Adding Magnesium Sulfate to Bupivacaine in the Thoracic Paravertebral Block in Open Renal Surgery

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ABSTRACT

Background: Renal surgery is frequently followed by postoperative nausea and vomiting (PONV), and restricted movement from pain. One of the most promising techniques in providing better postoperative analgesia for renal surgery patients is the paravertebral block (PVB). It is associated with better control of post-operative pain, less opioids requirement, decrease in postoperative nausea and vomiting (PONV), pulmonary complications and better outcome. Paravertebral blocks (PVBs) are effective techniques in controlling pain after lower thoracic and upper abdominal surgery. Magnesium has been used as an adjuvant to local anaesthetics in renal surgery and was found to improve analgesic efficacy.

Methods: Sixty patients (ASA I or II) undergoing elective open renal surgeries were included in a double blinded randomized study. Patients were randomly divided into two groups magnesium group (BM) and control group (B) of 30 patient each. BM group: received 0.3 ml/kg of 0.25 % Bupivacaine plus 100mg magnesium sulphate in the paravertebral space. Control group: received 0.3 ml/kg of 0.25 % Bupivacaine in the paravertebral space. Visual analog scale (VAS) was recorded at 30 min and subsequently 2, 4, 6, 12, and 24 h after the recovery. Rescue analgesia (pethidine) was given when VAS was >4. Time of administration was recorded and total dose of rescue analgesia was calculated. Onset and duration of sensory & motor block and also complications (hypotension, nausea and vomiting) related to regional anesthesia were recorded.

Results: Duration of block was significantly increased in Mg group more than in control group. First analgesic requirement time after surgery was significantly longer in Mg group compared to control group. The cumulative VAS score and total postoperative analgesic consumption were significantly less in Mg group than in control group. There were insignificant differences between the two groups as regarding hypotension, nausea & vomiting.

Conclusion: our study results suggest the significant role of magnesium sulphate as adjuncts to bupivacaine during paravertebral block for open renal surgery. In addition to relative safety, it improves postoperative pain scores (in the first 24 hours), decrease postoperative opioid consumption, and decrease postoperative nausea and vomiting.

Keywords: Magnesium Sulfate, paravertebral block, Bupivacaine, Analgesia, Renal Surgeries

1. INTRODUCTION

Renal surgeries (RS) are usually associated with significant postoperative pain. Ineffective postoperative pain management may result in clinical and psychological changes that increase morbidity and mortality. Postoperative analgesia following (RS) essential to allow effective coughing, early mobilization, and to reduce the incidence of postoperative respiratory complications. A considerable portion of those patients may suffer from comorbidities,
such as impaired renal function, hypertension, and ischemic heart diseases. So, morbidity rates can be reduced by analgesia after (RS) in such a high-risk group. A variety of techniques for postoperative analgesia following RS were applied. Administration of systemic analgesia after RS may be precluded by impaired renal function and respiratory complications from the use of opioids. Other techniques include intramuscular and/or intravenous injection of paracetamol or nonsteroidal anti-inflammatory drugs. However, none of these methods was proven to be highly effective. On the other hand, postoperative analgesia by utilizing epidural blockade (EP) demonstrated high rates of safety and efficacy in upper abdominal surgery, including RS.

Paravertebral blocks (PVBs) are effective techniques in controlling pain after lower thoracic and upper abdominal surgery. The use of paravertebral catheter to provide unilateral or bilateral analgesics has been described in adults and children. A single shot technique using bupivacaine, levobupivacaine, or ropivacaine can provide analgesia for up to 18 h. However, PVB has not been extensively studied as an analgesic tool in renal surgery.

Several adjuvants as fentanyl and clonidine have been reported to improve the clinical profile of paravertebral block in renal surgery but addition of these adjuvants was associated with more adverse effects as hypotension and vomiting. Paravertebral clonidine was also found to have a sedative effect. Hence the need to try another adjuvant with better analgesic profile and with less adverse effects.

Magnesium is a competitive NMDA (N-methyl D-aspartate) receptors antagonist. NMDA receptors are excitatory amino acid receptors which are activated by various excitatory amino acid neurotransmitters such as glutamate and aspartate in response to painful stimuli. Activation of NMDA receptors leads to calcium influx into the cells, the action which can be blocked by magnesium. Magnesium has been used as an adjuvant to local anaesthetics in renal surgery and was found to improve analgesic efficacy.

Objectives
This study was designed to evaluate the safety and efficacy of magnesium sulphate as an adjuvant in potentiating the analgesic effect of bupivacaine in paravertebral block in painful renal surgeries.

