COMPARATIVE OF BUPIVACAINE AND BUPIVACAINE WITH MAGNESIUM SULPHATE IN TRANSVERSUS ABDOMINISA PLANE BLOCK UNDER ULTRASOUND GUIDANCE FOR POST-OPERATIVE ANALGESIA IN PATIENTS SCHEDULED FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANESTHESIA

By

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DOCTOR OF MEDICINE

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ANAESTHESIOLOGY

ABBREVIATIONS

ASA	**American society of anaesthesiologists**
ATP	**Adenosine Tri Phosphate**
BP	**Blood pressure**
BMI	**Body mass index**
CNS	**Central nervous system**
CVS	**Cardiovascular system**
CSF	**Cerebrospinal fluid**
DBP	**Diastolic blood pressure**
EO	**External oblique(muscle)**
ERP	**Enhanced recovery procedure**
HR	**Heart rate**
hr	**Hours**
IO	**Internal oblique(muscle)**
IV	**Intravenous**
Group B	**Bupivacaine group**
Group BM	**Bupivacaine + Magnesium sulphate group**
MgSO4	**Magnesium sulphate**
MAP	**Mean arterial pressure**
No.	**Number**
NSAID‘s	**Non steroidal anti inflammatory drugs**
NMDA	**N-methyl-D-aspartate receptor**
NS	**Normal Saline**
PONV	**Post-operative nausea & vomiting**
PR	**Pulse rate**
SB	**Systolic blood pressure**
SAB	**Sub arachanoid block**
SPSS	**Statistical presenting system software**
SAPS	**short assessment of patient satisfaction score**
TAP	**Transversus Abdominis Plane**
TAH	**Total abdominal hysterectomy**
USG	**Ultrasound Guided**
VAS	**Visual analogue scale**

ABSTRACT

Introduction : To evaluate potency of magnesium sulphate as an adjuvant to bupivacaine compared to that of bupivacaine alone in ultrasound-guided T.A.P. block.

Aim : To compare the efficacy of 0.25% bupivacaine and 0.25% bupivacaine with magnesium sulfate for postoperative analgesia in ultrasound-guided T.A.P. block.

Objectives :

- To evaluate efficacy of transversus abdominis plane block for postoperative analgesia by VAS Score (Visual Analogue Score)
- To compare the time required for first rescue analgesia between the two study groups.
- Evaluate the total doses of rescue analgesic consumption.
- Evaluate the safety and adverse effects of TAP block like post operative nausea , vomiting, myositis and heamatoma.

Material and Methods:

Ethical committee permission: yes

Patient consent**:** attached

Randomization done by computer generated random numbers.

Group B - bupivacaine 0.25% (45 mg) with 2 mL of normal saline.

Group BM- bupivacaine 0.25% (45 mg) with MgSO4 50% w/v of 0.3 mL (150 mg).

Statistical tests: Chi squire test, Independent t-test , Mann Whitney U test .

INCLUSION CRITERIA

1. Female Patients aged between 35-60 years.
2. Patients with ASA Grade I & II.
3. Patients are scheduled for total abdominal hysterectomy under subarachnoid block.

EXCLUSION CRITERIA

1. Patient refusal.
2. Patient having bleeding disorders.
3. Patient having a local infection at the site of block to be performed .
4. Patients on calcium channel blockers
5. Patients with H/o Cardio-Respiratory disorders
6. Patients with H/o convulsions & neurological deficits.

Results: Timing of first rescue analgesic was significantly shorter in group B compared to group BM. Significantly lower visual analogue scores were observed in group BM compared to group B during the initial 24 hours .

Conclusion: Addition of Magnesium sulphate to bupivacaine in TAP block reduced the time to first rescue analgesia , lower visual analogue scores and decreased incidence of vomiting and nausea.

Keywords: TAP block , Magnesium sulphate , Visual analogue score.

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INTRODUCTION

Most of the patients scheduled for surgery endure emotional stress due to their fear of postoperative discomfort.[1] More than 80% of surgery patients report early postoperative pain, with 75% describing the severity as moderate, severe, or great.[2] According to studies, only around half of persons who have surgery report acceptable postoperative pain alleviation.[3]

Total abdominal hysterectomy (T.A.H.) is a frequent major surgical operation that results in increased postoperative discomfort and agony. Such patients necessitate a well-planned analgesic treatment with minimal postoperative adverse effects.[4,5]

The abdominal wall incision is typically the site of the most severe postoperative pain. Although there are many analgesic modalities available, managing postoperative pain is still difficult. Postoperative pain that is untreated or only partially managed is linked to worse patient satisfaction, slower healing times, longer stays in hospitals, and higher healthcare expenses.[5] As a result, postoperative analgesia following T.A.H. calls for a multimodal approach. Opioids have serious adverse effects like nausea, vomiting, respiratory depression, and sedation when used as part of a multimodal regimen. The possibility of long-term abuse is also increased. In addition to opioids, non-opioid painkillers have been shown to reduce opioid use and its negative effects.[6] Acetaminophen, aspirin, non-steroidal anti-inflammatory medicines (NSAIDs), and selective cyclo-oxygenase inhibitors are examples of non-opioid pain relievers.[7] Due to adverse effects such as hemorrhage, damage to the stomach mucosa, and renal toxicity, the use of intravenous NSAIDs, such as ketorolac, has been restricted.[8]

Following surgery, enhanced recovery procedures (ERP) are intended to speed up patients' return to baseline functionality while lowering morbidity and the postoperative stress response.[9] ERP includes early mobilisation, early enteral nutrition, and localised anaesthesia for the best pain control and surgical stress reduction.[10,11] Numerous studies, including randomised controlled trials, have shown that when ERP is used, hospital length of stay, postoperative ileus duration, morbidity, and time to recover to normal function all decrease .[9,12 -14] In order to achieve the best pain

treatment, many ERPs use a multimodal approach, decreasing the use of opioids as the primary analgesic in favour of neuraxial and regional anaesthetic techniques.[15-17] The transversus abdominis plane (TAP) block is a prime example of a regional anaesthetic technique that has been extensively used in abdominal surgery.[18,19] The T.A.P. block is favoured above other options for multimodal analgesia because to its technical simplicity and trustworthy analgesia.[20] Recent years have seen an increase in the accessibility of the transversus abdominis plane (TAP) block, a interfacial plane block of the anterior abdominal wall. This block involves injecting local anaesthetic into the space between the internal oblique and transversus muscles, which is marked by the lumbar Petit triangle. According to a recent analysis ultrasound guided T.A.P. block, minimises the number of attempts and the duration of application, which accelerates the block onset.[21] Because it is difficult to accurately localize muscles, especially the transversus abdominis muscle, which is deeper in obese patients and thinner in aged patients, block performed in conjunction with ultrasonography (USG) is safer and more effective. As a result of direct monitoring of all anatomical structures, the needle, and the local anesthetic's dissemination, the margin of safety was raised and the block was successfully accomplished utilising ultrasound guidance.[22] By combining an ultrasound approach with hydro dissection and keeping the needle below the fascia, analgesia can be administered more effectively.[23] Additionally, by altering the injection site used in the TAP block utilising USG, the usage of hydro dissection can be improved. TAP block-related vascular and visceral damage may be minimized by USG.[24]

The duration of the T.A.P. block is determined by the local anaesthetics used. To extend the analgesic effects of local anaesthetics, analgesic adjuvants like opioids, alpha 2 agonists, NMDA receptor antagonists, and other substances can be used. Peripheral nerve blocks are frequently treated with dexamethasone. According to a 2018 meta-analysis, transversus abdominis plane blocks can last about three hours longer with perineural dexamethasone (4 to 8 mg) than with saline. Transversus abdominis plane blocks have also been administered with alpha-2 agonist adjuvants, such as clonidine and dexmedetomidine. Analgesia was extended by 10 hours when

clonidine (1ug/kg each side) was added to plain bupivacaine; nevertheless, sedation occurred in approximately one-third of patients. Dexmedetomidine dosages studied include both fixed dosing and weight-based regimens (0.5 to 1 ug/kg per side) (100 ug per side). Transversus abdominis plane blocks with dexmedetomidine effectively decreased pain levels both at rest and during movement, according to a 2018 meta-analysis.[25] Dexmedetomidine, on the other hand, can cause a drop in heart rate for the first four hours after surgery and greater sedation during the first postoperative hour. The identification of N-methyl-D-aspartate (NMDA) receptors in the skin and muscles led to the development of magnesium sulphate (MgSO4), an NMDA antagonist, as an adjuvant for brachial plexus block and neuraxial route.[26] The anti-nociceptive effects of magnesium sulphate, an NMDA receptor antagonist, are brought on by calcium influx control in the cell.[27] Since 2016, multiple randomised controlled investigations have looked into how transverse abdominis plane blocks are affected by perineural magnesium.[28] Doses of 0.15 to 0.5 g (per side) lead to longer analgesic durations, less morphine use, and lower postoperative pain scores as compared to the control (for up to 12 h).[29-31] Despite possessing analgesic qualities, magnesium's use as a local anaesthetic adjuvant in peripheral nerve blocks has not been widely investigated.

In this study, the potency of magnesium sulphate as an adjuvant to bupivacaine was compared to that of bupivacaine alone in ultrasound-guided T.A.P. block.

AIMS AND OBJECTIVE

AIM

To compare the efficacy of 0.25% bupivacaine and 0.25% bupivacaine with magnesium sulfate for postoperative analgesia in ultrasound-guided T.A.P. block.

OBJECTIVES

PRIMARY OBJECTIVE

- To evaluate efficacy of transversus abdominis plane block for postoperative analgesia by VAS Score (Visual Analogue Scale)

SECONDARY OBJECTIVE

- To compare the time required for first rescue analgesia between the two study groups.
- Evaluate the total doses of rescue analgesic consumption.
- Evaluate the safety and adverse effects of TAP block like post operative nausea , vomiting, myositis and heamatoma.

REVIEW LITERATURE

TAP BLOCK

After major abdominal surgery, epidural analgesia is typically regarded as gold standard. However, there are few analgesic choices available when epidural analgesia is unfeasible. Large intravenous opiates doses may be required, which cannot be well tolerated. Transversus Abdominis Plane (TAP) Block was created in an effort to find an alternate method of effectively reducing pain.

Abdominal field blocks have been around for a long time and are widely used since they are usually technically unchallenging. The transversus abdominis plane (TAP) block is a form of abdominal field block that reduces pain by numbing the skin, muscles, and parietal peritoneum of the anterior abdominal wall.

TAP block is a efficient and safe complement to multimodal postoperative analgesia for abdominal surgery. Several trials have indicated that it is advanced than standard conventional therapy for postoperative pain control. It was first described a decade ago, but it has underwent numerous modifications since then, demonstrating its potential utility for a wide range of surgical procedures. TAP blocks are still massively underutilised, inspite of having less complications and a huge success rate when utilizing current methods.

HISTORY

Rafi described the transversus abdominis plane block for the first time in 2001. He applied the abdominal field block at the level of the Petit lumbar triangle. Rafi advised identifying

intermuscular plane between internal oblique and transversus abdominis muscles with a blunt needle and a single pop feeling .[32]

In 2006, O'Donnell popularised a term "transversus abdominis plane block" in.literature.[33] He also amended Rafi's original description by suggesting a double pop technique to determine planes between the fascial extensions of external oblique muscle and internal oblique muscle (first pop)[34] and internal oblique and transversus abdominis muscles (second pop).[33]

Triangle of Petit proved to be tricky to recognise in obese patients (because to its greater depth) and older people (because of a loss in muscle mass). Hebbard *et al.* supported the use of ultrasonography guidance to identify various intermuscular planes in 2007.[35]

ANATOMY

The anteriolateral abdominal wall is made up of four muscles: the rectus abdominis, the external oblique, internal oblique, and transversus abdominis. An anatomical plane situated between internal oblique and transversus abdominis muscles is the transversus abdominis plane compartment. Anterior rami of spinal neurons T6 to L1 innervate the anterolateral abdominal wall. The intercostal nerves (T6-T11), the subcostal nerve (T12), and the iliohypogastric and ilioinguinal nerves are among them (L1).

T6-T11 anterior divisions extend from the intercostal gap into the abdominal wall, passing through the internal oblique and transversus abdominis muscles before reaching the rectus abdominis.

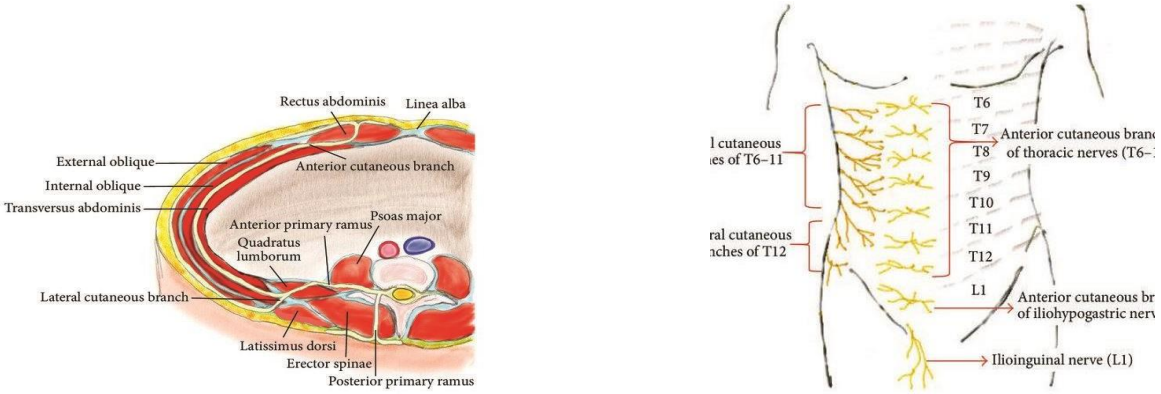
The T6-T11 segments gives off anterior cutaneous branch, which give branches to intercostal nerve ,supplying skin and muscles of anterior abdominal wall. Anterior and posterior

branches of the lateral cutaneous branch (from the T6-T11 segments) supply the external oblique muscle and the latissmus dorsi, respectively. (Fig. 1a)

Anterior branch of T12 interacts with the iliohypogastric nerve and gives a branch to pyramidalis. Its lateral cutaneous branch perforates the internal and external oblique muscles, descends over the iliac crest, and delivers sensation to the front section of the gluteal region.

L1 spinal nerve is divided into iliohypogastric and ilioinguinal nerves. Iliohypogastric nerve (L1) splits into lateral and anterior cutaneous branches around the iliac crest between the internal oblique and transversus abdominis. Skin of gluteal region is supplied by lateral cutaneous branches, while the skin of hypogastric region is supplied by anterior cutaneous branches.

The ilioinguinal nerve (L1) communicates with the iliohypogastric nerve between the internal oblique and transversus abdominis near the anterior part of the iliac crest. It supplies the upper and medial part of the thigh and part of the skin covering the genitalia.



(a) **(b)**

Figure 1 (a)Cross-sectional view of left abdomen showing pathway of thoracolumbar spinal nerves (T12). (b) Segmental division of cutaneous nerve on anterolateral trunk.

TAP BLOCK TECHNIQUES

Landmark-Guided TAP Block.

