wjpmr, 2018,4(7), 288-294

SJIF Impact Factor: 4.639

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

EFFECT OF ADDING MAGNESIUM SULPHATE TO PEDIATRIC CAUDAL BUPIVACAINE

***[1]Dr. Syeda Murwa Jilani, [2]Dr. Hussnain Qadir and [3]Dr. Ramsha Saqib**

[1]PMDC # 92892-P.
[2]PMDC # 85107-P.
[3]PMDC # 87259-P.

***Corresponding Author: Dr. Syeda Murwa Jilani**
PMDC # 92892-P.

Article Received on 19/05/2018 **Article Revised on 09/06/2018** **Article Accepted on 30/06/2018**

ABSTRACT

Background: Caudal anesthesia/analgesia is simple to perform, reliable and safe. Various adjuvants have been utilized with local anesthetic to prolong duration of post-operative analgesia of caudal block in pediatric patients, but with variable results. **Aim and Objective:** This study is conducted to evaluate the hemodynamics effects and surgical stress response of caudal magnesium sulfate with bupivacaine in children undergoing lower abdominal surgeries. **Methods:** The study was approved by the local ethics committee, and a written consent was obtained for each subject, and included 60 children ASA classification I and II, aged 1 year to 6 years scheduled for lower abdominal surgeries randomized into one of two groups. after inhalation induction of general anesthesia, standard caudal block was done the participants were randomized into one of two groups either receive 1ml volume containing 50mg of magnesium sulfate (group Mg) added to 1ml /kg bupivacaine 0.25% or 1ml saline as placebo added to the same dose of bupivacaine in group (C). Postoperative pain assessed by FLACC score (acronym for Face, Legs, Activity, Cry and CONSOL ability) and duration of analgesia, postoperative sedation as well as hemodynamic parameters were compared between the two groups. **Results:** Group Mg had significantly lower FLACC score than group C in the first six postoperative hours. The sedation score was significantly higher only during the first postoperative hours in group Mg compared to group C. There was no statistically significant difference between groups about hemodynamic parameters at any time during the study period. **Conclusion:** Caudal magnesium sulfate 50mg enhance caudal block and prolongs duration of analgesia with bupivacaine in pediatric patient undergoing lower abdominal surgeries under general anesthesia with minimum adverse effects.

KEYWORD: Caudal, Anesthesia, bupivacaine, FLACC.

INTRODUCTION

Postoperative pain in children is difficult to assess and associated with strong emotional component.[1] Caudal epidural anesthesia is a common technique providing intra and postoperative analgesia in pediatric infra umbilical surgical procedures.[2] Prolongation of caudal analgesia using a "single-shot" technique has been achieved by the addition of various adjuvant such as opioids, ketamine, clonidine, and dexmedetomidine.[3] However, their use has been limited by adverse effects in children, for example, opioids carry the risk of postoperative respiratory depression and ketamine has the potential of neurotoxicity if inadvertently injected Intrathecally.[4]

There is an increasing interest to study magnesium analgesic effects. It has antinociceptive effects in human and these effects are primarily based on its ability to regulate calcium influx into the cell, so it could be considered as a physiologic calcium antagonist. On the other hand, it can block N-methyl D-aspartate (NMDA) receptor and such NMDA antagonism prevents the central sensitization from nociceptive stimulation. Many studies suggested that epidurally administered magnesium as an adjuvant to local anesthetics could reduce the postoperative pain in adults. But few studies are available about its use as an adjuvant in caudal block for such purpose.[5] We designed this study to compare the intensity, safety and duration of postoperative pain relief using caudal magnesium sulfate as adjuvant with isobaric bupivacaine 0 .5% in pediatric patients undergoing lower abdominal surgeries.

