RESEARCH ARTICLE

Assessment of Magnesium Sulfate Infusion in Combination with Ketorolac for the Pain Management in Intertrochanteric Fractures; A Randomized Clinical Trial

Bijan Heidari, MD; Rasoul Salimi, MD; Hossein Saremi, MD; Mostafa Arab Ghahestani, MD

Research performed at Besat Hospital, Hamadan University of Medical Sciences, Hamadan, Iran

Received: 25 April 2022 *Accepted: 16 March 2023*

Abstract

Objectives: Intertrochanteric fracture is a common fracture that mainly occurs in the elderly. Diverse pain management strategies have been applied; however, considering the age of the patients, analgesia-related complications should be concisely considered. The current study aims to evaluate the efficacy and adverse effects of Ketorolac plus placebo versus Ketorolac plus magnesium sulfate for pain management in intertrochanteric fractures.

Methods: The current randomized clinical trial has been conducted on 60 patients with intertrochanteric fractures assigned into two groups of treatment with Ketorolac (30 mg) plus placebo (n=30) versus Ketorolac (30 mg) plus magnesium sulfate (15 mg/kg) (n=30). Pain scores using the visual analog scale (VAS), hemodynamic parameters, and complications (nausea and vomiting) were assessed at baseline and within 20, 40, and 60 minutes after the interventions. Additional morphine sulfate requirements were compared between the groups.

Results: Demographic characteristics in both groups were similar (P>0.05). All the assessments showed statistically significantly less pain severity in the magnesium sulfate/Ketorolac group (P<0.05), except for the baseline assessments (P=0.873). The two groups did not differ regarding hemodynamic parameters, nausea, and vomiting complaints (P>0.05). Although the frequency of additional morphine sulfate requirement was not different between the groups (P=0.06), the administered dose of morphine sulfate was significantly higher in those treated with ketorolac/placebo (P=0.002).

Conclusion: Based on the findings of this study, Ketorolac alone or in combination with magnesium sulfate led to significant pain reduction in patients with intertrochanteric fractures admitted to the emergency ward; however, the combination therapy had superior outcomes. Further studies are strongly recommended.

Level of evidence: II

Keywords: Femur intertrochanteric fractures, Ketorolac, Magnesium sulfate, Pain

Introduction

Hip fracture has become a crucial health challenge worldwide, affecting 1 million cases annually.[1] At age 50, low-impact injuries can lead to hip fracture in approximately 24 and 22.5 per 100,000 population for women and men, respectively; while by age 80 years, these rates dramatically increase to 1,290 per 100,000 in women and 630 per 100,000 for males .[2] Accordingly, considering the gradual upward trend of the aging phenomenon, up to 6-fold increase in the incidence of hip fractures has been estimated by 2050.[3]

As the geriatric population is the most common group of people influenced by hip fractures, pain management in these critical patients is a matter of debate. Inappropriate pain management accompanies delirium in 40% of the patients, while overmedication with an opioid is a leading cause of acute cognitive changes.[4-6] both delirium and uncontrolled pain are associated with increased lengths of stay, one-year mortality, hospital-related complications, and poor functional outcomes.[7, 8]

Corresponding Author: Mostafa Arab Ghahestani, Department of Orthopedics, School of Medicine, Besat Hospital, Hamadan

Email: mostafaarab0209@gmail.com

THE ONLINE VERSION OF THIS ARTICLE ABJS.MUMS.AC.IR

Older patients may more steeply experience opioid-associated complications, including respiratory depression, urinary retention, and constipation.[9, 10] Nevertheless, these agents have saved their place as the mainstay for pain management in hip fractures.[11] Therefore, numerous efforts have been made to assess the efficacy of other agents rather than opioids in the pain management of hip fractures in the elderly. Various medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and peripheral nerve block, have been accompanied by promising outcomes.[1,3,12]

Ketorolac is an injectable form of NSAIDs that has been widely administered for diverse conditions that could adequately decrease pain severity complaints and significantly lead to the decreased requirement for opioid use.[13-15]

Magnesium sulfate is a compound with an antagonizing effect on N-methyl-D aspartate (NMDA) receptors and modulates calcium ion entrance to the cells. The studies have revealed that NMDA receptor antagonists can inhibit nociceptive receptor stimulation by attenuating hypersensitivity. This agent has been successfully used for pain management in cesarean section and myocardial ischemia.[16, 17] However, the efficacy of this agent on hip fracture pain control has yet to be well established. Accordingly, the current study aims to compare the efficacy of magnesium sulfate in combination with Ketorolac versus placebo plus Ketorolac for pain management in patients with hip fractures.