Lumbar triangle of Petit is point of entry for blind TAP block. It is situated between lower costal border and iliac crest . It is bounded anteriorly by external oblique muscle and posteriorly by latissimus dorsi.(Fig.2)

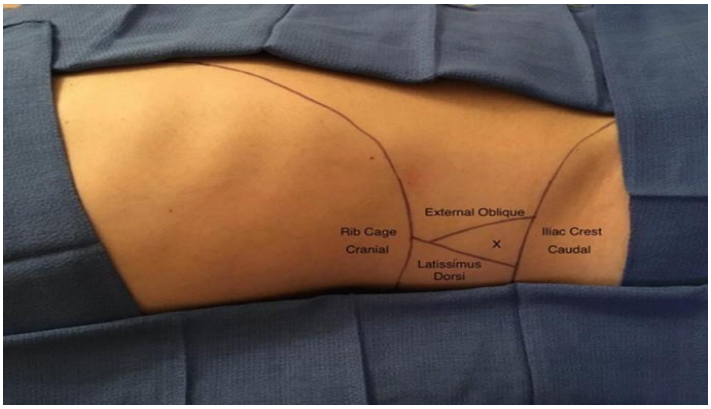


Figure 2: Lumbar triangle of petit

Approach is based on resistance loss as needle is passed through fascia layers of external and internal oblique muscles. Loss of resistance will be more noticeable with a blunt needle.[32] According to McDonnell *et al*., first pop indicates penetration of the fascia of the external oblique muscle, and the second pop indicates piercing of the fascia of the internal oblique muscle as well as entry of needle into TAP.[36,37] Rafi *et al*. proposed that first pop indicates needle has reached the plane between internal oblique and transversus abdominis, while second pop indicates that needle has advanced through transversus abdominis and thus went too far.[32,38] The efficacy of "single-pop",[32] "double-pop",[36] and structures responsible for "pop" are still being debated. Because of the ambiguity of the standard procedure sequence, the small size and wide variation of the Petit lumbar triangle, and the risk of peritoneal perforation during the blind technique, landmark-guided approach is no longer suggested.[38,39]

Ultrasound guided subcostal TAP block

Hebbard *et al*. (2008) described this block typically used for providing analgesia for upper abdominal procedures.[40] The subcostal approach targets transversus abdominis plane in the anterior abdominal wall (below the costal margin) anywhere between xyphoid process and anterosuperior iliac spine (fig. 2).[41] The subcostal method ideally anesthetizes intercostals nerves T6-T10 between the rectus abdominis sheath and the transverses abdominis muscle.

A probe is placed parallel to costal margin near xiphoid process. Transversus abdominis is visualized just below rectus abdominis. Needle is inserted in plane and should be always parallel to subcostal margin. Drug is administered between transversus abdominis and rectus abdominis, medial to linea semilunaris.

Hebbard *et al*. also established that subcostal TAP block is more appropriate for supraumbilical and periumbilical surgeries while lateral TAP block is appropriate for infraumblical surgeries.[42] Lee *et al*. demonstrated that there was a discrepancy in dermatomal spread between subcostal and lateral approaches.[43] A modified subcostal TAP block called oblique subcostal TAP block was first introduced by Hebbard *et al*.[42] The T6-L1 nerves may be covered by oblique subcostal line, which stretches from xiphoid toward anterior portion of iliac crest. By hydrodissecting TAP along oblique subcostal line, local anaesthetic solution covers the region of T6-L1 nerves. . Therefore, local anaesthetic solution in TAP along oblique subcostal line produces analgesia to above and below the umblicus, similar to a dual TAP block.

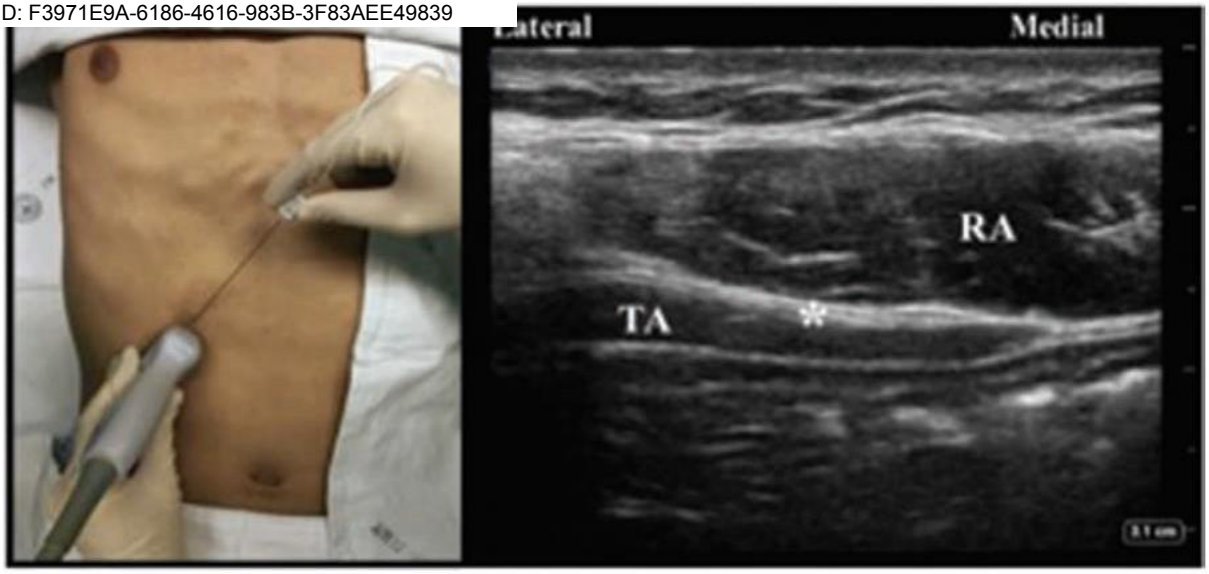


Figure 3: Probe position in USG Subcostal TAP block.

Ultrasound-guided Lateral TAP block

When doing a midaxillary or lateral TAP block, the probe is positioned anterior to the midaxillary line between costal margin and iliac crest. [44,45] Lateral approach focuses on transversus abdominis plane in lateral abdominal wall between midaxillary[35] and anterior axillary[46] lines. Shibata *et al*. recommended that only infra umbilical surgeries might be a signal for lateral TAP block due to restricted quantity of sensory block.[47]

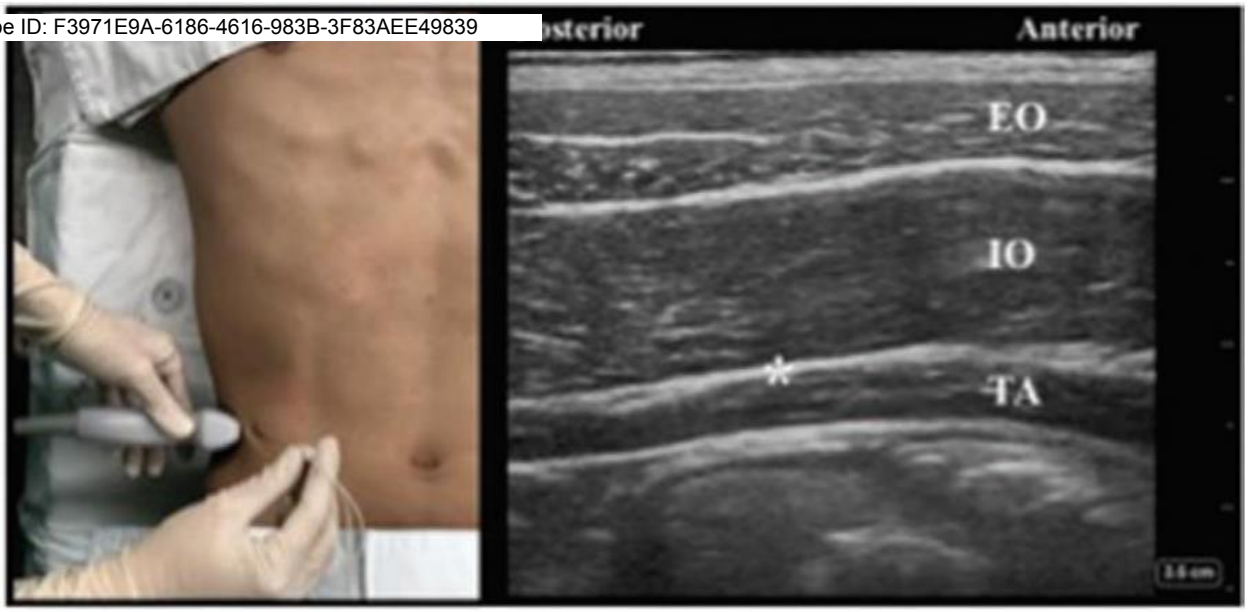


Figure 4: Probe position in USG Lateral TAP block.

Ultrasound-guided Posterior TAP block.

Posterior approach is comparable to lateral approach, but ultrasound probe is moved more posteriorly to midaxillary line. Posterior approach targets transverses abdominis plane at level of lumbar triangle of petit or anterolateral aspect of quadratus .lumborum muscle presumably anaesthetize T9-12 nerves .[48]

Abdallah *et al*.[44] reported that, posterior approach results in diminished pain and breakthrough opioid consumption upto 48hr after infraumbical surgeries. Such advantages vary with lateral approach. According to Abdallah *et al.*,[44] improved pain control observed with posterior TAP blocks is due to paravertebral local anaesthetic spread, resulting in sympathetic block and improved visceral analgesia.

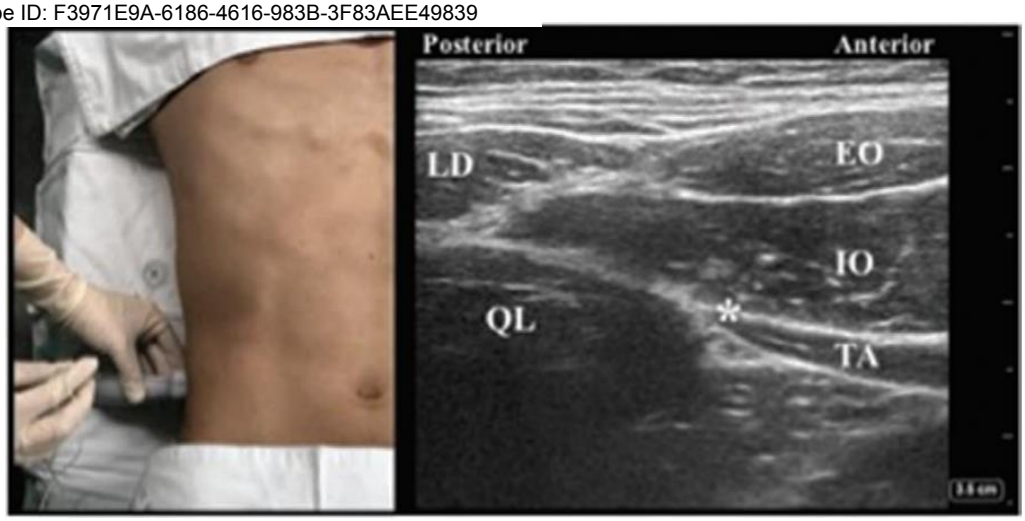


Figure 5 : USG Probe position in Posterior TAP block.

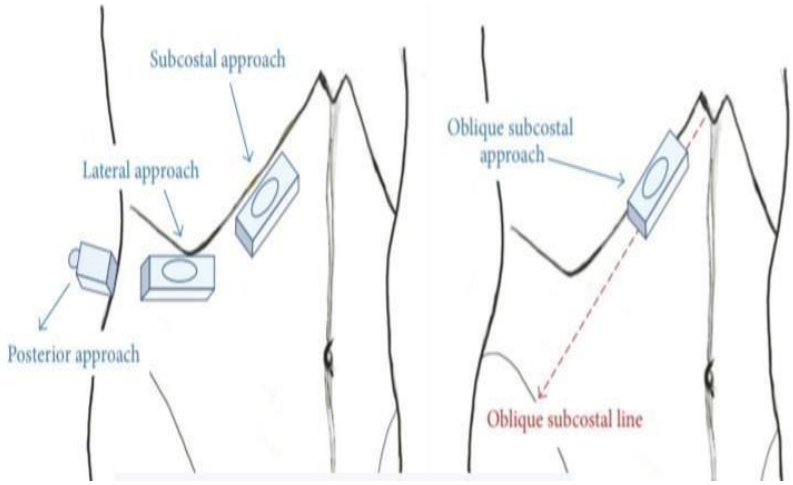


Figure 6: Four approach for ultrasound guided transversus abdominis plane block. Red dashed line represents the oblique subcoastal line , from xiphoid to the anterior part of the iliac crest.

TAP catheters

TAP catheters are placed in tranversus plane to increase duration of analgesia . Intermittently local anaesthetics can be given through these catheters or kept as infusion.[49] Catheter insertion is usually ultrasound guided.

Surgeon-Assisted Approaches:

A escalating number of reports have shown that surgeons can aid in the facilitation of these blocks. Chetwood *et al*. described a laparoscopic-assisted approach during which a classic TAP block was performed while the injection area was noted with an intra-abdominal laparoscopic camera.[50] After local anaesthetic was administered within the TAP, a peritoneal bulge was observed. Such direct visualisation helps in avoiding intraperitoneal injection.

A surgical TAP block using a trans-peritoneal approach was also described recently. A blunt-tipped block needle was advanced from inside the abdominal wall through the parietal peritoneum, the transversus abdominis muscle, and into the TAP as indicated by a single pop sensation.[51] Furthermore, Araco *et al*. described a surgical TAP block that involves blunt dissection through the external and internal oblique muscles, followed by injection of local anaesthetic into the TAP under direct visualisation.[52]

Extent of analgesia

Previously, McDonnell *et al.*[36] (2007) found that local anaesthetic administration into TAP caused a sensory block from T6 to L1. Other studies have published that with posterior TAP block T9-L1 nerves can be blocked. . In case of subcostal approach , from T6 to T10 block is extended. Hebbard *et al*[40]. (2007) compared height of block following classical and subcostal TAP blocks in an audit. Subcostal TAP block is preferable to a posterior TAP block for upper abdominal incisions.

TAP block only provides somatic analgesia. Visceral pain must be managed with conventional analgesics as usual. TAP block is an interesting approach since it reduces opioid requirements (up to 70% reduction in morphine requirement in some studies)[38] and related side effects such as nausea and vomiting, as well as respiratory depression. While the volume, concentration, and method of administration of local anaesthesia vary among studies, these regimen have yet to be compared. As a result, there is lacking evidence to recommend one combination over another.

Indications

Obstertic patients

The typical Pfannenstiel incision is located in a region that is easily anaesthetized by the often used lateral approach, making caesarean delivery the appropriate surgical background to study transversus abdominis plane blocks. Belavy *et al*. (2009)[53] utilised fentanyl with bupivacaine as an adjuvant for sub arachanoid block and discovered that TAP block reduced opioid demand in the

post-operative period, but there was no significant variation in vas scores between TAP and non-TAP groups.

Costello *et al.* (2009)[54] discovered that TAP blocks had no improved analgesic effects in patients administered with intrathecal morphine for caesarean delivery when combined with bupivacaine under spinal anaesthesia. In the United Kingdom, intrathecal diamorphine is frequently given in conjunction with bupivacaine in patients undergoing caesarean section . Post operatively, in most of cases, dimorphine provides tremendous analgesia up to 18-24 hours. As a result, there is no benefit in performing TAP block in patients undergoing caesarean section under sub arachnoid block who have already received intrathecal diamorphine. The potential of local anaesthesia toxicity must be considered if TAP block has been used as an adjunct method in patients who have previously had epidural or spinal anaesthesia.

In conclusion, De Q. Tran (2019) do not recommend lateral or posterior TAP block for caesarean delivery when intrathecal opioids were included in multimodal analgesic regimen. However , both approaches remains a important analgesic alternatives in patients who are undergoing ceasarean section under general anaesthesia or who are unable to get intrathecal morphine.[55,56]

Lower abdominal surgeries

After appendicectomy and inguinal herniorrhaphy, unilateral posterior TAP blocks give effective pain relief and reduce the requirement for opioids .[57] TAP block, local infiltration, and ilio-inguinal block are being studied against normal saline controls in patients scheduled for inguinal herniorrhaphy in a randomised controlled research in Copenhagen. The study's findings should help us to select best analgesic approach for treating post surgical pain in herniorrhaphy patients.

