

## Study of Analgesic Effect of Magnesium Sulphate with Bupivacaine in Ultrasonogram Guided Transversus Abdominis Plane Block for Post-Operative Analgesia in Lower Uterine Cesarean Section

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### Abstract

**Background:** Transversus abdominis plane (TAP) block has proven to be an effective component of postoperative pain management for different abdominal procedures particularly in Lower uterine cesarean section (LUCS) done under Sub arachnoid block. Magnesium sulphate (MgSO<sub>4</sub>) is a N-methyl-D-aspartate receptor antagonist has the potential to act as an adjuvant in TAP block. For this reason this study was planned to assess the role of Magnesium Sulphate as an adjuvant to bupivacaine in ultrasound-guided transverse abdominis plane (TAP) blocks for postoperative analgesia in patients undergoing LUCS after regression of block of Sub arachnoid block.

**Methods:** This was a hospital based randomized controlled trial which was conducted in Dhaka Medical College Hospital (DMCH) at the department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine for 2 years of period. Formal ethical approval was taken from the Ethical Review Committee (ERC) of DMC. Patients having LUCS were approached for the study. A total of 60 patients of LUCS under Sub arachnoid block were selected in the study among them 30 patients received TAP block with bupivacaine 0.25% with saline, and the other 30 received bupivacaine 0.25% with 150 mg Magnesium Sulphate immediately following surgery. Primary outcome was focused on duration of analgesia, pain score, time of first need of rescue analgesic and total opioid consumption. Pre-block and immediately post block Visual analog pain scores (VAS) (0–10) were obtained. After pre-anesthetic checkup & discussion about study procedures written informed consent was taken from the patient. Separate case record form was used in each case. Data analysis was done by SPSS version 22.

**Observation and Results:** Mean age of group B (GB) and group-BM (GBM) patients were 25.57± 2.76 & 25.9 ± 3.17SD (years). No significant difference demographic profile was observed (p>0.05). Mean duration of analgesia was significantly prolonged in Group BM compared to Group B (263.13 ± 34.39) min vs. 222.23 ± 30.58 min; P-value <0.001) which was evident by increased VAS score at 16<sup>th</sup> hour postoperatively in magnesium sulphate group than normal saline group. Total postoperative requirement of opioid was also lower in Group BM (p<0.05). **Conclusion:** Magnesium Sulphate could be used as an adjuvant with bupivacaine in ultrasound guided transversus abdominis plane (TAP) blocks for management of post-operative analgesia in LUCS patient.

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### Introduction

Uncontrolled pain after surgeries results surgical stress response that severely affects various physiological functions which may lead to increase perioperative morbidity and mortality. So, effective postoperative analgesia is an essential component of the care of surgical patients.<sup>1</sup> Regional anaesthesia with local anesthetic an agent inhibits the stress response to surgery and also improves the post-operative outcome. In patient of LUCS done under Sub arachnoid block, post-operative pain treated with multimodal approach combined with loco regional analgesia Transversus Abdominis

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Plane block, non-steroidal anti-inflammatory drugs and opioids.<sup>2</sup> The transversus abdominis plane (TAP) block is a regional technique used for postoperative analgesia in patients undergoing abdominal surgeries. TAP blocks can be done with ultrasound imaging to make the procedure more effective and safe.<sup>3</sup>

