



COMPARISON OF POST SURGICAL VAS VALUES IN SURGERY WITH SPINAL BUPIVACAINE ANESTHESIA USING ANALGETIC MAGNESIUM SULFATE AND KETOROLAC

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ABSTRACT

Magnesium sulphate is antagonists of the receptors of N-methyl-D-aspartate (NMDA) and as a calcium channel inhibitor (Cachannel blocker). The aim of this research is to determine the comparison of VAS and duration of analgesia on the use of MgSO₄ and intravenous ketorolac in dealing with pain during postoperative spinal anesthesia. This study was conducted by double blind randomized sampling method July - September 2018 at the Adam Malik General Central Hospital. The total samples obtained were 36 patients. The drug was prepared with the help of volunteer I who had randomized it (the researcher did not know the medication given). Recording and observation of patients on vital signs (blood pressure, heart rate, respiratory frequency) at T0 (2 hours after anesthesia), T1 (3 hours), T-2 (4 hours), T-3 (5 hours), T- 4 (6 hours), T-5 (7 hours), T-6 (8 hours), T-7 (9 hours), and T-8 (10 Hours) after anesthesia. From the result, samples based on age and sex, patients aged 18-32 years in the ketorolac group were 9 people (22.5%), while in the MgSO₄ group there were 9 people (22.5%). Patients aged 33-46 years in the ketorolac group were 12 people (30%) and in the MgSO₄ group as many as 15 people (37.5%), while patients aged 47-60 years in the ketorolac group were 19 people (47.5%) and in the MgSO₄ group there were 16 people (40%). Based on the age characteristics of patients, it was found that the data were relatively homogeneous ($p > 0.05$). Samples Based on Age, Gender and ASA PS, 43 men (53.75%) and women were 37 people (46.25%), with the youngest age 18 years and the oldest age 60 years, with average - average age of 42.9 years. In the ketorolac group, there were 21 male samples (52.5%) and 22 MgSO₄ groups (55%), while 19 females in the ketorolac group (47.5%) and MgSO₄ group was 18 people (45%). Based on the characteristics of the sample sex, it was found that the data were relatively homogeneous ($p > 0.05$) PS ASA 1 in the group that received ketorolac was 17 people (42.5%) and in the MgSO₄ group were 19 people (47.5%). While subjects with PS ASA 2 who received ketorolac were 23 people (57.5%) and in the MgSO₄ group 21 people (52.5%). Ketorolac has a stronger analgesic effect than MgSO₄ in patients who have undergone surgery with spinal technique. MGSO₄ can be used as an alternative as an analgesic for postoperative patients, but cannot be compared with ketorolac.

KEYWORDS : Magnesium Sulfate, Ketorolac, Spinal Bupivacaine Anesthesia, Visual analog scale

1. INTRODUCTION

Pain is a subjective feeling or experience that involves sensory, emotional and bad behavior are associated with tissue damage or potential damage to the tissue. If it is not treated, it would have a negative impact on postoperative sufferers such as anxiety (sleeping disturbances), immunosuppression, hyperglycemia, hemodynamic changes (hypertension, tachycardia), decreased breath movements that causes inability to cough, be able to facilitate the occurrence of atelectase, a mobilization fear will increase the risk of thromboembolic complications, and increase catecholamine discharge which causes increased vascular resistance, extension catabolic phase, decreasing blood flow to the inferior extremity and decreasing blood circulation to splanchnic. The above conditions will result a slow healing, impaired mobilization, risk factors for chronic pain, increased length of hospitalization and it will increase the cost of treatment.-(1,2)

The American Society of Anesthesiologists (ASA) states that multimodal analgesia is the key to treating postoperative pain. Good pain management will increase the end result of surgery by reducing morbidity and speeding up recovery time. Multimodal analgesia has been shown to reduce postoperative stress, reduce pain in patients with comorbidities related to breathing, heart disease, thrombotic complications, nausea, vomiting, ileus, increased catabolism, cognitive dysfunction, facilitate recovery by accelerating nutrition, mobilization, and also reduce hospitalization.

