The effect of intraoperative magnesium sulfate and ketamine infusion on post-operative pain in open gynecological surgeries

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Abstract

Background: besides an opioid analgesic, multimodal analgesia using a non-opioid analgesic, in atrial to decrease opioid use and to increase postoperative pain control.

Objectives: To compare the effect of intra-operative infusion of ketamine and magnesium sulphate in open gynaecological surgeries on post-operative pain, total morphine consumption, post-operative nausea, and vomiting in Qena University Hospitals.

Patients and methods: A prospective study. Conducted in Qena University Hospital, South Valley University, Qena, Egypt. The study was conducted on fifty patients (ASA I or II) scheduled for open gynaecological surgeries under general anaesthesia: group A: Ketamine (0.2 mg /kg) bolus than the continuous supply of ketamine (0.05 mg/kg/h), group B: Magnesium sulphate (50mg /kg) bolus and followed by continuous infusion of magnesium sulfate(10mg/kg /h).

Results: the visual analogue scale was found to be significantly higher in group B compared to group A in 2, 4, and 8 hrs time intervals. The mean opioid (Morphine/Pethidine) consumption doses over 24h were lower in group A compared to group B. There is no significant difference regarding adverse events between the two studied groups.

Conclusion: Intraoperative magnesium sulfate and ketamine infusion in patients exposed to gynecological surgeries with general anesthesia could and decreased the post-operative opioid requirement. Ketamine showed a significant preemptive analgesic effect compared to MgSO4 at 2 and 8 h postoperatively. VAS was significantly lowered in Ketamine than MgSO4.

Keywords: gynaecological surgeries, Ketamine, Magnesium sulphate

Introduction

Open gynaecological surgery is a major surgery associated with severe post-operative pain. Using morphine as analgesia with large doses might lead to many bad events, like nausea, vomiting, respiratory suppression, and hypotension. **(Ding et al., 2014)**

Besides an opioid analgesic, Multimodal analgesia using a non-opioid analgesic, in atrial to decrease opioid use and to increase postoperative pain control **(Evauxet al., 2003)**

Ketamine and magnesium have an established efficacy as morphine-sparing agents and their way of action varies from opioids one **(James, 2009).** The aim of this study is to compare the effect of intra-operative infusion of ketamine and magnesium sulphate in open gynaecological surgeries on post-operative pain, total

morphine consumption, post-operative nausea, and vomiting in Qena University Hospitals.

Patient and Method

Type of the study: a prospective hospital-based controlled analytical study.

Study Setting: Qena University Hospital in anaesthesia and ICU and Pain Management Department.

Study subjects: 50 cases undergoing open gynaecological surgeries under general anesthesia:

Group A: Ketamine (0.2 mg /kg) bolus then constant supply of ketamine (0.05 mg/kg/h)

Group B: Magnesium sulphate (50mg / kg) bolus then constant supply of magnesium sulfate (10mg/kg /h)

a. Inclusion criteria: ASA I and ASA II**.** Age from 30-70 undergoing the open gynaecological operation

b. Exclusion criteria: ASA III and ASAIV**.**last stages of renal, hepatic disorders. Cardiovascular impairment, neurological diseases.Sensitivity or allergy to the drugs in the study.

Methods: After local ethical committee approval, all of the patients will be subjected to the following:

1-Detailed History taking

2-laboratory investigations including:

Complete blood count, liver functions, kidney functions, and coagulation profile.

3- Routine basic monitoring is done containing after going to the operating room.

-An intravenous cannula will insert and fluids will be added regarding fasting protocol

- Start the operation using, general anaesthesia. Tracheal intubation wills bed one using 0.5 mg/kg of atracurium. Maintenance of anaesthesia will be established by isofluraine MAC 1,5. Mechanically controlled ventilation will be adjusted to maintain end-tidal PCO2 near 35 mmHg. Supplementary muscle relaxant was given through the surgery in response to the clinical need.

Group A: Ketamine (0.2 mg /kg) bolus then constant supply of ketamine (0.05 mg/kg/h)

Group B: Magnesium sulphate (50mg / kg) bolus then constant supply of magnesium sulfate (10mg/kg /h)

Anaesthesia will cease at the end of the operation, and the remaining neuromuscular blockade will antagonize by neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg). The trachea wills extubate when the patients become aware.

