Comparison between Intravenous Magnesium and Lidocaine Administration on Postoperative Pain during Spinal Anesthesia for Anal Surgery

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ABSTRACT

Background: Perioperative analgesia has been administered traditionally as opioid analgesics, but routine use of opioids for postoperative analgesia has recently been critically challenged. Excessive use of potent opioids may actually increase postoperative pain as a result of rapid elimination and development of acute tolerance and decrease patient satisfaction.

Objective: The aim of this study was to assess and compare the effect of IV infusion of lidocaine and magnesium sulphate (Mg) as adjuvant for postoperative pain in anal surgery after spinal anesthesia regarding duration, potency of analgesia, analgesic consumption and hemodynamics.

Patients and methods: In this prospective, observational, randomized, double blinded (nurse and junior doctor) placebo study, 150 patients of ASA (American Society of Anesthesiologists) physical status I and II with the age between 18-40 year, undergoing anal surgery under spinal anesthesia were included. The study was conducted in Al-Azhar University Hospital, Assiut during the period from June 2018 to Oct 2018.

Results: The results showed that there were significant differences between the three groups according to BP and HR. The patients in Mg group showed more hypotension and bradycardia than the patients in lidocaine and placebo groups. Patients in Mg group showed lower VAS score than lidocaine and placebo groups. The amount of analgesic consumption was lower in Mg group than lidocaine and placebo groups.

Conclusion: Usage of IV $MgSO_4$ at 50 mg/kg followed by continuous infusion of 10 mg/kg/h leading to decrease in postoperative pain and analgesic consumption in patients undergoing anal surgery under spinal anesthesia.

Keywords: Intravenous magnesium, lidocaine, Postoperative pain, Spinal anesthesia, Anal surgery.

INTRODUCTION

Surgical pain is due to inflammation from tissue trauma (surgical incision, dissection, burns) or direct nerve injury (nerve transaction, stretching, or compression). 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 [(1)]. 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 [(2)].

In order to reduce postoperative pain, opioids and NSAIDs are used on a routine basis; but the use of these drugs is associated with some side effects and risks [(3)]. 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 [(4)].

One IV adjuvant medication that has shown potential in preemptive analgesia is magnesium [(5)]. It can antagonize N-Methyl-D-aspartic acid receptor and it also inhibits the release of acetylcholine in the neuromuscular junction. It has 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 [(6)].

Another drug is lidocaine that is an amide-type of local anesthetic. The anti-nociceptive and analgesic effect are thought to be attributable to the blockade of neuronal sodium channels, blockade of potassium currents, interaction with nociceptive pathways, muscarinic receptor antagonist, blockade of dopamine receptors, glycine inhibitor, reduction in excitatory amino acids, reduction in thromboxane and release of endogenous opioid peptides [(7)].

AIM OF THE WORK

The aim of this study was to assess and compare the effect of IV infusion of lidocaine to the effect of IV infusion of magnesium sulphate as adjuvant for postoperative pain in anal surgery after spinal anesthesia regarding duration, potency of analgesia, analgesic consumption and hemodynamics.

PATIENTS AND METHODS

In this prospective, observational, randomized, double blinded (nurse and junior doctor) placebo study, 150 patients of ASA (American Society of Anesthesiologists) physical

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status I and II with the age between 18-40 year, undergoing anal surgery under spinal anesthesia were included.

The study was conducted in Al-Azhar University Hospital, Assiut during the period from June 2018 to Oct 2018.

Ethical consideration and written informed consent:

An approval of the study was obtained from Al-Azhar University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the operation.

Exclusion criteria

1- Patients with ASA physical status III and IV
2- Patients with known allergy from $MgSO_4$ or lidocaine.
3- Patients with drug or alcohol abuse.
4- BMI> 40.
5- Contraindicated spinal anesthesia (Relative-absolute)
6- Patients who refuse spinal anesthesia.
7- Failed spinal anesthesia.
8- Any anal surgery last for more than one hour.
9- Patients with renal impairment.

