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ORIGINAL ARTICLE

Could adding magnesium as adjuvant to ropivacaine in caudal anaesthesia improve postoperative pain control?

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Abstract Recently, most studies reported magnesium as a *N*-methyl-D-aspartate receptor antagonist and its analgesic and perioperative anaesthetic effects have been discussed with central desensitization pathway. We investigated the effects of caudal ropivacaine plus magnesium and compared with ropivacaine alone on postoperative analgesia requirements. After hospital ethic committee's consent, 60 patients (ASA I-II, 2–10 years old) who had lower abdominal or penoscrotal surgery were enrolled in the study. After general anaesthesia induction, caudal blockage was applied. Patients were randomly assigned in two groups. Ropivacaine 0.25% was administered to Group R ($n = 37$), ropivacaine 0.25% plus 50 mg magnesium to Group RM ($n = 23$) in 0.5 ml kg^{-1} volume. Postoperative analgesia level was recorded at 15 min and 1, 2, 3, 4, 6 h by using Paediatric Objective Pain Scale (POPS) and The Children's Hospital of Eastern Ontoria Pain Scale (CHEOPS). Postoperative motor blocks were evaluated with Modified Bromage Motor Block Scale. According to demographic characteristics, there were no significant differences between the two groups ($P > 0.05$). POPS, CHEOPS, Bromage Motor Scales, analgesia duration and adverse effects were similar in Group R and Group RM. It has been shown that addition of magnesium as an adjuvant agent to local anaesthetics for caudal analgesia has no effect on postoperative pain and analgesic need.

Keywords Anaesthesia · Caudal · Analgesics local · Ropivacaine · Pain postoperative · Adjuvant · Magnesium

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Introduction

Single shot caudal epidural blockade is one of the most widespread technique providing intra and postoperative analgesia in paediatric patients [1, 2]. Neuroaxial anaesthesia has been shown to have direct sedative effects and markedly to reduce the amount of hypnotic agents required for sedation [3].

In order to decrease intra and postoperative analgesic requirements after caudal epidural blockade, various additives, such as epidurally given morphine [4], fentanyl [5], clonidine [6] and ketamine [7, 8] with local anaesthetics have been investigated.

Recently, the importance of magnesium in an anaesthetic practice has been highlighted [9]. Magnesium blocks NMDA channels in a voltage-dependent fashion, and such NMDA antagonism prevents the induction of central sensitization from peripheral nociceptive stimulation [10]. Administration of i.v. magnesium sulfate during surgery reduces intra and postoperative opioid requirements [11]. Koinig and colleagues reported that magnesium administration led to a significant reduction in fentanyl consumption in the peri and postoperative periods [12]. However,

i.v. magnesium, even high doses, is associated with limited passage across the blood–brain barrier [13].

An experimental study has shown that intrathecally magnesium potentiates opioid antinociception in an acute incisional model of rats [14]. The suppression of nociceptive response by intrathecal magnesium has also been demonstrated in a rat model of neuropathic pain [15] and its safety profile has been evaluated, including histopathological analysis [16, 17].

Based on these findings, we hypothesized that the application of caudal epidural magnesium may better control the postoperative analgesia. This prospective randomized, double blind study investigates the effects of caudal ropivacaine plus magnesium compared with ropivacaine on postoperative analgesia in children.

Methods

After obtaining ethical committee approval and written parental consent from 60 patients, ASA I and II group infants and children aged from 2 to 10 years, presenting for elective minor surgery under general anaesthesia (inguinal herniotomy, orchidopexy and circumcision) were enrolled in this study. Exclusion criteria included major hepatic, renal or cardiovascular dysfunction, previously known allergy to magnesium sulphate or other study drugs, asthma, haematological disorders, obesity, prior treatment with opioids and anticoagulants. The children were randomized to receive, via caudal route in a double blind manner either ropivacaine 0.25% 0.5 ml kg^{-1} (Group R, $n = 37$) or a mixture of ropivacaine 0.25% 0.5 ml kg^{-1} and preservative free 15% MAG 50 mg (Group RM, $n = 23$). Patients were not premedicated. After inhalational induction of anaesthesia with sevoflurane 6% and N_2O in 50% O_2 the airway was secured by tracheal intubation or placement of a laryngeal mask. Anaesthesia was maintained by 2.5% sevoflurane. Caudal block was performed by the same anaesthetist as follows: for puncture of the caudal epidural space a 25-gauge caudal needle was used. When there was no evidence of intravascular or intrathecal malposition of the needle the study solutions were injected slowly with repetitive intermittent aspiration. Intraoperatively, no additional drugs were given. After anaesthesia induction, preoperative serum magnesium concentration in magnesium groups was measured by chlorophosphonazo III methods (Cobas Integra 700; Roche, Basel, Switzerland). Magnesium concentrations are expressed in milligrams per decilitre. The normal serum magnesium range in the child population in our laboratory is 1.7–2.2 mg dl^{-1}. During anaesthesia, heart rate and peripheral oxygen saturations were monitored continuously and arterial blood pressures were measured every 5 min by noninvasive means. Haemodynamic data were analysed to detect possible systemic effects of magnesium. Anaesthetic agents were discontinued after completion of surgery.