Materials and Methods

The current randomized clinical trial has been conducted on 60 patients with intertrochanteric fractures admitted to the emergency ward of Besat Hospital, affiliated with Hamadan University of Medical Sciences, Hamadan, Iran, from May 2020 to March 2021.

The study protocol that met the tents of the Helsinki Declaration was proposed to the Ethics Committee of Hamadan University of Medical Sciences and approved by code number IR.USHA.REC.1399.340. The study was also registered in the Iranian Registry of Clinical Trials and obtained code number IRCT20120215009014N373. The research objectives and procedures were explained to the patients, and they were reassured about their information confidentiality and signed written consent.

Over 18-year-old patients with intertrochanteric fractures were diagnosed through imaging and confirmed by an emergency medicine specialist or a radiologist included in the study. Unstable hemodynamic (systolic blood pressure<90 mmHg, pulse rate decrease to less than 60 per minute or respiratory rate<12 per minute), concurrent neurovascular injuries, open fracture, the history of chronic lower limb pain, hypersensitivity to or contraindication for each of the agents, medical history of peptic ulcer disease, cardiac arrhythmia, congestive heart failure, renal or hepatic failure, and unwillingness to participate in the study were determined as the exclusion criteria.

The patients entered the study through convenience sampling until achieving the desired number of the study population. Then, they were randomly assigned into two groups of treatment with Ketorolac plus magnesium sulfate or Ketorolac plus placebo using random allocation pockets. Accordingly, each patient was given a code, A or B, concealed in an envelope and divided into one of the medication strategies.

The study was triple-blindly designed, as the agents were administered intravenously. The patients and the physician who evaluated them were blinded to the type of regimen. The statistician who analyzed the data was the other blind person to the treatments.

Interventions

The first group was treated with 60 mg slow intravenous Ketorolac (Alborz-Darou, Iran) followed by 15 mg/kg magnesium sulfate 50% (Shahid Ghazi Pharmacy, Iran) diluted with normal saline until achieving 100 ccs of the solution infused in 20 minutes.

Ketorolac (Alborz-Darou, Iran) in an equivalent dose was injected intravenously for the second group, while 100 ccs of normal saline were infused as the placebo.

Outcomes

The patients' demographic characteristics (age, gender, and weight) and underlying etiology of death were recorded in the study checklist.

The study's primary outcome was to assess pain severity using the Visual Analogue Scale (VAS). VAS is a validated scoring system for pain severity determination ranking from 0-10 as the least to the most severe perception of pain.[18] Pain assessment was done at baseline and within 20, 40, and 60 minutes after the injections.

The effects of medications on the patient's hemodynamics were the secondary outcomes of the study evaluated by measuring blood pressure, respiratory and pulse rates, and oxygen saturation at similar target times.

In cases whose pain was not well-controlled (VAS≥6) within 40 minutes after the injections, 0.1 mg/kg morphine sulfate was applied. Nausea and vomiting as the adverse effects of the medications were recorded as well.

Statistical analysis

According to a study by Maleki Verki et al.[19] that compared the analgesic effects of magnesium sulfate with ketorolac in patients with renal colic, half an hour after the intervention, the mean pain scores in magnesium sulfate and ketorolac groups were 3.43±3.30 and 1.67±0.81, respectively.

The test power of 80%, the confidence interval of 95%, and the following formula were used to obtain a sample size of 30 cases per study group (60 people in total).