PATIENTS AND METHODS

This is randomized; double blind clinical study It was approved by our local institutional ethics committee and A written parental informed consent was obtained from one 60 children, ASA classification I and II, aged 1 year to 6 years, undergoing elective lower abdominal

surgeries. Study exclusion criteria were as followings: Parental refusal, allergy to local anesthetics, coagulation disorders, infection at site of injection, anatomic abnormalities and congenital anomalies e.g. spina bifida, the current use of calcium channel blockers or medication that may affect the neurologic system, the un avoided need for preoperative sedation or analgesia, and prolonged surgery (>90min). Randomization was attained though the research randomizer. The study drugs were prepared by clinical pharmacist who was not involved in the study in similar syringes (under complete aseptic conditions) that were only labeled with mixture's serial number. The drugs were handed to the anesthetist in charge who was blinded to the identity of the drug. All healthcare personnel providing direct patient care, parents, or guardians were blinded to the caudal medications administered. In the operating room, routine monitors were applied and baseline readings were recorded. Anesthesia was induced by face mask with sevoflurane 8% MAC in oxygen, then 22:24 gauge IV line was placed in the dorsum of the hand placement. The trachea was intubated without the use of a neuromuscular blocking agent and the lungs was ventilated by assisted manual ventilation until regular spontaneous breathing was achieved. Endotracheal tube was secured and the patient was placed in the lateral decubitus position and a single dose caudal block was performed using a 23g needle through standard loss of resistance technique.

Participants were randomly allocated into one of two groups

- **Group (C):** (n = 30) received 1 mL/kg bupivacaine 0.25% with 1 mL normal saline.
- **Group MG:** (n=30) magnesium sulfate (50mg) in 0.5 ml of 10% MgSO4, and 0.5 ml normal saline were added to same concentration of bupivacaine.

The child immediately turned supine after caudal anesthesia, and anesthesia was maintained with Isoflurane (0.6:1 % MAC Corrected for age) in air oxygen mixture (ratio 1:1), intravenous fluids were administered in flow rate of 3:5 ml/kg/hr. No extra analgesia or sedatives were administered.

The study period classified into two parts; Intraoperative part (in the operating room), and postoperative Part in the post anesthesia care unite (PACU) for the next three Hours. Hemodynamic parameters (Heart rate, arterial blood pressure and spo2) were recorded prior to induction (Baseline), after induction, before and after administration of caudal block, after skin incision and then every 10minutes till the end of surgery. During surgery, adequate analgesia was defined by hemodynamic stability, as indicated by the absence of an increase in heart rate (HR) or systolic blood pressure (SBP) of more than 20% compared with baseline values obtain just before the surgical incision, with Isoflurane concentration maintained at approximately 0.7 to 1 Minimum alveolar Concentration(MAC). The surgical incision was made at least 15 min after the Injection.

An increase in HR or SBP by more than 20% above pre-incision Values, the caudal block was deemed a failure, the child was withdrawn from the study, and the child managed with Fentanyl 1µg / kg.

Bradycardia was defined as 20% decrease in heart rate compared with preoperative values and treated with atropine 0.01 mg/kg I.V. hypotension was defined as 20% decrease in SBP compared with preoperative values and treated with rapid infusion of fluid, or if that was unsuccessful, with the use of ephedrine 5 mg I.V. as appropriate.

Anesthesia was discontinued when the wound dressing was applied; and all patients were transferred to PACU.

In the PACU monitoring included (SPo2, SAP and HR), with assessment of analgesia, sedation, and development of any side effects after Caudal block. Hemodynamic state (SBP, DBP, MBP, HR) were monitored every 15 minutes. Observations were performed by a PACU nurse blinded to the Analgesic used.

Any side effects of study drugs in the first 24 hours postoperative Hours was recorded: nausea, vomiting, lower limb weakness, Respiratory depression (Decrease in SPo2 of less than 90% Requiring supplementary oxygen), urinary retention, rash and Pruritus were noted and managed.