In Tanra's research, 2014, it was concluded that magnesium sulfate or MgSO₄ is an antagonist of N-methyl-D-aspartate (NMDA) receptors and calcium channel blockers (Cachannel blockers). As an NMDA receptor antagonist, magnesium sulfate works to inhibit central nerve sensitization due to peripheral stimulation and eliminates hypersensitivity reactions, magnesium sulfate has been

shown to have antinociceptive effects through calcium channel inhibition.(3)

In a research which conducted by Dhani et al in 2013 randomized, controlled, double-blind aims to assess the effect of intravenous magnesium sulfate bolus on visual analog scale (VAS) values and the number of pethidine analgesic requirements in 30 female patients with ASA I-II physical status, age 18-60 years old, who will undergo gynecological abdominal elective surgery under general anesthesia in the central operating room of the Dr. Hasan Sadikin Bandung in June-September 2013. The research subjects were divided into two groups which will get bolus and maintenance of intravenous MgSO₄ (group M) or 0.9% NaCl (group S). The results showed that the VAS value and the amount of pethidine analgesic given to M group were statistically lower compared to group S ($p < 0.05$). The conclusions of the study were perioperative intravenous bolus magnesium sulphate able to show VAS values when lower postoperative mobilization and reduce the need for pethidine analgesics in patients after gynecological abdominal surgery.

In a research which conducted by Hengki et al, 2014, the double blind block clinical trial method. Thirty-six subjects aged 21-55 years were allocated to group A who were given intravenous 15 minutes of MgSO₄ 30 mg / kg, continued 15 mg / kg / hr until the end of surgery and B group was given 0.9% NaCl with the same volume undergoing surgery. major in Sanglah Hospital Denpasar in June-August 2014. The results of the research were analyzed by Mann-Whitney Test. Visual analog scale (VAS) being silent and moving in 4th and 8th hours of the Mg group were significantly different ($p < 0.05$). The difference in postoperative morphine consumption at the 4th, 8th, and 24th hours was significantly different ($p < 0.05$). The conclusion of this research is that intravenous MgSO₄ administration during surgery improves the effect of analgesia and decreases postoperative morphine requirements.(4)

In the Atiyat B research, Cloub, 2009 Patients post abdominal surgery and thoracotomy who received multimodal pain therapy were shown to experience smaller metabolic and hormonal stress, shorter extubation time, lower pain score, and faster recovery time. Multimodal pain therapy is done by giving opioids as the main analgesic added with other analgesic drugs (eg paracetamol, cyclooxygenase inhibitors, or nonsteroidal anti-inflammatory drugs) and classes of coanalgesia drugs (clonidine and N-methyl-D-aspartate (NMDA) receptor antagonists, eg ketamine or MgSO₄ (magnesium sulfate) The use of combination therapy can strengthen the opioid class analgesic potential, reduce dosage requirements, tolerance and opioid side effects, and accelerate patient recovery.(5)

Lysakowsky's reserach in 2017 showed that there was a decrease in postoperative magnesium but postoperative hypomagnesaemia mechanism was not known with certainty, it was thought to be related to a decrease in albumin levels in the blood so that the protein and magnesium bonds also decreased. The decreased protein levels and albumin are closely related to the amount of fluid given. The incidence of hypomagnesaemia increased from 19.2% at preoperative to 71% immediately after surgery, and it will decrease to 65.6% after 24 hours later. Decreased magnesium levels in the blood below the physiological threshold can increase the responsiveness of N-methyl-D-aspartate (NMDA) receptors.(6)

In the 2013 research, it was found that morphine consumption in 24 hours postoperatively in the lower MgSO₄ group was 5.28 mg compared to the NaCl group. The results of this study are in line with the research conducted by Hwang et al. 10 and Pastore et al. 12 research using 50 mg / kgBg of intravenous bolus followed by 15 mg / kg / hour of total hip replacement surgery by using spinal anesthesia can reduce morphine requirements. postoperatively with a lower pain score. The study conducted by Dabbagh et al. 5 in lower extremity orthopedic surgery showed that the administration of 8 mg / kg of MgSO₄ until the end of the surgery showed a pain scale and lower morphine requirements compared to the control group.