Bilateral posterior TAP blocks provide effective post-recovery analgesia after abdominal hysterectomy, open retropubic prostatectomy, and caesarean delivery.[58] Carney *et al*. (2008)[59] conducted a prospective, randomised study to assess the analgesic effectiveness of TAP blocks administered under local anaesthesia vs TAP blocks under saline in patients following total abdominal hysterectomy. They came to the conclusion that local anaesthetic TAP blocks can cut down on the need for opioids for up to 48 hours following surgery. It is beneficial in reducing pain following anterior iliac crest bone graft in major orthopaedic surgery.[60]

Laproscopic surgeries

A prospective randomised controlled trial[23] comparing TAP blocks to conventional analgesia in patients having laparoscopic cholecystectomy discovered that TAP blocks are an effective analgesics and reduces need for both intraoperative and postoperative opioids. A case series was used to support the findings of Mukthar *et al.* (2009) about the reduced analgesic requirements of kidney transplant recipients.[61]

Presently, posterior TAP blocks are used for laparoscopic procedures like cholecystectomy, appendicectomy, and herniorrhaphy and have proven to be helpful. If the surgeon performs cholecystectomy using a supraumbilical port, a sub-costal TAP block should be admistered.

Paediatric and neonatal surgery

Two distinct case study on TAP blocks in neonates and children were published by Fredrickson *et al.*[62] These two articles make a compelling case for the viability of ultrasound-guided TAP blocks in newborns and children. TAP blocks has been effectively used by the authors

in neonates having difficult major surgeries such exomphalos major repair. This first result is expected to prompt additional studies contrasting TAP blocks with conventional analgesic methods in neonates.

TAP block in ICU

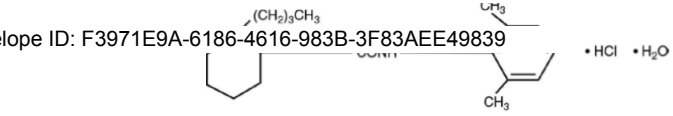
Niraj *et al*.[49] (2009) effectively delivered sub-costal TAP blocks in intensive care unit to provide analgesia. It also helped in providing chest physiotherapy in patients after abdominal surgeries.

Other indications

The use of continuous TAP blocks in nephrectomy , renal transplant and prostatectomy can be utilised to relieve pain.[50] It can be used for analgesia in thoraco-abdominal injuries acquired on the battlefield which has been described in recent papers. The bleak battlefield hospital was equipped with portable ultrasound machines.[63]

PHARMACOLOGY OF BUPIVACAINE

AF Ekenstam produced bupivacaine in Sweden in 1957. 1-Butyl-2'-6'-pipecoloxylidide monohydro-chloride mono-hydrate is a white crystalline powder , easily soluble in 95% ethanol, soluble in water, and partially dissolves in chloroform or acetone. It has following structural formula



Epinephrine is (-)-3,4-Dihydroxy-α-[(methylamino)methyl] ben
formula:

Figure 7: Structural formula of Bupivacaine.

Its chloride salt has a molecular weight of 325. The melting point is 258^0C. Chemically and pharmacologically, Bupivacaine hydrochloride is related to aminoacyl local anaesthetics. It is a Mepivacaine homologue and chemically related to Lidocaine. These three anaesthetics all have an amide connection between the aromatic nucleus and an amino or piperidine group. In this regard, they differ from procaine-type local anaesthetics, which has ester linkage.

Bupivacaine spinal comes in form of a sterile, hyperbaric solution for subarachnoid injection (spinal block). Each 1ml of bupivacaine spinal comprises 5 mg of anhydrous bupivacaine hydrochloride and 80 mg of anhydrous dextrose. There are no preservatives in bupivacaine spinal.

Mechanism of action

Bupivacaine, like all local anaesthetics, produces reversible nerve conduction blockage by lowering sodium permeability in neuron membranes. Local anaesthetic binding to voltage gated Na+ channel sites limits channel opening by inhibiting conformational changes. This reduces the rate of membrane depolarization, raising the threshold for electrical excitability. All nerves are affected in the following order: autonomic, sensory, and motor, with effects fading in reverse order. Clinically, nerve function loss includes pain, temperature, touch, proprioception, and skeletal muscle tone.

Effective anaesthesia requires direct nerve membrane penetration. During the onset and recovery of local anaesthesia, impulse blocking is incomplete, and partially blocked fibres are

further suppressed by repetitive stimulation, resulting in additional usage dependent binding to sodium channels.

Pharmokinetics

Bupivacaine is a weak base, with less than 50% of the medication existing in a lipid soluble non-ionized form at physiological pH. Absorption is affected by the dose, concentration, place of administration, and tissue vascularity.

The rate of tissue absorption, distribution, and elimination of the drug define the final plasma concentration of local anaesthetic. Distribution of a medicine in tissue is determined by the tissue blood flow and the drug's lipid solubility. Patient associated parameters such as age, cardiovascular health, and hepatic functions all have an impact on absorption and the resulting plasma levels. Bupivacaine can be extracted from circulation through the lungs. This reduces concentration of medication that reaches systemic circulation.

Propranolol can prevent this first pass pulmonary extraction, which is dose dependant. Propranolol lowers drug plasma clearance likely by reducing hepatic blood flow and competitive blocking at the receptor site. Peak blood levels are reached 30-40 minutes after injection for peripheral nerve blocks. Bupivacaine is a rapid acting (1-10 minutes) and lasts substantially longer than that of other local anaesthetics (3-9 hours). Bupivacaine is dispersed throughout the body, with the highest concentrations found in well-perfused organs such as the liver, lung, heart, and brain.

Metabolism

Local amide anaesthetics are metabolised at various rates in liver by microsomal enzymes. Intial step is to convert amide base to amino carboxylic and cyclic derivatives. Additional processes, such as dealkylation and hydroxylation, are required for full metabolism. Aromatic hydroxylation, N-dealkylation, amide hydrolysis, and conjugation are all possible mechanisms for bupivacaine metabolism. After epidural or spinal anaesthesia, only the N-dealkylated metabolite N-

desbutylbupivacaine has been calculated in urine or blood . Bupivacaine and its metabolite excretion in the urine accounts for more than 40% of the total anaesthetic dosage. The most important protein binding site for bupivacaine is alpha 1 glycoprotein I, and its concentration is elevated in various clinical conditions, including post-operative trauma.

Side effects

The most frequent side effects associated with the use of local anaesthetics include allergic reactions and systemic toxicity caused by high plasma and concentrations of drug in tissue , with most common cause being unintentional intravascular injection of the drug. Allergic responses are extremely uncommon and may be caused by the preservative methyl paraben. The presence of a rash, urticaria, and laryngeal oedema, with or without hypotension and bronchospasm, indicates an allergic reaction.

CNS Toxicity

Numbness of the tongue and circumoral tissues occurs at low bupivacaine concentrations. Vertigo, tinnitus, restlessness, and difficulty focusing are among symptoms of increasing plasma concentration. At 1 mcg/ml, an increase in concentration causes slurred speech and skeletal muscular twitching, followed by seizures (tonic clonic). Seizures are typically followed by central nervous system depression, hypotension, and apnea. The following is the rationale for the local anaesthetic seizures:

a) The medication selectively inhibits inhibitory cortical neurons.

b) Blocking the release of neurotransmitters such as gamma aminobutyric acid (GABA)

This is because of increased cerebral blood flow and drug delivery to the brain. A fall in arterial pH lowers the seizure threshold, most likely due to ion trapping and subsequent drug reduction in the brain. Mechanical ventilation and benzodiazepines are used to treat seizures.

CVS Toxicity

Because of the relaxation of arteriolar vascular smooth muscle and direct cardiac depression, local anaesthetics can cause significant hypotension. Hypotension is attributed to a reduction in both cardiac output and systemic vascular resistance. Part of cardiac toxicity caused by high plasma concentrations of local anaesthetics is generated by these medicines' ability to block cardiac sodium channels. Bupivacaine has a cardiotoxic plasma concentration of 8-10 mcg/ml. When plasma levels are high, enough cardiac sodium channels are blocked to impair conduction and automacity, resulting in a prolonged P-R interval and QRS complex on the ECG. Calcium and potassium ion channel effects, as well as local anaesthetic-induced suppression of cyclic adenosine monophosphate (cAMP) generation, may all contribute to cardiac toxicity. The protein binding sites for bupivacaine are soon saturated after inadvertent IV delivery, leaving a large amount of unbound drug available for diffusion into conducting tissues of the heart. Pregnancy may increase sensitivity to bupivacaine's cardiotoxic effects. In individuals receiving medicines that limit myocardial impulse propagation, the threshold of cardiac toxicity caused by bupivacaine may be reduced (beta blocker, digitalis and calcium channel blocker). At plasma concentrations of bupivacaine of 2-3 mcg/ml in the presence of propranolol, cardiac dysarrythmias occurred. Epinephrine and phenylephrine raise the concentration of bupivacaine by 2-3 mcg/ml. Bupivacaine-induced toxicity is increased by epinephrine and phenylephrine. Bupivacaine's sluggish dissociation from sodium

channel receptor sites accounts for the drug's sustained depressive effect on cardiac action potential and consequent toxicity. Bupivacaine's R enantiomer is more poisonous than its S counterpart. Tachycardia can improve bupivacaine's frequency-dependent blockage of cardiac sodium channels. Cardiovascular collapse caused by bupivacaine is difficult to resuscitate.

Indications

1. Infiltration anaesthesia

2. Intravenous regional anaesthesia

3. Peripheral nerve blockade

4. Central neuraxial blockade

Dosages

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

Figure 8 : 0.5% Anawin vial

PHARMACOLOGY OF MAGNESIUM SULPHATE

INTRODUCTION

Magnesium sulphate is the fourth most prevalent cation in the body and activates roughly 300 enzyme systems, many of which are involved in energy metabolism.[64] The ECF compartment has only 1-2% of total body magnesium reserves; bone contains 67%, while the remaining 31% is intracellular. Magnesium is a significant regulator for calcium entry into cell and calcium action within cell. Magnesium is important in controlling most of cellular functions . It can be thought of a natural physiologic calcium antagonist.[64] It is required for the manufacture and operation of ATP. Other processes that require magnesium include DNA, RNA, and protein synthesis.

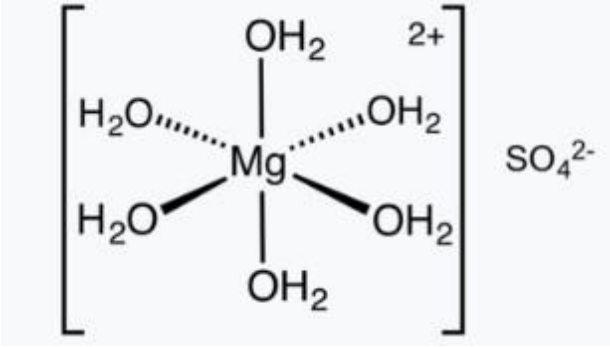


Figure 9 : Structure formula of Magnesium Sulphate.

MECHANSM OF ACTION

ACTION ON NMDA RECEPTORS

By inhibiting NMDA receptors in a voltage-dependent way, magnesium can stop peripheral nociceptive inputs from causing central sensitization at the spinal action site.[65,66,67] Through the same method, adding tiny amounts of magnesium sulphate to local anaesthetics for spinal anaesthesia increases duration of anaesthesia, decreased need for postoperative pain medication, and narrowed the negative consequences of using large doses of local anaesthetics and opioids.[68,69]

Anticonvulsant Activity of Magnesium Sulfate

Glutamate and other excitotoxic neurotransmitters are released in excess during seizures. The N-methyl-D-aspartate (NMDA) receptor might be activated by excessive glutamate, which causes huge depolarization of neuronal networks and bursts of action potentials. Magnesium may work to minimize the impact of glutamate and raises seizure threshold by blocking NMDA receptors.[70]

Vascular Effects

Magnesium has little effect on the cerebral arteries but has a powerful vasodilator action on uterine, mesenteric, and aortic arteries. Magnesium and calcium compete for binding sites in vascular smooth muscle, specifically for voltage operated calcium channels (VOCC).[64] Intracellular calcium is lowered via decreased calcium channel activity, resulting in vasodilation and relaxation. Magnesium helps in boosting Prostacyclin (also called prostaglandin I2 or PGI2) production in endothelium (via unidentified processes), which infact lowers platelet aggregation. It causes vasodilatation by NO production.

Effects on Cerebral Edema and the Blood-brain Barrier

Cerebral endothelium may be impacted by calcium - antagonistic effects of magnesium. Reduced cell calcium prevents opening of tight junctions . Reduced tight junction permeability restricts the movement of ions, proteins, and vascular contents outside of cells, which can lead to vasogenic edema and seizures. Magnesium sulphate may also reduce pinocytosis and reduces transcellular transport.

A water channel protein called aquaporin 4 (AQP4), which is found in astrocytic end feet and probably in the cerebral endothelium and has been linked to development of cerebral edema, may similarly be downregulated by magnesium (through unknown mechanisms).[64]

Pharmacokinetics:

Adults typically consume 20–30 mEq/d (240–370 mg/d) of magnesium. Kidneys are the primary route of elimination, with an average daily output of 6–12 mEq. In contrast to thick ascending limb of Henle loop, where 50–60% magnesium is reabsorbed, only 25% is reabsorbed in the proximal tubule. The distal small bowel absorbs most of the remaining 30–40%.

Effects on different systems of the body

CNS & PNS

Central nervous system depression is caused by magnesium. It was successfully utilised as a general anaesthetic in the early 1900s. However, magnesium has a weak ability to cross the blood-brain barrier, and an active transport system effectively regulates its concentration in the cerebrospinal fluid.[64] Magnesium inhibits neurotransmitter release at all synaptic connections in the peripheral nervous system and amplifies the effects of local anaesthetics.[64] Magnesium concentrations of 5 mmol/L significantly disrupt presynaptic neuromuscular transmission at the neuromuscular junction and improve the effects of nondepolarizing muscle relaxants. MgSO4 seems to have rather minor clinical effects on depolarizing muscle relaxants. MgSO4 does not affect onset or duration of succinylcholine-induced neuromuscular block, although it may appears to stop related muscle fasciculations and may reduce any potential serum potassium increases caused by succinylcholine.[71]

Cardiovascular system

Magnesium causes vasodilatation in the cardiovascular system by direct action on blood vessels. By inhibiting the release of catecholamines and blocking the sympathetic nervous system, it also lowers peripheral vascular tone.[64] Increased extracellular magnesium ion concentrations significantly reduce contractile force in isolated heart.

Respiratory system

No effect on central respiratory drive. The respiratory depressant effect is caused by neuromuscular blockade which it produces. Acts as a effective bronchodilator on bronchial smooth muscles .

Kidney

Magnesium is a renal vasodilator and a diuretic.

Role in Obstetrics

Magnesium is a powerful tocolytic and used in preterm labor. Magnesium also is used in obstetrics to prevent patients with preeclampsia from developing seizures.

HYPOMAGNESEMIA

SIGNS & SYMPTOMS:

Although the majority of individuals show no symptoms, some may exhibit anorexia, weakness, fasciculation, paresthesias, disorientation, ataxia, and seizures. Electrical irritability, a higher prevalence of atrial fibrillation, and a lengthening of the P-R and QT intervals are cardiac symptoms.

A patient with hypomagnesemia may experience intra-operative problems such as perioperative arrhythmias, reduced respiratory muscle power, hyperreflexia (such as the Chvostek sign), and agitation of the central nervous system with seizures .

CAUSES:

- **Primary nutritional disturbances**: Inadequate intake, total parenteral nutrition, re-feeding syndrome
- **Gastrointestinal disorders:** Specific absorptive defects, malabsorption syndromes, prolonged diarrhea, prolonged nasogastric suction, pancreatitis
- **Endocrine disorders:** Hyperparathyroidism, hypoparathyroidism, hyperthyroidism, primary hyperaldosteronism, Bartter's syndrome, diabetic or alcoholic ketoacidosis, administration of epinephrine, SIADH, hungry bone syndrome after parathyroidectomy .
- **Chronic alcoholism, alcoholic withdrawal, increased renal excretion :** Alcohol consumption; idiopathic; following renal transplantation; medications (Cisplatin, Aminoglycoside, Amphotericin B, diuretics, Pentamidine, Theophylline); acute tubular necrosis recovery phase.

TREATMENT:

Asymptomatic hypomagnesium can be treated orally or intramuscularly . Serious manifestations such as seizure shoud be treated with magnesium sulfate 1 to 2 g (8 to 16 mEq) over 15 minutes followed by 1g/hr until serial serum magnesium levels indicate the deficiency has been corrected.

