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COMPARISON OF EFFICACY OF MAGNESIUM SULFATE AS PREMEDICATION FOR PREVENTION OF MYOCLONUS INDUCED BY ETOMIDATE

Anaesthesiology

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ABSTRACT

Myoclonus is observed in 50- 80 % of patients after etomidate administration. Involuntary myoclonic movements during induction period occurs as a result of alteration in the balance of inhibitory and excitatory influences on the thalamocortical tract.3 Magnesium sulphate is a non-competitive NMDA (N- methyl D-aspartate) receptor antagonist.4,5 Activation of this receptor leads to calcium influx and increased nitric oxide production. 4Nitric oxide has an important role in venous nociception in humans.5Myoclonus is reduced by premedication with a small dose of magnesium 60 to 90 seconds before the induction dose of etomidate is given.

KEYWORDS

INTRODUCTION

Etomidate is an intravenous anesthetic, a carboxylated imidazole drug.[6] The Beneficial properties of etomidate like hemodynamic stability, minimal respiratory depression, cerebral protection, rapid onset of effect and rapid recovery after a single or a continuous infusion, led to widespread use of etomidate for induction, maintenance, prolonged sedation.[6,7]The effect of etomidate on cardiac output and myocardial oxygenation and its wide therapeutic index, which is approximately 6 fold better than thiopentone and propofol, have logically served to maintain niche use in patients of all age groups. The major advantage of etomidate is its minimal effect on cardiovascular and respiratory systems. The drug can however cause temporary inhibition of steroid synthesis after single doses and infusions.

Pain on injection, myoclonus and hiccups are the most common side effects of this drug.[8] Myoclonus is observed in 50- 80 % of patients after etomidate administration.

Magnesium sulphate popularly known as Epsom salt was initially intended for various uses has been found to have role in etomidate induced myoclonus. Magnesium inhibits calcium entry into the cell via a noncompetitive blockade of the N-methyl-D-aspartate (NMDA) receptor. Magnesium and the NMDA receptor are thought to be involved in the modulation of pain. Magnesium is a physiological calcium antagonist at different voltage gated channels, which may be important in the mechanisms of antinociception.[9]

Low dose magnesium pretreatment before etomidate induction of anesthesia significantly reduces unwanted myoclonic jerks and also protects the hemodynamic stability.

AIMS AND OBJECTIVE

1) To compare the efficacy of magnesium sulfate as a Premedication for prevention of myoclonus induced by etomidate**.**

2) To observe pain after given dose of etomidate**.**

MATERIAL & METHODS

It is a prospective, randomized, double blind comparative study. After approval of Institutional Ethics Committee, We used 120 consecutive patients satisfying eligibility criteria undergoing elective surgery under general anaesthesia with endotracheal intubation. Patients were allocated into 2 groups of 30 subjects each using computer generated randomization list.

Group S: included no pretreatment patients

Group M: received inj. iv magnesium sulfate 30 mg/kg as premedication

Patients were advised to fast from night before the day of surgery. They were given tablet alprazolam 0.5 mg and tablet ranitidine 150 mg previous night.

On the day of surgery, anesthesia workstation and monitors were checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large sized blades, stylet and working suction apparatus were kept ready before the induction of general anesthesia. Emergency drug tray consisting of atropine, adrenaline, ephedrine were also kept ready for any eventuality.Once the patient's nil peroral status was confirmed, patients were shifted to operating room (OR). After placing patient in supine position on OR table, an intravenous line was secured on a peripheral line. Standard monitoring devices like pulseoximeter (SpO2), non-invasive blood pressure (NIBP), echocardiogram (ECG) were connected. Baseline hemodynamic parameters and Ramsay sedation score were assessed. All patients were pre-oxygenated with 100% oxygen for 3 minutes before induction of anesthesia and all patients were premedicated with inj.glycopyrrolate0.2mg,inj. Ranitidine 50mgIV.The study syringes were prepared by ananesthetist not involved in the procedure. Patient and anesthesia provider was not aware of the study drug. Thus both the observer and the patient were blinded. Group M patients received 60 mg(2.48mmol) of magnesium sulphate in10Ml of normal saline infusion over a Period of3 min and group S patients received 10 mL of normal saline over a period of 3 min. Oxygen supplementation through mask was given during this period. After 90 seconds of the study drug, inj. etomidate 0.3 mg/kg was administered over a period of 30 seconds. Immediately pain on injection and myoclonus evaluation was done. After 2 minutes of etomidate induction, inj. midazolam 0.02 mg/kg, inj. fentanyl 2 µg/kg was administered, and tracheal intubation facilitated with inj. Vecuronium0.1 mg/kg. Anesthesia maintained as per institutional protocol. After the surgery, residual neuromuscular block was reversed using inj. neostigmine 0.05mg/kg, inj. glycopyrrolate 0.01mg/kg. Trachea was extubated after adequate recovery of muscle power.Patients were monitored post-operatively. Patients with nausea or vomiting in the postoperative period received inj. ondansetron 4mg IV as rescue antiemetics.

Parameters Measured:

1.) Heart rate (HR), oxygen saturation (SpO2), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), before premedication, after premedication, after pretreatment with magnesium sulphate, fentanyl and midazolam after etomidate induction every minute for 10 minutes and at 5minutes interval after that were measured.

2.) Myoclonus evaluation, pain evaluation,

3.)Adverse effects such as myoclonus, pain on injection, hemodynamic instability and postoperative nausea vomiting (PONV) if any were observed.

