Original Article

Effect of Magnesium Sulphate with Bupivacaine in Ultrasound-guided Transversus Abdominis Plane Block in patients undergoing Total Abdominal Hysterectomy

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ABSTRACT

Background: Transversus abdominis plane block is a valuable component of multimodal analgesia regimen. Magnesium sulphate has been shown to increase the duration of action of different peripheral nerve blocks. We assessed the efficacy of magnesium sulphate as an adjuvant to bupivacaine in transversus abdominis plane block in patients scheduled for total abdominal hysterectomy under general anaesthesia.

Methods: Sixty-six patients undergoing total abdominal hysterectomy under general anaesthesia were divided into two groups. Ultrasound guided bilateral transversus abdominis plane block was performed in both group before extubation. Bupivacaine alone group received block with 20ml of 0.25% bupivacaine while Bupivacaine with Magnesium group received block with 20ml of 0.25% bupivacaine with 150mg of magnesium sulphate on each side. Pain scores at 0, 2, 4, 6, 12 and 24 hours postoperatively along with time to first request of analgesia, total consumption of fentanyl and incidence of nausea or vomiting were noted.

Results: Group BM showed significantly lower pain scores at 4 and 6 hours (p=0.001 and 0.017 respectively). Time to first request of analgesia was significantly more in Group BM [285 minutes (85, 370) vs. 75 minutes (52.5, 150), (p<0.001)]. Total postoperative fentanyl consumption was significantly less in Group BM (230±59.06 mcg vs. 289.85±69.13 mcg, p<0.001).

Conclusions: Bupivacaine with magnesium sulphate in transversus abdominis plane block after total abdominal hysterectomy under general anaesthesia results in lower post operative pain scores, longer duration of analgesia and less postoperative fentanyl requirement with no difference in incidence of nausea/vomiting compared with bupivacaine alone.

Keywords: Bupivacaine; Magnesium sulphate; Postoperative analgesia; TAP block.

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INTRODUCTION

Hysterectomy is a common procedure in women. Patients undergoing abdominal hysterectomy complain of more pain than those undergoing vaginal hysterectomy.[1] For optimal post operative pain management in total abdominal hysterectomy (TAH), multimodal analgesia is recommended. Transversus abdominis plane (TAP) block, acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), steroids and opioids are thought to control the parietal pain, while NSAIDs, steroids and opioids also control the visceral pain.[2]

The evidence suggests that while TAP blocks can contribute to postoperative analgesia,[3-6] the benefit is limited to the early postoperative period. Different adjuncts have been used with local anaesthetics to increase the duration of analgesia.[7] Amongst the various adjuncts the most consistent prolongation of analgesia is shown by peripheral buprenorphine, clonidine, dexamethasone, dexmedetomidine and magnesium.[7]

This study was conducted with the hypothesis that the use of magnesium sulphate with bupivacaine in TAP block would increase the duration of post operative analgesia and decrease the total fentanyl consumption. We assume that this will help our patients receive better postoperative analgesia as well as decrease the need of opioids.

MATERIALS AND METHODS

This randomized, double blinded prospective, interventional study was done in Tribhuvan University Teaching Hospital, operation theatre, post anaesthesia care unit (PACU) and postoperative ward from November 23, 2018 to April 30, 2019 after the approval from the Institutional Review Board.

Sample size of 66 was calculated from the study done by Rana et.al[8] in 2016 in which the mean Numerical Rating Scale (NRS) for pain score difference at 6 hours between two groups was d= 4.53-2.4=2.13 and S=2.62 (larger SD of two groups), at 90% power and at 5% level of significance. Written informed consents were taken from all 66 participants during preanaesthetic checkup.

The American Society of Anesthesiologists (ASA) physical status (PS) I and II women aged 18-65 years scheduled for total abdominal hysterectomy via lower abdominal incision under general anaesthesia were included. Exclusion criteria were patient refusal to block, history of allergy to bupivacaine or magnesium sulphate and patients on calcium channel blockers or anticoagulants. Patients were screened for enrollment in the study by an anaesthesiologist not involved in the study and randomly divided in two groups using computer generated numbers and concealed in sequentially numbered opaque sealed envelopes (SNOSE).

The patients were divided into two groups:
Group B: 0.25% bupivacaine only
Group BM: 0.25% bupivacaine with 150mg of magnesium sulphate

The patients were kept nil per oral (NPO) as per the NPO guideline. Premedication was done with oral Diazepam 10mg on the night before surgery and in the early morning on the day of surgery.