HYPERMAGNESEMIA

SIGNS & SYMPTOMS: Symptoms and electrocardiographic changes of hypermagnesemia correspond to serum levels,

5 to 10 mEq/dL: Nausea ,vomiting, hyporeflexia **,** Depressed cardiac conduction, widened QRS complexes, prolonged P–R and QRS intervals

10- 15 mEq/dL: Hypoventilation, decreased deep tendon reflexes, and muscle weakness

15-20 mEq/dL: Hypotension, complete heart block , paralysis, asystole and death

CAUSES: Increases in plasma are almost always brought on by overconsumption (antacids or laxatives containing magnesium), renal impairment (GFR 30 mL/min), or both. Adrenal insufficiency, hypothyroidism, rhabdomyolysis, and lithium use are less frequent causes. Both the mother and the foetus may develop hypermagnesemia as a result of magnesium sulphate therapy for preeclampsia and eclampsia.

TREATMENT:

All that is required to treat mild hypermagnesemia is to stop the source of the condition. In patients with good renal function, a loop diuretic combined with intravenous fluid replacement increases urine magnesium excretion. Dialysis is a part of definitive treatment. With calcium therapy, the effects of magnesium can be momentarily reversed. Depolarizing and nondepolarizing muscle relaxants must be properly titrated in conjunction with an accurate assessment of neuromuscular blockade since hypermagnesemia enhances their effects.[64] It may be necessary to provide ventilatory, circulatory, or both in cases of extreme magnesium poisoning.

USES:

- Magnesium sulphate is frequently taken orally as an osmotic purgative.
- Hypomagnesemia treatment.
- It is a antiarrhythmic agent for torsades de pointes .
- Magnesium sulphate can be nebulized , in cases of severe asthma exacerbations.[72] For the treatment of severe asthma attacks, it is typically given intravenously.
- Pre-eclampsia progression risk can be reduced with magnesium sulphate. Magnesium sulphate I.V. is used to both prevent and treat eclampsia-related seizures.[73] The blood perfusion to the foetus is not impaired since it lowers the systolic blood pressure but does not affect the diastolic blood pressure. It is also frequently used to treat eclampsia, where it performs better than diazepam or phenytoin.[74,75]

Figure 10: Magnesium sulphate 50% w/v ampule.

Review of clinical study

The addition of nerve blockades as a multimodal analgesia can improve analgesic effects, reduce intraoperative opioid consumption, reduce postoperative VAS scores and fastens patient recovery. Several adjuvants (e.g., dexamethasone, , magnesium sulphate, , α-2 agonists , liposomal formulation ,opioids) has been studied for enhancing the analgesic duration of TAP block. Magnesium, in particular, is known to be an effective analgesic for both acute (e.g., postoperative) and chronic (e.g., neuropathic) pain in humans. It works primarily by blocking N-methyl-D-aspartate receptor ion channels and activating nitric oxide pathway, resulting in antinociceptive and analgesic effects.[76,77] A growing number of randomised controlled trials have been published recently testing the use of magnesium as an anaesthetic adjuvant in peripheral nerve blocks and truncal blocks.

In a study by Ae Ryoung Lee *et al*. (2012) researchers evaluated the effects of adding magnesium sulfate to 0.5% bupivacaine for interscalene nerve block in 66 patients posted for arthroscopic rotator cuff repair. Interscalene nerve block in one group was given with bupivacaine with 10% magnesium sulphate (2 ml) whereas in other group bupivacine alone was given. Magnesium sulphate group has longer duration of analgesia compared to bupivacaine group (665 ±187 min vs 551±156) min, respectively; p = 0.001) Magnesium sulphate group had notably lower VAS scores at 12 hr , but usage of fentanyl were same in both groups. Addition of magnesium sulphate to a bupivacaine for interscalene nerve block increases duration of analgesia and lowers VAS scores. [78]

In 2016 K AL-Refaey *et al*. studied effect of adding magnesium sulfate to bupivacaine in ultrasound guided TAP block in laparoscopic cholecystectomy patients. The study included 90 patients and were allocated into three equal groups: bupivacaine , magnesium and control

group. M group showed lower VAS (2.28 ± 0.51 for B group , 2.24 ± 0.51 for M group , 2.81 ± 0.61 for C group, $p < 0.001$), longer duration of analgesia (19 ± 2.2 h for M group, 16 ± 2.5 h for B group, 7 ± 2.8 h for C group, $p < 0.005$), lower morphine consumption (0.5 ± 0.1 mg for M group, 0.9 ± 0.1 mg for B group, 2 ± 0.1 mg for C group $p< 0.011$). Postoperative nausea and vomiting (PONV) was significantly less in group M . In laparoscopic cholecystectomy patients, adding magnesium sulphate as an adjuvant to bupivacaine in the TAP block enhanced postoperative analgesia in the form of longer duration, reduced analgesic needs, and PONV.[29]

Another study by Rana *et al*. (2016) evaluated magnesium sulfate's effectiveness as an adjuvant to 0.25% bupivacaine in T.A.P. block in patients undergoing total abdominal hysterectomy (TAH). Sixty-five women posted for TAH were included in study. Patients in Group B (n = 32) received bupivacaine (45 mg) alone , whereas those in Group BM (n = 33) receive bupivacaine (45 mg) with 1.5 mL (150 mg) MgSO4 and 0.5 mL NS in the ultrasound (USG)-guided on each side . After the completion of the surgery TAP block was given. They were evaluated for VAS at 0, 2, 4, 6, 12 and 24 hrs . Visual analogue scores were lower in Group BM at 4hr , 6hr and 12 hr ($p < 0.05$). Up to 12 hrs, mean duration of analgesia and time to first rescue analgesia was prolonged in group BM. Addition of MgSO4 to bupivacaine in ultrasound guided TAP block reduces VAS scores postoperatively , prolonged analgesia duration and decreased need for rescue analgesics. [20]

In a similar study by Abd-Elsalam *et al*. (2017) evaluated the efficacy of magnesium as an adjuvant to bupivacaine in TAP block for 60 women scheduled for total abdominal hysterectomy(TAH) . Group I received a TAP block with bupivacaine 0.25% plus 2 mL magnesium sulphate 10% (200 mg). Group II received a TAP block with bupivacaine 0.25% alone. Visual analogue scores , total morphine consumption, time to first analgesic request and any side effects were recorded.Up to 10 hours after surgery, the mean postoperative VAS score in group I was considerably lower than in group II. The mean time to rescue analgesia in group I (15.67 hrs.)

was substantially longer than in group II (7.33 hrs.) (P 0.001). Over the first 24 hours postoperatively, the mean total morphine intake was considerably lower in group I (7.64 ± 2.94 mg) than in group II (16.22 ± 3.21 mg) (P 0.001). In patients undergoing abdominal hysterectomy, the addition of 200 mg of magnesium sulphate to bupivacaine in an ultrasound-guided TAP block considerably reduced postoperative opioid needs, increased the duration of analgesia, and reduced the VAS score, all without severe side effects.[30]

In 2018 , Ammar AS *et al.* investigated the effect of adding adenosine to bupivacaine in transversus abdominis plane (TAP) block. Participants were allocated to TAP block using either 0.375% 20 mL of bupivacaine + 12 mg adenosine (adenosine group), 0.375% 20 mL of bupivacaine + 500 mg magnesium sulphate (magnesium group) or 0.375% 20 mL of bupivacaine alone (control group). At 6 and 12 hours postoperatively, VAS in adenosine and magnesium sulphate groups was lower than in control group. Duration of analgesia was relatively enhanced in the magnesium group when compared to adenosine group and control group. (402 vs. 446 vs. 320 mins respectively; p=0.003). Magnesium improved the quality and duration of TAP block even more compared to Adenosine.[31] Adenosine has a significant impact on both the central and peripheral mediation of pain.[79] Adenosine A1 receptors have been shown to have antinociceptive effects in the spine, but adenosine A2A and A3 receptors have been linked to peripheral pain mediation.[79,80,81]

Farnad Imani *et al.*(2018) aimed at investigating the effects of adding magnesium sulfate to ropivacaine in the transverse abdominis plane block in 60 patients after total abdominal hysterectomy. Ropivacaine group received 19 ml of 0.2% ropivacaine whereas Ropivacaine – Magnesium sulphate group received 19 ml of 0.2% ropivacaine plus 1 ml of 50% magnesium sulfate on each side. In group R and RM , mean VAS scores of patients at first hour after surgery were 5.72 ± 0.91 and 5.9 ± 1.12, respectively. At the second hour after surgery , scores reached 2.9 ± 0.5(group R) and 2.7 ± 0.4 (group RM) . Within the next 24 hours, VAS were 3.1 ±

0.7(group R) and 2.8 + 0.7(group RM). Upto 6 hrs after the block , rescue analgesic consumption was less in group RM compared to group R . The study concluded that on addition of magnesium sulfate to ropivacaine in TAP block minimized post hysterectomy pain.[82]

Gad M *et al.* (2019) conducted study on 60 patients posted for TAH . In group M , 200 mg of magnesium sulphate was added to bupivacaine , whereas in group D 8 mg of dexamethasone was added to bupivacaine. At 8 and 12 hr, VAS scores were elevated in group D compared to group M. In group M , prolonged duration of analgesia , lower opioid requirement and more patient satisfaction was seen . Therefore, on adding Magnesium sulfate in TAP block provided good analgesia compared with dexamethasone.[83]

Mayuresh Umalkar *et al.* (2020) conducted TAP block in sixty patients posted for elective cesarean section using 75 mg of magnesium sulphate as an adjuvant to bupivacaine. Results showed that duration of analgesia in Group B (12.03 hr ±1.24 hr) and Group BM (12.30 hr ±0.83 hr) were comparable (P = 0.3348). The mean VAS scores was also not significant at different time points between the two groups (P > 0.05). The study concluded that on adding 75mg of magnesium sulphate to bupivacaine is inadequate in providing longer duration of TAP block .[84]

In 2020 A M Kamaly *et al* aimed to compare the effectiveness of a transversus abdominis plane (TAP) block guided by ultrasonography with magnesium sulphate added to bupivacaine versus bupivacaine added to morphine. The study had 45 patients who were scheduled for inguinal herniorraphy and was separated into three groups. The study concluded that magnesium added to bupivacaine was better in providing better postoperative analgesia and low visual analogue scores. [85]

In 2021, Ezzat M Siam *et al*, studied the efficacy of $MgSO_4$ as an adjuvant to bupivacaine in TAP block in 50 adult patients posted for unilateral inguinal hernia repair . The dosage of $MgSO_4$ used in this TAP block was 200 mg. $MgSO_4$ group demonstrated a prolonged postoperative analgesia (p=0.001), lower postoperative VAS during rest and movement , longer period before rescue analgesia, a substantially lower opioid dose, and higher patient satisfaction. Adding $MgSO_4$ (150 mg) to bupivacaine in USG TAP block enhances analgesia duration, minimizes postoperative VAS scores and need for rescue analgesics.[86]

Nikita Gurung *et al* (2021), conducted a randomized double blind study, in a sixty-six patients scheduled for TAH under general anaesthesia. They were divided into two groups. Before extubation, both groups underwent a bilateral transversus abdominis plane block guided by ultrasound. Bupivacaine with Magnesium group received block with 20ml of 0.25% bupivacaine and 150mg of magnesium sulphate on each side, whereas Bupivacaine alone group received block with 20ml of 0.25% bupivacaine alone. Following surgery, pain scores at 0, 2, 4, 6, 12 and 24 hours were recorded, along with the first analgesic request time, the total amount of fentanyl consumed, and the frequency of nausea and vomiting. At 4 and 6 hours, the pain scores for the group BM were considerably lower (p=0.001 and 0.017, respectively). The time it took for a patient to request their first dose of analgesia was considerably longer in Group BM (285 minutes vs. 75 minutes, (p=0.001)]. Total postoperative fentanyl use was considerably lower in Group BM (230±59.06 mcg vs. 289.85±69.13 mcg, p=0.001). In comparison to bupivacaine alone, bupivacaine with magnesium sulphate results in lower post-operative pain scores, longer analgesic durations, and less postoperative fentanyl requirement in TAH patients. However, there is no difference in the incidence of nausea or vomiting.[87]

In 2022 Lipon Kanti Bhowmick *et al.,* conducted a randomized double blind study, in 60 patients posted for elective cesarean section. Study assessed the efficacy of Magnesium sulphate as an adjuvant to bupivacaine in USG TAP block for postoperative analgesia . VAS scores were noted before and immediately following the block. The mean duration of analgesia in Magnesium sulphate group was significantly longer than in another group. The study concluded that Magnesium Sulphate in conjunction with bupivacaine in USG transversus abdominis plane (TAP) blocks helps to manage post-operative pain in cesarean section patients.[88]

MATERIALS AND METHOD

SOURCE OF DATA:

This study was conducted in the Department of Anaesthesiology, Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijayapur. After obtaining approval of the Institutional Ethical Committee and written informed patient consent 70 adult patients of ASA I and II scheduled to undergo total abdominal hysterectomy under spinal anaesthesia were taken in the study and administered TAP block.

METHOD OF COLLECTION OF DATA:

Study Design: Randomized Prospective Comparative study.

Study Period: One and a half years from January 2021 to April 2022.

Sample Size: 70 female patients were randomly divided into two groups of 35 each. (by computer generated random numbers).

STATISTICAL DATA

Sample size calculation

The anticipated Mean ± S.D. of VAS score at 6th hour in group BM 2.4±1.33 and in group B 4.53± 2.62 . The required minimum sample size is 35 per group (i.e., a total sample size of 70, assuming equal group sizes) to achieve a power of 90% and a level of significance of 5%.

Formula used

$$n = \frac{(z\alpha + z\beta)^2 X\ 2\ X\ SD^2}{Md^2}$$

Z = Z statistics at a level of significance.

Md = anticipated mean difference.

S.D. = anticipated standard deviance

Statistical tests used

Independent t-test

Mann Whitney U test

Chi - square test

INCLUSION CRITERIA

- Female Patients aged between 35-60 years.
- Patients with ASA Grade I & II.
- Patients are scheduled for total abdominal hysterectomy under subarachnoid block.

EXCLUSION CRITERIA

- Patient refusal.
- Patient having bleeding disorders.
- Patient having a local infection at the site of the block.
- Patients on calcium channel blockers
- Patients with H/o Cardio-Respiratory disorders
- Patients with H/o convulsions & neurological deficits.

METHODOLOGY :

After a thorough preanesthetic check-up, patients satisfying the inclusion criteria were selected. The study protocol and procedure was explained to the patients. At the pre-operative visit , the VAS scale scoring system was explained to all patients. Written informed consent was obtained from all patients participated in the study. The patients were randomly allocated into two equal groups. A random number table created by a computer was used for randomization.

Group B - TAP block by18mL bupivacaine 0.25% (45 mg) with 2 mL normal saline

Group BM - TAP block by 18 mL bupivacaine 0.25% (45 mg) with MgSO4 50% w/v of 0.3 mL (150 mg) and 0.5 mL NS.

The study was double-blinded, where the anaesthetist who performs the technique was blinded to the drug solution. The preparation of drug solution was done by the anaesthetist who was not involved in the study . All the patients were kept nil orally for 6 hr before surgery . In the operation theatre 18-gauge intravenous (IV) cannula was secured and ringer lactate solution was infused 15 ml/kg body weight . Once the patient shifted to the operation theatre, standard monitoring devices were attached like pulse oximeter, sphygmomanometer cuff and E.C.G. leads and baseline readings were noted. A premedication of 1 mg Midazolam and 100mg of Rantidine was administered intravenously.

