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Original Research Article

A comparison of pretreatment with lignocaine versus dexmedetomidine in prevention of etomidate induced myoclonus- A randomised comparative trial

Vigneshwaran Swaminathan[1], Mohd Khalik[1,*], Neeharika Arora[1], Pallavi Ahluwalia[1], Akash Gupta[1], Ankur Garg[1]

[1] *Dept. of Anaesthesiology and Critical Care, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India*

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ABSTRACT

Background: Etomidate is a short-acting non-barbiturate intravenous anesthetic with rapid induction and rapid awakening. It is frequently utilized in clinical practice, especially for patients with an unstable cardiovascular system, due to its minimal influence on hemodynamics and respiratory depression. However, Etomidate might cause side effects during anaesthetic induction, such as injection discomfort, phlebitis, hemolysis, and myoclonus. This study was, therefore, conducted in order to compare the pre-treatment with lignocaine versus dexmedetomidine in deterrence of myoclonus resulting from Etomidate.

Materials and Methods: 60 patients were allocated randomly into two study groups. Each group comprising 30 patients. Patients in GroupI received injection Lignocaine (1 mg/kg)and Group II received injection Dexmedetomidine (0.5μg/kg) in 10 ml of normal saline over 10 min followed by Etomidate injection (0.3 mg/kg) over 30 s. Patients were observed for 2 minutes for occurrence of myoclonus and the intensity and time of occurrence was noted by a person blinded to the drug used.

Result: In our study, 90% patients were myoclonus grade zero, followed by 6.7%, 3.3% and no one of myoclonus grade one, two and three in dexmedetomidine group at 1 min. 60.0%, 10.0%, 13.3% and 16.7% patients had grade zero, one, two, three of myoclonus respectively in lignocaine group at 1 min. 80.0% patients were myoclonus grade zero, followed by 13.3%, 3.3%, 3.3% of patients had myoclonus grade one, two, three respectively in dexmedetomidine group at 2mins. 53.3%, 10.0%, 16.7%, 20.0% patients were myoclonus grade zero, one, two and three respectively in lignocaine group at 2mins. On the whole 46.7% patients in lignocaine group developed Myoclonus; but 20.0% in dexmedetomidine group shows the myoclonus.

Conclusion: We conclude that the prevalence of Etomidate-induced myoclonus was significantly decreased in patients who were pre-treated with dexmedetomidine in comparison with lignocaine.

1. Introduction

Etomidate, a carboxylated imidazole, is a hypnotic that acts mainly on the telencephalic neocortex [1] with limited effect on circulation and little respiratory depression. Etomidate-induced myoclonus (EIM), seen in 50%–80% of non-premedicated patients, limits its use. [2–4] Patients with open-globe damage, a full stomach, hypertension, coronary artery disease, and cerebral aneurysms may be more vulnerable. [5] Ideally, a pre-treatment drug for preventing myoclonic movements must be short acting, should not have significant effects on respiration and hemodynamics, and anaesthesia recovery should not be prolonged. [1] Lignocaine, a Class 1b antiarrhythmic and N-(2,6,Dimethylphenyl) an amide local anaesthetic, affects signal conduction in neurons by delaying the inactivation of the fast voltage-gated Na+

* *Corresponding author*.
E-mail address: ansarikhalik786@gmail.com (M. Khalik).

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channels in the neuronal cell membrane that are important for potential propagation.

Dexmedetomidine is an alpha-2 adrenoceptor agonist with a good selectivity. The locus coeruleus, which has one of the largest concentrations of alpha-2A adrenoreceptors in the brain, is where it works. Presynaptic activation of the alpha-2A adrenoreceptors in the locus coeruleus inhibits the release of norepinephrine resulting in sedative and hypnotic effects. Anxiolysis, analgesia, and sympatholysis with consequences of anaesthetic sparing and no substantial respiratory depression are some of the other pharmacological characteristics. Therefore, dexmedetomidine efficacy in relieving myoclonus may be related to its sedative and analgesic effects.[5] Few studies have evaluated the effect of dexmedetomidine on myoclonus after Etomidate injection. The goal of this study is to find an optimal pre-treatment medication that will eliminate or considerably reduce the incidence and severity of EIM, as well as to compare the effects of Lignocaine and dexmedetomidine on the occurrence of EIM.

