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Research Article

COMPARISON OF INTRAVENOUS MAGNESIUM AND PLACEBO ADMINISTRATION ON POSTOPERATIVE PAIN AND ANALGESIC CONSUMPTION DURING SPINAL ANESTHESIA FOR INGUINAL HERNIA REPAIR

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ABSTRACT
Previous studies have suggested that magnesium may be a useful adjuvant to postoperative analgesia.
We investigated efficacy of intravenous infusion of magnesium sulfate during spinal anesthesia to reduce post-operative pain and opioid consumption in patients undergoing inguinal hernia surgery.
We randomly divided one hundred patients' age 18-55 years old and ASA class I-II undergoing inguinal surgery into two groups. The magnesium group (Group M) received magnesium sulfate 50 mg/kg in 100 ml normal saline intravenously within 10 minutes and 15 mg/kg/h by continuous infusion during the operation in one hour. The control group (Group S) received the same amount of normal saline without magnesium sulfate. All patients received spinal anesthesia. Postoperative pain scores, meperidine consumption, and motor block were evaluated during 24 hours after surgery.
Postoperative pain scores were significantly lower in Group M at 2, 3, 4 and 6 hours after surgery ($P<0.05$). Motor block was longer in Group M ($P<0.05$). Cumulative postoperative meperidine consumptions were also significantly lower in Group M at 24 h after surgery ($P<0.05$). 12% nausea and 26% flashing have been reported in Group M.
A bolus and intravenous infusion of magnesium sulfate administration during spinal anesthesia improves postoperative analgesia. IRCT201201088645N1
Keywords: Magnesium sulfate; Spinal anesthesia**;** Post-operative pain

INTRODUCTION

Definition of pain according to the International Association the study for Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[1].

Surgical pain is due to inflammation from tissue trauma (surgical incision, dissection, burns) or direct nerve injury (nerve transaction, stretching, or compression)[2].

The sensory pathways for pain caused by tissue damage transmit information from the damaged tissue to the central nervous system (nociception). The nociceptive pain is accompanied by inflammatory, visceral, and neuropathic pain mechanisms. The sensitization of peripheral and central neuronal structures amplifies and sustains postoperative pain.

Pain after surgery is a compilation of several unpleasant sensory, emotional, and mental experiences, associated with autonomic, endocrine-metabolic, physiological, and behavioral responses [3,4]

The postoperative pain can have a significant effect on patient recovery and increases hospital stay and costs of care. In the long term, acute surgical pain is followed by chronic pain in 10%–50% of patients who undergo common surgical procedures[5]. Management of postoperative pain relief suffering and leads to earlier mobilization, shortened hospital stay, reduced hospital costs, increased patient satisfaction and improve quality of life [6,7].

In order to reduce post-operative pain, opioids and NSAIDs are used on a routine basis; but the use of these drugs is associated with some side effects and risks[8]. The major goal in the management of postoperative pain is minimizing the dose of medications to lessen side effects while still providing adequate analgesia. This goal is best accomplished with multimodal and preemptive analgesia[9,10]. Preventive analgesia results decrease in pain transmission in the central nervous system and subsequently decrease pain. It also prevents the occurrence of central excitability and thereby reduces pain after surgery or injury[11]. Some of the drugs that have been used as pre-emptive analgesia include gabapentin, ketamine, peripheral local anesthetics, opioids and NSAIDS[12].

Magnesium Sulfate has been used as a pre-emptive analgesia in clinical practice. It can antagonizes N-Methyl-D-aspartic acid receptor and it also inhibits the release of acetylcholine in the neuromuscular junction. It has recently been demonstrated that the receptor N-Methyl-D-aspartic acid (NMDA) plays a principle role in central excitability. Increased central excitability during surgery is more pronounced, so the idea that the addition of NMDA antagonists can reduce pain sensitivity seems innovative[13].

Some clinical trial studies have shown that intravenous infusion magnesium sulfate reduced intravenous anesthetics during general anesthesia and diminished postoperative analgesic consumption[14], whereas results of a few studies demonstrated that perioperative intravenous magnesium sulfate administration had little effect on postoperative pain reduction[15,16]. A few studies have been done on the effects of intravenous bolus or infusion of magnesium sulfate during regional anesthesia for postoperative pain

Objectives:

We investigated efficacy of intravenous infusion of magnesium sulfate during spinal anesthesia to reduce post-operative pain and opioid consumption in patients undergoing inguinal hernia surgery.