Under all aseptic conditions, patients undergoing T.A.H. were given spinal anaesthesia in left lateral position using a 25-gauge Quincke spinal needle at L3–L4 interspace. After confirming the free flow of CSF, 15 mg of 0.5% hyperbaric bupivacaine was injected. After confirmation of adequate level (T4), surgery was started. Once the surgery is over and the S.A.B. sensory level

regressed to T8 dermatome, under all aseptic precautions, a ultrasound guided T.A.P. block was performed. After draping the abdominal part between twelth rib and anterior superior iliac crest with umbilicus at the center- external oblique muscle, internal oblique muscle, transversus abdominis muscle, and their fascia were identified using a linear high-frequency probe (6–13 MHz) beneath the skin and the subcutaneous tissue. By in-plane technique , a 23-gauge spinal needle was advanced at the anterior axillary line and the exact location of the needle tip between internal oblique and transverse abdominis muscle was visualized . A 2 mL of normal saline was injected to open the plane. After confirmation of the hypoechoic area on the U.S.G. image, the study solution of 20 mL was injected. An equal amount of the same solution was also injected on the opposite side using identical techniques . The patients in Group A (n = 35) received 18 mL of 0.25% bupivacaine (45 mg) with 2 mL of NS , whereas the ones in Group B (n = 35) received 18 mL of 0.25% bupivacaine (45 mg) with 0.3 mL (150 mg) of MgSO4 50% w/v and 0.5 mL of NS. Postoperatively, the patients were assessed for pain, heart rate, blood pressure and any side effects like nausea , vomiting , haematoma in the post anaesthesia care unit at time 0 (time of completion of T.A.P. block),1, 2, 4, 6, 12 and 24 hr by an investigator blinded to the group assignment.

Post operatively, both the groups of patients received injection Paracetamol (1gm) intravenously every 8hrly as a part of multimodal analgesia. Whenever the VAS ≥4 or else on patient demand, injection Diclofenac 75mg IM was given as rescue analgesia. If pain persisted, Tramadol 2 mg/kg IV was administered .Visual analogue scale (VAS) consists of a 10cm line, marked at 1cm each on which the patient makes a mark on the line that illustrates the intensity of pain she is experiencing. Mark ‘0’ means no pain and mark ‘10’ means the worst possible pain. The numbers denoted by the patient was taken as units of pain intensity.

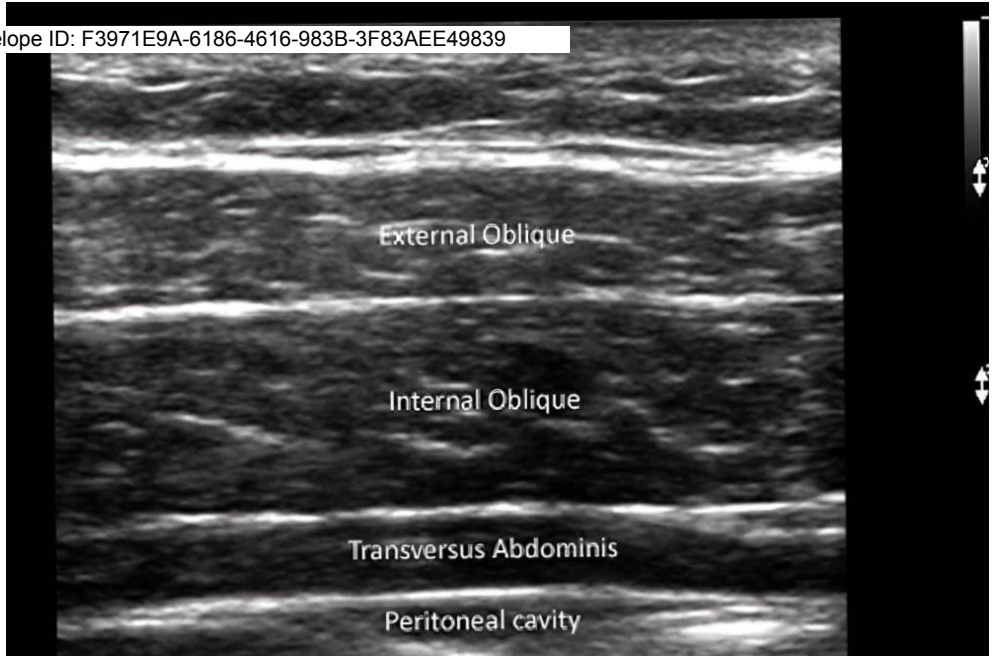


Figure 11: Sonoanatomical depiction of muscle layers and neuro-fascial plane.

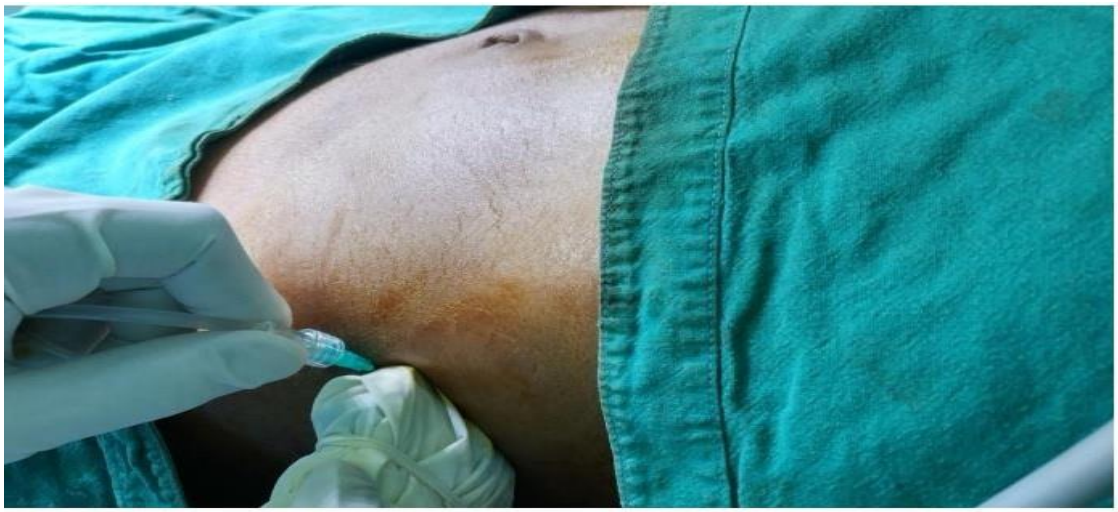


Figure 12 : Illustration of TAP block.

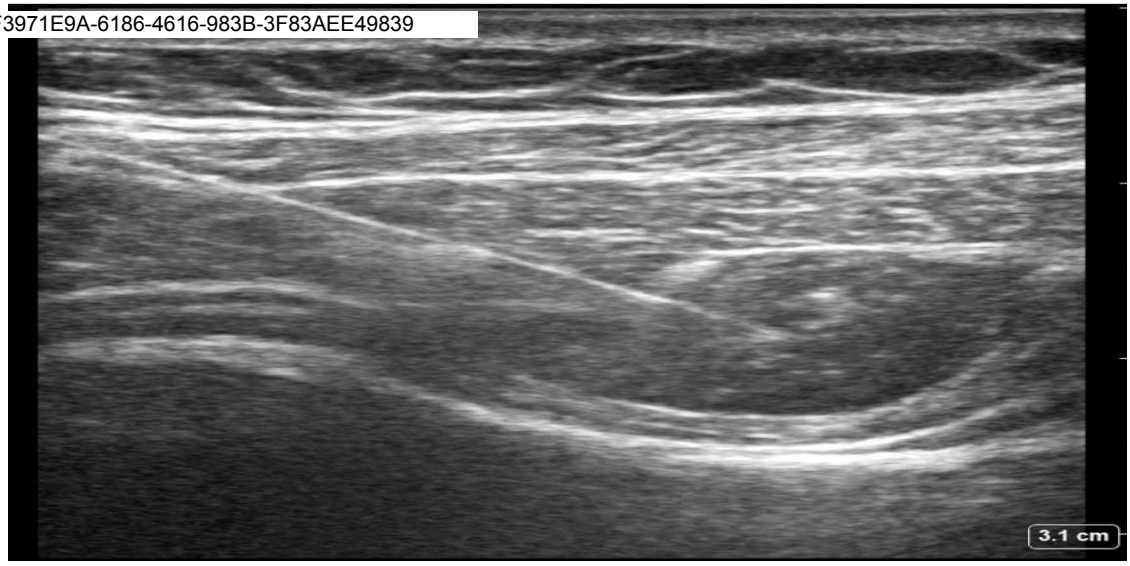


Figure 13: Spreading of local anesthetic drug in between internal oblique and transverse abdoiminis

- **VAS Score Intensity of pain**

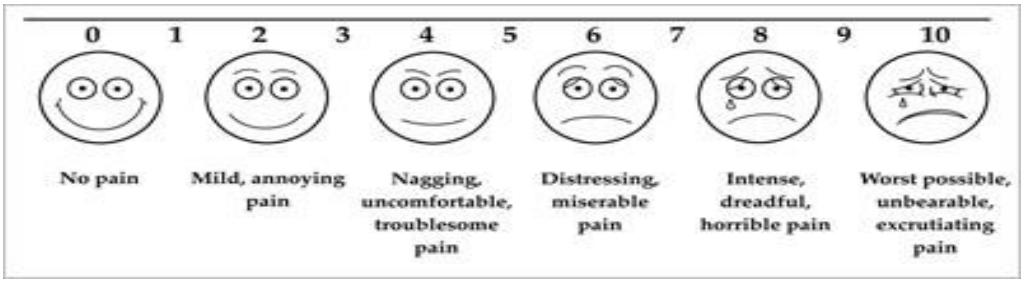


Figure 14 : Visual analogue scale

0 – 1 No pain to slight pain

2 – 4 Mild pain.

5 – 7 Moderate pain.

8 – 9 severe pain.

10- Worst possible pain.

- **SHORT ASSESSMENT OF PATIENT SATISFACTION SCORE**

  1- Highly dissatisfied

  2- Dissatisfied

  3- Neither dissatisfied nor satisfied

  4- Satisfied

  5- Highly satisfied

- **PONV SCORE:**

  0 = no nausea / vomiting.

  1 = nausea / retching.

  2 = Vomiting.

  3 = severe vomiting/projectile.

- **Following observations were recorded**.

  1. Postoperative VAS score.
  2. Duration of analgesia.
  3. Number of analgesic demands at various time intervals.
  4. Cardio-respiratory effects: Heart rate, blood pressure.
  5. Side effects / complications like nausea , vomiting , haematoma and myositis.
  6. Short assessment of patient satisfaction score (SAPS).

Statistical Analysis

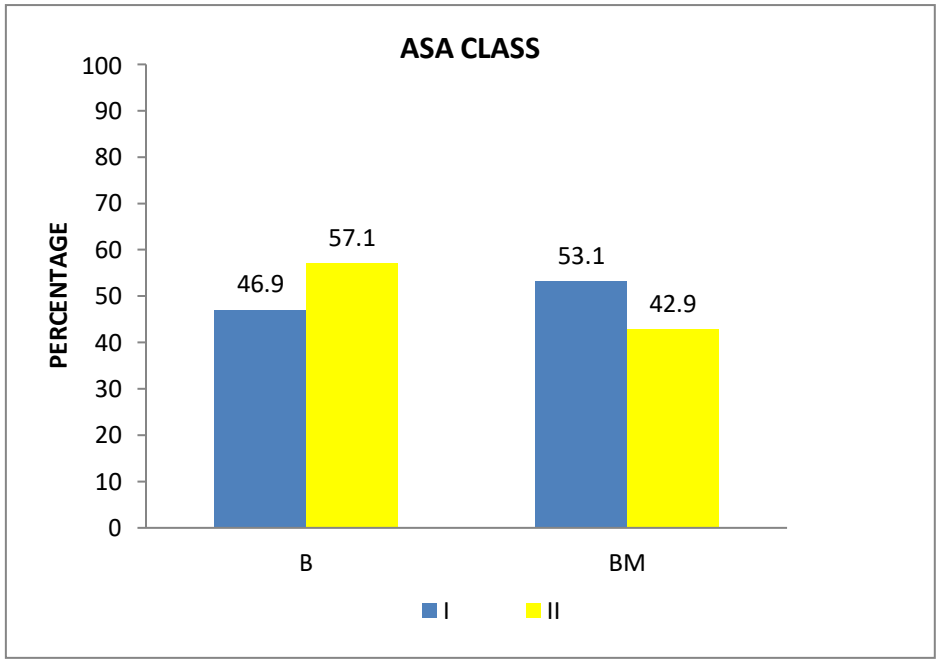
SPSS for Windows version 16.0 software was used for statistical analysis. Chi-square test was used for non continuous data. The mean and standard deviation of the parameters studied during observation period were calculated for two treatment groups and compared using Student 't' test. If p value <0.05 , it indicates that the study is siginificant .

All characteristics were descriptively summarized. Summary statistics of mean, standard deviation (SD) were used for continuous variables . The number and percentage were used for categorical data in the data summaries. Chi-square ($\chi 2$)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. Unpaired t test was used for the difference of the means of analysis variables between two independent groups. If the p-value was < 0.05, then the results were considered to be clinically statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office.

OBSERVATIONS AND RESULTS

TABLE 1: DISTRIBUTION OF CASES ACCORDING TO ASA CLASS IN GROUP B AND BM.

ASA CLASS	GROUP B		GROUP BM		p VALUE
	N	%	N	%	
I	23	46.9	26	57.1	0.434
II	12	53.1	9	42.9	
TOTAL	35	100	35	100	

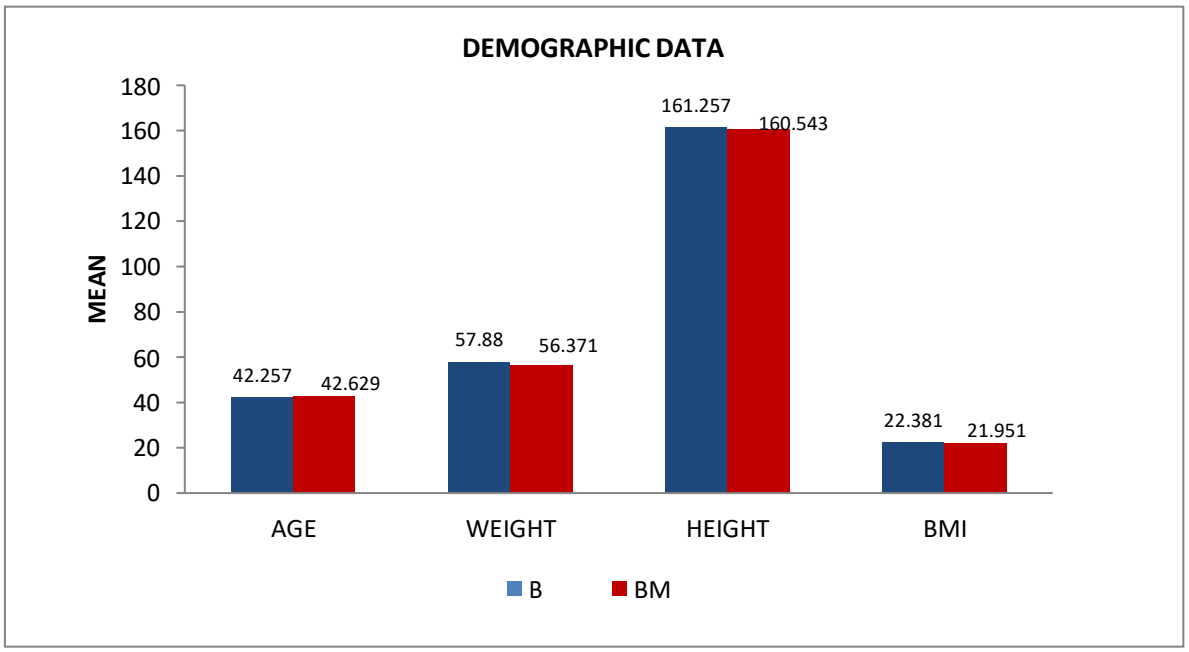


GRAPH 1: DISTRIBUTION OF CASES ACCORDING TO ASA CLASS IN GROUP B AND GROUP BM.

Total of 70 ASA class I and II subjects were studied. No statistical significance noted in any group. TAP block with bupivacaine alone or magnesium sulphate is not influenced by ASA class of the patient undergoing the block/procedure.