Analgesia assessments will make every 30 min in PACU by an FLACC is the acronym for Face, Legs, Activity, Cry and CONSOL ability. The patient is assessed in each of these categories with a score applied to behaviors evaluated. The five scores are totaled and the severity of pain is determined based on the 0-10 pain scale, patients with scores>7 were in severe pain. scores>4 indicate analgesic requirements with increasing urgency as scores increase, patients in severe pain were given paracetamol 15 mg/kg. This was repeated as necessary while in the PACU for adequate pain control. assessment was made every 30 min until 2 hours then 4,6,12,24 hours.[6,7] The time from caudal block to the first postoperative analgesic administration (paracetamol 15mg/kg) was the end-point of the study (Duration of analgesia). Ramsay Sedation Score was assessed every 30 min. a six-point patient sedation score (PSS), The PSS was used to quantify Sedation and to help to identify side effects, such as respiratory Depression from excess sedation, A Ramsey score of five or six was considered as a desirable

limit of sedation and score less than five was considered as insufficient rate of sedation.[8,9]

Statistical analysis

The data were tested for normality using the Anderson-Darling test and for homogeneity variances prior to further statistical analysis, the continuous variables were described by mean and standard deviation (Mean, SD) categorical data were compared with Chi Square test, continuous variables by Independent-Samples T test. A two-tailed $p < 0.05$ was considered statistically significant. We are used Pearson and spearman correlation to appear the association between variables. All analyses were performed with the IBM SPSS 20.0 software.

RESULTS

We enrolled 60 patients in this study with 30 patients in each group. There were no statistically significant differences between the two groups in patient's characteristics and operative time (Table 1).

Table 1: Shows demographic data between two groups.

	C	Mg	P. value
Male / female	24 / 6	26 / 4	
Age (years)	3.4±1.71	3.89±1.37	0.4
Weight (kilograms)	14.64±3.72	15.8±4.48	0.4
Operation Time (minutes)			
Mean ±SD	37.67±14.74	48.33±19.43	0.1

Intraoperative period figures shows perioperative changes in blood pressure and heart rate, and there were insignificant differences between the two groups (fig. 1-4).

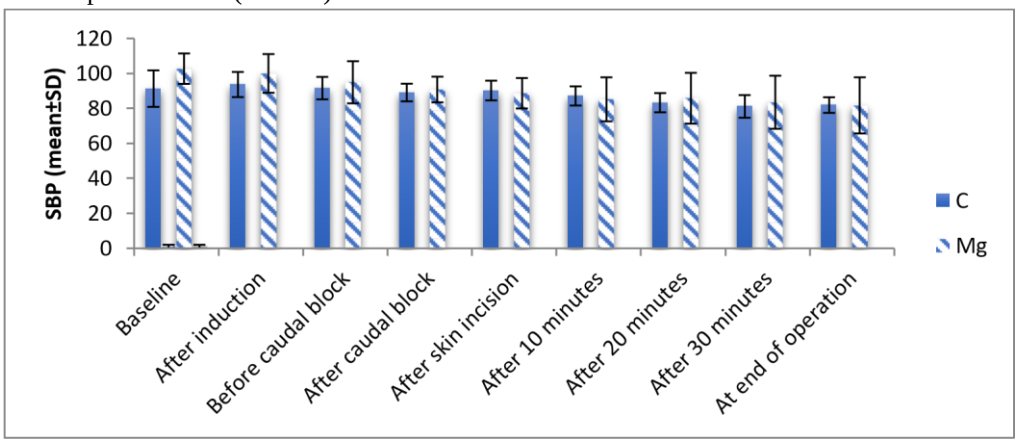

Fig. 1: Show perioperative changes in SAP.