Post-caesarean pain consists of both somatic and visceral component. Visceral pain arises from uterine incision and contractions. The somatic component originates from nociceptors within the surgical wound. Nerves supplying the anterior abdominal wall are originated from T6 to L1 and pass through the plane between the layers of the transversus abdominis and internal oblique muscles.<sup>4</sup> Introduction of local anaesthetics into the transversus abdominis plane (TAP), it is possible to block the sensory nerves (T6-L1) of the anterior abdominal wall and pierce the musculature to innervate the entire anterior abdominal wall. Although this block does not specifically target the individual nerves of the iliohypogastric and ilioinguinal nerve plexus, the spread of local anesthetic between the IO and TA muscles consistently anesthetize these pain fibers.<sup>5,6</sup> Regional nerve blocks technique reduces the requirement of opioids for optimal analgesic control that reduce unwanted adverse effects such as sedation, nausea, and vomiting.<sup>7,8</sup> Local anaesthetics used in regional anaesthesia provide good operative conditions but have shorter duration of post-operative analgesia. For this reason various adjuvants such as opioids, clonidine and ketamine are added to local anaesthetics to achieve a quick, dense and prolonged block, but their use is limited due to their side effects such as nausea, vomiting and pruritus.<sup>9</sup> Dexamethasone has been mostly used adjuvant to local anaesthetics in various nerve blocks resulting in variable effects on onset but prolonged duration of analgesia and motor block.<sup>10</sup> The analgesic efficacy of this block is described in the literature for various procedures including open appendectomy, laparoscopic cholecystectomy, nephrectomy, caesarean section and abdominal hernia repair.<sup>11-13</sup>

Evidence supports the presence of NMDA receptors in skin and muscles. N-methyl-D-aspartate (NMDA) receptors are found in deep tissues which play a role in deep tissue pain. Magnesium sulphate is the fourth major cation in our body. It has anti-nociceptive effects in animal and human models of pain. The role of supplemental Magnesium Sulphate in providing perioperative analgesia as this is a relatively harmless molecule, is not expensive and also because the biological basis for its potential anti-nociceptive effect is promising.<sup>14</sup> These effects are based on physiological calcium antagonism, that is voltage-dependent regulation of calcium influx into the cell, and noncompetitive antagonism receptors.<sup>15</sup>

Magnesium Sulphate shows antinociceptive effects in animal and human models by blocking the N-methyl-D-aspartate (NMDA) receptor and associated calcium channels which prevent central sensitization caused by peripheral nociceptive stimulation. The addition of Magnesium Sulphate to local anaesthetics for neuraxial anesthesia prolongs the duration of anesthesia and the quality of analgesia is also improved.<sup>16</sup>

The benefit of USG-guided TAP block regarding analgesia in LUCS done under Sub arachnoid block has already been established. USG guided TAP block is beneficial because it is related to enhanced accuracy of LA deposition. The analgesic effect of bupivacaine in TAP block has been studied.<sup>17</sup> So, the goal of this study was to determine the analgesic effect of 150 mg Magnesium Sulphate with standard TAP block solution (bupivacaine 0.25%) could prolong the duration of post-operative analgesia when used for patient of LUCS done under Sub arachnoid block.

## Methods

After approval by Ethical review committee this prospective, double-blinded, randomized controlled trial was conducted at the department of Anaesthesia, Analgesia, and Palliative & Intensive Care Medicine in collaboration with the department of Gynaecology and Obstetrics, Dhaka Medical College Hospital (DMCH) from March 2017 to

September 2019. This study was carried out in 60 adult patients (20–30 years age group) who provide informed written consent, belonging to American Society of Anesthesiologists physical status I or II scheduled for LUCS under Sub arachnoid block. But patient excluded who had following criteria: Obese patient (BMI >30 Kg/m<sup>2</sup>), Pre-eclampsia/ Eclampsia, coagulopathy, allergic to bupivacaine or magnesium sulphate, infection at the needle insertion site. Then the patients were randomly allocated into two groups that were group A and group B by computer generated random number table.

During pre-anesthetic visit, the patients were explained about the study purpose, advantages and risks of procedure and informed written consent was taken. Patients were educated about the 10 cm VAS during the preoperative assessment. All the patients were kept nothing per oral for 8 hours before surgery and no premedication was given. In the operation theatre, after securing 18-gauge intravenous (IV) cannula, Hartman solution infusion was started.

After establishing standard anaesthesia monitoring, baseline measurements such as heart rate (HR), non-invasive blood pressure, respiratory rate, temperature and peripheral oxygen saturation (SpO<sub>2</sub>) were recorded.