TABLE 2: COMPARISON OF MEAN DEMOGRAPHIC PARAMETERS IN GROUP B AND BM.

DEMOGRAPHIC PARAMETERS	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
AGE	42.257	5.305	42.629	5.926	0.845
WEIGHT	57.88	7.308	56.371	7.62	0.196
HEIGHT	161.257	6.635	160.543	7.743	0.663
BMI	22.381	3.289	21.951	2.776	0.557

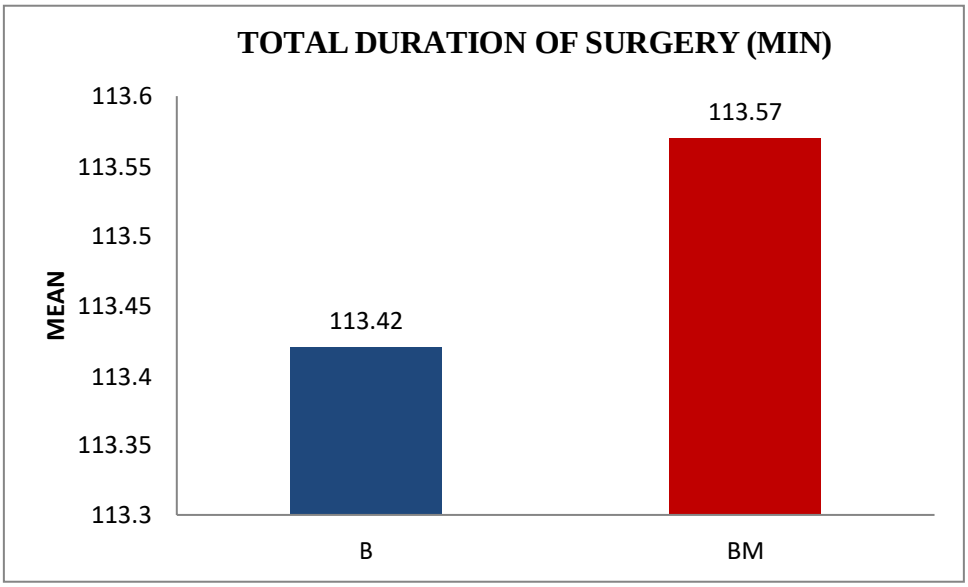


GRAPH 2: COMPARISON OF MEAN DEMOGRAPHIC PARAMETERS IN GROUP B AND BM.

Parameters like AGE/WEIGHT/ HEIGHT/BMI were assessed between both the groups and no clinically and statistical p value was not significant.

TABLE 3: COMPARISON OF MEAN DURATION OF SURGERY GROUP B AND BM.

PARAMETER	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
DURATION OF SURGERY	113.42	14.48	113.57	14.27	1.00

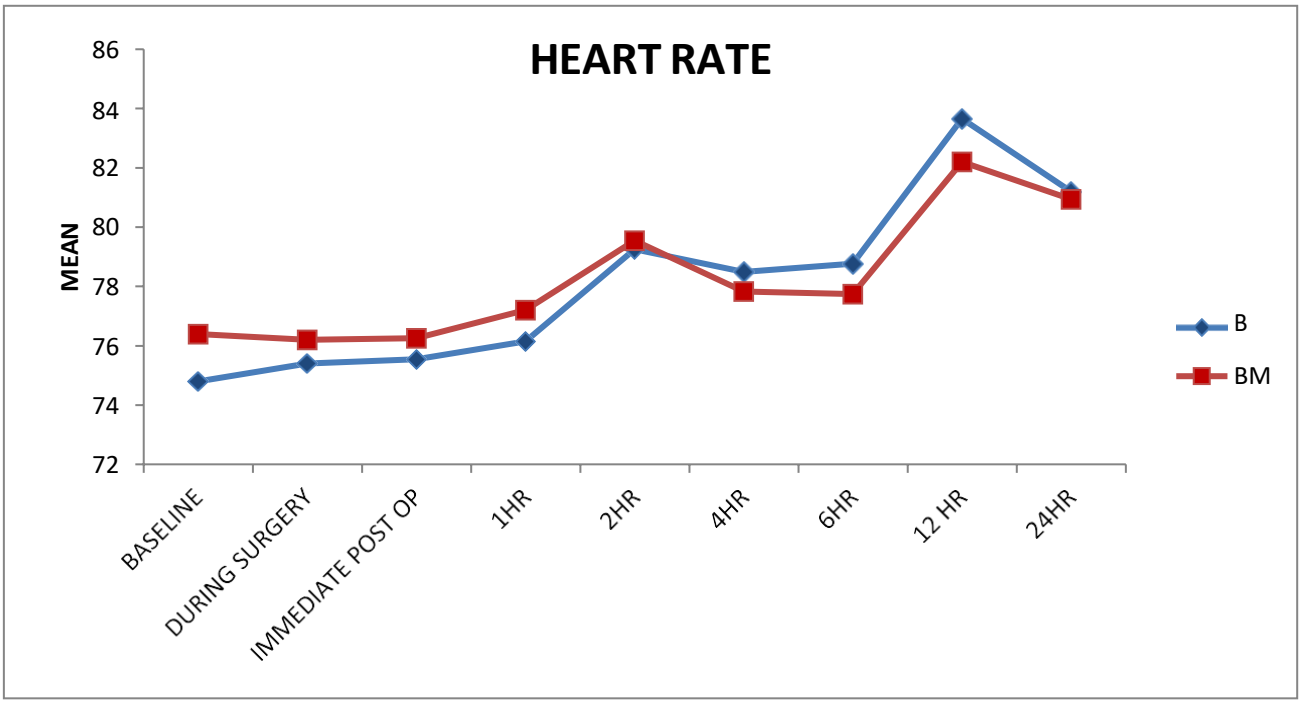


GRAPH 3 : COMPARISON OF MEAN DURATION OF SURGERY IN GROUP B AND BM.

In both groups, the total time of surgery was evaluated for its influence on the duration of post-operative analgesia with TAP block. No statistical p value determined.

TABLE 4: COMPARISON OF MEAN HEART RATE IN GROUP B AND GROUP BM.

HR	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
BASELINE HR	74. 80	6.99	76.40	8.21	0.383
DURING SURGERY	75.40	4.97	76.20	5.58	0.661
IMMEDIATE POST OP	75.54	3.86	76.25	4.15	0.303
1 HR	76.14	7.33	77.20	4.54	0.548
2 HR	79.25	4.81	79.54	5.33	0.736
4 HR	78.48	3.76	77.82	4.99	0.389
6 HR	78.77	6.92	77.74	8.22	0.573
12 HR	83.65	7.18	82.20	7.98	0.500
24 HR	81.20	5.91	80.94	6.48	0.990

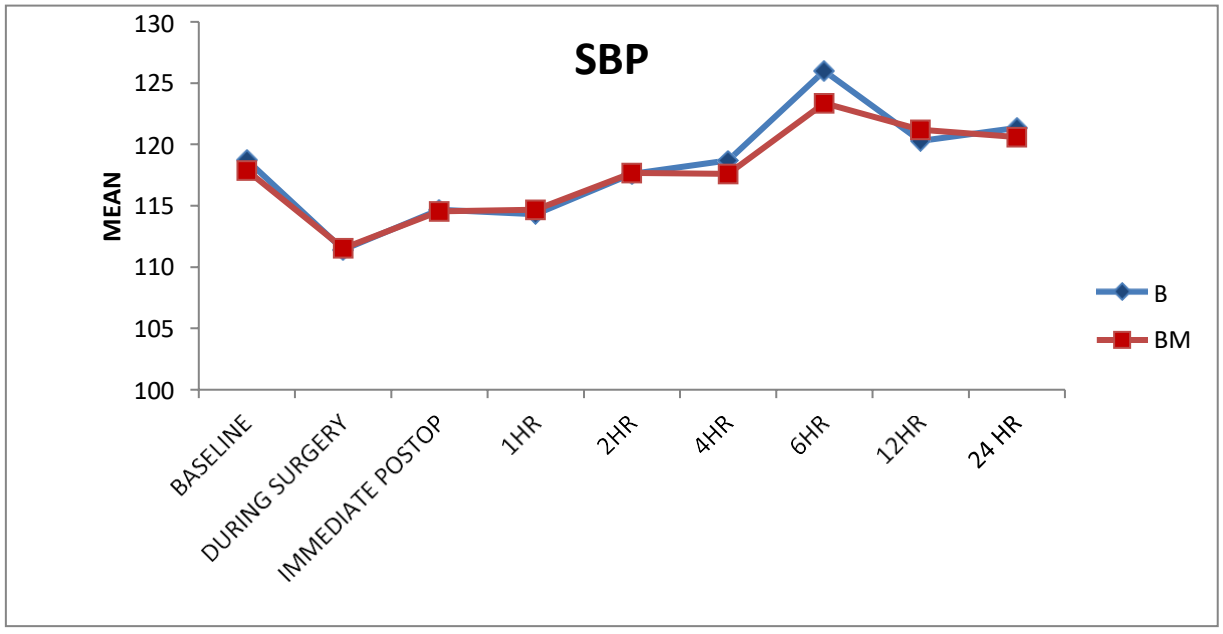


GRAPH 4 : COMPARISON OF MEAN HEART RATE IN GROUP B AND GROUP BM.

In both groups, heart rate was recorded for influencing the duration of analgesia. No significant p value was determined.

TABLE 5: COMPARISON OF MEAN SBP IN GROUP B AND GROUP BM.

SBP	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
BASELINE	118.743	10.22	117.886	10.40	0.775
DURING SURGERY	111.429	4.78	111.543	5.31	0.866
IMMEDIATE POST OP	114.686	7.74	114.543	8.76	0.845
1HR	114.314	4.65	114.686	4.75	0.714
2HR	117.600	8.32	117.686	7.27	0.728
4HR	118.714	7.60	117.600	8.05	0.612
6HR	126.000	7.74	123.371	9.34	0.192
12 HR	120.286	8.43	121.200	8.07	0.661
24 HR	121.371	10.28	120.600	9.26	0.752

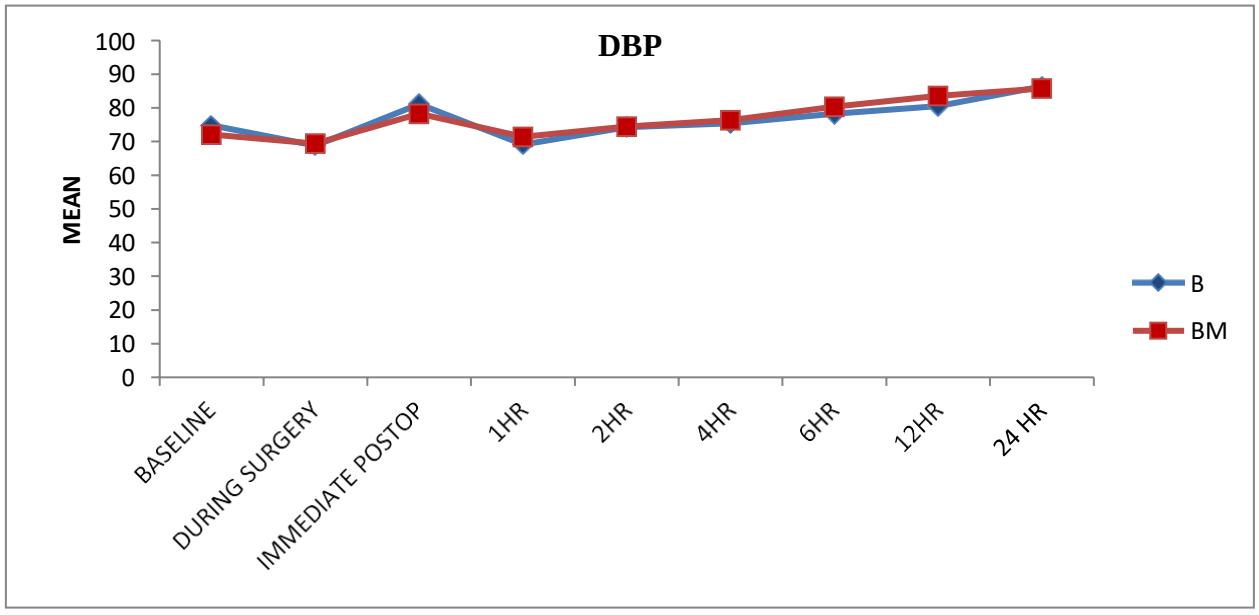


GRAPH 5: COMPARISON OF MEAN SBP IN GROUP B AND GROUP BM.

In both groups, the effect of systolic blood pressure on the duration of post-operative analgesia with TAP block was evaluated. No statistical P value determined.

TABLE 6 : COMPARISON OF MEAN DBP IN GROUP B AND GROUP BM.

DBP	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
BASELINE	74.857	9.114	72.143	7.305	0.171
DURING SURGERY	68.857	7.183	69.457	7.901	0.926
IMMEDIATE POST OP	81.143	18.907	78.286	7.947	0.793
1HR	69.143	8.179	71.429	9.360	0.262
2HR	74.286	10.084	74.486	8.836	0.684
4HR	75.429	6.683	76.429	8.005	0.686
6HR	78.314	3.571	80.371	6.160	0.237
12 HR	80.571	9.454	83.629	9.512	0.187
24 HR	86.400	4.797	85.771	6.454	0.765

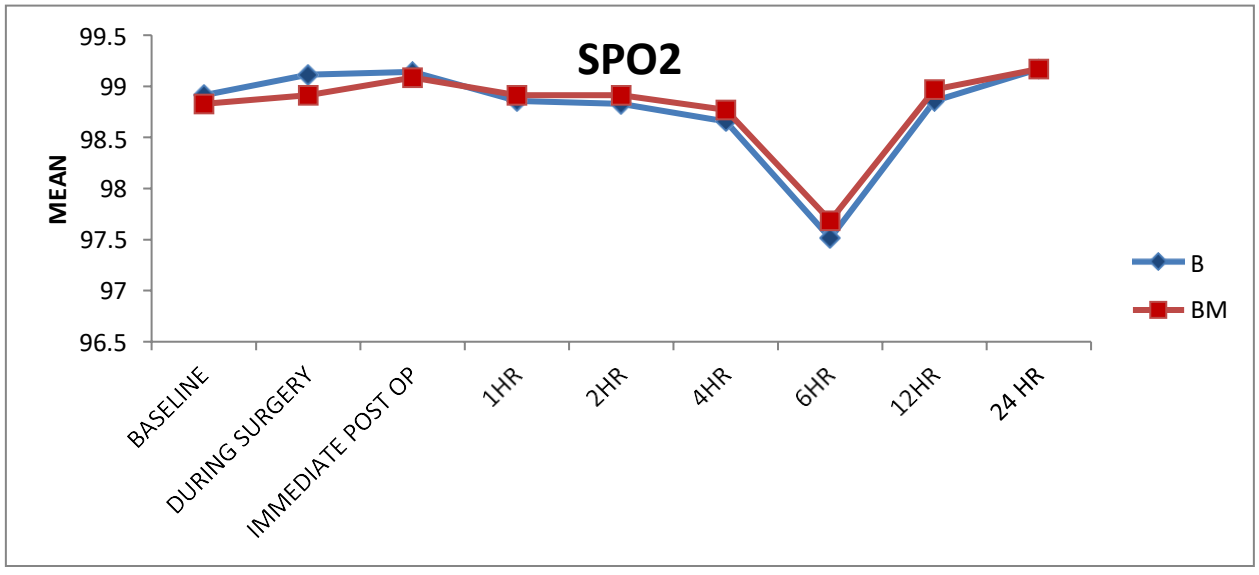


GRAPH 6: COMPARISON OF MEAN DBP IN GROUP B AND GROUP BM.

In both groups, the effect of diastolic blood pressure on the duration of post-operative analgesia with TAP block was evaluated. No statistical P value determined.

TABLE 7: COMPARISON OF MEAN SPO2 IN GROUP B AND GROUP BM.