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (\delta_1^2 + \delta_2^2)}{(\mu_1 - \mu_2)^2}$$

The obtained data were entered into the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 24. The qualitative data were presented as absolute numbers and percentages, and the quantitative as mean±SD. The normality of data distribution was assessed using the Smirnov-Kolmogorov test. The

categorical data were compared using the Chi-square test. The continuous data were compared using the independent t-test (or Mann-Whitney U test for data with non-normal distribution). A repeated measure ANOVA was applied to compare the trend of changes in the groups. A P-value of less than 0.05 was determined as the level of significance.

Results

The current study has been conducted on 60 patients with intertrochanteric fractures, and they were assigned into two groups of treatment with Ketorolac plus magnesium sulfate (n=30) or placebo (n=30). All the included patients fulfilled the study protocol. The consort diagram represents the participants in detail [Figure 1].

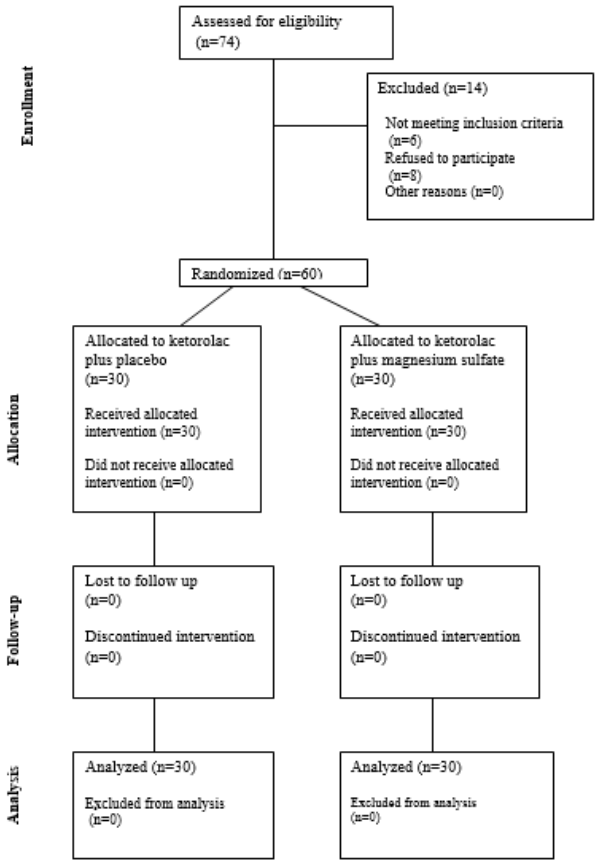

Figure1. Consort diagram of the study population

The studied population consisted of 34 females (56.7%) and 26 males (43.3%) and had a mean age of 68.6±9.91 years (age range: 34-93 years old). The two studied groups were similar regarding age (P=0.732), gender distribution (P=0.794), weight (P=479), baseline medical hemodynamic (P>0.05), and pain severity (P=0.823) which is demonstrated in [Table 1].

Table 1. The demographic and baseline characteristics of the studied population

	Ketorolac plus magnesium sulfate (n=30)	Ketorolac plus placebo (n=30)	P
Demographic characteristics			
Age (years), mean±standard deviation	69.4±9.6	67.5±10.1	0.732*
Gender (male), n (%)	12 (40)	14 (46.7)	0.794*
Weight (kg), mean±standard devistion	91.5±11.7	89.2±13.3	0.479*
Baseline medical condition			
Pain severity (VAS), mean±standard deviation	9.3±0.6	9.7±0.3	0.823*
Pulse rate (per minute), mean±standard deviation	96.1±17.7	91.7±16.4	0.421*
Systolic blood pressure (mmHg), mean±standard deviation	122.3±9.2	120.5±8.6	0.536*
Diastolic blood pressure (mmHg), mean±standard deviation	78.3±12.6	75.8±15.7	0.649*
Oxygen saturation (%), mean±standard deviation	94.7±4.8	92.8±5.5	0.159*
Respiratory rate (per minute), mean±standard deviation	18.2±2.3	16.7±1.9	0.257*

* Independent t-test

** Chi-square test

The VAS score has been compared between the groups. The baseline measurements revealed an insignificant difference (P=0873), while in all the further assessments, the pain severity was significantly less in the group treated with Ketorolac plus magnesium sulfate (P<0.05). In addition, both interventions led to significant pain reduction (P-<0.001), whereas those under Ketorolac plus placebo treatment presented significantly higher VAS scores in general (P<0.001) [Table 2].