After pre-oxygenation, intravenous (IV) fentanyl 2 mcg/kg body weight was given and induced with titrated dose of propofol followed by vecuronium 0.1 mg/kg body weight. Patients were intubated with appropriately sized endotracheal tube (ETT) and kept under intermittent positive pressure ventilation. General anaesthesia was maintained with isoflurane at 1-2 minimum alveolar concentration. Intravenous fentanyl 0.5mcg/kg was given every hourly and the total intraoperative consumption of fentanyl was noted. At skin closure, IV Ondansetron 0.1mg/kg and Paracetamol 1 gm infusion was given. IV Paracetamol 1gm was repeated every 6hrly thereafter.

Under aseptic precautions, lateral TAP block was performed according to standard protocol after skin closure. The study solution was made by another anaesthesiologist not involved in the study as per randomization in two 20ml syringes.

Group B: 20ml of 0.25% bupivacaine on each side for bilateral TAP block OR

Group BM: 20ml of 0.25% bupivacaine with 150mg of magnesium sulphate on each side for bilateral TAP block

Linear high frequency transducer of 38 x i/13-6 MHz of Sonosite Edge II total ultrasound machine was placed in the axial plane on the midaxillary line between the subcostal margin and the iliac crest. The three layers of abdominal wall muscles were visualized and identified: external oblique, internal oblique and the transversus abdominis muscles. A 25G Quincke's spinal needle was inserted in the anterior axillary line via in-plane technique. The needle tip was advanced until it reached the fascial plane between the internal oblique and transversus abdominis muscles. One ml of NS was injected to open the plane and after confirmation, 20ml of study solution was injected on each side as per randomization. Patient was extubated after neuromuscular blockade was reversed with neostigmine and glycopyrrolate then shifted to PACU.

Post operative pain was assessed using NRS. This consisted of a graduated, straight 10 cm line marked from 0 to 10 at each cm mark, 0 representing "no pain" and 10 representing "worst pain ever". NRS scores were noted at 0, 2, 4, 6, 12 and 24 hours along with the patient's vitals, 0 hour being when the patient was received in PACU. Rescue analgesic with intravenous fentanyl 1mcg/kg was given for NRS score ≥4.

Time for first request for analgesia (T rescue), as well as NRS for pain at that time (NRS T rescue), number of rescue analgesics, incidence of nausea and vomiting and requirement of antiemetic were noted. The primary outcome was post operative NRS scores and the secondary outcomes were the time to first request of analgesia, total postoperative fentanyl consumption and incidence of postoperative nausea/vomiting.

Data was collected in preformed data collection sheet and was filled in an Excel master sheet. Data analyses was performed using SPSS (Statistical Package for the Social Sciences) software, version 23 (SPSS Ltd, Chicago, IL, USA) and values presented as mean (standard deviation SD or range), median or number. Independent t test for normally distributed data, Chi square test for categorical data and Mann-Whitney U test for non-normally distributed (skewed) data were used with p value of <0.05 considered significant.

RESULTS

Total of 66 patients were studied (33 in each group). The demographic characters (age, weight) as well the mean duration of surgery (in minutes) in the two groups were found to be comparable (Table 1).

Table 1: General Characteristics

Parameter	Group B		Group BM		p value
	Mean	SD	Mean	SD	
Age in years	45.33	7.43	46.82	5.36	0.356
Weight in kg	59.21	6.24	59.85	5.59	0.664
Duration of Surgery in minutes	119.85	22.55	121.67	23.87	0.751
Data analyzed using independent t test and expressed as mean and standard deviation. P value <0.05 denotes statistical significance.					