From the background above, the researchers wanted to know whether the administration of Magnesium Sulfate 30 mg / kgBB mg intravenously as preemptive analgesia could further reduce the value of postoperative VAS compared with ketorolac 30 mg intravenously.

2. METHOD

This research used a double blind randomized clinical trial method to determine the comparison of Visual Analogue Scale from administration of 20% Magnesium sulfate 30 mg / kgBW with intravenous Ketorolac as a postoperative multimodal analgesia with spinal anesthesia.

Inclusion criteria in Willing to participate in research, Age 18-60 years., PS ASA 1-2., Pre operating VAS 0-1, Ideal, body weight according to BMI (18,5-24,9). Exclusion Criteria, patients with contraindications to spinal anesthesia, patients who have a history of hypersensitivity to 20% magnesium sulfate and ketorolac drugs., patients with impaired kidney function, patients with a history of taking pain relievers 24 hours earlier. After obtaining approval from the North Sumatera Medical Faculty Ethics Committee and the Haji Adam Malik General Hospital ethics committee, the patient received an explanation of the procedure to be followed and stated in writing his readiness on the *informed consent sheet*. This research first received approval from the research ethics committee in the field of health, Faculty of Medicine, University of North Sumatra and Haji Adam Malik General Hospital Medan. The researcher then conducted informed consent to the patient during the pre-trial visit. All samples will undergo surgery and comply with the inclusion criteria and are asked to sign an agreement for participation in the study. The patient is explained about the plan to give the drug for surgery and spinal anesthesia and research procedures that use drugs that are commonly used. Randomization by trained

volunteers, randomization was done using block method, each block consists of 6 sequences. Then with the eyes closed the pen is dropped over a random number. The number designated by the pen is the initial number to determine the appropriate sequence. Then choose 6 numbers with 2 digits to the side of the first number until you get the number of sequences that correspond to the size of the sample. Then the sequences obtained are arranged sequentially according to the envelope number. The drug was prepared with the help of volunteer I who had randomized it (the researcher did not know the medication given). After randomizing and preparing the medicine, (20% Magnesium sulfate and ketorolac drugs are put into a syringe and one in siringe pump, then volunteer I gives treatment to volunteer II to be given on the day of the research.

On the day of the research:

