

Pretreatment with dexmedetomidine and magnesium sulphate in prevention of etomidate induced myoclonus - A double blinded randomised controlled trial

INTRODUCTION

Etomidate is an imidazole derivative with potent hypnotic properties and better haemodynamic stability as compared to other induction agents.^[1] However, the most certain and undesirable side effect of etomidate is myoclonus; the incidence of which has been reported as much as 50%–80% after induction.^[2] We designed this study to compare the influence of dexmedetomidine with magnesium sulphate on incidence and severity of etomidate induced myoclonus. The secondary outcome was to compare the incidence of pain on etomidate injection and study the haemodynamic response during intubation.

METHODS

This randomised, double-blind clinical study was conducted from July to December 2019 on 100 patients posted for surgery under general anaesthesia after approval of the Institutional Ethics Committee. The study population consisted of 90 patients who consented for the study; of both the genders aged 18–50 years, with body mass index <25 kg/m², classified as American Society of Anesthesiologists (ASA) physical status I or II. The patients were randomly allocated into three groups using simple randomisation and closed envelope method based upon a computer-generated list and received pre-treatment of either normal saline, dexmedetomidine (0.5 µg/kg) or magnesium sulphate (30 mg/kg) 10 min before etomidate induction [Figure 1].

All patients received injection midazolam 0.03 mg/kg intravenously. Study drugs were prepared and coded in 10 ml syringes by an anaesthesiologist not involved in the study. Group C received 10-mL normal saline that acted as control group, group D received dexmedetomidine 0.5 µg/kg and group M received magnesium 30 mg/kg; both diluted up to 10 ml with normal saline and infused over 10 minutes. All

patients were preoxygenated with 100% oxygen via face mask for 3 min and induction was carried out with intravenous etomidate 0.3 mg/kg administered over 60 s. After evaluation of myoclonus, all patients received fentanyl 2 µg/kg and intubation was facilitated with injection vecuronium 0.1 mg/kg and further maintenance of anaesthesia carried out in the conventional manner.

Myoclonus was defined as involuntary, short muscle contractions, of a whole muscle, or of different muscles of one group leading to short observable movements of the corresponding body parts. The severity of myoclonus was graded as follows: 0—no myoclonus, 1—mild myoclonus (short movements of a body segment e.g., a finger or wrist), 2—moderate myoclonus (contraction of different groups of muscles, e.g., face and leg), 3—severe myoclonus (intense clonic movement in two or more muscle groups, e.g., fast adduction of a limb).^[3] The secondary objective was to study the incidence and intensity of pain on etomidate injection. The assessment of pain was done after 25% of total etomidate dose was administered and severity was graded using a 4-grade scale (McCGrirrick and Hunter scale)^[4] as 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 behavioural symptoms), and 3—severe (verbal response, grimacing, pulling the arm, tearing in the eyes).

Haemodynamic parameters were monitored as baseline, after study drug, before induction, immediately after intubation and 5 min after intubation.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 16.0 (SPSS, Chicago, Illinois). A value of $P < 0.05$ was considered as significant.

RESULTS

Demographic data represented in Table 1 show no significant difference between the three groups. The evaluation of myoclonus in the three groups is shown in Table 2. Myoclonus was observed in 20 patients in group C, 12 patients in group D and 8 patients in group M and the difference was of statistical significance ($P = 0.023$). More number of patients in group C had moderate i.e., grade 2 myoclonus and the difference was statistically significant ($P < 0.05$).