Patients were classified randomly into 3 equal groups as 50 patients in each one by closed envelope method according to the drug used into:-

Group I: called group L (Lidocaine group)

Group II: called group M ($MgSO_4$ group)

Group III: called group P (Placebo group)

Technique

An intravenous route was established with 18 gauge cannula at the dorsum of the left hand.

Continuous monitoring of ECG, non-invasive arterial blood pressure and pulse oximetry were carried out.

Under aseptic condition, dural puncture were performed using a standard midline approach in the sitting position at L4, L5 intervertebral space with a needle size 25 gauge, 5 mg hyperbaric bupivacaine 0.5% solution were injected intrathecally.

All patients remained in the sitting position for 10 minutes, then patients were asked if they perceive any change in motor power, if not, the patients were allowed to position themselves in the lithotomy position.

Immediately before surgery the level of sensory block was tested using along surgical toothless clamp gently applied radially starting from the anal orifice in different diagonal directions.

Patients randomly received:-

1- $MgSO_4$ 50 mg/kg in 100 ml of isotonic sodium chloride solution IV in 20 minutes (bolus dose) followed by continuous infusion of 10 mg/kg/h through syringe pump until 6 h postoperatively [$MgSO_4$ group].
2- Lidocaine as bolus dose of 2 mg/kg in 100 ml of isotonic sodium chloride solution IV in 20 minutes, followed by an infusion of 1.5 mg/kg/h through syringe pump until 6 h postoperatively [L group].
3- 100 ml isotonic sodium chloride IV in 20 minutes followed by an infusion of 100 ml of isotonic sodium chloride through syringe pump until 6 h postoperatively [P group].

Pain at rest was evaluated using visual analogue scale from 0 (no pain) to 10 (worst pain) at 2, 4, 8, 12, hrs after surgery.

The patients were kept at I.C.U and any patient reach score 4 or more; rescue analgesia was provided in form of IV infusion voltaren 75 mg (Novartis). The dosage and timing of analgesia were recorded blinded at 2, 4, 8, 12 hrs after operation. Toxicity of $MgSO_4$ was monitored by urine output, respiratory rate and knee jerk. Preoperative, intraoperative (each 5 min) and postoperative each one hour; hemodynamic parameters as Bp, HR, RR and saturation level were also noted until 12 hrs postoperatively.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

A one-way analysis of variance (ANOVA) when comparing between more than two means.

Post-hoc test: Least Significant Difference (LSD) was used for multiple comparisons between different variables.

Kruskall Wallis test: for multiple-group comparisons in non-parametric data.

Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

– P-value <0.05 was considered significant.

– P-value <0.001 was considered as highly significant.

– P-value >0.05 was considered insignificant.

RESULTS

Table (1): Comparison between groups according to demographic data.

Demographic Data	Mg Group (n=50)	Lidocaine group (n=50)	Placebo (n=50)	p-value
Age (years) Range Mean ± SD	 18-40 29.29±4.98	 18-40 28.79±4.89	 18-40 29.80±5.07	<0.05
Sex Male Female	 16 (32%) 34 (68%)	 17 (34%) 33 (66%)	 14 (28%) 36 (72%)	<0.05
Weight (kg) Range Mean ± SD	 73-95 84.84±14.42	 69-97 83.83±14.25	 72-95 84.34±14.34	<0.05
Height (cm) Range Mean ± SD	 152-178 166.65±28.33	 151-177 165.64±28.16	 154-179 168.17±28.59	<0.05
Duration of surgery (min) Range Mean ± SD	 15-20 17.68±3.00	 16-20 18.18±3.09	 17-19 18.18±3.09	<0.05

This table shows no statistically significant difference between groups according to demographic data.

Table (*2*): Comparison between groups according to heart rate (Beat/min).