2. Aim

To compare the effect of pre-treatment with lignocaine and dexmedetomidine on the occurrence and severity of Etomidate induced myoclonus.

3. Objectives

1. To determine the prevalence of myoclonus in both groups.
2. To determine the severity of myoclonus in both groups.

4. Materials and Methods

This prospective randomized comparative study was carried out in patients planned for elective surgeries of various specialities under general anaesthesia. The study was registered under CTRI with no CTRI/2020/04/024928.

The required sample size estimated was 30 per group. Following the approval by the Board of Thesis/Research committee, Anaesthesiology Department and Ethical committee IEC/IRB no IEC/62/2019/SEPT RMCH, Bareilly, 60 patients were randomly split into two groups. Informed consent was obtained from the patients participating in the study.

4.1. Inclusion criteria

American society of Anaesthesiologist (ASA) grade I or II, Age 18-60 years, either sex, weight between 45-80 kgs, Scheduled for elective surgeries under general anaesthesia.

4.2. Exclusion criteria

Patients refusal for procedure, ASA grade III, IV, V, Emergency surgeries, History of seizure disorder, History suggestive of any Drug Allergies, Anticipated difficult Airway, Known psychiatric disorders, Sepsis or Systemic infections, On Pacemakers or Beta blocker, Cardiovascular illness and uncontrolled hypertension, High intracranial pressure were excluded.

4.3. Methodology

The patients were allocated by sequentially numbered, opaque, sealed envelope technique randomly(randomised using chit in box method) into two study groups. Each group comprised of 30 patients. Two groups receiving injection Lignocaine and injection Dexmedetomidine were named as Group I and Group II respectively. To ensure blinding, syringes containing aqueous solution of either drug were prepared by a team member who was blinded to group allocation and also not a participant in the data recording. All patients were subjected to a detailed pre-anaesthetic evaluation. After intravenous cannulation, baseline parameters such as Blood pressure (BP) (systolic, diastolic, mean), pulse oximetry (SpO2), heart rate (HR), and electrocardiogram were recorded. Patients in Group I and Group II received injection Lignocaine and injection Dexmedetomidine (1 mg/kg) and (0.5μg/kg) respectively in 10 ml of normal saline over 10 min followed by Etomidate injection (0.3 mg/kg) over 30 s. Patients were observed for 2 minutes for occurrence of myoclonus and the intensity and time of occurrence was noted by a person blinded to the treatment group. Myoclonus was observed as involuntary, short contraction of some muscle fibres, of a whole muscle, or of different muscles of one group leading to short observable movements of the corresponding body parts. The intensity of myoclonus was graded as follows: 0 - no myoclonus, 1 - mild myoclonus (short contraction of some muscle fibres e.g., a finger or shoulder), 2 - moderate myoclonus (contraction of different groups of muscles, e.g., face and leg), 3 - severe myoclonus (at least two muscle units undergo strong clonic movement, e.g., whole-body movements or quick adduction of any limb). After 2 minutes of observation, Injection Butorphanol (0.02 mg/kg) was given and Injection Rocuronium (0.9 mg/kg) was given to facilitate intubation. Positive pressure ventilation was initiated using bag and mask with N_2O:O_2(70:30) and isoflurane (MAC- 0.6-1.6%) as an inhalational agent. Orotracheal intubation was done with an appropriately sized cuffed endotracheal tube by an experienced anaesthesiologist.

Patients were closely monitored during the course of intra- operative period. For reversal with inj. Glycopyrolate (0.01 mg/kg) iv and inj. Neostigmine (0.05 mg/kg) iv and. Pharyngo-tracheal suction and then extubation was

done. Amount of blood loss and fluid given were assessed. After the patient is able to keep his eyes open, elevate head and breathe normally, he/she was shifted to ward. Any complications, adverse effects up to 24 hours post-operatively were noted.