All patients undergoing LUCS were given Sub arachnoid block under all aseptic conditions in the left lateral position using 25-gauge Quincke spinal needle at L3–L4 interspace and 12.5 mg of 0.5% hyperbaric bupivacaine was injected after confirming free flow of CSF. After confirmation of adequate level (T4) of block surgery was started. When the surgery was over and the Sub arachnoid block sensory level regressed to T8 dermatome procedures for USG-guided TAP block (Sonosite Micromaxx, Sonosite Inc., WA, USA) with a linear ultrasound transducer (8–12MHz) was performed under all aseptic precautions. After draping the abdominal part between the 12<sup>th</sup> rib and iliac crest with umbilicus at the centre-external oblique muscle, internal oblique muscle,

transversus abdominis muscle, and their fascia were identified beneath the skin and the subcutaneous tissue under ultra-sonogram guidance. The needle was advanced by a USG-guided in-plane technique at the anterior axillary line. The exact location of the needle tip was confirmed via direct visualization with ultrasound. After checking the exact location of the needle tip, 1 ml of NS was injected to open the plane and after confirmation of hypoechoic area on USG image, the study solution of 20 ml was injected. Equal amount of the same solution was also injected on the opposite side using identical technique. The patients in Group B received 18 mL 0.25% bupivacaine with 2 mL NS on either side, whereas the ones in Group BM received 18 mL 0.25% bupivacaine with 1.5 ml (150 mg) of Magnesium Sulphate and 0.5 ml NS on either side.

Postoperatively, the evaluation of patient was done for pain, nausea or vomiting in the post-anaesthesia care unit at time 0 (time of completion of TAP block), 2 hours, 4 hours, 6 hours, 8 hours, 16 hours and 24 hours. Duration of analgesia was assessed by 0-10 Visual Analogue Scale.

The primary outcome measure of this study was the postoperative VAS score. The secondary outcome measures in this study included the number of supplemental analgesic requirements, duration of post-operative analgesia that is time of rescue analgesic request from the time of giving block, nausea & vomiting. All the patients were monitored closely in the perioperative period for hemodynamic stability and any side effects.

Each patient received I/V 1g Paracetamol in post-operative room at 0 hour. Rescue anti-emetics (Inj. Metoclopramide 10mg IV) were given. The presence and severity of pain were assessed using a visual analogue pain scale (VAS) and the rescue doses of opioid (morphine) requirements were documented. Rescue dose of morphine used in this study was I/V 0.1 mg/kg & incremental dose was given when VAS>4 in 1st 24 hours. Incidences of nausea, vomiting and pruritus were also recorded. It was considered as standard post-

operative care for patients of LUCS receive 6 hourly I/V 1gm paracetamol.

## Statistical Analysis

Following the collection of all necessary data, all of them were entered into SPSS 22.0 (IBM SPSS, Chicago, IL, USA). During analysis and thesis writings, continuous variables were expressed as mean  $\pm$  SD or median with interquartile range as appropriate. & categorical variables were expressed with frequency and/or percentage. Difference between the groups was estimated by using either student t test (in case of continuous data) or chi-square test was used (in case of categorical data). In all cases, P values were two tailed, and P value < 0.05 was considered significant.

Sample size was estimated using pain scores as the primary variable. Assuming a standard deviation (SD) of 10 mm, the minimum needed sample size to detect a difference of 10 mm on the VAS of 10 cm, with type I error of 0.05 and power of 80% was 54. Hence, each group required at least 30 patients. We included 60 patients in our study to account for probable block failures and drop out.<sup>18</sup> [Here, BMI was calculated by BMI= Weight in Kg/Height in m<sup>2</sup> (Kg/m<sup>2</sup>)].

## Results

In this study, population total 60. A patient who in Group B received 18 mL 0.25% bupivacaine with 2mL NS on either side, whereas the other one in Group BM received 18 mL 0.25% bupivacaine with 1.5 ml (150 mg) of Magnesium Sulphate and 0.5 ml NS on either side.

