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ORIGINAL RESEARCH

Comparison of Lidocaine-triamcinolone Injection with and without Magnesium Sulfate in Ankle Joint Osteoarthritis

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Abstract: **Background:** Currently available pharmacological therapies for osteoarthritis mainly target palliation of pain and include analgesics, intra-articular therapy, and topical treatment. We aimed to evaluate the effect of the concomitant use of magnesium sulfate in addition to a combination of triamcinolone and lidocaine.
Methods: To evaluate the changes in pain factor levels, sixty patients with ankle osteoarthritis were randomly divided into two control (Triamcinolone + Lidocaine) and intervention (Triamcinolone + Lidocaine + Magnesium sulfate) groups (n= 30, each group). In both groups, patients were injected with 80 mg triamcinolone and 0.5 cc of 2% lidocaine, while in the intervention group, 500 mg of magnesium sulfate was added to the injecting solution, and in the control group, an equivalent volume of 0.9% normal saline was added to the injecting solution. Patients were monitored after one week and one month and each completed the visual analog scale (VAS) and American Orthopedic Foot and Ankle Society (AOFAS) pain score questionnaires in addition to their demographic characteristics. The results were evaluated based on the design of the questionnaire and data were analyzed employing SPSS software, version 21, and using independent ttest.
Results: AOFAS and VAS scores were significantly different between the intervention and control groups within one week after treatment (p value= 0.018) but AOFAS and VAS scores after one month were not significantly different.
Conclusions: Using magnesium sulfate was effective in controlling the pain caused by ankle osteoarthritis at short intervals.

Keywords: Lidocaine, Triamcinolone, Magnesium sulfate, Osteoarthritis

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1. Introduction

Osteoarthritis (OA) is a mildly progressive joint disease that usually affects one or more joints (1). Dimensions and areas of involvement in patients with this disease include a wide range. However, the most common joints involved include the hip, knee, spine, and small joints of the arms and legs (2). Reducing the pain and inflammation caused by this disease has always been one of the challenges and priorities of treatment protocols (3). Currently, available pharmacological therapies for OA mainly target palliation of pain and include analgesics, intra-articular injection, and topical treatment. Intra-articular local anesthetics are often used for the prevention of pain after arthroscopic knee surgery (3,4). For this purpose, various drugs such as opioids, non-steroidal anti-inflammatory drugs, clonidine, neostigmine, and ketamine with variable effects are used (5,6).

The use of lidocaine to reduce the pain of tissue damage and limited surgery is very common (7), while triamcinolone has also been used because of its anti-inflammatory effects in various diseases such as eczema, allergies, lupus, psoriasis, alopecia, asthma, and autoimmune arthritis (8). The combined use of these drugs has been reported to help in many pain-related inflammatory disorders (9).

Magnesium is a calcium channel blocker that can regulate cell calcium influx (10). The N-methyl-D-aspartate (NMDA)

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receptor is an ionotropic receptor for glutamate and aspartate situated in the brain and spinal cord (11). NMDA receptor blockade can inhibit the induction of central sensitization due to peripheral nociceptive stimulation and abolish hypersensitivity (12). MgSO4 is an old and well-known therapeutic agent used in clinical practice which serves as a noncompetitive antagonist of NMDA receptors and their associated ion channels (13). On the other hand, magnesium sulfate, can also be considered as an alternative substance in controlling inflammatory conditions (14). However, its effectiveness as an intra-articular NMDA receptor antagonist in reducing pain sensation, or as an adjunct to local intra-articular anesthesia is not known (15).

Therefore, in the present study, an attempt was made to evaluate the effect of concomitant use of magnesium sulfate in addition to the previous combination, while using the combination of lidocaine and triamcinolone as a treatment-control method for patients with OA of the ankle.

2. Material and Methods

The present interventional, randomized, and double-blind study was approved by the Ethics Committee in Biomedical Research of Shahid Beheshti University of Medical Sciences in Tehran (code: IR.SBMU.RETECH.REC.1400.054). Patients with ankle OA aged 18-60 years who had no concurrent comorbidities were included in this research. Those who did not give their informed consent and patients with rheumatoid arthritis, ankle malalignment, ipsilateral knee or hip OA were excluded. To evaluate the changes in pain factor levels (AOFAS score and VAS score) following the injection of lidocaine + triamcinolone with and without magnesium sulfate addition in patients with OA of the ankle, sixty OA cases were randomly divided into two control (Triamcinolone + lidocaine) and intervention (Triamcinolone + lidocaine + Magnesium sulfate) groups (n= 30, each group). The study was conducted in a referral university hospital, Akhtar Hospital, Tehran, Iran, from October 2020 to October 2021, though, the individuals were from the whole country. In both groups, patients were injected with 80 mg triamcinolone and 0.5 cc of 2% lidocaine, while in the intervention group, 500 mg of magnesium sulfate was added to the injecting solution, and in the control group, an equivalent volume of 0.9% normal saline was added to the injected solution. Patients were monitored after one week and one month and each completed the visual analog scale (VAS) and American Orthopedic Foot and Ankle Society (AOFAS) pain score questionnaires in addition to their demographic characteristics. The results were evaluated based on the design of the questionnaire and data were analyzed using SPSS software, version 21. Following confirmation of a normally distributed population, an independent t-test was applied.