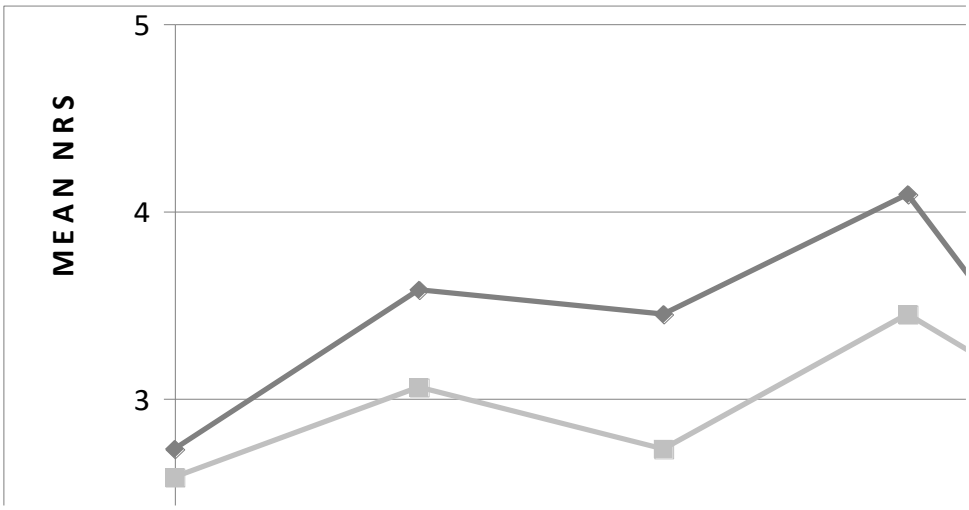

Figure 1: Comparison of post operative NRS between Group B and Group BM
* Represent statistical significance (p<0.05)

Table 2: Time to first request of analgesia (T first)

	Group B	**Group BM**	**p value**
T first (time in min) [Median (Q1, Q3)]	75 (52.5, 150)	285 (85, 370)	<0.001*
Mann-Whitney U test used to analyze data. P value <0.05 denotes statistical significance (represented by *)			

The NRS for pain was taken at 0, 2, 4, 6, 12 and 24 hours, 0 hour being when the patient was received in PACU. Significant difference in NRS was seen at 4 hours and 6 hours (p=0.001 and 0.017 respectively) with less NRS in Group BM at 0, 2, 4 and 6 hours (Fig 1.)

Time to first request of analgesia was statistically significant with longer time to request of first analgesia in BM group (Table 2). The minimum time to first request of analgesia in Group B was 45 min whereas it was 55 min in Group BM and the maximum time to first request of analgesia in Group B was 255 min and in Group BM it was 555 min.

Group BM showed significantly less consumption of fentanyl compared with Group BM (p<0.001) postoperatively (Table 3). The minimum total postoperative fentanyl consumption in Group B was 150mcg and in Group BM was 120mcg whereas the maximum total postoperative fentanyl consumption in Group B was 420mcg and in Group BM was 390mcg.

The incidence of nausea/vomiting 24 hours postoperatively was similar (p=0.779) in both the groups (Table 4). Five patients in Group B and 4 patients in Group BM received rescue antiemetic.

Table 3: Total postoperative fentanyl requirement

	Group B		Group BM		p value
	Mean	SD	Mean	SD	
Total postoperative fentanyl consumption (in mcg)	289.85	69.13	230.15	59.06	<0.001*
Data analyzed using independent t test and expressed as mean and standard deviation. P value <0.05 denotes statistical significance (represented by *).					

Table 4: Total incidence of postoperative nausea/vomiting

Nausea/Vomiting	Group B	Group BM	Chi square	p value
Yes	9	8	0.079	0.779
No	24	25		
Chi square test used to analyze data. P value <0.05 denotes statistical significance.				

DISCUSSION

Use of magnesium sulphate as an adjunct to bupivacaine in TAP block for postoperative analgesia was studied in this study. The primary outcome was post operative NRS scores between the two groups. The patients in magnesium sulphate group had lower pain scores at 0, 2, 4 and 6 hours with significant difference at 4 and 6 hours. Our results are comparable with a similar study by Rana et al,[8] Abd-Elsalam et al,[9] and Haider.[10]

Although magnesium sulphate has been studied in various peripheral nerve blocks like brachial plexus block, axillary nerve block, interscalene block, the study of magnesium sulphate with TAP block is quite recent.[8] Though it has been found that the duration of analgesia with magnesium sulphate in TAP block is prolonged, it is also found to be variable.

Different studies show that the duration analgesia in TAP block with magnesium sulphate varies according to the dose of magnesium sulphate, the time of application of block (preoperative or postoperative) and the technique of TAP block. Magnesium is an N-methyl-D-aspartate (NMDA) receptor antagonist and has been studied for the control of pain. It is thought to prevent central sensitization because of peripheral nociceptive stimulation and to abolish hypersensitivity once it is established. These effects are primarily based on the regulation of calcium influx into cell and antagonism of NMDA receptor. Calcium ions have an important role in the analgesia mediated by the local anaesthetics (LA). Calcium permeability is reduced by LA and it has been shown that calcium channel blockers can potentiate the analgesic effect of LA.

