ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Comparative study of midazolam and fentanyl for the prevention of etomidate-induced myoclonus

Sophiya Rasool[1], Radha Gupta[2], Sukriti Prakash[3]

[1]Senior Resident, Department of Anaesthesiology, S.V.D, Savarkar Municipal General Hospital, Mumbai, Maharashtra, India, [2,3]Senior Consultant, Department of Anaesthesiology, Jaipur Golden Hospital, New Delhi, India

Submission: 06-11-2022 Revision: 04-01-2023 Publication: 01-02-2023

ABSTRACT

Background: Etomidate is one of the popular rapidly acting inducing agents with cardio-stable profile but associated with side effects such as myoclonus. Myoclonus can lead to regurgitation, prolapse of vitreous in open globe or many other complications. **Aims and Objectives:** The objectives are as follows: To compare the efficacy of Fentanyl and midazolam for prevention of Etomidate induced myoclonus. To study the hemodynamic parameters and side effects of midazolam and fentanyl in patients with myoclonus after etomidate injection. **Materials and Methods:** Eighty patients scheduled for elective surgeries under general anesthesia were randomly allotted into two groups of 40 patients each. Group F – fentanyl 1 μg/kg and Group M – midazolam 0.03 mg/kg were administered as pre-treatment before induction by Etomidate. After injection of Etomidate, incidence of myoclonus was observed along with the change in hemodynamic parameters (heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], and mean arterial pressure [MAP]). Comparison of hemodynamic parameters between 2 groups was done at pre-treatment, 1 min and 2 min after induction and 1 min after intubation. **Results:** Both fentanyl and midazolam reduced the incidence of myoclonus. However, fentanyl was more effective in decreasing incidence as well severity of myoclonus. Fentanyl was associated with more stable hemodynamic parameters such as HR, SBP, DBP, and MAP 1 min after intubation ($P<0.05$). In both the groups, there was no increased incidence of PONV. **Conclusion:** Fentanyl 1 μg/kg or midazolam 0.03 mg/kg can reduce etomidate induced myoclonus. However, fentanyl was more effective in decreasing incidence as well severity of myoclonus and was associated with stable hemodynamic parameters as compared to midazolam.

Key words: Fentanyl; Midazolam; Etomidate induced myoclonus; Hemodynamic parameters

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i2.49267

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

The intravenous route of the administration of drugs is recognized as being the most convenient means of inducing general anesthesia. In fact, the efficacy of this method was appreciated long before a suitable agent was available as a result of which intravenous anesthesia awaited only the development of suitable drug. Ideal intravenous anesthetic agent for the induction of general anesthesia should be stable in solution, have cardiovascular stability, minimal respiratory side effects, no histamine release, rapid onset and complete return of consciousness and also absence of post-operative effects such as nausea, vomiting, and delirium.[1]

At present, Etomidate is one of the popular rapidly acting inducing agents.[2] Etomidate is an imidazole-derived, sedative hypnotic agent. Etomidate causes minimal histamine release, has very stable hemodynamic profile due to lack of effect on the sympathetic nervous system and on baroreceptor function.[3] Etomidate has minimal effects on respiratory system. However, pain on injection and

Address for Correspondence:
Dr. Sophiya Rasool, Senior Resident, Department of Anaesthesiology, S.V.D, Savarkar Municipal General Hospital, Mumbai, Maharashtra, India. **Mobile:** +91-7517639894. **E-mail:** rasoolsophiya@gmail.com

myoclonus are the most common side effects of this drug. Pain on injection, venous irritation, and hemolysis were virtually abolished by the new fat emulsion preparation of etomidate.[4] but it failed to reduce the incidence of myoclonus. Myoclonic movements after etomidate injection develop in nearly 80% of the non-pre-medicated patients which may lead to regurgitation and aspiration in the non-fasting patients, may even raise the risk of prolapse of the vitreous in patients with open globe injury.[5]