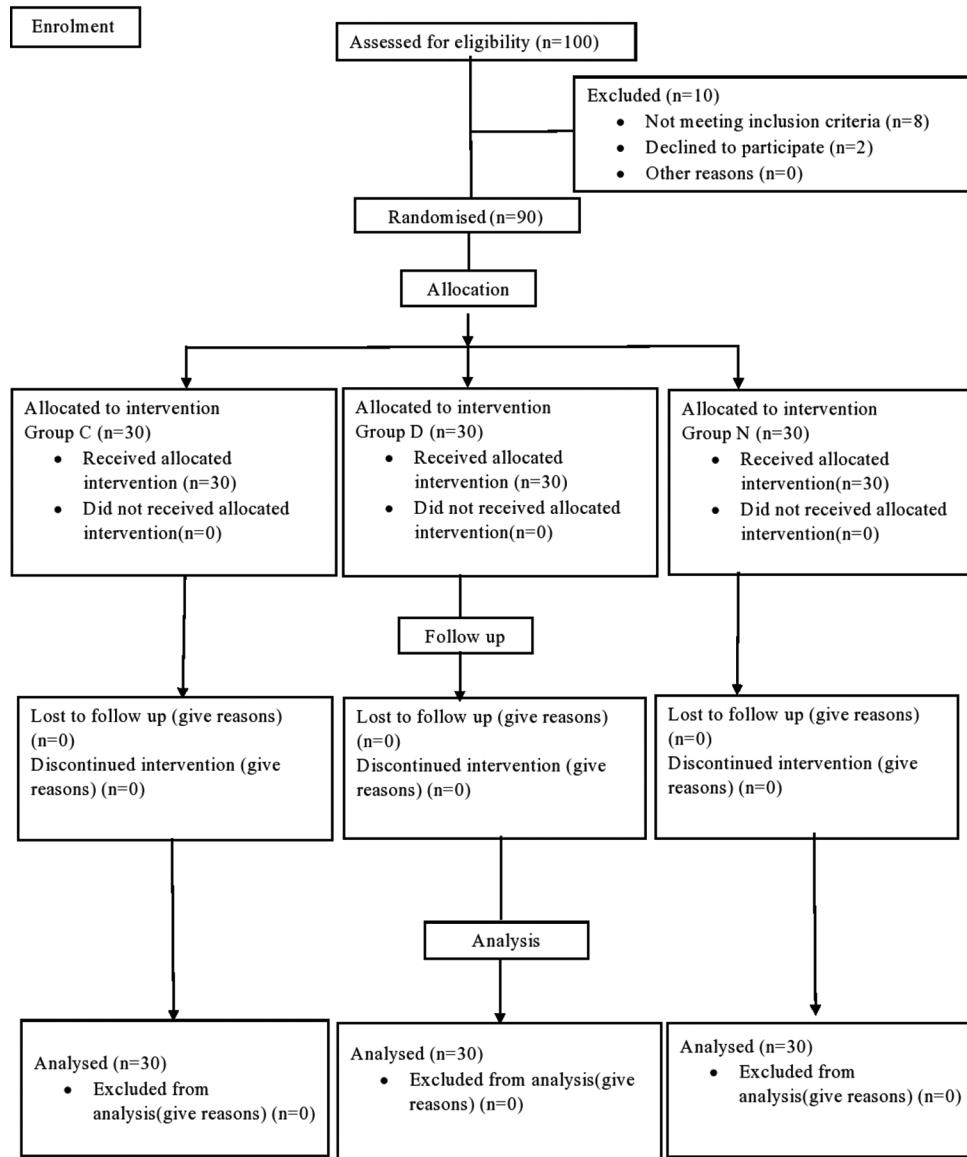


Figure 1: CONSORT chart

Additionally, the severity level in group M was significantly lower as compared to other 2 groups, the median intensity of grade 2 myoclonus being one patient in group M as compared to six patients in group D ($P = 0.028$).

Regarding the pain on etomidate injection, we found a statistically significant difference ($P = 0.002$) in its incidence between the three groups [Table 3]. Between the study drugs, we observed that a smaller number of patients in group M ($n = 3$) had moderate to severe pain as compared to group D ($n = 7$) and the difference was statistically significant ($P = 0.036$). Without pre-treatment as in group C, the number of patients with moderate to severe pain was statistically high ($n = 17$).

The haemodynamic variables between the three groups during and after intubation were comparable. [Figures 2 and 3].

DISCUSSION

Our present study demonstrates that pre-treatment with both dexmedetomidine and magnesium reduces the incidence of myoclonus induced by etomidate. However, magnesium appears to be more effective than dexmedetomidine in not only decreasing the incidence but also reducing the intensity of myoclonus. The study also shows that pain on etomidate injection is reduced more efficiently by magnesium when compared to dexmedetomidine.