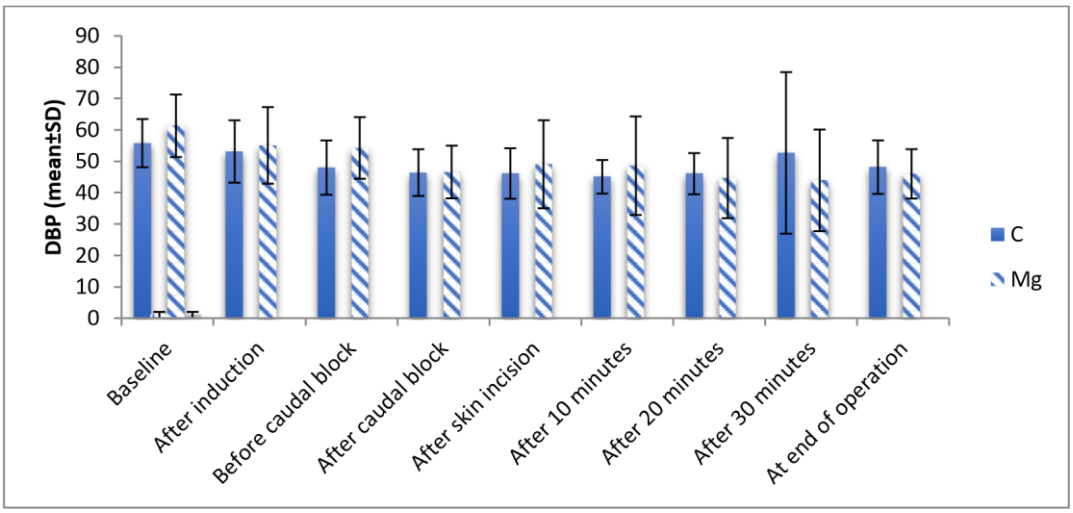

Fig. 2: Shows perioperative changes in DAP.

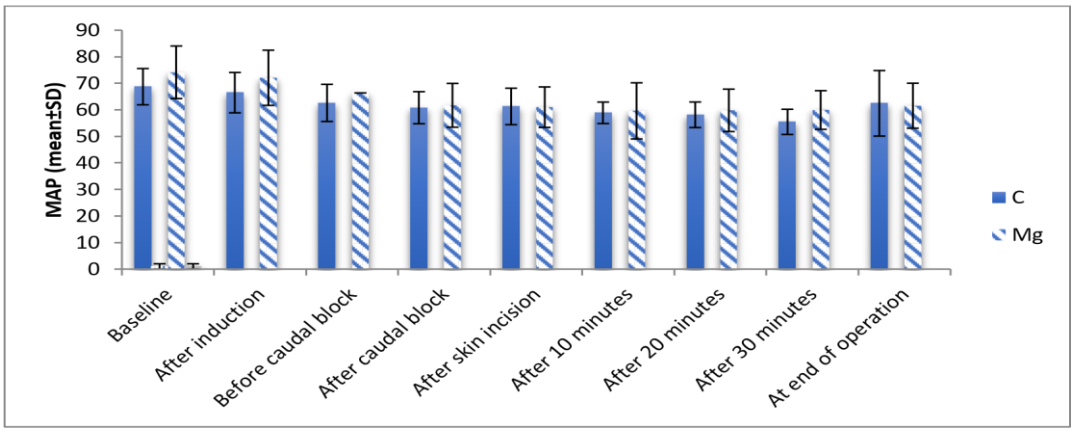

Fig. 3: Shows perioperative changes in MAP.

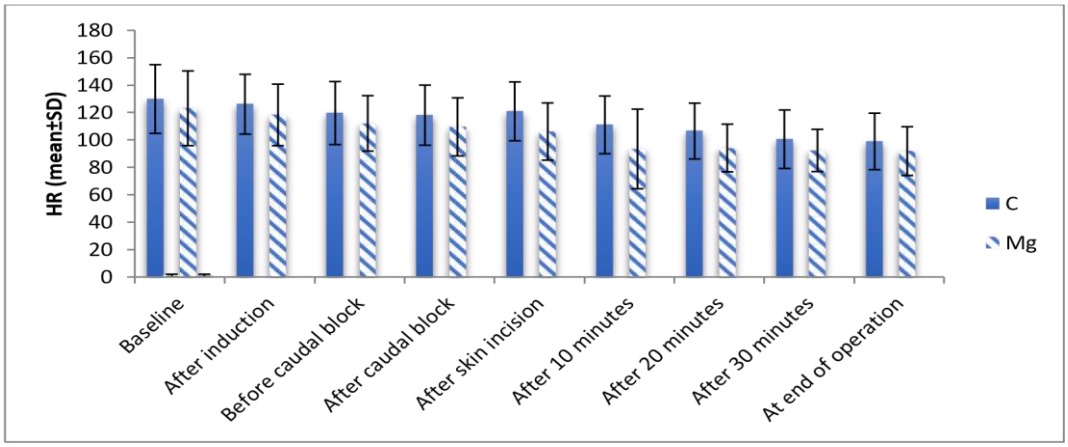

Fig. 4: Shows perioperative changes in heart rate.