Although the probable mechanism of etomidate induced myoclonus is alteration in the balance of inhibitory and excitatory influence on the thalamocortical tract, and number of drugs has been investigated for their ability to suppress these myoclonic movements. Pre-treatment with benzodiazepines, opioids, dexmedetomidine, propofol, and Ketamine have been used to suppress etomidate induced myoclonus.[6]

Ideally, a pre-treatment drug for prevention of etomidate induced myoclonus should be short acting, without any significant effect on respiration and hemodynamic and should not prolong recovery from anesthesia. Midazolam is a water-soluble benzodiazepine having fast-action, short half-life, and rapid bioavailability >90%. Under physiological pH, midazolam can quickly enter into the central nervous system through the blood-brain barrier, thus rapidly playing its pharmacological role.[7] One potential reason for the prevention of etomidate-induced myoclonus by midazolam is that midazolam interferes with neurohumoral GABA reuptake, leading to accumulation of GABA. Small doses of midazolam have been found to readily suppress the effect of stimulation of the medullary reticular formation on electrochemical responses, leading to relaxation of central muscles, thus inhibiting or mitigating myoclonus.[8]

Fentanyl is a phenyl-piperidine derivative synthetic μ-opioid antagonist that causes dose dependent analgesia, respiratory depression, and sedation. Myoclonus also occurs through cortical disinhibition.[9] Fentanyl is known to inhibit subcortical neuronal activity which form its basis in myoclonus suppression.

We conducted this study to evaluate and compare effectiveness of midazolam and fentanyl for prevention of etomidate induced myoclonus.

Aims and objectives

The objectives are as follows:

1. To compare effectiveness of midazolam and fentanyl for prevention of myoclonic movements following Etomidate injection
2. To study the hemodynamic parameters and side effects of midazolam and fentanyl in patients with myoclonus after etomidate injection.

MATERIALS AND METHODS

This prospective study was carried out on American Society of Anesthesiologists (ASA) Grades I and II patients of either sex, aged 18–60 years, undergoing elective surgical procedures requiring general anesthesia in Jaipur Golden Hospital, Rohini, New Delhi. The study was conducted from January 2021 to June 2022. A total of 80 patients scheduled for elective surgical procedure requiring general anesthesia and endotracheal intubation were screened and recruited for the study on the basis of a predefined inclusion and exclusion criteria. Patients were randomly divided into two groups as per intervention by two study drugs. Group F consisted of 40 patients who received 1 μg/kg fentanyl whereas Group M comprised of 40 patients who received 0.03 mg/kg midazolam. Sample size calculation was calculated on the basis of pilot studies done for analysis of effects of fentanyl or midazolam on etomidate-induced myoclonus. Keeping power (1-Beta error) at 80% and confidence level (1-alpha error) at 95%, the minimum sample size required in each group was 35 patients; therefore, we included 40 patients in each group. The patient and observer of this study were blinded of group allocation of the patient. In the pre-operative reception area, the study drug was prepared by a specially designated nurse according to group allocation in a volume of 10 ml and the same were coded and handed over to the anaesthesiologist who intervened and observed the patient parameters under study.

All the patients were advised to be nil by mouth for at least 8 h. On arrival in the pre-operative area, the patient's vital parameters were recorded and considered as baseline parameters. Group allocation was done as per randomization protocol. In the operation theater iv line was established and multi-parameter monitors were connected (NIBP, SPO_2, and ECG) and vitals were monitored at the start of pre-treatment followed by 1 and 2 min after induction and 1 min after intubation in addition to preset monitoring cycles every 3 min. Inj glycopyrrolate 0.2 mg iv was given, patient was administered either a precalculated dose of fentanyl or midazolam. While, the patient was preoxygenated by 100% oxygen through Bain's circuit. Two minutes after intravenous injection of pre-treatment drugs, anesthesia was induced with etomidate 0.3 mg/kg iv over a period of 20–30 s. After the end of etomidate injection occurrence of myoclonic movements was observed for 2 min and was graded according to clinical severity. After that muscle relaxation was achieved by 0.1 mg/kg vecuronium and endotracheal intubation was done.