Table 2. The comparison of pain severity between the groups

	Visual Analog Scale mean±standard deviation		P*
	Ketorolac plus magnesium sulfate (n=30)	Ketorolac plus placebo (n=30)	
Baseline	9.7±0.3	9.3±0.7	0.873
Within 20 minutes	8.1±0.6	8.8±0.9	<0.001
Within 40 minutes	6.2±0.5	7.4±0.6	<0.001
Within 60 minutes	3.1±1.8	4.9±2.1	0.033
P**	<0.001	<0.001	
P**	<0.001		

* Mann-Whitney U test

**Repeated measure ANOVA

Table 3 represents the trend of hemodynamic changes in the studied groups and revealed insignificant differences between those treated with Ketorolac plus placebo versus magnesium sulfate (P>0.05) [Table 3].

Table 3. The comparison of hemodynamic parameters between the groups

	Ketorolac plus magnesium sulfate (n=30)	Ketorolac plus placebo (n=30)	*P* *
	mean±standard deviation		
Systolic blood pressure (mmHg)			
Baseline	122.3±9.2	120.5±8.6	0.536
Within 20 minutes	121.6±10.3	121.1±9.4	0.736
Within 40 minutes	122.2±10.8	120.3±10.7	0.591
Within 60 minutes	119.5±11.6	117.6±12.5	0.544
*P***	0.603	0.512	
Diastolic blood pressure (mmHg)			
Baseline	78.3±12.6	75.8±15.7	0.649
Within 20 minutes	77.4±9.5	74.3±10.2	0.228
Within 40 minutes	76.3±11.2	75.5±11.3	0.784
Within 60 minutes	77.1±11.8	73.2±12.4	0.219
*P***	0.503	0.423	
Pulse rate (per minute)			
Baseline	96.1±17.7	91.7±16.4	0.421
Within 20 minutes	93.4±16.1	90.4±15.9	0.516
Within 40 minutes	91.6±13.9	89.9±14.5	0.645
Within 60 minutes	95.3±15.4	91.6±11.7	0.299
*P***	0.781	0.639	
Oxygen saturation (%)			
Baseline	94.7±4.8	92.8±5.5	0.159
Within 20 minutes	95.2±3.6	93.5±3.1	0.051
Within 40 minutes	94.2±4.1	92.2±4.6	0.097
Within 60 minutes	95.7±3.7	94.1±3.6	0.095
*P***	0.291	0.307	
Respiratory rate (per minute)			
Baseline	18.2±2.3	16.7±1.9	0.25
Within 20 minutes	16.25±2.33	16.38±2.26	0.82
Within 40 minutes	14.84±5.04	14.13±4.56	0.13
Within 60 minutes	16.40±6.11	16.55±5.15	0.91
*P***	0.46	0.25	

The mean dosage of morphine sulfate administration in the patients treated with ketorolac plus magnesium sulfate was 12.51±4.59 mg versus 10.59±3.45 mg in the latter group, which revealed a significant difference (P=0.002). Morphine sulfate was administered to 8 (26.67%) patients treated with the combination of magnesium sulfate and Ketorolac, while 14 (46.67%) cases received this agent as an add-on analgesic therapy (P=0.06). There was no differencbetween the groups regarding nausea and vomiting complaints in any of the assessment intervals (P>0.05) [Table 4].