Postoperative period

Hemodynamics parameters (HR, DAP, MAP) were significantly decreased on arrival to PACU, after 15 minutes and after 30 minutes in group Mg compared to Group C. while SAP was significantly decrease on arrival to PACU in group Mg compared to group C.

Table 2: Shows comparison between groups in postoperative hemodynamics parameters.

PACU	C	Mg	P. value
On arrival of PACU			
HR	102.5±17.08	89.4±8.01	0.012*
Spo2	97±2	99.67±1.05	0.233
SBP	97.73±5.51	90±21	<0.001**
DBP	60±4	54.4±6.63	0.003*
MAP	85±2	68.38±5.44	<0.001**
After 15 min			
HR	103.7±16.08	90.8±7.01	0.008*
Spo2	97±1	99.67±1.05	0.233
SBP	103±5.7	103.2±3.8	0.912
DBP	65±4.2	58.4±6.8	0.003**
MAP	77.7±4.7	73.3±5.8	0.030*
After 30 min			
HR	105.2±11.2	95.8±10.4	0.024*
Spo2	99±1	99.67±1.05	0.233
SBP	102±6.3	102.1±7.6	0.969
DBP	66±4.7	58.9±6.1	<0.001**
MAP	78±5.2	73.3±6.6	0.039*

*PACU (post anesthesia care unit)

FLACC score

On evaluation of the FLACC score within the two groups, a significant difference decrease in pain scores was found, there were significant decrease in pain score in group Mg compared to group C at 30 minutes, after 120 minutes up to 6 hours postoperatively as Table(3).

Table 3: Shows FLACC score for the two groups.

FLACC	C	Mg	P. value
After 30 min	0.67±0.72	0±0	<0.001**
After 60 min	0.6±0.74	0.6±0.74	1.00
After 90 min	0.93±0.7	0.8±0.68	0.610
After 120 min	2±1	0.53±0.92	<0.001**
After 4 h	3.2±0.77	0.53±0.92	<0.001**
After 6 h	2.93±1.33	1.2±0.94	<0.001**
After 12 h	1.53±1.13	2.27±1.44	0.129
After 24 h	1.33±0.9	1.6±1.24	0.500

Duration of analgesia (hours)

There were significant increase in duration of first analgesic requirement in group Mg (15.27±4.65) compared to group C (6±2.31) (p value <.001). Sedation score was significantly higher only during the first hour postoperatively in group Mg than group C (Table 4). The two groups were comparable as regards to residual motor blockade at recovery and at 3 hours after recovery. The overall incidence of postoperative side effects was comparable in all groups.

Table 4: Shows sedation score for two groups.

Sedation	C	Mg	P. value
After 30 min	1.53±0.74	3.47±1.73	<0.001**
After 60 min	1.87±0.35	2.27±0.46	0.012*
After 90 min	1.93±0.26	2±0	0.306
After 120 min	1.93±0.26	2±0	0.306

DISCUSSION

We designed this study to compare whether the magnesium sulfate to bupivacaine, when administered caudally, would prolong the duration of postoperative analgesia in children undergoing inguinal orchidopexy, distal hypospadias surgery or inguinal herniorrhaphy. Our results revealed that caudal administration of 50mg magnesium sulfate with bupivacaine (0.25%) in a total volume 1 ml/kg significantly prolonged the mean duration of postoperative analgesia by about 15 hours compared with caudal injection of 0.25% bupivacaine and at a volume of 1mL/kg (up to 6.5 h). Caudal administration of bupivacaine alone at a dose of 2-2.5 mg/kg can provide adequate analgesia in the early postoperative period only for the duration of the local anesthetic; 24 h.[10] Hence, early postoperative adjuvant systemic analgesia is usually required.