Heart rate (Beat/min)	Mg Group (n=50)	Lidocaine group (n=50)	Placebo (n=50)	p-value
Preoperative	89.94±11.29	92.34±11.07	93.34±11.07	>0.05
Intraoperative				
At 5 min.	65.90±13.24	73.48±12.13	90.88±12.52	**<0.001***
At 10 min.	66.48±11.82	71.34±11.45	90.58±11.9	**<0.001***
At 15 min.	63.60±11.97	72.38±11.15	87.92±11.34	**<0.001***
Postoperative				
PACU	79.28±11.6	82.7±11.19	90.34±11.46	**<0.001***
After 1hr	90.58±12.23	93.56±11.95	94.56±12.65	>0.05
After 2hrs	89.60±12.78	92.56±11.97	93.12±12.68	>0.05
After 3hrs	88.06±11.6	91.30±10.79	91.92±11.1	>0.05
After 4hrs	84.94±11.28	87.88±10.64	88.34±11.07	>0.05
After 5hrs	90.9±13.24	93.48±8.17	93.88±12.52	>0.05
After 6hrs	90.48±11.81	93.34±11.44	93.58±11.99	>0.05
After 7hrs	87.6±11.96	90.38±11.14	90.92±11.51	>0.05
After 8hrs	88.28±11.6	91.7±11.18	92.34±11.45	>0.05
After 9hrs	90.58±12.22	94.08±11.46	94.56±11.86	>0.05
After 10hrs	89.6±12.77	92.56±11.97	93.12±12.39	>0.05
After 11hrs	88.06±11.59	91.3±10.79	91.92±11.09	>0.05
After 12hrs	88±11.57	91.34±10.86	91.96±11.05	>0.05

This table shows statistically significant difference between groups according to heart rate (Beat/min) at 5, 10 and 15 min intraoperatively.

Table (*3*): Comparison between groups according to respiratory rate.

Respiratory Rate	Mg Group (n=50)	Lidocaine group (n=50)	Placebo (n=50)	p-value
Preoperative	15.15±1.36	15.31±1.43	15.70±1.50	>0.05
Intraoperative				
At 5 min.	15.30±1.38	15.47±1.45	15.87±1.52	>0.05
At 10 min.	14.14±1.27	14.85±1.34	15.59±1.40	>0.05
At 15 min.	15.15±1.36	15.91±1.43	16.70±1.50	>0.05
Postoperative				
PACU	14.28±1.29	14.99±1.35	15.74±1.42	>0.05
After 1hr	15.15±1.36	15.91±1.43	16.70±1.50	>0.05
After 2hrs	15.15±1.36	15.91±1.43	16.70±1.50	>0.05
After 3hrs	15.30±1.38	16.07±1.45	16.87±1.52	>0.05
After 4hrs	15.15±1.36	15.91±1.43	16.70±1.50	>0.05
After 5hrs	14.28±1.29	14.99±1.35	15.74±1.42	>0.05
After 6hrs	15.15±1.36	15.91±1.43	16.70±1.50	>0.05
After 7hrs	14.14±1.27	14.85±1.34	15.59±1.40	>0.05
After 8hrs	14.28±1.29	14.99±1.35	15.74±1.42	>0.05
After 9hrs	15.15±1.36	15.91±1.43	16.70±1.50	>0.05
After 10hrs	15.30±1.38	16.07±1.45	16.87±1.52	>0.05
After 11hrs	14.24±1.27	14.45±1.34	14.59±1.40	>0.05
After 12hrs	14.34±1.27	14.45±1.34	14.59±1.40	>0.05

This table shows no statistically significant difference between groups according to respiratory rate.

Table (*4*): Comparison between groups according to SPO_2%

SPO_2%	Mg Group (n=50)	Lidocaine group (n=50)	Placebo (n=50)	p-value
Preoperative	99.10±0.72	98.80±0.89	99.40±0.75	>0.05
Intraoperative				
At 5 min.	99.55±0.69	99.40±0.60	99.55±0.69	>0.05
At 10 min.	99.65±0.59	99.30±0.66	99.30±0.66	>0.05
At 15 min.	99.35±0.75	99.45±0.69	99.40±0.75	>0.05
Postoperative				
PACU	99.40±0.75	99.30±0.66	99.35±0.75	>0.05
After 1hr	99.35±0.75	99.45±0.69	99.45±0.69	>0.05
After 2hrs	99.55±0.60	99.40±0.68	99.55±0.60	>0.05
After 3hrs	99.60±0.50	99.55±0.51	99.40±0.68	>0.05
After 4hrs	99.55±0.69	99.40±0.60	99.55±0.69	>0.05
After 5hrs	99.35±0.81	99.65±0.49	99.65±0.49	>0.05
After 6hrs	99.55±0.60	99.10±0.85	99.55±0.60	>0.05
After 7hrs	99.40±0.68	99.30±0.66	99.40±0.68	>0.05
After 8hrs	99.35±0.81	99.65±0.49	99.65±0.49	>0.05
After 9hrs	99.55±0.60	99.35±0.59	99.55±0.60	>0.05
After 10hrs	99.68±0.27	99.59±0.35	99.40±0.75	>0.05
After 11hrs	99.40±0.75	98.80±0.89	99.40±0.60	>0.05
After 12hrs	99.35±0.75	99.40±0.60	99.65±0.49	>0.05