Hemodynamic parameters (systolic blood pressure [SBP], diastolic blood pressure [DBP], mean arterial pressure

[MAP], and heart rate [HR]) were recorded before induction, during 1 and 2 min after induction and 1 min after intubation. Incidence and severity of myoclonus, pain and post-operative nausea and vomiting was compared in both the groups.

Myoclonus was graded as Grade 0 (no myoclonus), Grade 1: Mild myoclonus (Small movements in 1 body segment, such as finger or wrist), Grade 2: Moderate myoclonus (slight movements in 2 or more muscle areas, such as face or shoulder), and Grade 3: severe myoclonus (intense movements in 2 or more muscle areas, sudden adduction of an extremity) Normally, distributed continuous variables were compared using the unpaired t-test, whereas the Mann–Whitney U-test was used for those variables that were not normally distributed. SSPS 21.0 software was used for statistically analysis and $P<0.05$ was taken as statistically significant.

Inclusion criteria

The following criteria were included in the study:

1. ASA Grade I or II
2. 18–60 years of age
3. Ready to give written informed consent.

Exclusion criteria

The following criteria were excluded from the study:

1. Difficult airway
2. Patients with an allergy to opioids or benzodiazepines or etomidate
3. History of seizure disorder
4. Patient with neuropsychological illness
5. Patient who had received analgesics or sedatives within the previous 24 h
6. Patient undergoing emergency surgery.

RESULTS

The study was conducted in a prospective randomized way in 80 patients scheduled for elective surgery requiring general anesthesia. The patients were divided into two groups, Group F and Group M of 40 in each group. Group F received fentanyl 1 μg/kg and Group M received midazolam 0.03 mg/kg as pre-treatment for the prevention of etomidate induced myoclonus demographic and anthropometric data were tabulated and test of statistical significance performed for inter group comparison. The analysis of age and gender distribution showed that the mean age in Group F was 39.47±10.71 years and in Group M was 39.22±10.17 years. There was no significant difference in age distribution between the groups (P=0.866). Out of 40 patients in Group F, 22 patients were female and 18 patients were male. In Group M, 27 patients were female and 13 patients are male. There was no significant difference in gender distribution between the groups (P=0.2520). Only patients of ASA I and II were included in the study. Distribution of ASA Grades I and II patient in both groups was similar without any statistically significant difference (P=0.576) (Table 1).

The mean weight and distribution range of subjects of both the groups was comparable with no statistically significant difference. (P=0.285) Mean weight in Group F was 65.45±5.72 and in Group M was 64.05±5.90. Distribution range in Group F was 52–76 kg and in Group M was 53–80 kg. Similarly, in both the groups mean height and distribution range was comparable with no statistically significant difference (P=0.443). Mean height in Group F was 167.6±9.27 cm and Group M was 166.2±6. 8 cm. Distribution range in Group F was 150–185.4 and in Group M was 152–182.9. The mean BMI distribution in two groups was also comparable with no statistically significant difference (P=0.760). Mean BMI in Group F was 23.15±1.46 and in Group M was 23.25±1.45 (Table 2).

On comparison of mean HR between two groups, we found that baseline HR in Group F was 78±11.16 and HR in Group M was 82±10.27 which was without any statistically significant difference. (P=0.099) On 1 min and 2 min after induction the mean HR in Group F was

Table 1: Comparison of age, gender distribution, and ASA grades in studied cases

Parameters	Group F (n=40)	Group M (n=40)	P-value
Gender distribution			
Male/Female	22/18	27/13	0.252 (Not significant) *Fisher test
Age distribution			
18–30	8 (20%)	8 (20%)	0.866 (Not significant) *Mann–Whitney test
31–40	14 (35%)	13 (32.5%)	
41–50	11 (27.5%)	14 (35%)	
50–60	7 (17.5%)	5 (12.5%)	
Mean±SD	39.47±10.71	39.22±10.17	
ASA grades			
ASA I/II	31/9	33/7	0.576 (Not significant) *Fisher test

