogue scale |
| Hrs | - | Hours |
| Yrs | - | Years |
| mg | - | milligram |
| Group 1 | - | Bupivacaine |
| Group 2 | - | Bupivacaine + Fentanyl |

# ANNEXURE – VI – ETHICAL CLEARANCE LETTER

K.L.E.UNIVERSITY'S
**JAWAHARLAL NEHRU MEDICAL COLLEGE,**
**NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)**
**(Accredited 'A' Grade by NAAC)**

Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

**Ref: MDC/DOME/** 369.

**Date: 16/11/2015**

To,

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled

**"A COMPARISON OF PREEMPTIVE TRANSVERSUS ABDOMINIS PLANE BLOCK WITH 0.25% BUPIVACAINE AND 0.25% BUPIVACAINE WITH 20MCG FENTANYL FOR POST OPERATIVE ANALGESIA IN LAPAROSCOPIC APPENDICECTOMY - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"** is ethical

and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

**(Dr. Arathi Darshan)**
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

**(Dr. Ganga Pilli)**
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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