1. This research was conducted under the supervision of an anesthetist consultant on duty on that day.
2. Both groups underwent elective surgery preparation procedures.
3. After the patient arrives at the operating room waiting room, the patient is re-examined by the researcher for identity, diagnosis, plan for anesthesia, access to infusion.
4. Both groups are given an infusion of preload of lactate ringer fluid as much as 10 ml / kg of fluid before spinal anesthesia was performed.
5. The patient is informed of the sense of pain described to the patient before carrying out the operation with the prepared VAS numerical scale. Then the VAS value, and the initial measurement of blood pressure, pulse frequency, breathing frequency.
6. Before the patient enters the operating room, an anesthetic machine is connected to an oxygen source. Also prepared is an endo tracheal intubation set (ETT), injection emergency medication such as epinephrine, sulfas atropine, ephedrine and dexamethasone.
7. After the patient enters the operating room, lying on his back, a monitoring device is installed in the form of an ECG monitor, tensimeter, oxygen saturation on the patient's body.
8. After that, the patient is tilted to the lateral decubitus position for spinal anesthesia with a 0.5 mg hyperbaric bupivacaine 15 mg after being positioned supine or sloping position depending on the operating action, and given 2 L / minute oxygen nasal prong. Spinal anesthesia is performed by PPDS anesthesia.
9. The block height is set as high as Thorakal 6 by performing a head up position which is confirmed by the prick test pin.
10. Recording and observation of patients on vital signs (blood pressure, heart rate, respiratory frequency) at T0 (2 hours after anesthesia), T1 (3 hours), T-2 (4 hours), T-3 (5 hours), T- 4 (6 hours), T-5 (7 hours), T-6 (8 hours), T-7 (9 hours), and T-8 (10 Hours) after anesthesia is carried out. VAS score is assessed when the room is post-surgery using a table VAS images are asked to the patient by showing images that correspond to the pain perception felt by the patient. This assessment was carried out directly by researchers and volunteers III who were not involved in giving drugs to these patients at T0 (2 hours after anesthesia), T1 (3 hours), T-2 (4 hours), T-3 (5 hours), T-4 (6 hours), T-5 (7 hours), T-6 (8 hours), T-7 (9 hours), and T-8 (10 hours)
11. Side effects that occur after surgery are noted T0 (2 hours after anesthesia), T1 (3 hours), T-2 (4 hours), T-3 (5 hours), T-4 (6 hours), T-5 (7 hours), T-6 (8 hours), T-7 (9 hours), and T-8 (10 hours) decreased physiological reflexes, anuria, decreased frequency of breathing, allergic reactions, nausea and vomiting other complaints that may occur, or even shortness of breath.
12. The research will be stopped when there is a total spinal block, a warning of airway, heart, lung and brain emergency.
13. If the patient has an elevated spinal block exceeding th4 then the patient will be given oxygen therapy by using a hood. Treatment of hypotension due to spinal action, where systolic blood pressure <90 mmHg and MAP <60 mmHg, will be treated with administration of 10 mg of ephedrine and infusion of RL 20 cc / kgBB resuscitation fluid for 30 minutes.

14. If the patient feels a total spinal or respiratory depression, the patient will be given a breath assistance.
15. The length of surgery in minute will be calculated starting from the operator to cut the skin until accomplish sewing / closing the skin.
16. Bromage Score is a criterion for assessing the patient's general condition during treatment in the observation room.

3. RESULTS

This research has been carried out in July - September 2018 at the Central Surgical Installation of H. Adam Malik General Hospital Medan. This study was conducted by double blind randomized sampling method. Patients aged 18-32 years in the ketorolac group were 9 people (22.5%), while in the MgSO4 group there were 9 people (22.5%). Patients aged 33-46 years in the ketorolac group were 12 people (30%) and in the MgSO4 group as many as 15 people (37.5%), while patients aged 47-60 years in the ketorolac group were 19 people (47.5%) and in the MgSO4 group there were 16 people (40%). Based on the age characteristics of patients, it was found that the data were relatively homogeneous ($p > 0.05$).

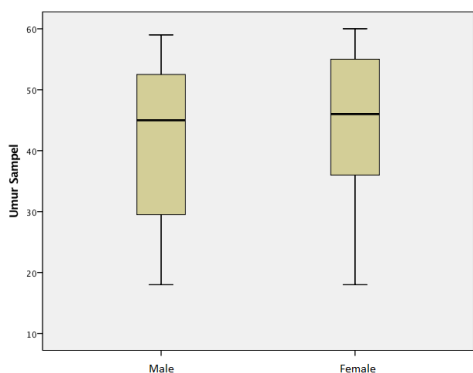


Figure 4.1. Description of Sample Characteristics based on age and gender

This study was followed by 43 men (53.75%) and women as many as 37 people (46.25%), with the youngest age 18 years and the oldest age 60 years, with an average age of 42.9 years. In the ketorolac group, there were 21 male samples (52.5%) and 22 MgSO4 groups (55%), while 19 females in the ketorolac group (47.5%) and MgSO4 group was 18 people (45%). Based on the characteristics of the sex, the sample was found to be relatively homogeneous ($p > 0.05$).