SPO2	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
BASELINE	98.914	0.853	98.829	1.014	0.800
DURING SURGERY	99.114	0.832	98.914	0.742	0.288
IMMEDIATE POST OP	99.143	0.430	99.086	0.612	0.851
1HR	98.857	0.912	98.914	0.887	0.775
2HR	98.829	0.514	98.914	0.562	0.530
4HR	98.657	0.482	98.771	0.646	0.535
6HR	97.514	0.507	97.686	0.676	0.347
12 HR	98.857	0.912	98.971	0.891	0.586
24 HR	99.171	0.382	99.171	0.514	0.929



GRAPH 7 : COMPARISON OF MEAN SPO2 IN GROUP B AND GROUP BM.

In both groups, standard oxygen saturation parameters were evaluated for their ability to influence the duration of post-operative analgesia with TAP block. There was no statistical p value determined.

TABLE 8 : COMPARISION OF MEAN VAS IN GROUP B AND GROUP BM.

VAS	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
IMMEDIATE POST OP	0.28	0.32	0.11	0.45	0.076
1 HR	0.54	0.49	0.37	0.50	0.127
2 HR	1.17	0.85	1.02	0.29	0.427
4 HR	2.40	1.31	1.74	0.70	0.001
6 HR	4.51	0.95	2.48	0.78	0.001
12 HR	3.87	1.14	3.13	1.55	0.026
24 HR	3.19	0.93	2.14	0.34	0.001

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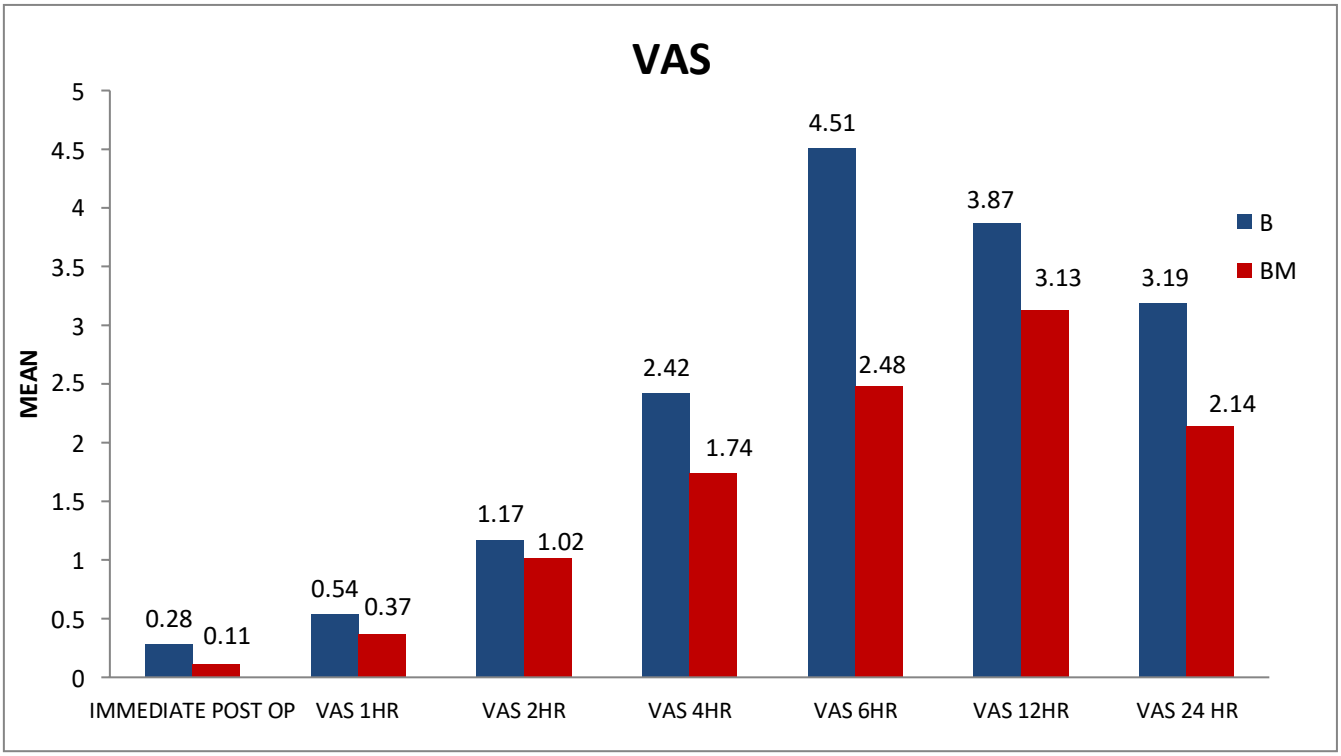

GRAPH 8 : COMPARISION OF MEAN VAS IN GROUP B AND GRUPO BM.

Difference in mean VAS at 0, 1 hr and 2 hr was found to be clinically and statistically insignificant. However, there was statistically significant decrease in VAS scores at 4, 6 , 12 and 24 th hr in group BM compared to group B. Higher VAS was recorded in Group B in 6^{th} hr (4.51 ± 0.95) and Group BM at 12th hr (3.13 ± 1.55).

TABLE 9: ANALGESIC REQUIREMENT BETWEEN GROUP B AND GROUP BM.

ANALGESIC REQUIREMENT	GROUP B		GROUP BM		p VALUE
	N	%	N	%	
IMMEDIATE POST OP	0	0	0	0	0
1 HR	0	0	0	0	0
2 HR	0	0	0	0	0
4 HR	2	5.71	0	0	0.001
6 HR	8	22.85	0	0	0.001
12 HR	31	88.57	5	14.28	0.001
24 HR	10	28.57	25	71.42	0.002

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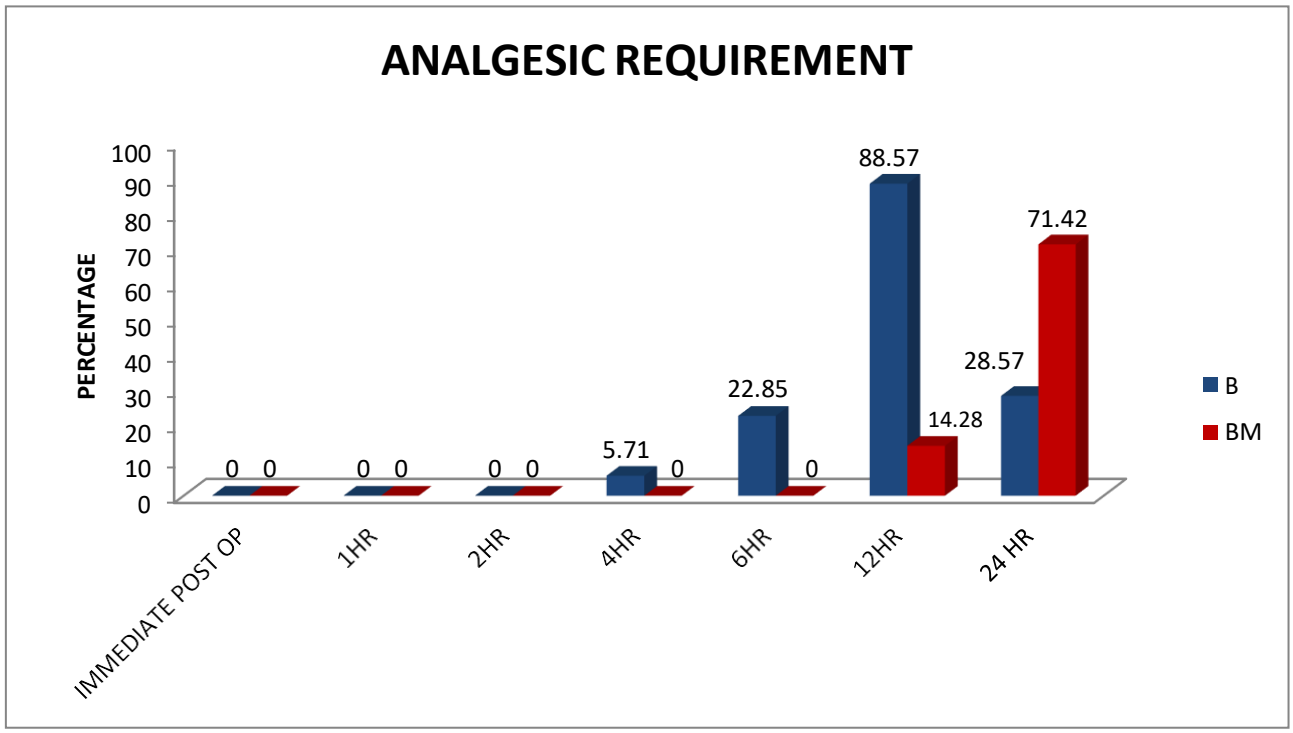
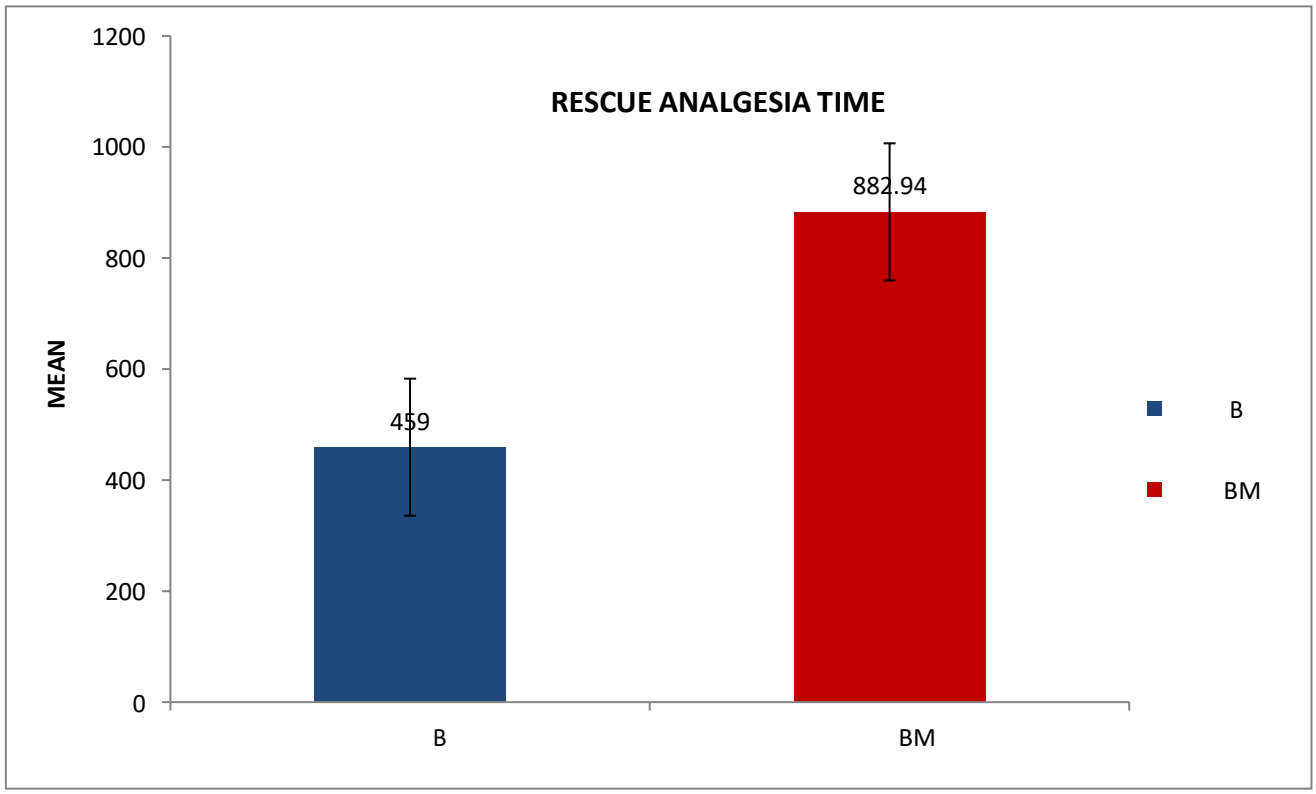


GRAPH 9 : ANALGESIC REQUIREMENT BETWEEN GROUP B AND GROUP BM.

In first 4hr, there were 2 demands for rescue analgesic in Group B (5.71%) and none in Group BM. Between 4 and 6 hr, 8 patients in Group B (22.85%) demanded rescue analgesia with none in Group BM. Between 6 and 12hr , 31 patients in Group B (88.57%) and 5 in Group BM (14.28%) demanded rescue analgesic. Between 12 and 24hr, 10 patients in Group B (28.57%), and 25 patients in Group BM (71.42%) demanded rescue analgesia. In first 12 hours, Group B required more rescue analgesics than group BM. The patients in the BM group needed rescue analgesia after 12^{th} hr($p = 0.001$).

TABLE 10 : TIME TO FIRST RESCUE ANALGESIA (MINS).

PARAMETER	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
Time to first rescue analgesia (mins)	459	100.53	882.94	70.228	<0.001

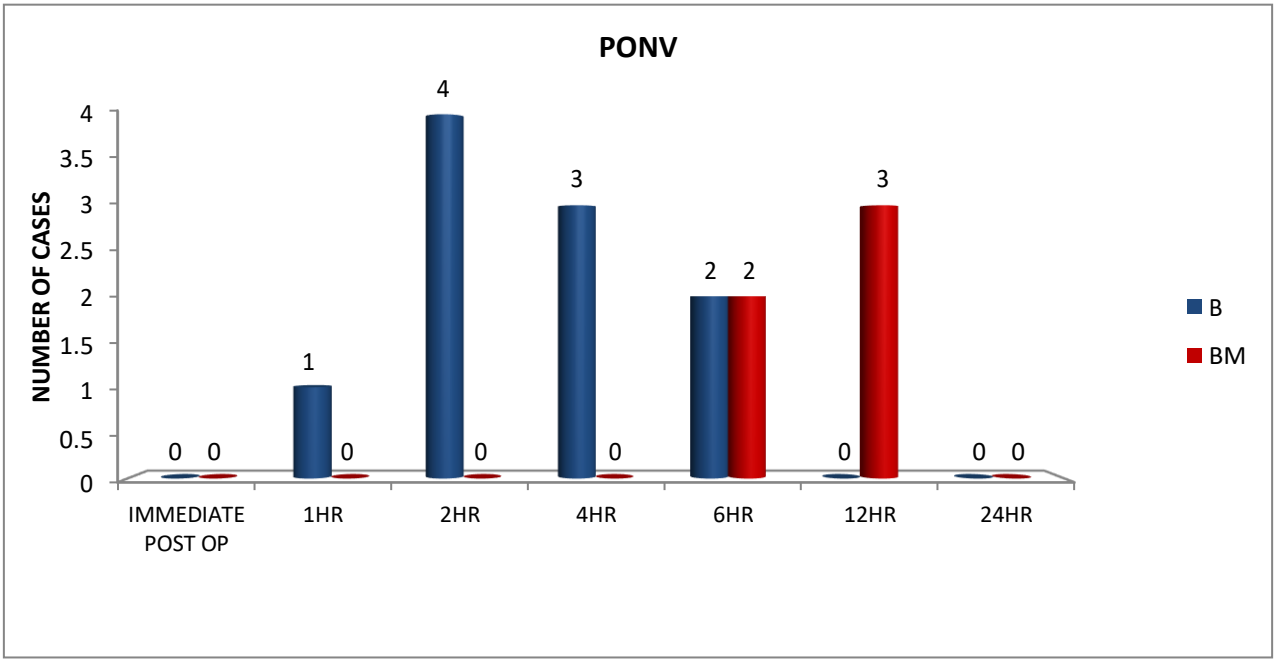


GRAPH 10 : TIME TO FIRST RESUCE ANALGESIA (MINS) EXPRESSED IN MEAN ± STANDARD DEVIATION.

The time to first rescue analgesia was significantly increased in group BM (882.94 ±70.22 mins) group compared to group B (459 ±100.53 mins).

TABLE 11: PONV BETWEEN GROUP B AND GROUP BM.