2. METHODS

Eligibility and Randomization
After approval from the local ethics committee of faculty of medicine, Assiut University, written informed consent from all patients before participation was obtained. The study started on January 2015 and finished on August 2016.

Setting
Urology & Nephrology Hospital, Assiut University.

Study Design
This study was a randomized double-blind controlled study. It was carried out on sixty patients (ASA I or II) 18-60 years old of both sex underwent open renal surgery under general anesthesia were included in the study. Neither the investigator nor the participant was aware of the group allocation or the drug used. The drugs used were prepared by one of the supervisor anesthesiologists (not included in the procedure, observation or in the data collection).

Patients
Sixty patients were randomly divided into two equal groups: Magnesium sulfate group (BM); 30 patients received 0.3 ml/kg of 0.25 % Bupivacaine plus 100mg magnesium sulphate in the paravertebral space. Control group (B); 30 patients received 0.3 ml/kg of 0.25 % Bupivacaine in the paravertebral space.

Inclusion criteria
Age 18 to 60 years, ASA physical status I-II, scheduled for elective open renal surgery under general anesthesia.

Exclusion criteria
Patient refusal, patients with a history of cardiac, liver diseases, allergy to amide local anesthetics or medication included in the study, any contraindication of regional anesthesia.

Anesthetic Technique
Standard preoperative data were collected prospectively for all patients undergoing open renal surgery. Upon arrival of patients into the operating room & basic monitoring was initiated using non-invasive blood pressure measurements, continuous electrocardiography and pulse oximetry. After intravenous line was secured with cannula 18G, general anesthesia was induced by propofol 1.5-2 mg/kg IV and cisatracurium 0.1 mg/kg IV to facilitate

The patients were then assigned to two groups by closed-envelope randomization. In both groups, anesthesia was maintained with Controlled ventilation was done with tidal volume of 8-10 mL/kg and I/E ratio 1:2 to maintain end-tidal carbon dioxide tension around 35 mmHg. All patients were placed in the lateral position with the side of the surgery upwards. all patients received ultrasound-guided (US) thoracic paravertebral block (TPVB). The spinous process of T10 is palpated and marked at its superior aspect. The site of paravertebral block was sterilized using iodine solution and the ultrasound probe was covered by a disposable sterile cover. After location of the paravertebral space, a 24 G Touhy needle was inserted 2.5 cm lateral to the cephalic edge of the T10 thoracic vertebral spinal process and perpendicular to hit the transverse process. After hitting this bony structure, the needle was redirected cephalic at 15° towards the paravertebral space. After localization of the needle in the paravertebral space and negative aspiration, injection of the medication prepared for each group of the study was carried out. The correct placement of the injected drug was confirmed by expansion of the paravertebral space between the pleura and the superior costo-transverse ligament (11).

Electrocardiography, noninvasive blood pressure, pulse oximetry, and endtidal carbon dioxide (ETCO2) was monitored throughout surgery. At the end of surgery neuromuscular block was antagonized in all patients with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg.

Data Monitoring
Vital signs: as non-invasive mean arterial blood pressure (MABP), HR, SaO₂, RR were assessed at the first 15 minutes and 30 minutes thereafter every half an hour until the end of the surgery.

After recovery from anaesthesia, all patients were assessed for the following parameters:

- Hemodynamics: mean arterial blood pressure and heart rate were monitored every 30 min, 1 h, 4, 8, 12, 16, and 24 hr postoperatively.
- Peripheral oxygen saturation and respiratory rate: were monitored during the first 24 hr postoperatively.
- Pain: post-operative pain was assessed over 24 h using Visual analogue scale (VAS) score was used to assess the pain scores in the patient at 30 min and subsequently 2, 4, 6, 12, and 24 h after the recovery. The VAS is approach to pain measurement [12]. The most common VAS consists of a 10-cm line with one end labeled “no pain” and the other end labeled “worst pain imaginable.” The patient marks the line at the point that best describes the pain intensity. The length of the line to the patient’s mark is measured and recorded in millimeters.

- Time till the first analgesic requirement: which was the time interval from recovery of the patient from anaesthesia till time of his first analgesic request. Total opioid consumption during the first postoperative 24 hrs. When the patients experienced pain (VAS ≥4) pethidine was given intramuscularly 50-100 mg. Total pethidine consumption were recorded.
- PONV: was assessed as number of attacks of nausea or vomiting in the first 24 h after surgery and metoclopramide 10 mg i.v. was given for every attack of nausea or vomiting. The patients were evaluated for any other complications or side effects up to 24 h after the surgery.