Table 2: Anthropometric parameters in studied cases

Anthropometric parameters	Group F	Group M	P-value
Height (cm)			
Mean±SD	167.6±9.27	166.2±6.8	0.4435
Median (range)	165.1 (150–185.4)	165.1 (152–182.9)	
Weight (kg)			
Mean±SD	65.45±5.72	64.05±5.90	0.285
Median (Range)	65.5 (52–76)	64.0 (53–80)	
Body mass index (kg/m^2)			
Mean±SD	23.15±1.46	23.25±1.45	0.760
Median	22.8 (20–26.6)	23.5 (19.4–26)	

77.37±10.65 and 76.45±10.33, respectively, and mean HR in Group M at 1 min and 2 min after induction was 82.23±9.13 and 81.38±9.23. On intergroup comparison, the difference was statistically significant. In Group F, at 1 min after intubation mean HR was 84.02±10.43 representing a rise of 6 bpm from base line. While in Group M, at 1 min after intubation mean HR was 89.30±9.33 representing a rise of 7 bpm from baseline. Both groups showed peak rise in mean HR at 1 min after intubation but in Group M the rise was greater and the difference was statistically significant (P=0.019).

In Group F, at 1 min after intubation mean SBP increased to 124.075±4.731 representing a rise of 9 mmHg while in Group M, at 1 min after intubation mean SBP increased to 129.05±6.377 representing a rise of 11 mmHgThe SBP reached its highest peak at 1 min after intubation in both groups but the increase in SBP was greater in Group M and was found to be statistically significant (P=0.0002) on comparison between the two study groups. In Group F at 1 min after intubation mean DBP increased to 77.95±7.18 representing a rise of 6 mmHg. Similarly in Group M at 1 min after intubation mean DBP increased to 81.02±5.29 representing a rise of 10 mmHg. The DBP reached its highest peak at 1 min after intubation in both groups but the increase in DBP was greater in Group M and was found to be statistically significant on comparison between the two groups (0.0002).

In Group F at 1 min after intubation MAP increased to 92.88±5.65 representing a rise of 7 mm Hg. Similarly in Group M at 1 min after intubation MAP increased to 96.15±5.35 representing a rise of 10 mm hg The MAP reached its peak at 1 min after intubation in both groups but the increase in MAP was greater in Group M and was found to be statistically significant on comparison between the two groups (P=0.0095) (Table 3).

In Group F, 32.5% (13 patients) experienced myoclonus and in Group M, 65% (26 patients) experienced myoclonus with regard to severity of myoclonus 22.5% (9 patients) had Grade I, 7.5% (3 patients) had Grade II and 2.5% (1 patient) had Grade III myoclonus in Group F while in Group M 30.5% (12 patients) had Grade 1, 27.5% (11 patients) had Grade II, and 7.5% (3 patients) had Grade III myoclonus. On comparison of the incidence of myoclonus between Groups F and M, the difference was statistically significant (P=0.0069) (Table 4).

In Group F, the incidence of pain on injection was 12.50% (5 patients) and in Group M the incidence of pain was 22.50% (9 patients). On comparison between the study groups, the statistically difference was found to be insignificant (P=0.3781). In Group F, the incidence of post-operative nausea and vomiting was 5% (2 patients) and in Group M the incidence of post-operative nausea and vomiting was 7.5% (3 patients). On comparison between the study groups, the statistically difference was found to be insignificant (P=1) (Table 5).

DISCUSSION

Etomidate administration is often associated with myoclonic movements that are not only bothersome but may also interfere with patient monitoring and have deleterious consequences as well. It has been suggested that large doses of etomidate depress cortical activity causing myoclonus.[10] The incidence of myoclonus is influenced by the speed of etomidate injection This effect as a confounding factor in our study has been eliminated by keep the speed of etomidate injection same in both the study groups.

Several pharmacological agents have been studied to prevent etomidate induced myoclonus; benzodiazepines, opioids, dexmedetomidine, propofol, ketamine, and some of the agents were associated with side effects such as bradycardia or chest rigidity.[11] Therefore, we have chosen two pharmacological agents (Fentanyl and Midazolam) for comparison in prevention of etomidate induced myoclonus considering their minimum effects on respiration and hemodynamic.