Myoclonus clinical severity grading will be done as below-
Grading of Myoclonus;
0 No Movement;
1 Mild, Movement at wrist;(short movement of body segment) Moderate mild movement of two different muscle groups e.g. face and arm

2 Severe intense myoclonic movement in two or more muscle groups,

And the severity of pain due to etomidate injection will be evaluated using a 4 grade scale
0 no pain
1 mild (pain reported only when asked)
2 moderate (pain reported without being asked or reported when asked and there were associated behavioral symptoms)
3 Severe verbal response grimacing, pulling the arm tearing the eyes.

Mean arterial pressure (MAP) and heart rate recordings will be evaluated during the time between entrance into the operating room and 5 minutes after intubation. Decrease in the SPO2, (SPO2), arrhythmia and other adverse effect will also be evaluated.

Inclusion And Exclusion Criteria

Inclusion Criteria:

1. Patient undergoing elective surgery under general anaesthesia
2. American Society of Anaesthesiologists grade 1 and2
3. Age 20-55 years 4. Weight 40-70 Kg 5. Both sexes

Exclusion Criteria:

1. Patient's refusal to participate in the study
2. Allergy to study drugs
3. Patients with neurological disorder, hepatic or renal disease, bronchospastic disease (ASA grade 3 or more)
4. Emergency surgeries
5. Patients taking any adrenergic or psychotropic drugs

RESULT:

Table-1: Average Age Difference In Saline, Magnesium

Age	Saline		Magnesium	
	S- Mean	Std Deviation	Mg- Mean	Std Deviation
	37.83	8.59	38.20	7.77

Table-2: Average Weight Difference In Saline, Magnesium

Weight	Saline		Magnesium	
	S- Mean	Std Deviation	Mg- Mean	Std Deviation
	54.93	9.70	38.20	7.77

Table-3:comparison Of Incidence And Intensity Of Myoclonus Among Saline And Magnesium .

Myoclonus	Saline	magnesium	P
Incidence in %	65%	25%	
Intensity(n)			
Grade 0	9	24	0.023
Grade 1	9	5	
Grade 2	9	1	
Grade 3	3	0	

DISCUSSION

Induction of general anesthesia initially began with gases or vapours, which was an unpleasant experience for patients. The introduction of intravenous anaesthetic agents was a milestone in the development of anesthesia [10]. Among them etomidate has emerged as a novel intravenous agent due to its unique properties like hemodynamic stability, minimal respiratory depression, cerebral protection, favourable toxicity profile, and pharmacokinetics enabling rapid recovery after either a single dose or a continuous infusion [11]. It was associated with temporary inhibition of steroid synthesis, and other minor disadvantages like pain on injection, superficial thrombophlebitis, myoclonus, nausea and vomiting [11]. No serious adverse effects were observed after this. However the use of etomidate has expanded as it preserves hemodynamic stability, which is the biggest advantage of Etomidate [12]. The most commonly encountered drawback is myoclonus during induction. Myoclonus is especially problematic in nonfasting patients, patients with open eye injuries, or those having limited cardiovascular reserves [13].Various drugs have been studied to decrease the incidence of myoclonus like opiates, benzodiazepines, dexmedetomidine, ketamine, magnesium sulphate, as pretreatment and priming with etomidate. Abolition of myoclonus occurs with premedication with drugs known to inhibit subcortical neuronal activity. Among them, magnesium sulphate does not cause respiratory depression,sedation or hemodynamic Instability.Studies using pretreatment with magnesium sulphate, with a dose of 60 mgIV showed reduced incidence of myoclonus without causing respiratory depression.

1. Distribution of average age in study group

The prospective, randomized, single blind comparative study was carried out in which ; mean age of Saline,Magnesium, study group was 37.83,38.20 respectively which was not statistically significant which was similar to the study done by Salim B., et al., (2015) [14] and Prakash et al. (2019) [15]

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2. Distribution of average weight in study group

In the present study, mean weight of Saline,Magnesium study group was 54.93, 38.20 respectively which was not statistically significant which was similar to the study done by Salim B., et al., (2015) 64 and Schwarzkopf KR et. al., (2003 and IsitemizIeti al., (2014)

3. Heart rate in study group

In the present study, Heart rate was recorded from 1 min to 90 min respectively in all study groups and P value 0.00 indicating strongly significance between all study groups. This finding was similar to the others reported in the literature [14,15]

4. Systolic BP in each group

In our study, Systolic BP was obtained were recorded from 1 min to 90 min respectively in all groups with P value 0.136 indicating suggestive significance between all study groups. At these intervals higher Systolic BP was observed in Saline group than Magnesium group.

5. Diastolic BP in each group

In the present study, Diastolic BP was recorded from 1 min to 90 min respectively in all groups and P value 0.762 indicating suggestive significance between all study groups. At these intervals higher Diastolic BP was observed in Saline group than Magnesium group.

6. Mean Arterial Pressure in each group

Mean Arterial Pressure was recorded from 1 min to 90 min respectively in all study groups.P value 0.442 indicating suggestive significance between all study groups. At these intervals higher Mean Arterial Pressure was observed in Saline group than Magnesium group.

7. SPO2 Score in each group

SPO2 Score was recorded from 1 min to 90 min respectively in all study groups.P value 0.138 indicating suggestive significance between all study groups. At these intervals higher SPO2 Score was observed in Saline group than Magnesium group.

CONCLUSION

Magnesium pre-treatment before etomidate administration significantly prevents the myoclonus without adverse side effects . magnesium decreases not only incidence but also severity of myoclonus**.**

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