Postoperative pain was assessed using an established Paediatric Objective Pain Score (POPS) and The Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) at 15th min, 1st, 2nd, 3rd, 4th and 6 h. POPS of more than four points was taken as an indication of inadequate analgesia and rectal paracetamol was administered if necessary.

Residual motor block in the lower extremity was assessed using a modified Bromage scale (0 = no residual motor block, 1 = inability to raise extended legs, 2 = inability to flex knee and 3 = inability to flex ankle). Postoperative sedation was evaluated using a three-point scale (0 = awake, 1 = drowsy and 2 = asleep) immediately after arrival to the recovery room. After transfer to the recovery area, patients were assessed neurologically for any sign of hypermagnesaemia. Any adverse events or side effects were recorded during the perioperative and postoperative periods. To ensure that the anaesthetist who performed the caudal block and was responsible for the child during the operation was blind to drug administration, study solutions were outside the induction room and syringes were labelled with randomization numbers. In the postoperative observation period, all assessments and recordings of parameters were made by another anaesthetist.

Statistical analysis

Statistical analyses were performed using the statistical package SPSS 9.0 (SPSS, Inc., Chicago, IL, USA). All values are expressed as mean ± SD. Demographic variables were compared using chi-square test. Heart rates were analysed between groups using two-way repeated measures ANOVA. POPS, CHEOPS, Sedation scores, Modified Bromage scale were evaluated between groups using the Mann–Whitney U test. $P < 0.05$ was considered significant.

Results

Demographic characteristics of the groups were shown in Table 1 ($P > 0.05$). Two groups were comparable with regard to these characteristics. The types of surgery were presented in Table 1. During surgery, additional analgesics were not required in any child. On the

Table 1 Patient characteristics and type of surgery

	Group RM (n = 23)	Group R (n = 37)
Age (years)	6.34 ± 2.41	4.31 ± 2.59
Weight (kg)	19.6 ± 5.8	17.6 ± 6.7
Female/male	2/21	4/33
Type of surgery		
Inguinal hernia	8	2
Hernia + circumcision	4	4
Orchiodopexy	6	5
Circumcision	19	12

Values are mean ± SD

other hand three children in Group R, nine children in Group RM required additional analgesics with paracetamol in the postoperative period but these were not statistically significant ($P > 0.05$). There was no statistically significant difference between the Group R and Group RM for sedation scores and heart rates ($P > 0.05$). During following period, we did not observe any deep sedation in patients and all patients were fully awake before transfer from operative theatre (sedation scale = 0). Although the patients' motor block levels were evaluated with Bromage motor block scale, we did not observe any motor block. Postoperative pain scale was shown in Table 2. According to CHEOPS and POPS score, there was no statistically significant difference between Group R and Group RM ($P > 0.05$). Serum magnesium levels did not change between preoperative (1.89 ± 0.3 mg dl^{-1}) and postoperative (1.9 ± 0.3 mg dl^{-1}) period in Group RM ($P > 0.05$). No patients showed respiratory depression, neurological or other negative side effects.

Discussion

Magnesium is known to be an NMDA receptor antagonist [18]. It is assumed that NMDA receptors play an important role in the development of central sensitivity after noxious peripheral stimulations [10]. There are studies demonstrating that magnesium is effective by way of preventing nociceptive related central sensitization through NMDA receptor blockage [10]. Very few publications are available about the use of magnesium that is NMDA receptor antagonist magnesium in children. To our knowledge this is the first randomized human study concerning the use of magnesium, an NMDA receptor antagonist, as an adjuvant agent for the caudal epidural block in children.