Table 4.1. Sample Characteristics Based on Age, Gender and ASA PS

| Characteristic | | | Amount | P value* |
|-----------------------|------------|------------|-------------|----------|
| | Ketorolac | MgSO4 | | |
| 1. Age (Years) | | | | |
| 18-32 | 9 (22,5%) | 9 (22,5%) | 18 (22,5%) | 0,272 |
| 33-46 | 12 (30%) | 15 (37,5%) | 27 (33,75%) | |
| 47-60 | 19 (47,5%) | 16 (40%) | 35 (43,75%) | |
| Total | 40 (100%) | 40 (100%) | 80 (100%) | |
| 2. Gender | | | | |
| Male | 21 (52,5%) | 22 (55%) | 43 (53,75%) | 0,127 |
| Female | 19 (47,5%) | 18 (45%) | 37 (46,25%) | |
| Amount | 40 (100%) | 40 (100%) | 80 (100%) | |
| 3. PS ASA | | | | |
| ASA 1 | 17 (42,5%) | 19 (47,5%) | 36 (45%) | 0,229 |
| ASA 2 | 23 (57,5%) | 21 (52,5%) | 44 (55%) | |
| Amount | 40 (100%) | 40 (100%) | 80 (100%) | |

*Fisher exact test

Based on table 4.1., Subjects with PS-ASA 1 in the group that received ketorolac were 17 people (42.5%) and in the MgSO4 group as many as 19 people (47.5%). While subjects with PS-ASA 2 who received ketorolac were 23 people (57.5%) and in the MgSO4 group 21 people (52.5%).

Table 4.2. Characteristics of Samples Based on Average Age

| Gender | Age average | N | CI 95% | Std. Deviation |
|--------|-------------|----|------------|----------------|
| Male | 42.21 | 43 | 42.21 3.94 | 12.813 |
| Female | 43.70 | 37 | 43.70 4.08 | 12.231 |
| Amount | 42.90 | 80 | | 12.491 |

Based on the results of the study the average time to reach VAS > 3 in the ketorolac drug group for 200.4 ± 56.6 minutes was longer than the average time to reach VAS > 3 in the MgSO4 group. Statistical Tests with Mann-Whitney test showed a significant difference in the time to reach VAS > 3 between the two groups of study subjects ($p < 0.05$).

Table 4.3 The average difference in time to reach VAS > 3 based on the drug given

| | Drug | N | Mean | P Value* |
|---------|-----------|----|--------|----------|
| Outcome | Ketorolac | 40 | 200.4 | .000* |
| | MgSO4 | 40 | 143.42 | |
| | Total | 80 | 171.91 | |

*Mann-Whitney Test

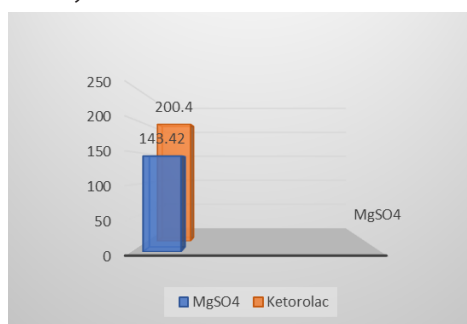


Figure 4.2. Average Difference The time needed to reach VAS > 3



Figure 4.3. Graph of the time difference needed to reach VAS > 3

From the graph above (figure 4.3.) It can be seen that the ketorolac group has a longer time value compared to the MgSO4 group at T1 - T4. In T0 both groups have the same VAS value. This is because there are still effects of analgesic drugs used during surgery.

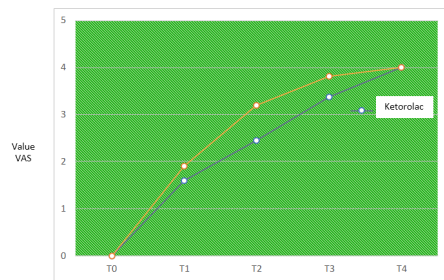


Figure 4.4. Graph difference in average time needed to reach VAS > 3

From the graph above (figure 4.4.) It can be seen that the ketorolac group has a longer average time span compared to the MgSO4 group at T1 - T4. In T0 both groups have the same VAS value. This is because there are still effects of analgesic drugs used during surgery.

