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Original Contribution

Comparison the analgesic effect of magnesium sulphate and Ketorolac in the treatment of renal colic patients: Double-blind clinical trial study☆,☆☆

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ABSTRACT

Background: Ureter muscles contraction movements caused pain in renal colic. Magnesium sulphate could influence the pain by reducing acetylcholine in the nerve terminals. We have aimed to evaluate the analgesic effects of magnesium sulphate on acute renal colic pain.
Method: In this double-blind clinical trial study, the patients with renal colic pain were randomly divided into 2 groups; Group I received an intravenous infusion of 30 mg of Ketorolac and normal saline as placebo, Group II 50 mg/kg magnesium sulphate 50%/100 ml normal plus 30 mg of Ketorolac. The pain severity of patients was assessed using the visual analog scale (VAS) at baseline, and 15 and 30 min after intervention.
Results: Baseline pain score and demographic characteristics did not significantly different between the groups. After 30 min the pain score significantly reduced in both groups. While, at 15 and 30 min, mean pain score did not show statistically significant differences.
Conclusion: Our findings indicated that Magnesium sulphate did not influence renal colic pain relief.

1. Introduction

One of the most clinical manifestation of renal lithiasis is renal colics (RC). It also is the common cause for admitting to hospital emergency departments [1]. It presents as acute pain in the flanks because of the stone passage from the ureter. The acute renal colic presentations could be included: a pain diffuse; the flanks to the groin, nausea, vomiting, and microscopic hematuria. Moreover, hydronephrosis, urinary infection and continuous colic attacks can be presented in patients with renal colic [2]. It is a relatively most common condition and affected 10–12% of the industrialized countries population. The risk of stone formation during the life estimated between 5 and 10% [3]. While, in Iran, it was reported as 5.7%, that is more frequent in males than females (6.1% vs. 5.3%, respectively) [4]. Ureteral obstruction by stones leads to major alterations of renal blood flow, pressure of intralumin and also glomerular filtration rate. The changes make up by prostacyclin and prostaglandin E2 (PGE2). Moreover, NO release in the kidney is elevated by ureteral obstruction. Therefore, eicosanoids especially prostaglandins have a central role in the creation of pain [5].

Pharmacological management of patients with renal colic performs by prescribing non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and paracetamol [6]. It has been showed that NSAIDs is prior to opioids in relieving patients with renal colic, because of fewer adverse effects and also less rescue analgesia requirement. Moreover, intravenous opioid analgesia could be caused acute respiratory depression and also disruption in gastrointestinal motility [7]. The evidences showed that NSAIDs seems as an ideal analgesics in the renal colic due to many unique properties. They act through inhibition of prostaglandin synthesis that subsequently leads to reduces glomerular filtration, renal pelvic pressure and also stimulation of stretch receptors. Ureteric oedema and inflammation reduction are also caused by NSIADs that facilitate better drainage. Hence, all of them lead to a decrease in ureteric activity or peristalsis. Moreover, NSAIDs could make a direct effect on ureteric smooth muscles and their relaxation [8].

Magnesium is an intracellular ion with diverse physiological functions in human that included enzymes activation, protein synthesis, vasomotor tone regulation, signaling and also neurotransmission. It also is a non-competitive antagonist of *N* methyl D aspartate (NMDA) glutamate receptors that which are participate in pain feeling and persistence. The Pharmacological form of magnesium, Magnesium sulphate ($MgSO_4$), indicated in different clinical conditions including: myocardial and neuronal ischaemia, tachyarrythmia, asthma, pre-eclampsia and spasmophilia [9]. NMDA antagonists were reported as useful agents in the alleviation of acute post-operative pain. Moreover, the effect of

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magnesium sulphate on postoperative pain relief and its effects on reduction of postoperative opioid consumption have been studied in different clinical situations such as ophthalmic, orthopedic and gynaecological surgery [10,11]. While, there is limited studies in respect to the role of Magnesium sulphate on renal colic pain relief. Therefore we have aimed to evaluated the analgesic effect of magnesium sulphate in compared with Ketorolac to treatment the patients with renal colics.