Patients will receive ketorolac (IV: 30 mg as a single dose or 30 mg q6hr; not to exceed 120 mg/day). The severity of pain will be assessed every 4, 8, 12, 16, 20, and 24 hours after surgery and according to the visual analog scale (VAS), no pain (0), mild pain (1-3), moderate pain (4_6), severe pain (7-9), worst pain (10). The patient which (VAS) >5 will receive morphine (0,1 mg /kg/dose) and re-assess after fifteen minutes to ensure that there is no respiratory depression if there is any respiratory depression (respiratory rate < 8 / minute) or manifestation of hypercarbia, the patient will shift to intensive care unit(ICU) for close monitoring.

Statistical analysis

Our data were analyzed by the statistical Package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). continues data were expressed as mean± standard deviation (SD). Qualitative data

were expressed as frequency and percentage. Test of significances: chi-square test was used to compare the difference in the distribution of frequencies among different groups. For continuous variables; an independent T-test was carried out.

Results

There was a significant difference in MAP between the two studied groups at 2 and 8 hrs intervals, where MAP significantly higher in group A compared to group B. However, there is no significant difference in MAP between the two studied groups in the remaining studied intervals postoperatively (**Table.1**).

We found that VAS was significantly higher in group B compared to group A in 2, 4, and 8 hrs time intervals (Table**. 2**).

The mean opioid (Morphine/Pethidine) consumption doses over 24h were lower in group A compared to group B(**Table. 3**).

There is no significant difference regarding adverse events between the two studied groups (**Fig.1**).

Table 1. MAP (Mean Arterial blood Pressure) changes postoperatively between the two studied groups

Variables	Group A (N=25)	Group B (N=25)	t	P
Baseline	84.5 ± 2.43	84.94 ± 4.79	.409	.684
2hr	85.83 ± 3.35	78.61 ± 5.62	**5.52**	**.000****
4hr	84.17 ± 4.17	83.72 ± 3.41	.418	.678
8hr	86.44 ± 3.2	84.39 ± 2.21	**2.64**	**.011***
12hr	88.59 ± 3.46	86.89 ± 3.58	1.71	.094
16hr	88.83 ± 3.01	87.11 ± 3.63	1.82	.074
20hr	84.4 ± 2.24	86.53 ± 5.16	1.96	.06
24hr	85.2 ± 3.15	86.94 ± 4.24	1.65	.106

*P-value <0.05 was considered significant

** P-value <0.001 was considered highly significant

Table 2. Visual Analogue Scale (VAS) score of the two studied groups postoperatively.

Variables	Group A (N=25)	Group B (N=25)	t	P
2hr	1.44 ± 0.511	2.11 ± 0.758	**3.66**	**.001****
4hr	1.89 ± 0.583	2.61 ± 0.502	**4.68**	**.000****
8hr	1.78 ± 0.732	2.28 ± 0.752	**2.38**	**.021***
12hr	2.56 ± 1.09	2.94 ± 1.32	1.11	.273
16hr	1.86 ± 0.616	2.11 ± 0.837	1.21	.235
20hr	1.63 ± 0.924	1.96 ± 0.951	1.24	.219
24hr	1.5 ± 0.707	1.72 ± 0.826	1.01	.317

*P-value <0.05 was considered significant

** P-value <0.001 was considered highly significant

Table 3. Postoperative opioid (Morphine/Pethidine, mg) consumption among the studied groups

Variables	Group A (N=25)	Group B (N=25)	t	P
2h	25.6 ± 2.1	30.2 ± 1.7	**8.51**	**.000****
6h	30.8 ± 3.5	39.5 ± 3.8	**8.42**	**.000****
12h	46.3 ± 4.2	54.4 ± 5.1	**6.13**	**.000****
24h	50.9 ± 2.8	58.2 ± 3.5	**8.14**	**.000****