Fentanyl is an opioid and has been consistently associated with suppression of etomidate induced myoclonus. Therefore, in our study, we have chosen to compare the

Table 3: Comparison of hemodynamic parameters in studied cases

Hemodynamics	Group	n	Mean	SD	t-test	P-value
Heart rate (per minutes)						
Basal	Group F	40	78	11.16	1.668	0.099
	Group M	40	82	10.27		
At pre-treatment	Group F	40	77.97	11.03	1.617	0.109
	Group M	40	81.85	10.39		
1 min after induction	Group F	40	77.37	10.65	2.187	0.031
	Group M	40	82.23	9.13		
2 min after induction	Group F	40	76.45	10.33	2.251	0.027
	Group M	40	81.38	9.23		
1 min after intubation	Group F	40	84.02	10.43	2.386	0.019
	Group M	40	89.30	9.33		
Systolic blood pressure (mmHg)						
Basal	Group F	40	115.02	6.14	1.170	0.2455
	Group M	40	117.22	10.15		
At pre-treatment	Group F	40	115.87	5.91	1.299	0.1978
	Group M	40	118.10	9.11		
1 min after induction	Group F	40	110.1	4.58	1.454	0.1499
	Group M	40	112.42	8.99		
2 min after induction	Group F	40	106.25	3.86	1.452	0.1505
	Group M	40	108.12	7.197		
1 min after intubation	Group F	40	124.075	4.731	3.963	0.0002
	Group M	40	129.05	6.377		
Diastolic blood pressure (mmHg)						
Basal	Group F	40	72.60	5.98	1.004	0.3183
	Group M	40	71.30	5.59		
At pre-treatment	Group F	40	71.85	5.59	1.322	0.1899
	Group M	40	70.25	5.23		
1 min after induction	Group F	40	68.02	5.19	0.858	0.3934
	Group M	40	67.02	5.23		
2 min after induction	Group F	40	65.95	4.70	0.334	0.739
	Group M	40	66.30	4.66		
1 min after intubation	Group F	40	77.95	7.18	2.161	0.0337
	Group M	40	81.02	5.29		
Mean arterial pressure (mmHg)						
Basal	Group F	40	85.78	6.18	0.364	0.7167
	Group M	40	86.28	6.10		
At Pre-treatment	Group F	40	86.15	6.31	0.162	0.8719
	Group M	40	85.93	5.84		
1 min after induction	Group F	40	81.55	5.34	0.342	0.7330
	Group M	40	81.13	5.63		
2 min after induction	Group F	40	78.5	4.75	1.365	0.1761
	Group M	40	79.95	4.75		
1 min after intubation	Group F	40	92.88	5.65	2.658	0.0095
	Group M	40	96.15	5.35		

Table 4: Comparison of severity of myoclonus in both the groups

Group	Number	Severity of myoclonus								P-value
		Grade 0		Grade 1		Grade 2		Grade 3		
		n	%	n	%	n	%	n	%	
Group F	40	27	67.5	9	22.5	3	7.5	1	2.5	0.0069 Significant
Group M	40	14	35	12	30.5	11	27.5	3	7.5	
Total	80	41	51.25	20	25	15	18.75	4	5	

efficacy of fentanyl at a dose of 1 μg/kg iv with that of midazolam 0.03 mg/kg iv in the prevention of etomidate induced myoclonus.