2. Material and methods

2.1. Study design

In this double blind randomized clinical trial, renal colic suspicious patients who admitted to emergency department, Ahvaz, Iran were enrolled to the study. Inclusion criteria were symptoms associated with acute renal colic, age of 18 to 65 years, kidney-bladder-urinary tract ultrasound or computed tomography scan confirmed stone. Exclusion criteria were patients under 18 or above 65 years old, history of renal or hepatic disease, blood systolic pressure lower than 90 mm Hg, patients with sings related to fever (temperature greater than 38 °C), pregnancy, patients suspected to Peritonitis, absence of stone in radiologic evaluations and abnormality in urinary tract and patients that consumed Ca blockers. The study approved by Jundishapour University of medical sciences ethic committee. Also study protocol was described for all of the patients and signed informed consent was given by the patients.

2.2. Therapeutic intervention

Demographic characteristics of patients included gender, age and weight were registered by a questionnaire. Thereafter, patients randomly divided in two groups by block randomization procedure. Patients and also residents who measured answers were not informed of what treatment every person has received. Patients in group A were treated by a standard protocol; 30 mg I.V. Ketorolac along with 100 cc I.V. normal saline as a placebo. Patients in group B received 50 mg/kg Magnesium sulphate 50% (diluted by normal saline). The pain was measured by visual analog scale (VAS) before the intervention, 15 min and 30 min after intervention. The VAS scale is an eleven point unidimensional measure of pain intensity in adults that quantified pain severity.

2.3. Statistical analysis

To have 80% power, detect a correlation as small as 0.25, with a type I error of 0.05, we needed at least 42 samples in each groups. The data obtained were showed by descriptive indicators; mean, standard deviations. Kolmogorov-Smirnov (K-S) used to test the normal distribution of data. After that, to compare numerical variables between the groups, according to normality of data, *t*-test and Mann-Whitney were used. Moreover, repeated measures ANOVA was used to determine the significance of VAS changes. Statistical analyzes were performed using the SPSS version 20. A *p*-value less than 0.05 was considered as significance level.