Visual analog scale (VAS): It is often used in epidemiologic and clinical research to measure the intensity or frequency of various symptoms. For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain (16).

American Orthopedic Foot and Ankle Society (AOFAS): Ankle-Hindfoot Score is among the most commonly used instruments for measuring the outcome of treatment in patients who sustained a complex ankle or hindfoot injury (17).

3. Results

Of the 60 patients included in this study, 30 (50%) were men and 30 (50%) were female. Among them, the intervention group consisted of 14 (46.7%) men, and the control group comprised 16 (53.3%) men. However, there was no significant difference between the sex ratios of the two groups (P = 0.606). The mean±SD ages of patients in the intervention and control groups were 51±7.47 and 48.3±7.47 years, respectively (P = 1.00, Figure 1).

Baseline AOFAS scores (mean ± SD) for intervention and control groups were 68.1±6.50 and 65.8±5.83 respectively. Moreover, their VAS scores (mean ± SD) were also comparable; 7.2±1.15 in the group receiving Triamcinolone + lidocaine and 6.9±1.24 in Triamcinolone + lidocaine + Magnesium sulfate group. Table 1 shows the monitoring of AOFAS and VAS indices in two time periods (one week and one-month following injection). Accordingly, AOFAS and VAS scores were significantly different between the intervention and control groups within one week after treatment but AOFAS and VAS scores after one month were not significantly different.

4. Discussion

Although the direct analgesic effects of magnesium have not yet been proven, we do know that the analgesic effects of this element are due to blocking NMDA receptors and preventing calcium ions from entering the cell. To be precise, it can be said that this analgesic effect is related to the prevention of central sensitivity caused by damage to peripheral tissue. Such sensitivity is due to the increase of neural properties in the pain pathways of the central nervous system which in such cases, repetitive pain afferent inputs are stimulated and eventually appear as a long-term decrease in pain threshold. With wind-up or long-term pain potentiation, it causes pain even when peripheral stimuli are not severe and continues to cause pain even after the initiating stimuli have disappeared.11 Given these cases, it can be expected that increased intracellular calcium plays a major role in initiating central sensitization, and its accumulation is related to various receptors in spinal dorsal horn postsynaptic neurons (such as NMDA, amino 3-hydroxy-5 methyl receptors Isoxazole is propionate and kainite) (12, 14). Activation

Table 1: Examination of AOFAS and VAS indices in two time periods "after one week and after one month" shown in two groups of intervention (Triamcinolone + lidocaine + Magnesium sulfate) and control (Triamcinolone + lidocaine).

Variable	Triamcinolone + Lidocaine + Magnesium sulfate (mean± SD)	Triamcinolone + Lidocaine (mean± SD)	p-value
AOFAS score (first week)	86.7±3.5	75.46±5.6	0.018
AOFAS score (first month)	71±4.3	69.8±3.9	0.279
VAS score (first week)	2.06±0.86	6.00±1.36	0.08
VAS score (first month)	7.16±1.2	6.83±1.57	0.11