The analysis of hemodynamic parameters in both the groups showed that both groups showed peak rise in mean HR, systolic as well as DBP and MAP was seen at 1 min after intubation but in Group M the rise was greater and the difference was statistically significant. Isitemiz et al., conducted a retrospective study to compare the effectiveness of fentanyl, midazolam, and a combination of fentanyl and midazolam to prevent etomidate-induced

Table 5: Comparison of pain on injection and post-operative nausea vomiting in both the groups

Parameters	Group F (n=40)	Group M (n=40)	P-value
Pain Present/Absent	5/35	9/31	0.378 (Not significant)
PONV Present/Absent	2/38	3/37	1.0 (Not significant)

myoclonus.[12] In this study depending on the drugs that was given before the induction of anesthesia with etomidate, the patients were divided into four groups: No pre-treatment (Group NP), fentanyl 1 μg/kg (Group F), midazolam 0.03 mg/kg (Group M), and midazolam 0.015 mg/kg + fentanyl 0.5 μg/kg (Group FM). The study found that the MAP measurements after induction were significantly lower in Groups F and FM compared to the no pre-treatment group ($P<0.001$). Intragroup comparison showed that MAP had significant reductions to the basal values in Groups F and FM ($P<0.001$ and $P<0.01$, respectively). All groups except Group FM had significant increases in MAP 2 min after intubation. The severity of pain due to etomidate injection, MAP, HR, and adverse effects was also evaluated. The study found that myoclonus incidence was 85%, 40%, 70%, and 25% in Group NP, Group F, Group M, and Group FM, respectively, and was significantly lower in Group F and Group FM. On the basis of these findings, the authors concluded that pre-treatment with fentanyl or combination of fentanyl and midazolam was effective in preventing etomidate-induced myoclonus. Similar findings were also reported by the authors such as Huter et al.[13]

In our study, we evaluated the etomidate induced myoclonus for 2 min, beginning of which was marked by the end of etomidate injection. We also noted the grade of severity of myoclonus, time of initiation, and other side effects such as pain on injection or incidence of post-operative nausea and vomiting. The analysis of severity of myoclonus in both the groups showed that both drugs showed reduction in incidence of myoclonus after etomidate injection but fentanyl was more effective in decreasing incidence as well as severity of myoclonus after etomidate injection. Smita Prakash concluded that incidence of etomidate induced myoclonus was 48% and 78.6% in fentanyl and midazolam pretreated groups, respectively.[14] These findings were coherent with our study. Khteishat et al., found 5.6% and 11.8% incidence of myoclonus in fentanyl and midazolam pre-treated groups.[15] The less incidence of myoclonus as compared to ours may be due to shorter duration of observation (60 s) in their study. However, the overall conclusion of fentanyl being more effective in prevention of etomidate induced myoclonus was similar to our study.

The incidence of pain on etomidate injection and incidence of post-operative nausea vomiting were compared between the Groups F and M and the difference was found to be statistically insignificant ($P>0.05$).

Limitations of the study

The study included only ASA I/II patients whereas ASA III/IV patients with significant co-morbidities (cardiovascular and neurological). Emergency surgeries were excluded from the study. These higher risk patients (ASA III, IV) and emergency situation have more risk of myoclonus associated side effects. Moreover, study was conducted in surgeries requiring general anesthesia for longer duration, so effects of study drugs on rapid awakening required in short procedures (cardioversion) could not be evaluated. These were limitations of our study.

CONCLUSION

Fentanyl as well as midazolam is effective in reducing incidence of etomidate induced myoclonus; however, fentanyl is not only more efficacious in reducing etomidate induced myoclonus but also provides better hemodynamic profile after intubation

ACKNOWLEDGMENT

The authors would like to acknowledge the support extended by the staff of Department of Anaesthesiology, Jaipur Golden Hospital, Rohini, New Delhi, for their valuable support in undertaking this study.

REFERENCES

1. Mahmoud M and Mason KP. Recent advances in intravenous anesthesia and anesthetics. F1000Res. 2018;7:F1000 Faculty Rev-470.
   https://doi.org/10.12688/f1000research.13357.1
2. Valk BI and Struys MM. Etomidate and its analogs: A review of pharmacokinetics and pharmacodynamics. Clin Pharmacokinet. 2021;60(10):1253-1269.
   https://doi.org/10.1007/s40262-021-01038-6
3. Bergen JM and Smith DC. A review of etomidate for rapid sequence intubation in the emergency department. J Emerg Med. 1997;15(2):221-230.
   https://doi.org/10.1016/s0736-4679(96)00350-2
4. Geng D, Li Y, Wang C, Ren B, Wang H, Wu C, et al. Optimization, and *in vitro* and *in vivo* evaluation of etomidate intravenous lipid emulsion. Drug Deliv. 2021;28(1):873-883.
   https://doi.org/10.1080/10717544.2021.1917729
5. Aissaoui Y, Belyamani L, El Wali A, Hajjouji SM, Atmani M and Kamili ND. Prevention of myoclonus after etomidate using a