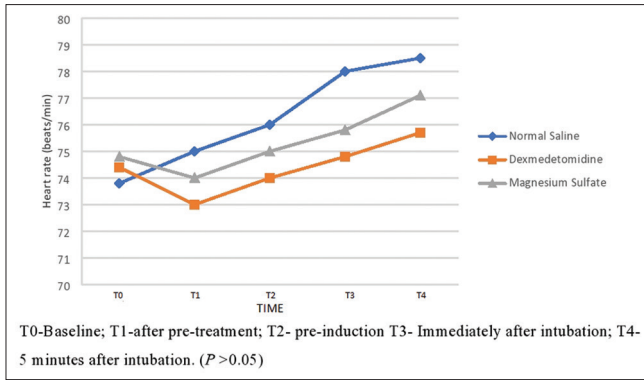


Figure 2: Comparison of heart rate (per minute) in the three groups

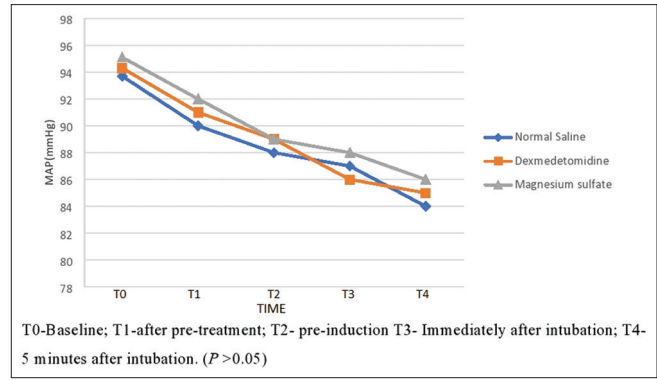


Figure 3: Comparison of mean arterial pressure (mm Hg) in three groups

Table 1: Comparison of demographic profile between the three groups

	Group C n=30	Group D n=30	Group M n=30
Age (years)	42.5±9.3	41.5±11.2	40.3±10.5
Gender			
Male	15 (50%)	16 (53.33%)	14 (46.66%)
Female	15 (50%)	14 (46.66%)	16 (53.33%)
Weight (kg)	62.3±8.2	61.1±6.2	63.2±7.3
ASA			
I	19 (63.33%)	20 (66.66%)	21 (70%)
II	11 (36.66%)	10 (33.33%)	09 (30%)

Data represented as mean (±standard deviation) ($P>0.05$, non-significant). ASA-American Society of Anesthesiologists

Table 2: Comparison of incidence and intensity of myoclonus among the 3 groups

Myoclonus	Group C n=30	Group D n=30	Group M n=30	P
Incidence in %	66.6%	40%*	23.3%	0.023
Intensity (n)				
Grade 0	10	18	22#	
Grade 1	08	06	07	
Grade 2	09	06*	01	
Grade 3	03	00 [§]	00	

$P=0.028$ as compared to group M, * $P=0.009$ as compared to group D, $^{\S}P>0.05$ as compared to group M

Table 3: Comparison of incidence and severity of pain among the 3 groups

Pain	Group C n=30	Group D n=30	Group M n=30	P
Incidence in %	67%	40%	33%	0.002
Pain Severity (n)				
Grade 0	10	18	20	
Grade 1	03	05	07*	
Grade 2	08	04	02**	
Grade 3	09	03	01	

* $P=0.036$, ** $P=0.001$, as compared to group D

Etomidate because of its beneficial effects is widely used induction agent in clinical practice.^[1,2] Pain on injection and myoclonus remain the consistent and most undesirable effects of etomidate. Many studies have demonstrated that etomidate-induced myoclonus might be associated with a seizure-like activity.^[5] Opioids like

nalbuphine and fentanyl have been studied either alone or in combination with benzodiazepines.^[6] Choi *et al.*^[7] reported pre-treatment with rocuronium significantly decreased the myoclonus; however, it was accompanied with disadvantages of muscle relaxants (airway obstruction, regurgitation and aspiration). Drugs like lignocaine, and small priming doses of either thiopental or etomidate have been tried with variable results.^[8,9] Dexmedetomidine, a highly selective α_2 agonist is widely used in anaesthesia as an anaesthetic adjuvant. The effect of dexmedetomidine in relieving myoclonus may be related to the analgesic effects.^[3] Dexmedetomidine has been found to be more effective than midazolam for decreasing the etomidate-induced myoclonus.^[10] Dexmedetomidine has been evaluated in the doses of 0.5-1 $\mu\text{g}/\text{kg}$ as a pre-treatment to reduce etomidate induced myoclonus. In our study no incidence of significant haemodynamic instability warranting treatment was observed in group D. These findings are in concordance with results of study by Luan *et al.*^[3]

Magnesium on the other hand is an antagonist of N-methyl D- aspartate (NMDA) receptor. Activation of NMDA receptor leads to calcium influx and also catalyses the production of nitric oxide which is associated with nociception.^[11] Thus blocking these receptors imparts magnesium its analgesic property. Magnesium has been shown to prevent etomidate-related myoclonus when compared to normal saline.^[12] Magnesium has been compared with ketamine, another NMDA antagonist and has been proven to be more efficient in decreasing the myoclonus. This may be because magnesium in addition also blocks inositol 1, 4, 5-triphosphate (IP3) mediated calcium channels which are responsible for preventing pain of etomidate injection.^[11,12] The incidence of myoclonus is highly dependent upon the dosage and speed of injection. A slower rate of

infusion was found to be effective in reducing the myoclonic jerks in a study by Sang Hwan Do *et al.*^[13] Therefore, we kept the etomidate dose fixed with slow rate of injection in all our cases.