Mean age was  $25.57 \pm 2.76$  years in group-B and majority were >25 years of age (63.3%) and  $25.9 \pm 3.17$  years in group BM and majority were in >25 years age group (53.3%) also. No statistical difference was found between the two study groups regarding age (p-value>0.05) (Table I).

**Table I: Age distribution of study population according to groups (n=60).**

Age group	Group B		Group BM		p-value*
	N	%	N	%	
$\leq 25$ years	11	36.7 %	14	46.7%	<b>0.601*</b>
>25 years	19	63.3 %	16	53.3%	
<b>Total</b>	<b>30</b>	<b>100%</b>	<b>30</b>	<b>100%</b>	
<b>Mean <math>\pm</math> S D (years)</b>	<b><math>25.57 \pm 2.76</math></b>		<b><math>25.9 \pm 3.17</math></b>		<b>0.666**</b>

\*p-value determined by chi-square test. \*\*p-value determined by student 't' test

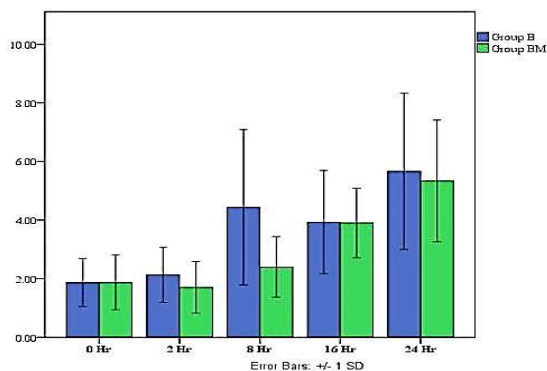
Different demographic profile as height, weight, BMI (body mass index), gestational age and duration of surgery of study population was tabulated above. All the parturient were comparable to each other with respect to above variables. (Table II)

**Table II: Other demographic profile of study population according to groups (n=60).**

Variables	Group B	Group BM	p-value*
<b>Height (cm)</b>	153.3 5.25 $\pm$	153.53 4.94 $\pm$	<b>0.860</b>
<b>Weight (kg)</b>	57.5 3.77 $\pm$	58.43 3.51 $\pm$	<b>0.325</b>
<b>BMI (kg/m<sup>2</sup>)</b>	24.48 1.48 $\pm$	24.85 2.01 $\pm$	<b>0.430</b>
<b>Gestational age (weeks)</b>	38.40 1.73 $\pm$	37.93 1.76 $\pm$	<b>0.305</b>
<b>Duration of surgery (min)</b>	39.40 9.71 $\pm$	38.13 6.67 $\pm$	<b>0.558</b>

Values expressed as mean  $\pm$  SD.\*p-value determined by one-way ANOVA.

**Figure 1: Mean visual analogue score over 24 hours postoperatively. Values expressed as Mean  $\pm$  SD.**



The VAS (Visual Analogue Score) was measured postoperatively for 24 hours. The difference in mean VAS at 0 h and 2 h (VAS-0, VAS-2 h) was found to be statistically insignificant (mean  $\pm$  SD:  $1.87 \pm 0.82$ ,  $2.13 \pm 0.93$  vs.  $1.87 \pm 0.94$ ,  $1.70 \pm 0.88$ ) in Groups B and BM, respectively ( $P > 0.05$ ). However, there was statistically significant decrease in VAS scores at 4 and 8 h (Group BM:  $1.47 \pm 0.93$ ,  $2.40 \pm 1.03$  vs. Group B:  $2.40 \pm 1.48$ ,  $4.43 \pm 2.65$ ; [P-value 0.005 and P-value  $< 0.001$ ]). Higher VAS was recorded in Group B than in group BM at 16h and 24 h. (Figure 1).