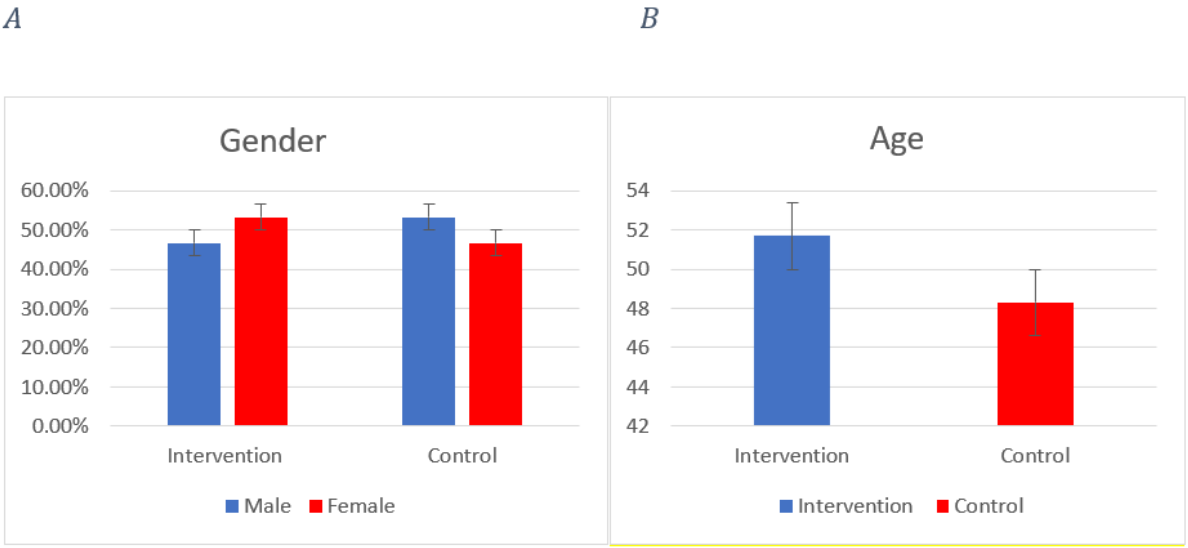

Figure 1: Comparison of gender ratio (A) and age of patients (B) in the two groups of Intervention (Triamcinolone + Lidocaine + Magnesium sulfate) and Control (Triamcinolone + Lidocaine) of patients with ankle joint osteoarthritis.

of the NMDA receptor is a necessity to establish and maintain central sensitivity. These receptors are a type of membrane ion channels expressed in the central nervous system that regulates Na + and Ca2 + cell flow and K + output. Extracellular magnesium blocks these receptors in a voltage-dependent manner.11 In addition to central sensitivity, calcium channels have been reported for therapeutic purposes in neuropathic pain conditions (18). Since magnesium is a natural calcium antagonist, magnesium analgesics should include calcium channel blockade (19).

Despite various studies on the analgesic effects of magnesium sulfate, the results have been contradictory. Thus, according to the results of some studies, MgSO4 reduces analgesic consumption during and after surgery. Tramer and colleagues first mentioned in 1996 that individuals' morphine administration following surgery was found to be less in the group of patients being treated simultaneously with intravenous magnesium (20). In one study, a dose of magnesium was given to patients undergoing orthopedic lumbar surgery during anesthesia, based on which a decrease in opioid use after surgery was evident during the 24-hour study period (21). However, the average VAS is about 5, so pain management with this method is not desirable.

In this study, two indicators of the AOFAS score and VAS score were evaluated to evaluate patients' pain after intervention in two time periods of one week after surgery and one month after intra-articular injection. Data analysis shows AOFAS (P = 0.018) and VAS (P = 0.08) score indices of the experimental group were significantly and non-significantly different from the control group within one week after the procedure, respectively.

Earlier, Sadoni and co-workers studied the effects of intra-articular injection of magnesium sulfate on postoperative pain in knee arthroscopy, stated that the magnesium sulfate group showed a significant reduction in VAS score, a significantly increased time to first postoperative analgesic request as well as significantly reduced total analgesic requirement than the control group (22).

In a study entitled "Intraarticular Injection of Magnesium Sulphate and/ or Bupivacaine for Postoperative Analgesia after Arthroscopic Knee Surgery", the researchers demonstrated that in group MB (Magnesium combined with bupivacaine) VAS scores significantly reduced both at rest and on movement, a significantly increased time to first postoper-

ative analgesic request, as well as significantly reduced total analgesic requirement than other groups were reported (23). Although the beneficial effect of magnesium might be the result of antagonism of NMDA receptors, magnesium's inhibitory properties for calcium channels may play a role as well. The analgesic effect of magnesium may be the result of pharmacodynamics rather than a pharmacological receptor effect (11, 13). In another study, magnesium used as an adjunct to lidocaine improved the quality of anesthesia and analgesia for IV regional anesthesia (24).

5. Conclusion

According to the results of the present study and the evaluation of two parameters, AOFAS score, and VAS score, it can be said that the use of magnesium sulfate is effective in controlling the pain caused by ankle OA at short intervals.

6. Appendix

6.1. Acknowledgment

None.

6.2. Conflict of interest

The authors declare no conflict of interest.

6.3. Funding support

None.

6.4. Author's contributions

All the authors had the same contribution.

6.5. Ethical approval

We obtained full ethical approval from the Biomedical Research Ethics Committee of the Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1400.054).

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