PONV	GROUP B		GROUP BM		p VALUE
	N	%	N	%	
IMMEDIATE POST OP	0	0	0	0	-
1HR	1	2.9	0	0	0.31
2HR	4	11.4	0	0	0.04
4HR	3	8.6	0	0	0.07
6HR	2	5.7	2	5.7	-
12 HR	0	0	3	8.6	0.07
24 HR	0	0	0	0	-

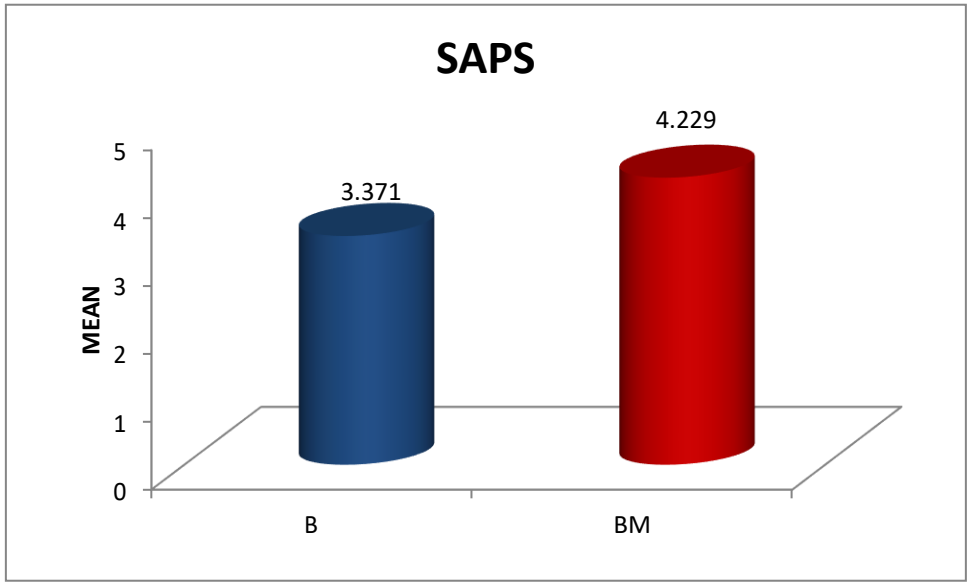


GRAPH 11 : PONV BETWEEN GROUP B AND GROUP BM.

On comparision of PONV score in both groups , the highest incidence was noticed in 2nd hr of group B (p value=0.04*). It indicates that group BM has less incidence of post operative nausea and vomiting compared to group B.

TABLE 12: COMPARISION BETWEEN MEAN SHORT ASSESSMENT OF PATIENT SATISFACTION SCORE

PARAMETER	GROUP B		GROUP BM		p VALUE
	MEAN	SD	MEAN	SD	
SHORT ASSESSMENT OF PATIENT SATISFACTION SCORE	3.37	0.770	4.22	0.731	<0.001*



GRAPH 12 : SAPS BETWEEN GROUP B AND GROUP BM.

Patient satisfaction score was better in group BM (4.22±0.73 compared to group B (3.37± 0.77).

DISCUSSIONS

This randomised clinical trial demonstrated that the TAP block with magnesium sulphate as an adjuvant added to bupivacaine when used as a part of multimodal analgesia provides effective analgesia for patients undergoing TAH . It lowered the severity of breakthrough pain and the need for opiods after surgery. All blocks were performed under ultrasound guidance, ensuring precise placement. No block-related complications occurred.

In our study , parameters like ASA grade, age , weight, height ,BMI and duration of surgery have no influence on the duration of analgesia provided by the TAP block. Intial 2 hrs visual analog scores were lower in both groups , may be due to residual effects of sub arachanoid block. Our study shows VAS scores were siginificantly less in 6^{th} , $12^{th}$and 24 th hrs after the block in group BM compared to group B .It indicates that the addition of magnesium sulphate to bupivacine has led to lower the VAS pain scores upto 24 hrs significantly (p = <0.001). Shelly Rana *et al.*[20] conducted the same study in total abdominal hysterectomy patients and reported that addition of 150 mg of magnesium sulphate reduced the post-operative visual analogue scale (VAS) score in 4, 6 and 12 h ($P < 0.05$). Abd-Elsalam *et al.* [30] conducted a prospective, randomised, double-blind study on 60 women undergoing total abdominal hysterectomy . Over the first 24 hours after surgery, the MgSO4 group had a significantly lower postoperative VAS score for pain than the bupivacaine group. At the end of arthroscopic knee surgery, R S Bondok *et al.*[89] noticed that intra-articular administration of MgSO4 (50 mg / ml) reduced postoperative VAS scores. Additionally, it delays the first rescue analgesic request and reduces the demand for further analgesic drugs. During the first 8 hours after surgery, the intra-articular magnesium group had lower VAS scores than the intra-articular saline group.

In terms of rescue analgesia consumption, the plain bupivacaine group required the most rescue boluses between the 6th and 12th hr, whereas the magnesium sulphate group required more rescue analgesia after 12 hours of post surgery. It indicates shorter pain free period and increased demand of rescue analgesia with plain bupivacaine. Therefore, magnesium typically decreased the need for analgesics on the first postoperative day. The main mechanism could be magnesium's voltage-dependent antagonism of N-methyl-D-aspartate receptors, which regulate calcium ion influx and prevent central sensitization of peripheral nociceptive stimulation, thereby reducing acute pain after tissue injury.[90]Another possible mechanism is that magnesium enhances excitatory neurotransmitter release at the synaptic junction, which may improve local anaesthetic effects**.**[64,91] The surface charge theory also helps to explain the analgesic effects of magnesium sulphate on peripheral neurons. Magnesium ions have been shown to increase the firing threshold in myelinated and unmyelinated axons.[92] It has been proposed that divalent cations decrease the fixed negative surface charge on the outer neuronal membrane, increasing the transmembrane potential , causing hyperpolarization.[93,94-97] When a fibre is hyperpolarized, it is more difficult for it to achieve the threshold level, resulting in conduction block. Akutagawa *et al.*[98] demonstrated that modulating the external magnesium concentration bathing a nerve bundle improved nerve blockade caused by local anaesthetics. Mohamed A. Elshahaly *et al*.[86] reported that magnesium sulphate as an adjuvant to TAP block in patients undergoing unilateral open inguinal hernia repair had a lesser requirement of rescue analgesia post operatively.

The magnesium dose employed in this investigation was based on data from the Gunduz A *et al*.[99] study. He concluded that adding 150 mg of magnesium to prilocaine increases the duration of the axillary plexus block compared to 100mg of magnesium without causing systemic effects or neurotoxicity. Similarly, Goyal P *et al*.[100] reported that MgSO4 in 200 mg and 100 mg doses was employed as the sole agent for postoperative analgesia in axillary block, and the duration of analgesic relief in MgSO4 groups was longer than in control groups. Although pain alleviation with 200 mg MgSO4 was longer than with 100 mg MgSO4, and morphine use was lower in both study

groups than in the control group. Mayuresh Umalkar *et al.*[84] employed 75 mg of MgSO4 as an adjuvant to bupivacaine in TAH cases and found that it did not extend the duration of post-operative analgesia, might be due to inadequate dosage of magnesium sulphate. In our study , the usage of MgSO4 150 mg in group BM provided good post operative analgesia, with increased time to first rescue analgesia compared to group B (882.94 ±70.228 mins vs. 459 ±100.53 , P = 0.001). When the PONV score in both groups was compared, the highest incidence was observed in the second hour of group B (p value=0.04). It suggests that group BM has a lower incidence of post-operative nausea and vomiting than group B. A statistically significant difference in satisfaction score was also observed in the magnesium group. The mean patient satisfaction score in group BM was higher (4.22 ± 73) than in group B (3.37 ± 0.77). Our data demonstrates that not only analgesic requirements were lower in group BM , but so are VAS scores and PONV incidence. Many direct and indirect causes could have contributed to PONV's desired outcome. Aside from the direct relationship of opioid consumption, higher pain scores are known to directly enhance PONV. Soltani Mohammadi *et al.*[101] and Parikh *et al.*[102] indicated that the overall numeric rating scale (NRS) for pain had much lower values with the application of TAP block because it produced analgesia for a significantly longer duration. As a result of minimising the use of opioids for postoperative pain, the incidence of PONV will be reduced. In estimating the incidence of PONV, any score greater than zero at any time point was considered an indication that the patient had PONV. No injury to viscera or haematoma was observed in this study as blocks were performed under ultrasound guidance.

An area of limitation in this study was that serum Mg levels were not evaluated and study group was less in number. To generalise the results large group studies are required.

CONCLUSION

The addition of MgSO4 to bupivacaine in an ultrasound-guided TAP block substantially decreased VAS scores ,reduced postoperative analgesic requirement and increased time to first request analgesia in patients undergoing abdominal hysterectomy without notable side effects compared to bupivacaine alone . More research is needed, however, to determine the optimum dosage by conducting the investigation in a variety of ways (e.g., increasing magnesium doses, using alternative pain control modalities with continuous infusion or various combinations of local anaesthetics), as well as to evaluate the safety profile of magnesium before its routine use as a perineural adjuvant can be advocated.

SUMMARY

This randomized double blind controlled study was conducted in the Department of Anaesthesiology, B.L.D.E (deemed to be university) SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR. KARNATAKA. After obtaining approval by the Institutional Ethical Committee and written informed patient consent, seventy adult patients of ASA I and II scheduled to undergo abdominal hysterectomy under spinal anaesthesia in the age group of 35-60 years were randomized into two groups comprising thirty-five each. **Group B** - TAP block by18mL bupivacaine 0.25% (45 mg) with 2 mL normal saline . **Group BM** - TAP block by 18 mL bupivacaine 0.25% (45 mg) with MgSO4 50% w/v of 0.3 mL (150 mg) and 0.5 mL NS. Pain was assessed in both the groups by VAS score postoperatively. Rescue analgesics (Inj. Paracetamol and Inj. Diclofenac) were given as per requirement for the management of pain. All findings were noted by a blinded observer. All data were analyzed statistically by Students t test and Chi-Square test. Data were considered clinically significant when $p < 0.05$. Group BM provided good post operative analgesia, reduced VAS scores and increased time to first rescue analgesia compared to group B . From our study we found out that under ultrasound guidance TAP block is easy to perform and use of magnesisum sulphate as an adjuvant to bupivacaine increased the time to first rescue analgesia . There was no drug related complication and it provided effective analgesia. Thus T.A.P. block is favoured above other options for multimodal analgesia and provide efficient analagesia in patients undergoing total abadominal hysterectomy.

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ANNEXURES

I. ETHICAL CLEARANCE CERTIFICATE

IEC/NO-09/2021
22-01-2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Comparison of Bupivacaine and Bupicacaine with magnesium sulphate in transversus abdominis plane block for post operative analgesia in patients scheduled for total abdominal hysterectomy under spinal Anaesthesia

Name of PG student: Dr Komalea Priya Balakrishna Department of Anaesthesiology

Name of Guide/Co-investigator: Dr K Nirmaladevi Associate Professor of Anaesthesiology

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

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

II .INFORMED CONSENT FORM

B.L.D.E.(DU)'S SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR – 586103, KARNATAKA

TITLE OF THE PROJECT :" COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH MAGNESIUM SULFATE IN TRANSVERSUS ABDOMINIS PLANE BLOCK UNDER ULTRASOUND GUIDANCE FOR POST OPERATIVE ANALGESIA IN PATIENTS SCHEDULED FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA"

PRINCIPAL INVESTIGATOR : DR.KOMALEA PRIYA BALAKRISHNA

Department of Anaesthesiology

BLDE (Deemed to be university)

Shri B.M. Patil Medical College Hospital &Research Centre,

Sholapur Road Vijayapur-586103

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PG GUIDE : Dr.K.NIRMALA DEVI

Associate Professor

Department Of Anaesthesiology

BLDE (Deemed to be university) Shri B.M. Patil

Medical College Hospital & Research Centre, Sholapur Road Vijayapura.

Email: nirmalakagalkar77@gmail.com

PURPOSE OF RESEARCH:

I have been informed that this study is **"COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH MAGNESIUM SULFATE IN TRANSVERSUS ABDOMINIS PLANE BLOCK UNDER ULTRASOUND GUIDANCE FOR POST OPERATIVE ANALGESIA IN PATIENTS SCHEDULED FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA"**

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

PROCEDURE:

I understand that I will be participating in the study: **"COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH MAGNESIUM SULFATE IN TRANSVERSUS ABDOMINIS PLANE BLOCK UNDER ULTRASOUND GUIDANCE FOR POST OPERATIVE ANALGESIA IN PATIENTS SCHEDULED FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA."**

BENEFITS: I understand that my wards participation in this study will help in finding out "**COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH MAGNESIUM SULFATE TRANSVERSUS ABDOMINIS PLANE UNDER ULTRASOUND GUIDANCE BLOCK FOR POST OPERATIVE ANALGESIA IN PATIENTS SCHEDULED FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA."**

CONFIDENTIALITY:

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

REQUEST FOR MORE INFORMATION:

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

REFUSAL OR WITHDRAWL OF PARTICIPATION:

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

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

INJURY STATEMENT:

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

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

Date: **Dr. KOMALEA PRIYA BALAKRISHNA**

(Investigator)

Patient's signature Witness to above signature

STUDY SUBJECT CONSENT STATEMENT:

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

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

III . PROFORMA

STUDY: "COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH MAGNESIUM SULFATE IN TRANSVERSUS ABDOMINIS PLANE BLOCK UNDER ULTRASOUND GUIDANCE FOR POST OPERATIVE ANALGESIA IN PATIENTS SCHEDULED FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA"

PATIENT DETAILS: **DATE:**

I. Name: **Age :** **Sex:** **I.P No:**

Ward: **Group allotted by randomization: Group B / Group BM**

II . 1. Type of the surgery: **Duration of surgery (min):**

2. Indication:

III. Significant History:

IV. General Physical Examination:

Pallor **Icterus** **Cyanosis** **Clubbing** **Koilonychia** **Lymphadenopathy** **Edema**

V. Vital Parameters :

Pulse **Blood Pressure** **Respiratory Rate** **Temperature**

VI. Systemic Examination:
CVS
RS
CNS
P/A

VII. Airway Assessment: **Mouth opening** **Neck movements**
Teeth **ASA Grade**
MP Grade

VIII. Investigation :

1. Hemodynamic variables during intraoperative period.

OBSERVATION	HR	SBP/DBP	SPO2
BASELINE			
5 MINS			
15 MINS			
30 MINS			
60 MINS			
END OF SURGERY			

2. Haemodynamic variables during postoperative period.

OBSERVATION	HR	SBP/DBP	SPO2	VAS(1-10)	RESCUE ANALGESIA TIME(T RESCUE)	ANALGESIC CONSUMPTION	PONV	SAPS
IMMEDIATE POSTOP								
1 HRS								
2 HRS								
4 HRS								
6 HRS								
12 HRS								
24 HRS								

T RESCUE : Time for Request of Analgesia

SAPS : Short assessment of patient satisfaction score

PONV: Post operative nausea , vomiting

PRIMARY INVESTIGATOR SIGNATURE:-

GUIDE SINATURE :-

BIO-DATA OF THE GUIDE

GUIDE NAME : DR. K.NIRMALA DEVI

DATE OF BIRTH : 24/04/1976

EDUCATION : MBBS 2000, KURNOOL MEDICAL COLLEGE,
KURNOOL ANDHRA PRADESH
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QUALIFICATION : M.B.B.S., DR.PINNAMNENI SIDDHARTHA INSTITUTE OF MEDICAL SCIENCE AND RESEARCH FOUNDATION, VIJAYAWADA ANDHRA PRADESH

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KEY TO MASTER CHART

SL NO : Serial number

Group B : Bupivacaine group

Group BM: Bupivacaine + Magnesium sulphate group

ASA_Class : American society of anaesthesiologists classification

BMI : Body mass index

HR : Heart rate

SBP : Systolic blood pressure

DBP : Diastolic blood pressure

SPO2 : Oxygen saturation

VAS : Visual analogue score

PONV : Post operative nausea vomitting

T RESCUE : Time for Request of Analgesia

SAPS : Short assessment of patient satisfaction score

MASTER CHART

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