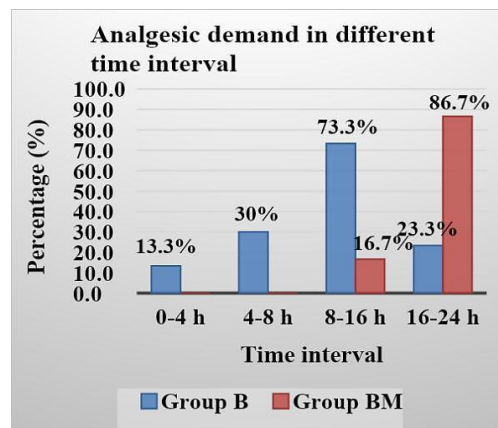
Postoperatively, time required for first analgesic dose was significantly more in Group BM  $263.13 \pm 34.39$  min than Group B  $222.23 \pm 30.58$  min. There was a significant decrease in total analgesic requirement in Group BM  $5.84 \pm 2.93$  mg compared to Group B  $11.5 \pm 3.24$  mg.

**Table III: Time interval of first analgesic requirement and total rescue analgesic requirement (n=60).**

Parameter	Mean $\pm$ SD		P-value *
	Group B	Group BM	
Postoperative first requested analgesic dose required (min)	222.23 $\pm$ 30.58	263.13 $\pm$ 34.39	$< 0.001^*$
Total analgesic requirement Postoperatively in 1 <sup>st</sup> 24 hours (mg)	11.5 $\pm$ 3.24	5.84 $\pm$ 2.93	$< 0.001^*$

\*P-value determined by student 't' test

**Figure 2: Number of analgesic demands at different time intervals.**



In the first 4 hours postoperatively, there were 4 demands for rescue analgesic in Group B (13.3%) and none in Group BM. Between 4 and 8 hours, 9 patients in Group B (30%) demanded rescue analgesia with none in Group BM. Between 8 and 16 hours, 22 patients in Group B (73.3%) and 5 in Group BM (16.7%) demanded rescue analgesic. Between 16 and 24 hours, 7 patients in Group B (23.3%), and 26 in Group BM (86.7%) demanded rescue analgesia. The number of requirements of rescue analgesic was more in Group B as compared to BM in the first 16 hours, and patients in BM group required analgesia after 16 hours.

**Table IV: Incidence of side effect in between groups (n=60).**

Variables	Group B		Group BM		P-value*
	N	%	N	%	
Nausea	12	40%	11	36.7%	0.5
Vomiting	6	20%	5	16.7%	0.5
Pruritus	1	3.3%	2	6.7%	0.5

P-value determined by chi-square test\*

Incident of side effects in our study population is tabulated in table-6. The result shows no significant difference in between groups.



## Discussion

The aim of the present study is designed to evaluate the analgesic effect of magnesium sulphate with bupivacaine in ultrasound guided TAP block. Water *et al.* described a technique in 2008 where TAP blocks can be done with ultrasound imaging to make the procedure more effective and safe.<sup>19</sup>

In this study, we discussed about 60 patients who were admitted for LUCS under Sub arachnoid block and receiving ultrasound guided TAP block. We divided the patients into two groups: Group B- who received Bupivacaine 0.25% 18 ml with 2 ml normal saline (in each side) and Group BM- who received Bupivacaine 0.25% 18 ml with 150 mg magnesium sulphate (1.5 ml) with 0.5 ml normal saline (in each side). 30 patients were included in each group.

Sixty three percent of patients in group B were >25 years of age with mean value of  $25.57 \pm 2.76$  years while in group BM, 53.3% were >25 years of age with mean value of  $25.90 \pm 3.17$  years. The study was non-significant which implies that, all the parturient were comparable to each other irrespective of maternal age. Other demographic data as height, weight, BMI, gestational age and duration of surgery indicate all the parturient were comparable to each other.

Magnesium sulphate with bupivacaine produces a reduction in postoperative pain when given intra-articularly in comparison to either bupivacaine or magnesium sulphate alone or to saline placebo.<sup>20</sup> The epidural administration of single dose magnesium sulphate with bupivacaine in labour analgesia resulted in significantly faster onset and longer duration of action of epidural analgesia compared to bupivacaine and fentanyl combination.<sup>21</sup> These studies support the prolong duration of action of bupivacaine along with Magnesium Sulphate than normal saline.