PATIENTS AND METHODS:

This study was approved by the Institutional Ethics Committee with Institutional ethical clearance number: U-90132 and written informed consent was obtained from all patients.

In a randomized, double -blind, prospective study, we investigated efficacy of intravenous infusion of magnesium

sulfate to reduce post-operative pain in patients undergoing inguinal surgery. We randomly divided one hundred patients' age 18-55 years old and ASA class I-II undergoing inguinal surgery into two groups. The exclusion criteria were as follows: ASA class III & IV patients, patients with a history of opioid or cannabis abuse, and patients with allergy to NSAIDs or narcotic analgesics. If hemodynamic instability happened after spinal injection, which required medication, or if the operation duration was more than two hours, the patients were excluded.

Spinal anesthesia was performed for all patients through the L3-L4 interspace in the sitting position. After dural puncture with a needle size 25 G, 12.5 mg Bupivacaine 0.5% solution was injected intrathecally. After administration of bupivacaine the patient was immediately turned to the supine horizontal position for Development of the aesthesia level to T10. The level of sensory block to reach the T10 dermatome level was determined based on the loss of sensation to pin-prick testing in the mid-clavicular line (using a 20G hypodermic needle). Ten minutes after intrathecal injection, 50 mg / kg magnesium sulfate in 100 mL of normal saline was infused over 10 minutes followed by 15 mg / kg magnesium sulfate through pump infusion within one hour in group A. Group B were given the same volume of normal saline instead of magnesium sulfate. After the operation, the pain and the ability of toes move were checked.

Pain was measured by visual analogue scale (VAS) from zero as no pain to ten as the worst pain for patients. Meperidine consumption and the ability of toes move at 1, 2, 3, 4, 6, and 12 and 24hours after intrathecal injection were recorded as well. Any kind of symptoms, flushing, restlessness or other complaints were registered.

After collecting the data from both groups, they were analyzed by SPSS program. The study data were expressed as mean ± standard deviation for the quantitative variables percentages for the categorical variables. The parametric data of the patients were compared using the student t-test for the continuous variables and the chi-square test for the categorical variables. A P-value < 0.05 was considered significant.

Table 1: Mean age, operation time and sex distribution in the case and control groups.

Groups	n	Mean age(Y/O) (P-value=0.26)	Mean Time(min) (P-value=0.87)	Sex (P-value=0.77)
Case group	50	32.40±9.33	55.90±9.77	Male = 86% Female = 14%
Control group	50	34.64±10.49	56.20± 9.06	Male = 84% Female = 16%

Table 2: Average pain score in case and control groups at different duration after spinal anesthesia

Time(After spinal anesthesia)	2nd hour	3rd hour	4th hour	6th hour	12th hour	24th hour
Mean pain score in case group(n=50)	0.84±0.81	1.46±0.93	2.22±1.05	3.4±0.96	3.9±0.58	3.42±0.57
Mean pain score in control group(n=50)	1.48±0.88	2.22±1.11	2.92±1.29	3.96±1.04	4.1±0.46	3.58±0.64
p-value	0.0001	0.0001	0.004	0.007	0.06	0.19

Table 3: Mean time the ability of toes moving after spinal block in the case and control groups (P-value=0.002)

Groups	n	ability of toes moving (Hour)	SD
Case group	50	2.52	0.5
Control group	50	2.22	0.41

Table 4: Average meperidine consumption at the first day of operation in the case and control groups (P-value=0.0001)

Groups	n	Average meperidine consumption(mg)	SD
Case group	50	17.6	8.09
Control group	50	37.5	7.3

RESULTS:

Patients' mean age was 52.94 ± 9.33(SD) years old. Age (P-value = 0.26) and sex (P-value = 0.77) distribution were similar in both groups (Tables 1). Mean operation time was 56.05 ± 9.38 (SD) minutes and there was no significant difference between groups (Table1, P-value = 0.87).

In the first hour after intrathecal injection, there was no pain in both groups. At the second, third, fourth and sixth hours the mean pain scores was significantly lower in the case group than the control group (P-value <0.05). After twelve hours the mean pain score in case and control groups were 3.9 ± 0.58(SD) and 4.1 ± 0.46(SD) respectively, but it was not significant (P-value = 0.06). Although after 24 hours mean pain score was lower in case group, but it was not significant (P-value = 0.19)(Table 2).