** P-value <0.001 was considered highly significant

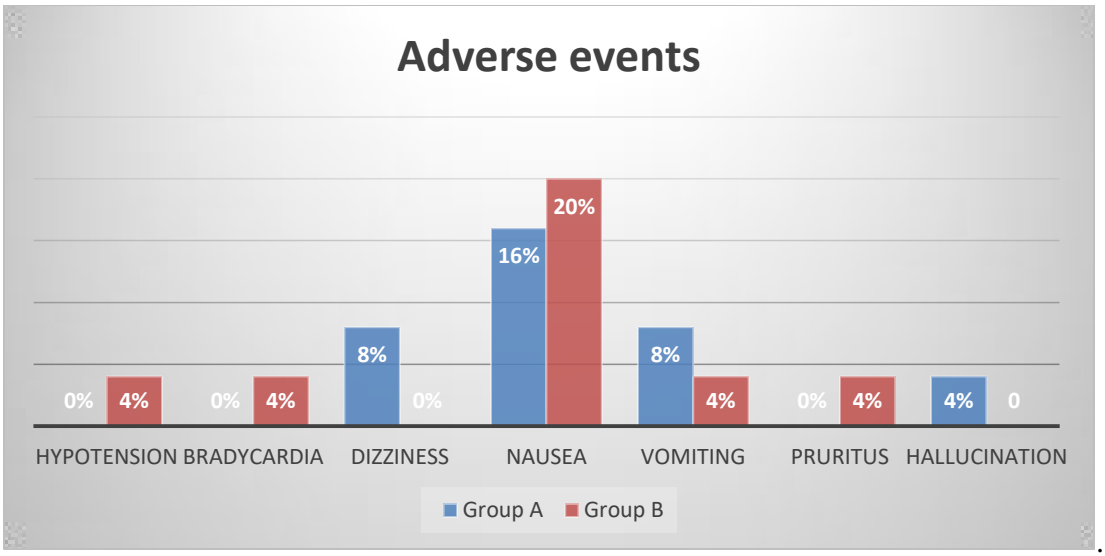

Fig.1. Adverse events between the two studied groups

Discussion:

In our study, regarding MAP, there was a significant difference in MAP between the two studied groups at 2 and 8 hrs intervals, where MAP significantly higher in group A compared to group B at 2 and 8 hrs intervals (P=.000, P=.011). However, there is no significant difference in MAP between the two studied groups in the remaining studied intervals postoperatively.

Magnesium is a well-known antiarrhythmic drug act by regulation of voltage-dependent K+, Na+, and Ca2+ channels. Acting on those channels, magnesium can prolong atrioventricular-nodal conduction times. So, the effects of Mg+ on the variability of heart rate can be clarified by its ability to act on myocardial cells. But, the antinociceptive actions of Mg+ could have a role. Sufficient analgesia is connected with stable heart rates **(Baker, 2016).** in our study, we explain the transient tachycardia which occurred between 2-8 hr in group B as a reflex to the hypotension. It can make vasodilatation in the small vascular tree small arteries because of its action as a Ca2+ channel blocker **(Kamel et al., 2008)**.

Using ketamine as a pretreatment has been confirmed to advance the antinociceptive outcome of magnesium **(SavicVujovic et al., 2015).**

The visual analog scale (VAS) is a validated, subjective measure for acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between "no pain" and "worst pain." **(Delgado et al., 2018).**

In our study, as regarding the VAS (Visual Analogue Scale) score of the two studied groups postoperatively. VAS was found to be significantly higher in group B (Magnesium group) compared to group A (Ketamine group) in 2, 4 and 8 hrs time intervals (P=.001, .000, and .021 respectively).

In agreement with our study, **Arıkan et al.,2016** made a study to compare the outcomes of magnesium and ketamine on postoperative severity of pain and amount of morphine intake. They viewed that VAS was significantly

higher in the Magnesium group than the Ketamine group (P=0,000).

Numerous studies have confirmed the analgesic effectiveness and role of perioperative ketamine during the acute postoperative period. **Himmelseher et al., 2005** reported the analgesic advantages of ketamine, particularly in operations that are associated with increasing degrees of postoperative pain.

Typically consistent with our results **(Helmy et al., 2015)**, made their study to compare the effect of the intraoperative analgesia of low dose ketamine versus magnesium sulfate on parturient undergoing cesarean section under general anesthesia. There was a statistically significant difference between the studied groups regarding mean VAS score at 2 and 6 h post-operatively. But there were no statistically significant differences 12 and 24 h post-operatively.

Our study was similar to those obtained by **(Behdad et al., 2011)** where They viewed that the VAS score was lower in the ketamine group in comparison to the control group, the ketamine group had a longer time for analgesic request and the recommended amount of postoperatively Pethidine injections in the first day was higher in the control group.

(Bhatia et al., 2004) reported similar results regarding the postoperative analgesic outcome of magnesium sulfate. Another finding of **(Jabbour et al., 2019)**, where they reported that VAS was a statistically significant difference between the 2 groups being lower in (Mg + Ketamine) group compared to the Mg, K, and placebo group (P=0.0001). which is consistent with our results.

Regarding Postoperative opioid (Morphine/Pethidine, mg) consumption among the studied groups, the mean opioid (Morphine/Pethidine) consumption doses over 24h were significantly lower in the A group, comparing to the B group (P=0**.000**). **Helmy et al., 2015** obtained similar results.

Conclusion

Intraoperative magnesium sulfate and ketamine infusion in patients exposed to gynecological surgeries with general anesthesia could and decreased the post-operative opioid requirement. Ketamine showed a significant preemptive analgesic effect compared to MgSO4 at 2 and 8 h postoperatively. VAS was significantly lowered in Ketamine than MgSO4.

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