Intrathecal administration of magnesium has been reported as adjunct to both anesthesia and postoperative analgesia. The possible analgesic effect of magnesium sulfate occurred at the central level and might be due to its absorption to the systemic circulation.[11] Perioperative efficacy of adjuvant addition of magnesium (10mL of 5% magnesium sulfate) to epidural bupivacaine (10 mL of 0.25% plain bupivacaine) and fentanyl (100µg) was demonstrated in women undergoing elective caesarean section,[12] Ghatak et al. evaluate the effect of 50 mg magnesium sulfate versus 150 mg clonidine as adjunct to 19 mL of epidural bupivacaine on 90 patients undergoing lower abdominal and lower limb surgeries; the onset of anesthesia in the magnesium group was faster. No statistically significant differences for both groups regard perioperative hemodynamics and postoperative side effects. Onset of anesthesia was more rapid with magnesium sulfate group.[13]

Magnesium sulphate is found to have analgesic effects, mediated through antagonism of NMDA receptors in the CNS.[14] and related to regulation of calcium influx into the cells. Several small studies investigating the analgesic potency of intravenous magnesium is being published, which shows conflicting results. But, a meta-analysis of all available trials of intravenous administration of magnesium shows reduction of postoperative opioid requirements. Animal studies shows direct intrathecal administration of magnesium increases the antinociceptive effect of opioids.[15] Intrathecal and epidural administration of magnesium also increase the mean duration of analgesia. But, the dose of neuraxial magnesium that produce safe anesthesia without any major side effects remain unclear.

Arcioni, et al. observed that intrathecal and epidural magnesium sulfate potentiated and prolonged motor block. They concluded that patients undergoing orthopedic surgery, supplementation of spinal anesthesia,[16] with combined intrathecal and epidural MgSO4 significantly reduces patients' postoperative analgesic requirements.[16]

In agree with our results Gamal et al. (2014), found in their study that caudal supplementation of ropivacaine (0.15% 1.5ml /kg) with (50mg) magnesium sulfate in children undergoing inguinal hernia repair significantly prolonged duration of analgesia (5-11h). The results of this study showed that the usage of same dose of magnesium sulfate (50mg) with bupivacaine (0.5% 0.5 ml/kg) also prolonged duration of analgesia (10-16 h) but more than Gamal et al. Also, their study revealed that the incidence of postoperative rescue analgesia was significantly higher in ropivacaine group compared with magnesium group. The time of first analgesic request

was significantly longer in magnesium groups (500 ± 190 min) compared with ropivacaine group (260 ± 65 min). Ropivacaine group patients achieved significantly higher Children's Hospital of Eastern Ontario Pain Scale and Faces Legs Activity Cry CONSOL ability scores (4th hourly) compared with magnesium group (8th hourly)[17] In contrast to our study Birbicer et al., compared bupivacaine 0.5% plus 50 mg magnesium to bupivacaine 0.5% alone for caudal anesthesia in children. They concluded that that addition of magnesium as an adjuvant agent to local anesthetics for caudal analgesia has no effect on postoperative pain and analgesic need. Birbicer et al., studied the effects of caudal magnesium administration on anesthesia depth and analgesia requirement on 32 patients (ASA I–II, aged from 2–8 years) who had lower abdominal or penoscrotal surgery.[18] In the present study, there were no significant hemodynamic changes between groups. This is in agreement with many authors who used epidural MgSO4,[19] and did not report any hemodynamic or respiratory instability during the observation period. The results revealed significant difference regarding the sedation score during first hour postoperatively. This is disagreed with Bilir et al.[20] and El-Kerdawy,[21] who did not report any case with drowsiness or respiratory depression when using epidural magnesium.this may explain Post anesthesia care unit results in first half hour.

CONCLUSION

Administration of regional anesthesia before surgery is a safe and widely accepted technique, providing adequate pain relief, pediatric caudal bupivacaine with magnesium sulfate in dose 50 mg improve quality of caudal block and postoperative analgesia.