In our study the time to first request of analgesia showed wide variation, hence we used median for analysis of the skewed data. The median time to first request of analgesia in Group B was 75 mins (52.5, 150) and in Group BM was 285 mins (85, 370). The reason for the skewed data may be because of the wide variation in spread and success of nerve block in TAP block that has been seen.[11] Stoving et al. showed a large variation in the spread of the block and the duration of analgesia after TAP block.[12] They showed that TAP block results in a non-dermatomal cutaneous sensory block area with a more lateral orientation and a relatively small and variable medial effect. The block also does not cross the midline and hence incisions in the midline may not be well covered by the TAP block. According to a cadaveric dissection study, the T9-L1 nerves are likely to be blocked by the lateral TAP block approach like the one that we performed on our patients. However a wide variation in success rates of affecting all these nerve roots was seen with reported low rate of success of affecting T10 (only 50%) and L1 (only 43%).[11-13] This variation in success of nerve block may be related to individual differences in the branching position of the anterior ramus of the spinal nerve and the L1 nerves are also not easy to block with the lateral TAP approach.[13] These may also be the reason for the large variation in the time to first request of analgesia seen in our study.

The benefit of TAP block in post operative analgesia has been reported in various review articles and meta-analysis.[14-16] Use of USG for TAP block has become popular because of increase in successful injection of LA in the plane with reduction in block time, number of attempts and complications like accidental puncture and injury to internal organs. The efficacy of TAP block in

TAH in terms of reduced post operative pain scores with reduced total opioid consumption has also been seen.[3-5, 8,17] However, Chin et al stated that the benefit of TAP block for postoperative analgesia may be limited only to the early postoperative period.[18] Gasanova et al showed that although TAP block reduces parietal pain from the skin and muscles, it does not influence the visceral pain generated from the fallopian tubes, uterus and vagina that are innervated by the sympathetic (L2-L4 roots) and the parasympathetic (S2-S5) roots.[2] Thus TAP block has been recommended for postoperative analgesia in TAH not as a sole analgesic but as a part of multimodal analgesia to address both the visceral and parietal pain. Because of this reason, we used acetaminophen 1gm 6hrly in addition to the bilateral TAP block along with fentanyl for postoperative analgesia as a multimodal analgesic regimen.

Whenever NRS was ≥ 4 at any time in the 24 hours postoperative period, 1mcg/kg fentanyl was given and the total dose of fentanyl given was calculated. The mean fentanyl consumption 24 hours postoperatively in Group B was 289.85±69.13mcg and 230.15±59.06mcg in Group BM. The total postoperative fentanyl consumption was significantly lower in Group BM compared to Group B ($p<0.001$). This finding is similar to other studies that have been done using magnesium sulphate as an adjuvant in TAP block.[8-10] All these studies have shown consistent decrease in total opioid requirement in the postoperative period in patients who received magnesium sulphate as an adjuvant.

In our study we also compared the incidence of nausea/vomiting between the two groups. No significant difference was found in the incidence of nausea/vomiting. This is similar to the study done by Abd-Elsalam et al,[9] which showed no significant difference in side effects between the two groups. In the study done by Rana et al,[8] higher mean postoperative nausea and vomiting was recorded in the group that received only bupivacaine compared to the group that received bupivacaine with magnesium sulphate but it was not statistically significant (1.17±0.38 vs. 1.07± 0.25, $p= 0.488$).

This study enrolled relatively healthy ASA I and II patients, so how the addition of magnesium sulphate in bupivacaine in TAP blocks behaves in sicker patient cannot be obtained from the study. Similarly, our study was done on female patients scheduled for elective, gynecological, lower abdominal surgeries. So, the results of this study cannot be applied to other surgical disciplines or male patients. This study is a single cantered study. Larger studies are needed to make definite conclusions.

CONCLUSIONS

We conclude that addition of 150mg Magnesium sulphate in 0.25% bupivacaine in ultrasound guided TAP block after total abdominal hysterectomy under general anaesthesia via lower abdominal incision results in lower postoperative NRS scores, longer duration of analgesia and less postoperative fentanyl requirement with no difference in incidence of nausea and vomiting when compared with bupivacaine alone. We recommend adding magnesium sulphate in bupivacaine in ultrasound guided TAP block for postoperative analgesia in patients undergoing total abdominal hysterectomy.

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