The major advantage of etomidate is its stable cardiovascular profile that aids in counteracting the sympathetic stress response during laryngoscopy and intubation.^[1] In our study we observed that both dexmedetomidine and magnesium preserved this haemodynamic stability and there were no incidences of either bradycardia or hypotension.

There are certain limitations of our study. Firstly, we only studied the incidence and severity of etomidate induced myoclonus and not the duration of myoclonus which may also have an adverse effect. Secondly, infusing the drug slowly over 10 minutes using infusion pump maybe time-consuming and not suitable under some emergency situations. Other measures like bolus injection of lignocaine may be convenient and need to be compared with these study drugs.

CONCLUSION

In conclusion, both dexmedetomidine and magnesium pre-treatment before etomidate administration significantly prevents the myoclonus without adverse side effects. Magnesium, however, is superior to dexmedetomidine in decreasing not only the incidence but also the severity of myoclonus.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

- Komatsu R, You J, Mascha EJ, Sessler DI, Kasuya Y, Turan A. Anesthetic induction with etomidate, rather than propofol, is associated with increased 30-day mortality and cardiovascular morbidity after noncardiac surgery. *Anesth Analg* 2013;117:1329-37.
- Morel J, Salard M, Castelain C. Haemodynamic consequences of etomidate administration in elective cardiac surgery: A randomized double-blinded study. *Br J Anaesth* 2011;107:503-9.
- Luan HF, Zhao ZB, Feng JY. Prevention of etomidate-induced myoclonus during anaesthetic induction by pretreatment with dexmedetomidine. *Braz J Med Biol Res* 2015;48:186-90.
- McCrirrick A, Hunter S. Pain on injection of propofol: The effect of injected temperature. *Anaesthesia* 1990;45:443-4.
- Kadiyala PK, Kadiyala LD. Anaesthesia for electroconvulsive therapy: An overview with an update on its role in potentiating electroconvulsive therapy. *Indian J Anaesth* 2017;61:373-80.
- Isitemiz I, Uzman S, Toptaş M, Vahapoglu A, Gül YG, Inal FY, *et al.* Prevention of etomidate-induced myoclonus: Which is superior: Fentanyl, midazolam, or a combination? A Retrospective comparative study. *Med Sci Monit* 2014;16:262-7.
- Choi JM, Choi IC, Jeong YB, Kim TH, Hahm KD. Pretreatment of rocuronium reduces the frequency and severity of etomidate-induced myoclonus. *J Clin Anesth* 2008;20:601-4.
- Gupta P, Gupta M. Comparison of different doses of intravenous lignocaine on etomidate-induced myoclonus: A prospective randomised and placebo-controlled study. *Indian J Anaesth* 2018;62:121-6.
- Nyman Y, von Hofsten K, Ritzmo C, Eksborg S, Lönnqvist PA. Effect of a small priming dose on myoclonic movements after intravenous anaesthesia induction with Etomidate-Lipuro in children. *Br J Anaesth* 2011;107:225-8.
- Dey S, Kumar M. Comparison of pretreatment with dexmedetomidine with midazolam for prevention of etomidate-induced myoclonus and attenuation of stress response at intubation: A randomized controlled study. *J Anaesth Clin Pharmacol* 2018;34:94-8.
- Kiran S, Gupta R, Verma D. Evaluation of a single-dose of intravenous magnesium sulphate for prevention of postoperative pain after inguinal surgery. *Indian J Anaesth* 2011;55:31-5.
- Guler A, Satilmis T, Akinci SB, Celebioglu B, Kanbak M. Magnesium sulfate pretreatment reduces myoclonus after etomidate. *Anesth Analg* 2005;101:705-9.
- Do SH, Han SH, Park SH, Kim JH, Hwang JW. The effect of injection rate on etomidate induced myoclonus. *Korean J Anesth* 2008;55:305-7.

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