priming dose. Ann Fr Anesth Reanim. 2006;25(10):1041-1045.
https://doi.org/10.1016/j.annfar.2006.07.079

6. Wang J, Li QB, Wu YY, Wang BN, Kang JL and Xu XW. Efficacy and safety of opioids for the prevention of etomidate-induced myoclonus: A meta-analysis. Am J Ther. 2018;25(5):e517-e523.
https://doi.org/10.1097/MJT.0000000000000404
7. Van Keulen SG and Burton JH. Myoclonus associated with etomidate for ED procedural sedation and analgesia. Am J Emerg Med. 2003;21(7):556-558.
https://doi.org/10.1016/j.ajem.2003.08.004
8. Schwarzkopf KR, Hueter L, Simon M and Fritz HG. Midazolam pretreatment reduces etomidate-induced myoclonic movements. Anaesth Intensive Care. 2003;31(1):18-20.
https://doi.org/10.1177/0310057X0303100103
9. Pathan H and Williams J. Basic opioid pharmacology: An update. Br J Pain. 2012;6(1):11-16.
https://doi.org/10.1177/2049463712438493
10. Luan HF, Zhao ZB, Feng JY, Cui JZ, Zhang XB, Zhu P, et al. Prevention of etomidate-induced myoclonus during anesthetic induction by pretreatment with dexmedetomidine. Braz J Med Biol Res. 2015;48(2):186-190.
https://doi.org/10.1590/1414-431X20144100
11. Zhang KD, Wang LY, Zhang DX, Zhang ZH and Wang HL. Comparison of the effectiveness of various drug interventions to prevent etomidate-induced Myoclonus: A Bayesian network meta-analysis. Front Med (Lausanne). 2022;9:799156.
https://doi.org/10.3389/fmed.2022.799156
12. 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;20:262-267.
https://doi.org/10.12659/MSM.889833
13. Huter L, Schreiber T, Gugel M and Schwarzkopf K. Low-dose intravenous midazolam reduces etomidate-induced myoclonus: A prospective, randomized study in patients undergoing elective cardioversion. Anesth Analg. 2007;105(5):1298-1302.
https://doi.org/10.1213/01.ane.0000287248.25610.c0
14. Prakash S, Mullick P, Virmani P, Talwar V and Singh R. Effect of pre-treatment with a combination of fentanyl and midazolam for prevention of etomidate-induced myoclonus. Turk J Anaesthesiol Reanim. 2021;49(1):11-17.
https://doi.org/10.5152/TJAR.2019.90248
15. Khteishat B, Salaytah W, Qatawneh T and Alsagheer M. The effect of preinduction with midazolam, fentanyl, and ketamine on etomidate induced myoclonic muscle movements. J R Med Serv. 2011;18:38-41.

Authors' Contributions:
SR - Concept and design of the study; interpreted the results, prepared first draft of manuscript and critical revision of the manuscript; **RG -** Statistically analysed and interpreted; reviewed the literature and manuscript preparation; **SP -** Design of the study, statistically analyzed and interpreted, preparation of manuscript and revision of the manuscript.

Work attributed to:
Department of Anaesthesiology, Jaipur Golden Hospital, New Delhi, India.

Orcid ID:
Dr. Sophiya Rasool - https://orcid.org/0000-0001-8989-3754
Dr. Radha Gupta - https://orcid.org/0000-0001-6130-6423
Dr. Sukriti Prakash - https://orcid.org/0000-0003-3631-2965

Source of Support: Nil, **Conflicts of Interest:** None declared.