Checking the ability of toes moving had been done as well; In case group motor blockade took 2.52 ± 0.6(SD) hours and in control group took 2.22 ± 0.41(SD) hours (Table 3) which was significant(P-value = 0.002).

Mean of meperidine consumption was 17.6 ± 8.09(SD) mg in case group and 37.5 ± 7.3(SD) mg in the control group (Table 4). That it was significant (P-value = 0.0001) between two groups.

DISCUSSION:

The aim of this study was to evaluate the effect of intraoperative infusion of magnesium sulfate on the pain and analgesic consumption after spinal anesthesia in patients undergoing inguinal hernia. The inguinal herniorrhaphy is usually associated with moderate to severe postoperative pain. All patients had no pain in the first hour after intrathecal injection, so it was predictable because of successful spinal anesthesia. During Six hours after intrathecal injection, the case group had significantly less pain than the control group; however the difference in pain levels decreased gradually and after 12 hours was not significant. This study showed that infusion of magnesium sulfate during operation under spinal anesthesia reduced postoperative pain and analgesic consumption. The mechanism of analgesic effect of

magnesium sulfate is unknown, but interference of NMDA receptors and calcium channels may have an important role. The first possibility is based on the observations of Miranda and his colleagues and another research by Wong and his colleagues, that calcium channel blocker drugs like nifedipine have an antinociceptive action in algesiometric tests in rats[17,18].

In humans, calcium channel blockers can enhance opiate analgesia in patients with cancer chronically treated with morphine he analgesic action of calcium channel blockers could be mediated by interference with calcium influx, which this influx has important role in the release of neurotransmitters and other substances implicated in nociception and inflammation[19.]

The second possible mechanism for the analgesic effect of magnesium is its antagonism of the NMDA receptor. Magnesium seems to prevent central sensitization after peripheral tissue injury or inflammation because of inhibition of dorsal horn NMDA receptors[20].

A study was done by Tramer and his colleagues[21], observed that IV magnesium sulfate had no analgesic efficacy and no reduction in postoperative analgesic requirements, but they used only diclofenac suppository preoperatively and local nerve block at the end of hernia repair surgery resulting in consistently decreased pain scores.

The result of our study reveals that intravenous magnesium sulfate reduces postoperative pain, which corroborates with previous studies [22-25]. However, in two studies (Do SH study and Paech MJ study) have demonstrated that magnesium sulfate does not reduce the severity of postoperative pain[26, 27]. In these two studies after operation, epidural analgesia was used for postoperative pain relief. Thus, it is possible that the analgesic effect of epidural block have masked the analgesic effect of magnesium sulfate in these two studies.

In the some studies a single bolus injection of magnesium sulfate were used before or during operation for reducing postoperative pain[28]. It seems effective bolus and adequate infusion dosages of magnesium sulfate are important for produce pain relief in the postoperative period. Seyhan and his colleagues studied the effects of three different dose regimens of magnesium on postoperative pain relief and morphine consumption in gynecological surgery[29]. Based on their observations a single bolus injection at 40 mg/kg of magnesium sulfate was found to reduce postoperative morphine consumption, and when this was followed by infusion of 10 mg/kg/h, the effect was enhanced. In another study, patients receiving general anesthesia with total intravenous anesthesia, a bolus dose of 50 mg/kg and maintenance 15 mg/kg/h of magnesium sulfate reduced muscle relaxant requirement and enhanced postoperative analgesia without any significant side-effects[30,31]. According these studies, we selected a bolus dose 50 mg/kg of the magnesium sulfate and a maintenance dose of 15 mg/kg/h.

In this study up to fourth hour, motor blockade was checked every one hour and it was significantly greater in the case group. Magnesium has been reported enhance the activity of local anesthetic agents[32]. Magnesium competitively blocks calcium entry at the motor nerve terminal. There may also be a milder postsynaptic affect. Moreover it is well known that magnesium sulfate inhibits acetylcholine release at motor nerve terminals, thus potentiating the effect of neuromuscular blocking agents[33].

CONCLUSION

A bolus and intravenous infusion of magnesium sulfate during spinal anesthesia for inguinal hernia surgery improves postoperative analgesia.

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