Any other postoperative events like shivering or respiratory distress (through counting the respiratory rate) were recorded.

Statistical analysis
Statistical Package for Social Sciences (SPSS) version 20.0 was used for data analysis. Mean± standard deviation was used for the description of VAS scores, time to first analgesic requirement and total 24 h pethidine consumption. Median and range was used for the description of attacks of vomiting. Parametric and non-parametric independent t test compared mean and medians of the 2 study groups. P values were set significant at 0.05 level.

Confidentiality & Ethical Consideration
All data taken from all participants in this research work either from history, examination or investigations were dealt with in a confidential manner. There was no risk affecting patients in the study.

3. RESULTS
Sixty patients were included in our study and were randomly assigned to two equal groups. All patients completed the study and no one was excluded due to any serious complications from the maneuver. There were no statistically significant differences between groups as regard patients’ demographic data. (Table 1)

Table (1): Patients demographic data

<table>
<thead>
<tr>
<th></th>
<th>BM</th>
<th>B</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36.76±13.02</td>
<td>33.74±11.66</td>
<td>0.348</td>
</tr>
<tr>
<td>Weight</td>
<td>75.69±10.86</td>
<td>75.74±10.88</td>
<td>0.985</td>
</tr>
<tr>
<td>Sex</td>
<td>No. %</td>
<td>No. %</td>
<td>0.795</td>
</tr>
<tr>
<td>Male</td>
<td>17 56.7</td>
<td>16 53.3</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13 43.3</td>
<td>14 46.7</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as Mean ± standard deviation (SD), numbers, and percentages.

The intra-operative and post-operative mean arterial blood pressure monitoring was significantly decrease in group (BM) [(81+5.8 mmHg), (77.5+7.5 mmHg)] respectively in comparison to group (B) [(86.5+6.4 mmHg), (85.6+4.7 mmHg)] (p=0.001, p=0.000).

The reading of the heart rate during intra-operative monitoring showed no statistical significant difference between the two study groups till the end of operation with p value > 0.05.

During the post-operative period, the mean arterial blood pressure in group (B) was 78.2+8.1 b/ min, while in group (BM) was 71.2+4.6 b/ min mmHg, with p value of 0.000 which indicate that there was statistical significant difference between the two study groups.

The reading of the arterial oxygen saturation during intra-operative monitoring showed no statistical significant difference between the two study groups till the end of operation with p value of > 0.05. During the post-operative period, the arterial oxygen saturation in group (B) was 99.5+0.5 %, while in group (BM) was 99.6+0.6 %, with no statistical significant difference between the two study groups till the end of operation with p value > 0.05.

The reading of the respiratory rate during intra-operative monitoring was the same 12+0 breath/min, while in group (BM) was 13.6+1.7 breath / min, with no statistical significant difference between the two study groups as p value > 0.05.

Table (2): mean arterial pressure, heart rate, peripheral oxygen saturation and respiratory rate

<table>
<thead>
<tr>
<th>Vital signs</th>
<th>Intra-operative</th>
<th>Post-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BM</td>
<td>B</td>
</tr>
<tr>
<td>MABP</td>
<td>81±5.8</td>
<td>86.5±6.4</td>
</tr>
<tr>
<td>HR</td>
<td>81.3±10.8</td>
<td>85.5±12.1</td>
</tr>
<tr>
<td>SaO2</td>
<td>99.3±0.7</td>
<td>99.2±0.6</td>
</tr>
<tr>
<td>RR</td>
<td>12±0</td>
<td>12±0</td>
</tr>
</tbody>
</table>

Data are expressed as Mean ± standard deviation (SD). ** Statistically significant difference (p<0.01).

As regard pain profile, The addition of magnesium sulphate to bupivacaine 0.25% in the paravertebral space significantly reduced VAS scores at 4, 6, 12, 16 hours assessment points (p<0.001, 0.020), with Mean±SD of accumulated VAS score in group (B) was 3.5+0.2, while in group (BM) was 2.8+0.4 (p<0.001).

The times to first analgesic request after surgery was significantly increased in group (BM) (4.19±0.79 hours) compared to group (B) (7.24±1.14 hours) with P value < 0.001.