4. DISCUSSION

This study was conducted to determine the comparison of VAS and duration of analgesics on the use of MgSO₄ and intravenous ketorolac in dealing with pain during postoperative spinal anesthesia. The American Society of Anesthesiologists (ASA) states that multimodal analgesia is the key to treating postoperative pain. Good pain management will increase the end result of surgery by reducing morbidity and speeding up recovery time. Multimodal analgesia has been shown to reduce postoperative stress, reduce pain in patients with comorbidities related to breathing, heart disease, thrombotic complications, nausea, vomiting, ileus, increased catabolism, cognitive dysfunction, facilitate recovery by accelerating nutrition, mobilization, and also reduce stay in hospital.

The main working mechanism of ketorolac is inhibiting prostaglandin synthesis by acting as a competitive inhibitor of the enzyme cyclooxygenase (COX) and producing analgesia. Like NSAIDs in general, ketorolac is a non-selective COX inhibitor. Magnesium has a large effect on ion transport in the heart cell membrane, contributing to activating around 300 enzymatic reactions, including enzymes that play a role in energy metabolism and nucleic acid synthesis.⁽⁷⁾ Besides that magnesium also plays a role in hormone and receptor bonds, regulation of calcium channels, muscle contraction, neuronal activity, vasomotor tone control, cardiac excitability, and neurotransmitter release.⁽⁸⁾ This study was attended by 80 people who met the inclusion and exclusion criteria. From the characteristics of the research sample in table 4.1 (consisting of gender categories) and table 4.2 (consisting of the sample age group categories) which were assessed by statistical tests, there were no significant differences in all samples. This aims to avoid bias in the results of this study, in the absence of differences in the characteristics of all samples, it is expected that the results of this study are truly accurate and reliable.

Based on Table 4.4. The research results obtained and analyzed showed that ketorolac had a longer analgesic effect compared with MgSO₄ with p value <0.05 using Mann-Whitney statistical test. Post-operative pain causes marked distress and anxiety and is a major factor influencing recovery from anesthesia and surgery. Despite major improvements in understanding the pathophysiology of acute pain over the past decade, about 80 percent of patients undergoing surgical procedures experience mild to severe postoperative pain. Kumar and Sherif found that patients who received ketorolac 30 mg iv had a much better VAS score. No significant side effects were recorded.⁽⁹⁾

Oliveira et al in his meta-analysis said that administration of ketorolac was able to reduce the dose of opioid drugs. In 5 studies, patients received several ketorolac doses, 13-17 studies evaluated continuous infusion, 18 studies evaluated ketorolac as postoperative medication, and 2 studies did not report results determined by our inclusion criteria. Dosages range from 30 to 60 mg of systemic ketorolac. Oliveira et al did not take unpublished data.⁽¹⁰⁾

Hwang et al said in their study that postoperative pain scores were significantly lower in the MgSO₄ group at 4, 24, and 48 hours after surgery (p <0.05). Postoperative magnesium concentration was higher in Group M (p, 0.05 at 4, 24, and 48 hours after surgery), but no side effects associated with hypermagnesemia were observed. Hemodynamic variables and incidence of chills, nausea, and vomiting were similar in the two groups.⁽¹¹⁾ Magnesium acts as a stabilizer for cell membranes and intracytoplasmic organelles by intervening in the activation of Ca ATPase and Na-K ATPase membranes which are involved in the transmembrane ion exchange during the depolarization and repolarization phases. Mg also inhibits Ca from the sarcoplasmic reticulum through its effect on the L-type calcium channel in the membrane and the sarcoplasmic reticulum. In addition, Mg has a vasodilator effect by increasing prostacyclin synthesis and inhibiting angiotensin-converting enzyme activity.

5. CONCLUSION

There is a distinction the VAS and the duration of the analgetik on the grant of Magnesium sulfate with intravenous ketorolac in patients post operative with spinal anesthesia. Ketorolac is better in decrease the value of the VAS than MgSo₄ in patients post surgery with spinal anesthesia. Ketorolac has a duration analgetik longer than Mgso₄ in patients post operation with spinal anesthesia.

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