Table 4. The comparison of nausea and vomiting complaints in the studied groups

		Within 20 minutes	Within 40 minutes	Within 60 minutes
Ketorolac plus magnesium sulfate (n=30)	**Nausea**	12 (40)	12 (40)	10 (33.3)
Ketorolac plus placebo (n=30)		14 (46.67)	6 (20)	6 (20)
P		**0.47**	**0.17**	**0.34**
Ketorolac plus magnesium sulfate (n=30)	**Vomiting**	6 (20)	4 (13.33)	0 (0)
Ketorolac plus placebo (n=30)		5 (16.67)	2 (6.67)	0 (0)
P		**0.58**	**0.26**	**N/A**

Discussion

Inappropriate pain control can lead to delayed rehabilitation, increased hospital stay, and hospitalization.[15] Although various medications have been applied to control pain in surgery, the regimen by which ultimate pain control with minimum adverse effects can be achieved remains a question.[5, 6]

To the best of our knowledge, the current study is the first one assessing the use of magnesium sulfate for preoperative pain management of intertrochanteric fractures. Accordingly, it was found that magnesium sulfate in combination with Ketorolac led to significantly lower levels of pain severity complaint and less need for additional analgesia; hemodynamic parameters and adverse effects, including nausea and vomiting, did not differ between the groups.

Surfing the literature revealed that up to 60% of the adults with lower limb fractures have not achieved reasonable pain control in the emergency room before fixation, and even 30% have not received any analgesia.[20] Proper pain management is one of the critical steps in

traumatic fractures. In contrast, factors, including age, pain severity, adverse effects, and cost-benefit of the applied analgesics should be concisely considered.[7] Most of the guidelines recommended acetaminophen or NSAIDs as the first line of therapy for mild,[21, 22] acetaminophen combined with opioids for moderate,[20, 23] and high doses of opioids for severe pains.[20,24] Nevertheless, the excellent use of opioid compounds to achieve early and adequate pain control has led to significant complications, such as urinary retention, constipation, and cognition impairment.[4-6]

The use of magnesium sulfate for pain management in surgical settings has been primarily investigated in 1996.[25] The promising outcomes of this study led to further investigation in which the researchers have presented significant pain improvement by postoperative continuous or bolus infusion of magnesium sulfate.[26, 27] Even a systematic review stated that significantly fewer complaints of postoperative pain accompanied the infusion of this agent during the surgery under general anesthesia without significant adverse effects.[28] In addition, Peng et al. presented that fewer pain complaints by magnesium sulfate administration in diverse orthopedic surgeries led to a remarkable reduction in the requirement for further analgesia; therefore, the related complications, including nausea, vomiting, and shivering, occurred in fewer cases.[29] Similar outcomes were achieved by the intravenous infusion of magnesium sulfate in spinal anesthetized patients for total hip replacement.[30] Even intrathecal use of this compound caused considerably less requirement for anesthetics and postoperative pain complaint.[31]

Ketorolac is one of the NSAIDs used through injecting routes. Our findings showed an acceptable pain decrease when this agent was used alone. In agreement with these outcomes, the previous studies reported successful pain control in conditions, such as distal radius [32] and mandibular fractures.[32,22] The other study presented that interarticular injection of Ketorolac for the patients undergoing arthroscopy was accompanied by significant pain reduction.[33]

Ketorolac and magnesium sulfate have yet to be concurrently administered for lower limb fractures. Maleki et al. applied this combination for renal colic management and revealed significant pain reduction within 30 minutes; however, the comparison of Ketorolac alone versus in combination with magnesium sulfate did not reveal a statistical difference. This result was in contrast to our findings.[34]

Conclusion

Based on the findings of this study, Ketorolac alone or in combination with magnesium sulfate led to significant pain reduction in patients with intertrochanteric fractures admitted to the emergency ward; however, the combination therapy had superior outcomes. Therefore, further studies are recommended.

Acknowledgement

We are grateful to the officials of emergency ward of Besat Hospital affiliated at Hamadan University of Medical Sciences.

Conflict of interest: None

Funding: None

Bijan Heidari MD [1]

Rasoul Salimi MD [2]

Hossein Saremi MD [1]

Mostafa Arab Ghahestani MD [1]