REFERENCES

1. Hannam JA, Anderson BJ, Mahadevan M, et al. Postoperative analgesia using diclofenac and acetaminophen in children. Pediatric Anesthesia, 2014; 24: 953-961.
2. Bailey B, Trottier ED. Managing Pediatric Pain in the Emergency Department. Paediatr Drugs, 2016; 18: 287-301.
3. Kalappa S, Sridhara RB, Kumaraswamy S. Dexmedetomidine as an Adjuvant to Pre-Emptive Caudal Epidural Ropivacaine for Lumbosacral Spine Surgeries. J Clin Diagn Res, 2016; 10: UC22-24.
4. Singhal NR, Jones J, Semenova J, et al. Multimodal anesthesia with the addition of methadone is superior to epidural analgesia: A retrospective comparison of intraoperative anesthetic techniques and pain management for 124 pediatric patients undergoing the Nuss procedure. J Pediatr Surg, 2016; 51: 612-616.
5. Yousef GT, Ibrahim TH, Khder A, et al. Enhancement of ropivacaine caudal analgesia using dexamethasone or magnesium in children undergoing inguinal hernia repair. Anesth Essays Res, 2014; 8: 13-19.
6. Junghans-Rutelonis A, Weiss K, Tamula M, et al. (493) Pediatric pain assessment methods and interventions used by mental health providers: a survey by the Pain Special Interest Group of the Society of Pediatric Psychology. J Pain, 2016; 17: S98.
7. Redmann AJ, Wang Y, Furstein J, et al. The use of the FLACC pain scale in pediatric patients undergoing adenotonsillectomy. Int J Pediatr Otorhinolaryngol, 2017; 92: 115-118.
8. Akin A, Esmaoglu A, Tosun Z, et al. Comparison of propofol with propofol–ketamine combination in pediatric patients undergoing auditory brainstem response testing. Int J Pediatr Otorhinolaryngol, 69: 1541-1545.
9. Riessen R, Pech R, Tränkle P, et al. Comparison of the RAMSAY score and the Richmond Agitation Sedation Score for the measurement of sedation depth. Critical Care, 2012; 16: P326-P326.
10. Kim EM, Kim MS, Han SJ, et al. Magnesium as an adjuvant for caudal analgesia in children. Paediatr Anaesth, 2014; 24: 1231-1238.
11. Buvanendran A, McCarthy RJ, Kroin JS, et al. Intrathecal magnesium prolongs fentanyl analgesia: a prospective, randomized, controlled trial. Anesthesia & Analgesia, 2002; 95: 661-666.
12. Yousef AA, Amr YM. The effect of adding magnesium sulphate to epidural bupivacaine and fentanyl in elective caesarean section using combined spinal-epidural anaesthesia: a prospective double blind randomised study. Int J Obstet Anesth, 2010; 19: 401-404.
13. Ghatak T, Chandra G, Malik A, et al. Evaluation of the effect of magnesium sulphate vs. clonidine as adjunct to epidural bupivacaine. Indian J Anaesth, 2010; 54: 308-313.
14. Jaoua H, Zghidi SM, Wissem L, et al. [Effectiveness of intravenous magnesium on postoperative pain after abdominal surgery versus placebo: double blind randomized controlled trial]. Tunis Med, 2010; 88: 317-323.
15. Tramer MR, Schneider J, Marti RA, et al. Role of magnesium sulfate in postoperative analgesia. Anesthesiology, 1996; 84: 340-347.
16. Arcioni R, Palmisani S, Tigano S, et al. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double-blind, controlled trial in patients undergoing major orthopedic surgery. Acta anaesthesiologica scandinavica, 2007; 51: 482-489.

17. Yousef GT, Ibrahim TH, Khder A, et al. Enhancement of ropivacaine caudal analgesia using dexamethasone or magnesium in children undergoing inguinal hernia repair. Anesthesia: Essays and Researches, 2014; 8: 13.
18. Birbicer H, Doruk N, Cinel I, et al. Could adding magnesium as adjuvant to ropivacaine in caudal anaesthesia improve postoperative pain control? Pediatric surgery international, 2007; 23: 195-198.
19. Aly Kandil AH, Hammad RAEA, Shafei MAE, et al. Preemptive use of epidural magnesium sulphate to reduce narcotic requirements in orthopedic surgery. Egyptian Journal of Anaesthesia, 2012; 28: 17-22.
20. Bilir A, Gulec S, Erkan A, et al. Epidural magnesium reduces postoperative analgesic requirement. Br J Anaesth, 2007; 98: 519-523.
21. El-Kerdawy H. Analgesic requirements for patients undergoing lower extremity orthopedic surgery--the effect of combined spinal and epidural magnesium. Middle East J Anaesthesiol, 2008; 19: 1013-1025.