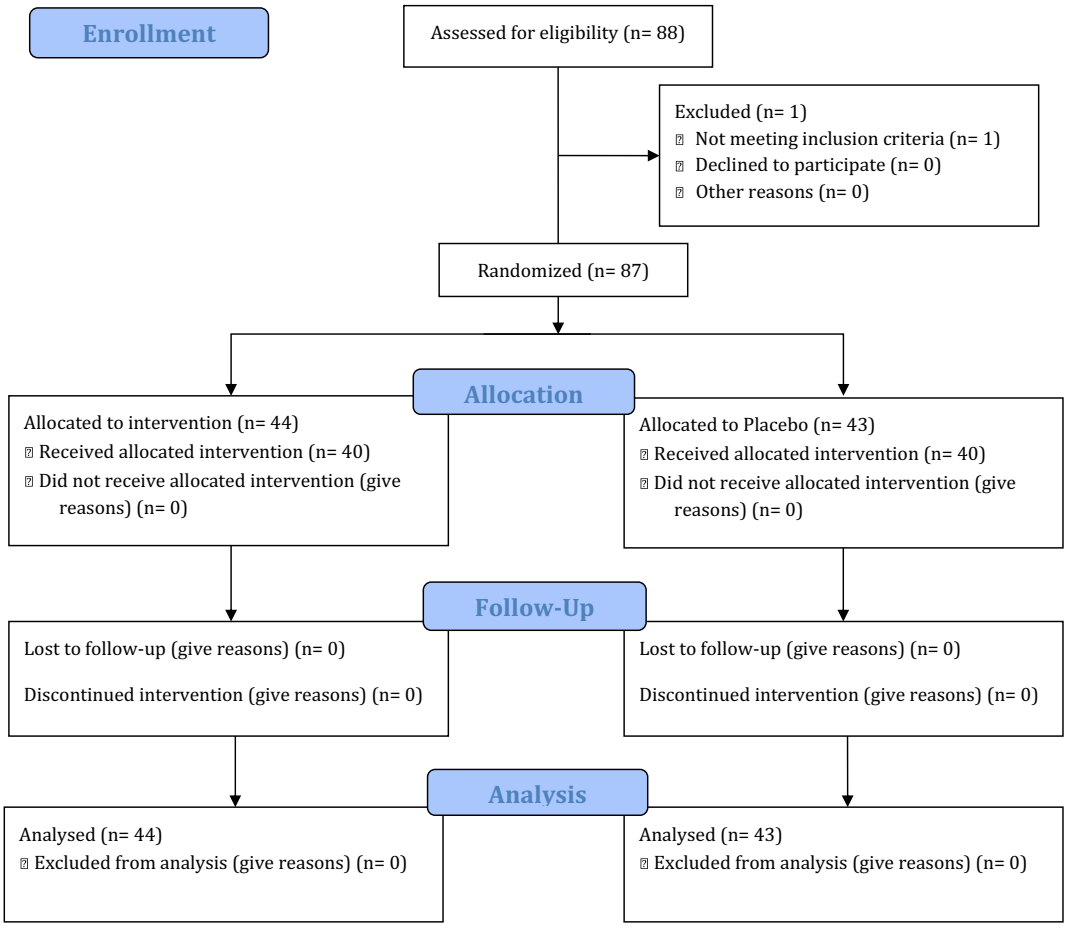

Fig. 1. Study flow diagram.

Table 1
Patient's characteristics.

Variables		Intervention n = 44	Control n = 43	P-value
Age year (Mean ± SD)		39.43 ± 12.089	37.19 ± 10.032	0.256
Gender F (%)		5 (11.4%)	9 (20.9%)	0.359
Weight Kg (Mean ± SD)		78.98 ± 9.62	76.19 ± 11.77	0.232
Temperature median (Celsius)		36.75	36.90	0.099
Before treatment	Oxygen saturation	98.45	98.60	0.496
	Respiratory rate	16.48	17.93	0.381
	Heart rate	83.11	81.26	0.509
	Systolic blood pressure	133.82	129.23	0.318
	Diastolic blood pressure	81.09	79.86	0.656
After 15 min	Oxygen saturation	98.41	98.63	0.573
	Respiratory rate	14.32	13.96	0.632
	Heart rate	81.91	81.09	0.752
	Systolic blood pressure	119.64	116.26	0.257
	Diastolic blood pressure	71.14	70.87	0.925

Table 2
Comparison of drug efficacy in tow group.

Variable	Intervention n = 44	Control n = 43	P-value
Before treatment	7.56 ± 1.84	7.81 ± 1.59	0.493
After 15 min	3.20 ± 2.45	3.62 ± 2.27	0.424
After 30 min	3.43 ± 3.309	1.67 ± 0.81	0.232

3. Results

During the study 88 patients were included into the study that one of them lost follow up. Other 87 patents randomly allocated into two groups (Fig. 1). The mean age of patients was 31.38. The gender distribution in the groups was not significantly different. Moreover, the mean of age of patients in both group were not significantly different (39.43 and 37.19, p = 0.35). Also, the patient's weight did not showed statistically significant differences (p = 0.232) (Table 1).

The hemodynamic factors including: oxygen saturation, respiratory rate, heart beat and blood pressure did not significantly changed after intervention and showed similar levels in both groups (Table 2). Before the intervention, VAS in the control and intervention groups were 7.56 and 7.81, respectively, that showed insignificantly differences (p = 0.49). After 30 min pain score significantly reduced in both groups (Fig. 2). While, in the time point of 15 min and also 30 min the VAS did not show significantly differences between the groups (Table 2).