Furthermore, patients in group (BM) required less amount of intra muscular pethidine in the first 24 h of postoperative period (88.2±33.4 mg) compared to bupivacaine group (157.5±44.5 mg) with p-value <0.001. (Table 3)
Table (3): Pain profile

<table>
<thead>
<tr>
<th></th>
<th>BM Mean±SD</th>
<th>B Mean±SD</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>2.21±0.41</td>
<td>2.45±0.68</td>
<td>0.098</td>
</tr>
<tr>
<td>30 min</td>
<td>3.14±0.64</td>
<td>3.42±0.76</td>
<td>0.129</td>
</tr>
<tr>
<td>1 hr</td>
<td>2.52±0.83</td>
<td>2.58±0.81</td>
<td>0.765</td>
</tr>
<tr>
<td>4 hr</td>
<td>2.62±0.68</td>
<td>3.84±1.46</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>6 hr</td>
<td>3.03±1.4</td>
<td>4.39±1.48</td>
<td>0.001**</td>
</tr>
<tr>
<td>12 hr</td>
<td>3.21±0.73</td>
<td>4.84±1</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>16 hr</td>
<td>2.76±1.38</td>
<td>3.55±1.18</td>
<td>0.020*</td>
</tr>
<tr>
<td>24 hr</td>
<td>2.41±0.57</td>
<td>2.52±0.85</td>
<td>0.589</td>
</tr>
<tr>
<td>Accumulated VAS</td>
<td>2.8±0.4</td>
<td>3.5±0.2</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Time to 1st rescue analgesia (hours)</td>
<td>7.24±1.14</td>
<td>4.19±0.79</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>No. analgesia</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>26.7</td>
<td>0</td>
</tr>
<tr>
<td>Once</td>
<td>17</td>
<td>56.7</td>
<td>1</td>
</tr>
<tr>
<td>Twice</td>
<td>5</td>
<td>16.7</td>
<td>23</td>
</tr>
<tr>
<td>Three times</td>
<td>0</td>
<td>0.0</td>
<td>6</td>
</tr>
<tr>
<td>Total analgesic Consumption (mg)</td>
<td>88.2±33.4</td>
<td>157.5±44.5</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

Data are expressed as Mean ± standard deviation (SD), numbers, and percentages. * Statistically significant difference (p<0.05). ** Statistically significant difference (p<0.01).

Seven patients in group (BM) in the first 24 hours postoperatively; showed one attack of PONV (23.3%) compared to twenty-one patients showed one attack of PONV (70%) and four patients showed two attacks of PONV (13.3%) in group (B) (P value = 0.001). (table 4)

Shivering occurred in five patients in group(BM) (16.7%) and seven patients in group (B) (23.3%) with no significant difference between the two groups (P value =0.729). (table 4)

Respiratory distress didn’t occur in any patient of the two groups. (table 4)
Table (4): Incidence of side effects

<table>
<thead>
<tr>
<th></th>
<th>BM</th>
<th>B</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>PONV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>23</td>
<td>76.7</td>
<td>5</td>
</tr>
<tr>
<td>Once</td>
<td>7</td>
<td>23.3</td>
<td>21</td>
</tr>
<tr>
<td>Twice</td>
<td>0</td>
<td>0.0</td>
<td>4</td>
</tr>
<tr>
<td>Shivering</td>
<td>5</td>
<td>16.7</td>
<td>7</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are expressed as numbers, and percentages. ** Statistically significant difference (p<0.01).

4. DISCUSSION

The results of our study demonstrated that the addition of magnesium sulphate (100 mg), as adjuvant to bupivacaine (0.25% 0.3 ml/kg) during paravertebral block had the best analgesic results in postoperative pain scores and reduces postoperative analgesic consumption than using bupivacaine (0.25% 0.3 ml/kg) alone for patients undergoing open renal surgery.

Our results confirm the findings of previous studies showing that addition of magnesium to local anesthetics improved the efficacy and quality of various regional anesthetic procedures, such as intrathecal, epidural, caudal, brachial plexus blocks and intravenous regional anesthesia (IVRA)\(^{13,14}\).

All patients in the two groups exhibited adequate postoperative analgesia as judged by the decreased VAS score and increased the time of rescue analgesia which was (4.19±0.79 hr) for B group and (7.24±1.14 hr) for BM group that was pronounced in decreasing the percentage of patients needed supplementary analgesia.