This table shows no statistically significant difference between groups according to SPO_2%.

Table (*5*): Comparison between groups according to visual analogue scale score.

VAS score	Mg Group (n=50)	Lidocaine group (n=50)	Placebo (n=50)	p-value
After 2 hrs.	1 (0-2)	1 (1-2)a	2 (2-3)ab	0.021*
After 4 hrs.	1 (1-2)	2 (1-2)a	4 (1-5)ab	<0.001**
After 8 hrs.	2 (1-3)	3 (1-4)a	5 (2-6)ab	<0.001**
After 12 hrs.	4 (2-5)	5 (2-5)a	6 (2-4)ab	<0.001**

Data are expressed median and Interquartile range (IQR)
a: Significant difference compared to Mg group
b: Significant difference compared to lidocaine group
This table shows highly statistically significant difference between groups according to visual analogue scale score.

Table (*6*): Comparison between groups according to postoperative analgesic consumptions (mg).

	Mg Group (n=50)	Lidocaine group (n=50)	Placebo (n=50)	p-value
After 2 hrs.	14.66±4.99	21.60±7.72a	25.46±8.70ab	0.021*
After 4 hrs.	19.27±6.55	29.13±9.90	32.04±10.89ab	<0.001**
After 8 hrs.	22.30±7.58	33.07±11.24	36.38±12.37ab	<0.001**
After 12 hrs.	28.57±9.71	48.55±16.51a	53.41±18.16ab	<0.001**

a: Significant difference compared to Mg group
b: Significant difference compared to lidocaine group

This table shows highly statistically significant difference between groups according to postoperative analgesic consumptions (mg).

DISCUSSION

This study was conducted aiming to compare the effect of IV infusion of lidocaine to the effect of IV infusion of magnesium sulphate as adjuvant for postoperative analgesia after spinal anesthesia for anal surgery. For that purpose we divided the 150 patients study population into 3 groups; one received magnesium sulfate, the second received lidocaine and the third group received isotonic saline as placebo.

The results were in accordance with that of the study of **Saadawy *et al.* [8].** It was a double-blinded study aimed at evaluating and comparing the effects of magnesium and lidocaine on pain, but it differed from this study in that the patients were under general anesthesia. They agreed with our results in that they found both lidocaine and magnesium sulfate had significantly lower VAS score than the control group. They also agreed with this study in that both lidocaine and magnesium sulfate resulted in significantly lower rated analgesic consumption. They also found that lidocaine had lower VAS score and analgesic consumption than Mg group.

The study of **Kim *et al.* [9]** also partially agreed with these results, they aimed to compare the effects of postoperative lidocaine and magnesium on postoperative functional recovery and pain after mastectomy due to breast cancer. They divided their population into three groups one for magnesium sulfate, one for lidocaine and one as a control group. Moreover, they measured the outcome using quality of recovery (Qor) survey and found that both lidocaine and magnesium sulfate had significant better results of Qor than the control group. They also found that lidocaine had significantly better Qor results than magnesium sulfate. Although they showed better results with both lidocaine and magnesium sulfate groups that had better results of pain scores immediately postoperatively, they found that both of them attenuated the intensity of chronic pain in patients undergoing breast cancer surgery.

The pain relief effects of lidocaine and magnesium sulfate were compared in the study of **Safavi *et al.* [10].** They found that about 60% of patients in the control group had pain as compared to 22.2% and 40% in the lidocaine and magnesium sulfate groups, respectively. The other finding was that there was difference in induction pain score between the three treated groups significantly, and observed that the differences in pain scores between "normal saline and lidocaine group" and "normal saline and magnesium sulfate groups" were statistically meaningful.