4. Discussion

Renal colic is a sudden onset severe pain that initiated from flanks and radiated to the groin. The patients experience an increasing recurrent pain. The mail goal in the treatment is alleviation of pain. Ketorolac is NSAID with analgesics and anti-inflammatory effects that frequently used in patients with renal colic. The drug controlled pain and inflammation by inhibition of prostaglandins synthesis [12]. In the emergency department is administered routinely. But it could be caused upper gastrointestinal bleeding, gastric ulcers, hemostatic impairment, renal dysfunction and bronchospasm. Hence it is contraindicated in some predisposed patients [13]. Moreover, its analgesic effect is short term and usually patient is re-admitted to the ED. So, the emergency physicians are seeking for a more effective analgesic in controlling the renal colic pain. In the current study, we have aimed to evaluate the effect of magnesium sulphate as an adjunct to Ketorolac in the alleviating renal colic pain.

Our results showed that, baseline pain score (before intervention) in the control and intervention groups were 7.56 and 7.81, respectively, that showed insignificantly differences. After 30 min pain score significantly reduced in both groups. While, in the time point of 15 min and also 30 min the VAS did not showed significantly differences between the groups. So, the results indicated that adding magnesium sulphate to Ketorolac did not cause a significant analgesic effect. Joker et al. in a similar randomized clinical trial study evaluate the analgesic effects of magnesium sulphate on renal colic pain. They compared the pain severity using VAS in patients either received standard protocol for renal colic pain relief (intravenous infusion of 0.1 mg/kg morphine sulphate and 30 mg of Ketorolac) with or without magnesium sulphate. Contrary to our results they found that mean pain severity on VAS is significantly lower in the groups received magnesium sulphate [14]. The differences may be due to the Jokar et al. study protocol, they also administrated morphine along with Ketorolac. In the RCT study, Sun et al. assessed the perineural magnesium sulphate analgesic effects for diabetic toe amputation, they showed that $MgSO_4$ as an adjunctive drug did not enhance analgesic quality [15]. Similarly, Frassanito et al. evaluated the effect of IV magnesium sulphate on postoperative total knee arthroplasty pain severity. They found that perioperative infusion of IV magnesium

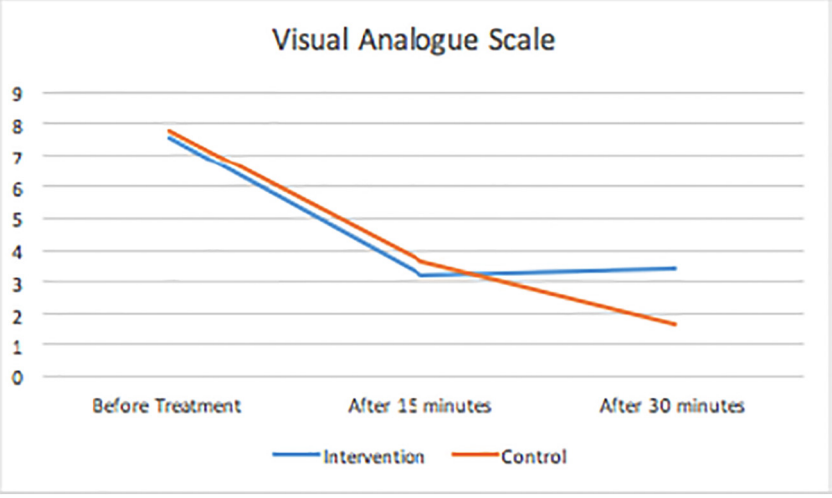

Fig. 2. Pain score changes during the study.

sulphate could not influence postoperative pain [16]. Moreover it has been reported that magnesium sulphate did not also effect on opioid consumption [17].

4.1. Limitation

Short follow up duration and also small sample size are the limitations of our study. We also did not compare the side effects between the groups.

5. Conclusion

Collectively, our finding emphasized that adding magnesium sulphate to Ketorolac could not influence the renal colic pain relief.

Conflict of interest

The authors declare that they have no conflict of interest.

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