1 Department of Orthopedics, School of Medicine, Besat Hospital, Hamadan, Iran

2 Department of Emergency Medicine, School of Medicine, Besat Hospital, Hamadan, Iran

References

1. Wennberg P, Norlin R, Herlitz J, Sarenmalm EK, Möller M. Pre-operative pain management with nerve block in patients with hip fractures: a randomized, controlled trial. Int J Orthop Trauma Nurs. 2019; 33:35-43. doi.org/10.1016/j.ijotn.2018.11.003.
2. Sanzone AG. Current challenges in pain management in hip fracture patients. J Orthop Trauma. 2016; 30:S1-S5. doi: 10.1097/BOT.0000000000000562.
3. Dixon J, Ashton F, Baker P, Charlton K, Bates C, Eardley W. Assessment and early management of pain in hip fractures: the impact of paracetamol. Geriatr Orthop Surg Rehabil. 2018; 9:2151459318806443. doi.10.1177/2151459318806443.
4. Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Elsevier; 2010:18-26. doi.10.1177/2151459318806443.
5. Zanker J, Duque G. Rapid geriatric assessment of hip fracture. Clin Geriatr Med. 2017; 33(3):369-382. doi.org/10.1016/j.cger.2017.03.003.
6. Maxwell L, White S. Anaesthetic management of patients with hip fractures: an update. Continuing Education in Anaesthesia, Critical Care & Pain. 2013; 13(5):179-183. doi.org/10.1093/bjaceaccp/mkt006.
7. Rantala M, Kankkunen P, Kvist T, Hartikainen S. Post-operative pain management practices in patients with dementia-the current situation in Finland. Open Nurs J. 2012; 6:71. doi: 10.2174/1874434601206010071.
8. Garlich JM, Pujari A, Moak Z, et al. Pain management with