In our study, the VAS score was measured for 24 hours. The difference in mean VAS at 0 h and 2 h (VAS-0, VAS-2 h) was found to be statistically insignificant (mean  $\pm$  SD:  $1.87 \pm 0.82$ ,  $2.13 \pm 0.93$  vs.  $1.87 \pm 0.94$ ,  $1.70 \pm 0.88$ ) in Groups B and BM, respectively ( $P > 0.05$ ). But there was statistically significant decrease in VAS scores at 4 and 8 h in group BM than in group B (p-value 0.005). Higher VAS was recorded in group B than in group BM at 16 h and 24 h. So, in this study, the addition of Magnesium Sulphate with bupivacaine in a dose of 150 mg has led to lower VAS pain scores, prolongation of duration of analgesia and less requirement of rescue analgesia. This study shows significantly lower VAS scores with the use of Magnesium Sulphate at 4, 8 and 16 h after the block. The results of this study are comparable to the other studies as the authors also found significant reductions in postoperative VAS scores with the use of Magnesium Sulphate in intra articular blocks and femoral nerve blocks, respectively (Bondok and Abd El-Hady, 2006; Elshamaa, Ibrahim and Eldesuky, 2014).<sup>22,23</sup>

Postoperatively, time required for first rescue analgesic dose was significantly more in Group BM than Group B. The mean value was respectively  $263.13 \pm 34.39$  and  $222.23 \pm 30.58$ . There was a significant decrease in total analgesic requirement in Group BM  $5.84 \pm 2.93$  mg compared to Group B  $11.5 \pm 3.24$  mg. The studies by Lee *et al.* and Kiran *et al.* are not exactly the same scenario as this current study but this study also demonstrated less requirement of analgesics in patients receiving IV Magnesium Sulphate as it prolongs the duration of analgesia and reduces postoperative pain and reduce the requirement of opioid analgesics (Lee *et al.*, 2012; Thiele *et al.*, 2013).<sup>24,25</sup>

Regarding the number of rescue analgesics in TAP block, maximum numbers of demand boluses were observed between 4 and 24 hours with plain bupivacaine<sup>26</sup> while this study shows maximum demands between 6 and 16 hours. The reason for initial discrepancy may

be the difference in anaesthesia technique that is general anaesthesia versus Sub arachnoid block (present study). The bupivacaine group required rescue analgesic from 4 to 16 hours and Magnesium Sulphate group demanded rescue analgesic after 16 hours postoperatively which indicate shorter pain-free period and more requirement of analgesia in the bupivacaine group. Use of Magnesium Sulphate in TAP block has a beneficial effect in reducing the number of systemic analgesic requirement. The prolonged duration with bupivacaine in TAP block has also been attributed to the poor vascularity of TAP as demonstrated in the study using ropivacaine in TAP.<sup>27</sup>

This data supports specific action of Magnesium Sulphate on peripheral nerves leading to improve VAS pain scores and reduce post-operative analgesic requirement. TAP block has no effect on visceral component of pain as it is a peripheral nerve block technique which mainly reduces the pain from skin and muscle of the abdominal wall by blocking thoracolumbar nerves (T6-L1).<sup>28,29</sup> So, it is more beneficial when supplemented with systemic analgesics as a part of multimodal regimen for post-operative pain management.

### Limitations of the study

These were all patients of Group-BM got magnesium sulphate 150 mg irrespective of body weight & all patients of both groups got 0.25% Bupivacaine irrespective of body weight. Another limitation of the study was due to lack of facility to measure plasma concentration of magnesium sulphate.

### Conclusion

Magnesium Sulphate is effective as an adjuvant with bupivacaine in transversus abdominis plane (TAP) blocks for prolongation of postoperative analgesia.

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### Conflicts of interest

There are no conflicts of interest.

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