Table 2 POPS, CHEOPS for both groups during the postoperative period

Time	POPS		CHEOPS	
	Group R	Group RM	Group R	Group RM
15 min	1.8 ± 2.0	1.9 ± 1.7	5.3 ± 1.8	6.0 ± 1.8
1 h	1.6 ± 1.6	1.7 ± 1.6	5.0 ± 1.6	5.2 ± 1.5
2 h	1.1 ± 1.3	1.0 ± 1.4	4.0 ± 1.2	4.4 ± 1.1
3 h	1.2 ± 1.7	0.6 ± 1.1	3.8 ± 1.2	3.8 ± 0.9
4 h	0.5 ± 0.9	0.2 ± 0.7	3.5 ± 0.8	3.5 ± 0.7
6 h	0.2 ± 0.7	0.2 ± 0.7	3.1 ± 0.3	3.5 ± 0.7

Our results revealed that there is no effect of magnesium added as an adjuvant agent to caudal ropivacaine on postoperative analgesia and analgesia requirement. Magnesium may be used via i.v. and intrathecal pathways for postoperative analgesia in clinics. There are publications with different results about the effects of intravenous use of magnesium in adults in clinical applications on postoperative pain and need for analgesic. Koinig et al. [11] showed that i.v. magnesium application reduced the need for intra-postoperative analgesic, whereas Ko et al. [12] showed that it did not. Intravenous magnesium was used for posttonsillectomy pain in children and reported to have no effect on analgesia [18]. It was demonstrated that the ineffectiveness of magnesium in intravenous applications may be due to its inability to form effective cerebrospinal fluid concentrations because of inadequate penetration through the blood–brain barrier [13]. For this object, Buvanendran et al. [20] used magnesium intrathecally and demonstrated that 50 mg intrathecal use of magnesium prolonged analgesia in adults. In the light of these data, we thought that we could get the same effect through epidural caudal use of magnesium.

Although there have been many studies about the intravenous use of magnesium, there is little clinical experience on its intrathecal and epidural applications. Lejuste [19] accidentally injected 1,000 mg magnesium intrathecally and described an intensive motor block which was completely reversed 90 min later and no neurological deficit was determined in the long-term follow-up.

The reliability of intrathecal magnesium application has been evaluated with experimental studies. In a 30-day period, rats were given 1.26 mg bolus magnesium intrathecally on various days and as a result, a motor and perceptive block similar to lidocaine occurred. In the histological examination of the spinal cord at the end of this period histopathologically abnormal findings were not encountered other than those observed in the animals which were attempted for isotonic, lidocaine or intrathecal catheter without a drug [16]. In another randomized controlled study, dogs were given 3 mg kg^{-1} intrathecal magnesium preoperatively. No neurological deficit was observed in

the dogs after the operation and no pathological findings were encountered in the histopathological examination of the spinal cord [17]. Based on these studies, we used magnesium epidurally and did not detect any neurological deficit in the patients in the postoperative period.

Buvanendran et al. in the first randomized clinical study in literature, took as a reference 188 μg of intrathecal magnesium potentializing morphine antinociception for postoperative pain by taking a rat model that they used in their previous study [20, 21]. The differences between rats and humans in cerebral fluid amount and body weight were taken into account. An equivalent dose of 50 mg was suggested against 188 μg dose. No neurological findings were reported to be observed in short term about the intrathecal use of magnesium at this dose in human [21]. In our study, we accepted this dose as reference and at this dose the postoperative magnesium level was at normal range.

We figured that the results we obtained might be due to the following reasons: (1) it may be possible that epidurally applied magnesium is less effective in passing the blood–brain barrier compared to its intrathecal use and is unable to form efficient CSF concentration, (2) the dose we applied was based on the reference of intrathecal application, and may not be sufficient for postoperative analgesia to be achieved through epidural use.

In conclusion, it has been shown that addition of magnesium as an adjuvant agent to local anaesthetics for caudal analgesia has no effect on postoperative pain and analgesic need. In our opinion especially in children additional studies may have been done with different magnesium doses.

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