early regional anesthesia in geriatric hip fracture patients. J Am Geriatr Soc. 2020; 68(9):2043-2050. doi.org/10.1111/jgs.16547.
9. Edlund MJ, Steffick D, Hudson T, Harris KM, Sullivan M. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. Pain. 2007; 129(3):355-362. doi.org/10.1016/j.pain.2007.02.014.
10. Chau DL, Walker V, Pai L, Cho LM. Opiates and elderly: use and side effects. Clin Interv Aging. 2008; 3(2):273.
11. Lindenhovious AL, Helmerhorts GT, Schnellen AC, Vrahas M, Ring D, Kloen P. Differences in prescription of narcotic pain medication after operative treatment of hip and ankle fractures in the United States and The Netherlands. . J Trauma. 2009; 67(1):160-164. doi: 10.1097/TA.0b013e31818c12ee.
12. Abdolrazaghnejad A, Banaie M, Tavakoli N, Safdari M, Rajabpour-Sanati A. Pain management in the emergency department: a review article on options and methods. Adv J Emerg Med. 2018; 2(4). doi: 10.22114/AJEM.v0i0.93.
13. Haddadian A, Pourmoteabed S, Nasiri Gigloo K, Ghorbani Amjad G, Bahrami A. Comparison of Ketorolac and Ibuprofen IV Infusion Effect on Radius Distal Fracture Pain Control. Avicenna Journal of Clinical Medicine. 2018; 25(2):79-84. doi. 10.21859/ajcm.25.2.79.
14. McDonald E, Winters B, Nicholson K, et al. Effect of postoperative ketorolac administration on bone healing in ankle fracture surgery. Foot Ankle Int. 2018; 39(10):1135-1140. doi.org/10.1177/1071100718782489.
15. Eftekharian HR. Effect of intravenous ketorolac on postoperative pain in mandibular fracture surgery; a randomized, double-blind, placebo-controlled trial. Bull Emerg Trauma. 2017; 5(1):13.
16. Sedighinejad A, Haghighi M, Nabi BN, et al. Magnesium sulfate and sufentanil for patient-controlled analgesia in orthopedic surgery. Anesth Pain Med. 2014; 4(1). doi: 10.5812/aapm.11334.
17. Bolcal C, Iyem H, Sargin M, et al. Comparison of magnesium sulfate with opioid and NSAIDs on postoperative pain management after coronary artery bypass surgery. J Cardiothorac Vasc Anesth. 2005; 19(6):714-718. doi.org/10.1053/j.jvca.2005.08.010.
18. Fan X, Cao F, Luo A. Femoral nerve block versus fascia iliaca block for pain control in knee and hip arthroplasties: A meta-analysis. Medicine (Baltimore). 2021; 100(14). doi: 10.1097/MD.0000000000025450.
19. Maleki Verki M, Porozan S, Motamed H, Fahimi MA, Aryan A. Comparison the analgesic effect of magnesium sulphate and Ketorolac in the treatment of renal colic patients: Double-blind clinical trial study. Am J Emerg Med. 2019; 37(6):1033-1036. doi:10.1016/j.ajem.2018.08.040.
20. Griffioen MA, O'Brien G. Analgesics administered for pain during hospitalization following lower extremity fracture: a review of the literature. J Trauma Nurs. 2018; 25(6):360-365.doi: 10.1097/JTN.0000000000000402.
21. Molina-Praena J, Ramirez-Baena L, Gómez-Urquiza JL, Cañadas GR, De la Fuente EI, Cañadas-De la Fuente GA. Levels of burnout and risk factors in medical area nurses: A meta-analytic study. Int J Environ Res Public Health. 2018; 15(12):2800. doi.org/10.3390/ijerph15122800.
22. Aliuskevicius M, Østgaard SE, Rasmussen S. No influence of ibuprofen on bone healing after Colles' fracture–A randomized controlled clinical trial. Injury. 2019; 50(7):1309-1317. doi.org/10.1016/j.injury.2019.06.011.
23. Cowan R, Lim JH, Ong T, Kumar A, Sahota O. The challenges of anaesthesia and pain relief in hip fracture care. Drugs Aging. 2017; 34(1):1-11. doi.org/10.1007/s40266-016-0427-5.
24. Sousa AM, Rosado GM, Neto JdS, Guimarães GM, Ashmawi HA. Magnesium sulfate improves postoperative analgesia in laparoscopic gynecologic surgeries: a double-blind randomized controlled trial. J Clin Anesth. 2016; 34:379-384.
25. Tramer MR, Schneider J, Marti R-A, Rifat K. Role of magnesium sulfate in postoperative analgesia. Anesthesiologists. 1996; 84(2):340-347. doi.org/10.1097/00000542-199602000-00011.
26. De Oliveira Jr GS, Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2013; 119(1):178-190. doi.org/10.1097/ALN.0b013e318297630d.
27. Albrecht E, Kirkham K, Liu S, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia. 2013; 68(1):79-90. doi.org/10.1111/j.1365-2044.2012.07335.x.
28. Stomatology FM, Yan Q. Effects of systemic magnesium on post-operative analgesia: is the current evidence strong enough. Pain Physician. 2015; 18:405-417.
29. Peng Y-N, Sung F-C, Huang M-L, Lin C-L, Kao C-H. The use of intravenous magnesium sulfate on postoperative analgesia in orthopedic surgery: A systematic review of randomized controlled trials. Medicine (Baltimore). 2018; 97(50). doi: 10.1097/MD.0000000000013583.
30. Hwang J-Y, Na H-S, Jeon Y-T, Ro Y-J, Kim C-S, Do S-H. IV infusion of magnesium sulphate during spinal anaesthesia improves postoperative analgesia. Br J Anaesth. 2010; 104(1):89-93. doi.org/10.1093/bja/aep334.
31. 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 Anaesthesiol Scand. 2007; 51(4):482-489. doi.org/10.1111/j.1399-6576.2007.01263.x.
32. Barata I, Spencer R, Suppiah A, Raio C, Ward MF, Sama A. Emergency ultrasound in the detection of pediatric long-bone fractures. Pediatr Emerg Care. 2012; 28(11):1154-1157. doi: 10.1097/PEC.0b013e3182716fb7.
33. Navali M, Mohammad A, Moradi M, Mokhtari M. Intra-Articular Injection of Ketorolac for Post-Arthroscopic Pain Control. Iranian Journal of Orthopedic Surgery. 2020; 13(1):16-21. doi.10.22034/ijos.2020.121285.
34. Verki MM, Porozan S, Motamed H, Fahimi MA, Aryan A. Comparison the analgesic effect of magnesium sulphate and Ketorolac in the treatment of renal colic patients: Double-blind clinical trial study. Am J Emerg Med. 2019; 37(6):1033-1036. doi.org/10.1016/j.ajem.2018.08.040.