Our results are in agreements with Lee ARand Yi HWand their colleges (2012) in their study on the effect of adding magnesium sulphate to bupivacaine to prolong the duration of analgesia after interscalene nerve block. The interscalene nerve block was performed with 0.5% bupivacaine 20 mL with epinephrine (1:200,000) plus either 10% magnesium sulphate 2 mL (Magnesium Group) or normal saline 2 mL (Saline Group). The following data were recorded for 24 hr after surgery: onset times and durations of sensory and motor blocks, analgesic duration, the pain numeric rating scale (NRS), postoperative fentanyl consumption, and complications. They observe that the duration of analgesia was longer in the Magnesium Group than in the Saline Group (mean and standard deviation) 664 (188) min vs 553 (155) min, respectively; \( P = 0.017 \). Patients in the Magnesium Group had significantly reduced pain NRS scores at 12 hr (\( P = 0.012 \)), but the cumulative fentanyl consumption was similar in both groups. The onset times and durations of sensory and motor blocks were not significantly different between the two groups.

Also our results are in agreements with Buvanendran A, McCarthy and their colleges (2002) in their clinical study in obstetrics requesting labor analgesia, intrathecal magnesium sulphate (MgSO4) 50mg increased the duration of spinal opioid analgesia without additional side effects.

The direct action of magnesium on the peripheral nerves is supported by the study done by Belgin Buyukakilli and his colleges (2006). they found that magnesium added to bupivacaine resulted in better impulse inhibition in a frog sciatic nerve. This was in agreement with what Goyal P and his colleges (2008). They found that administration of a small dose of magnesium only in the axillary sheath during brachial plexus analgesia resulted in prolonged time of postoperative pain relief with reduction of post-operative analgesic requirement and without any major side effects.

Different theories have been suggested to explain the antinociceptive effect of magnesium that include interference with calcium channels and noncompetitive blocking of N-methyl-Daspartate receptors\(^{11}\). Also, these results are consistent with Manjushree Ray and his collages (2010) in their study on effect of...
clonidine and magnesium sulphate, they found that use of both clonidine and magnesium sulphate significantly reduced the requirement of propofol and fentanyl citrate. They were able to attenuate the hemodynamic response to tracheal intubation. Both clonidine and magnesium sulphate resulted in bradycardia and hypotension. Magnesium sulfate administration may cause cardiovascular depression by acting as a calcium channel blocker. The consequent inhibition of catecholamine release reduces plasma epinephrine and norepinephrine concentrations after endotracheal intubation, and therefore reduces hypertensive responses during anesthesia induction\(^{(15)}\).  

The efficacy of adding magnesium to bupivacaine in paravertebral block to control post-operative pain in thoracic surgery is evaluated in a study done by Ammar and Mahmoud (2014). The results of their study was in agreement with that of our study and this agreement support the good analgesic efficacy of adding magnesium as an adjuvant to bupivacaine in paravertebral block. They divide their patients into two equal groups. Group I received 12 ml of 0.5 % bupivacaine plus 0.9 % saline (3 ml) whereas Group II received 12 ml of 0.5 % bupivacaine plus 150 mg magnesium sulphate (in 3 ml 0.9 % saline) for TPVB. Group II patients showed a significantly longer sensory block duration (224.6 ± 59.3 vs 160.1 ± 55.2 min, P < 0.05), longer duration of analgesia (388.8 ± 70.6 vs ± 61.6 min, P < 0.05), less VAS during the postoperative 48 h, less need for postoperative analgesia during the first 24 hours, less need for postoperative morphine (16.2 ± 7.4 vs 29.5 ± 11.1 mg, P < 0.05). The duration of analgesia and the need of opioid are longer than that of our study may due to the higher doses of local anaesthetic and magnesium used in their study.

In contrast with our results, a study done by Birbicer et al. (2007), found no difference in analgesia by adding 50 mg of magnesium to 0.25 % ropivacaine for caudal anesthesia in pediatrics. The mechanism of this contradictory finding is unclear but appears to be independent of the action of ropivacaine and MgSO\(_4\) at the receptors within the Na channel but may be due to a relatively insufficient dose of MgSO\(_4\) used in that study.

Absence of complications related to the paravertebral block technique as pneumothorax and epidural spread may be due to the use of ultrasound guided technique which allows better localization of the needle in the paravertebral space\(^{(16)}\). Expansion of the paravertebral space and displacement of the pleura by the injected medications was an additional sure sign of a good and safe site of the needle, which minimize the risk of pleural puncture. This may reduce the incidence of respiratory distress. Respiratory distress didn’t occur in any patient of the two groups.

5. CONCLUSION

Our study results suggest the significant role of magnesium sulphate as adjuncts to bupivacaine during paravertebral block for open renal surgery. In addition to relative safety, it improves postoperative pain scores (in the first 24 hours), decrease postoperative opioid consumption, and decrease postoperative nausea and vomiting.

REFERENCES