For comparison, a few studies had used $MgSO_4$ following regional anesthesia as compared to general anesthesia. In the study of **Hwang *et al.* [11]** an

administration of $MgSO_4$ as bolus followed by IV infusion under spinal anesthesia was associated with postoperative increased time to analgesic requirement, significantly lower pain score and lower cumulative patient controlled analgesia drug consumption.

The result the study of **Levaux *et al.*** [12] agreed with the results of this study as they found that postoperative opioid consumption and pain scores were lower in the magnesium groups as well as the first night's sleep and the global satisfaction scores, but it differed from this study as it was under general anesthesia.

The current results were also consistent with **Ryu *et al.*** [13] **study** which was randomized, double-blind, prospective study and was undertaken to evaluate the effects of magnesium sulphate on anesthetic requirements and postoperative analgesia in patients undergoing total IV anesthesia. Their findings were that patients in magnesium group required less rocuronium than those in saline group. They found also postoperative pain scores, cumulative analgesic consumption, and shivering incidents were significantly lower in magnesium sulfate group. They also found that BP was significantly lower in magnesium sulfate group. Mg may induce hypotension by vasodilatation, sympathetic blockade and inhibition of catecholamine release.

Nevertheless, some studies disagree with the results of this study. **Ko *et al.*** [14] found that perioperative intravenous administration of magnesium sulfate did not increase CSF magnesium concentration and had no effects on postoperative pain. However, an inverse relation between cumulative postoperative analgesic consumption and the CSF magnesium concentration was observed. These results suggest that perioperative intravenous magnesium infusion may not be useful for preventing postoperative pain.

Tramèr and Glynn [15] also mismatched the results of this study as their conclusion was that in operations under general anesthesia supplemented with other analgesic adjuvants, single preoperative IV bolus dose of $MgSO_4$ had no impact on postoperative pain and analgesic consumption.

As regards to lidocaine as adjuvant to postoperative analgesia, the results were also conflicting. **Kaba *et al.*** [16] aimed to test the hypothesis that perioperative lidocaine infusion facilitates acute rehabilitation protocol in patients undergoing laparoscopic colectomy. They matched the results of this study in that intravenous lidocaine improves postoperative analgesia, fatigue, and bowel function after laparoscopic colectomy. They found also that these benefits are associated with a significant reduction in hospital stay [16].

The study of **Frédéric Martin *et al*.** [17] mismatched this study. They aimed to evaluate a possible opioid-sparing effect of intravenous lidocaine so; they conducted a randomized, double-blind clinical trial on patients undergoing total hip arthroplasty under general anesthesia. They divided the patients into two groups:-

- One for lidocaine group that received lidocaine 1.5 mg/kg (bolus) in ten minutes followed by IV infusion of 1.5 mg/kg/h.
- Another group was placebo.

Their results found that, in comparison with placebo, lidocaine did not induce any opioid-sparing effect during the first 24 h. There was no significant difference regarding the effect of lidocaine and placebo on pain score.

Excessive use of opioids could prolong intestinal transit time and result in impaired colonic transport, while local anesthetics have a direct excitatory effect on intestinal smooth muscle by blocking the inhibitory reflexes that are activated once the parietal peritoneum is entered. In addition, lidocaine reduces the inflammatory process in the gut by inhibiting cytokine secretion and triggering the secretion of anti-inflammatory mediators [18].

In addition to that an inverse relationship was demonstrated between pain severity and serum magnesium level. As in a large study, the magnesium group experienced better sleep quality during the first postoperative night than the other groups, which might be related to the sedative effect of magnesium. NMDA-glutamate receptor antagonists exhibit an anxiolytic effect through interaction with benzodiazepine/GABAA receptors [19].

CONCLUSION

Usage of IV $MgSO_4$ at 50 mg/kg followed by continuous infusion of 10 mg/kg/h leading to decrease in postoperative pain and analgesic consumption in patients undergoing anal surgery under spinal anesthesia.

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