4.4. Statistical analysis

Data was entered in MS Excel spread sheet and analysed using SPSS (Statistical Package for Social Science) version 22 software for statistical analysis. Frequency distribution tables was produced, and the chi square test was used to asses associations of variables. Data was present in standard deviation and mean. Independent t-test was performed to find significant difference in different variables in between two groups. A p-value less than 0.05 was considered statistically significant. Summarized as standard deviation and mean with confidence interval of 95%.

5. Results

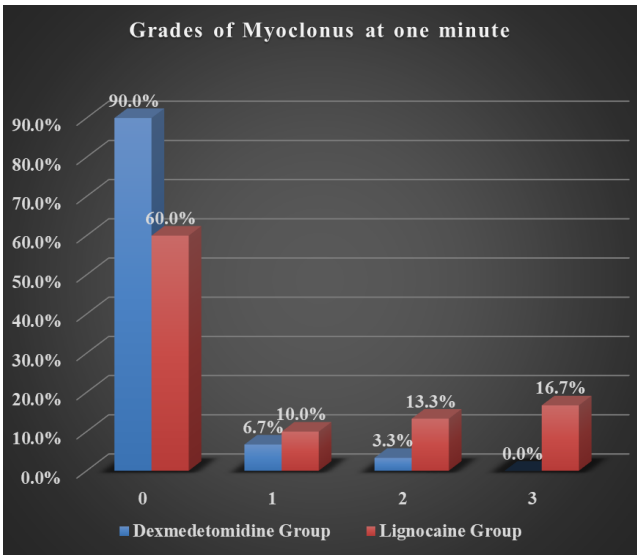

Fig. 1: Grades of myoclonus at one minute

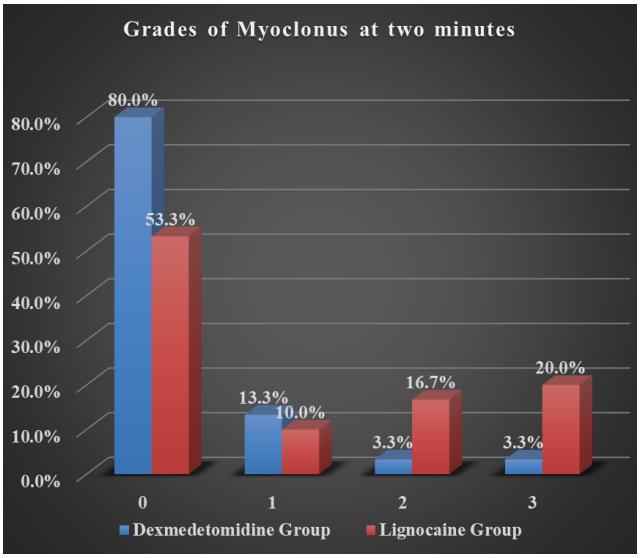

Fig. 2: Grades of myoclonus at two minutes

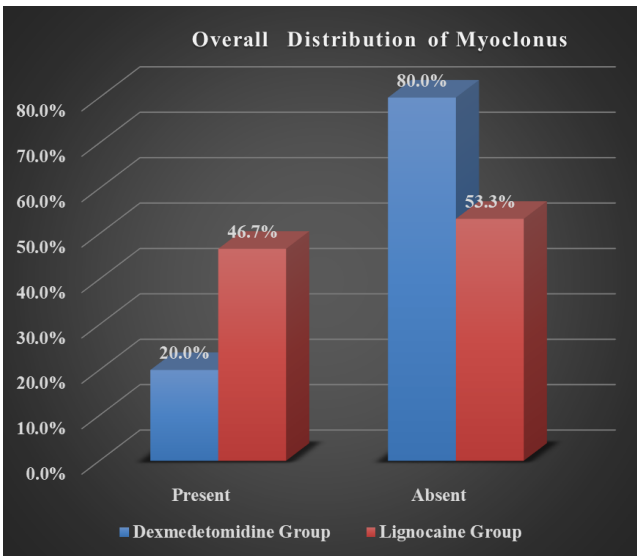

Fig. 3: Overall distribution of myoclonus

6. Discussion

Etomidate is a short-acting non-barbiturate intravenous anesthetic with rapid induction and rapid awakening. It is frequently utilised in clinical practice, especially for patients with an unstable cardiovascular system, due to its minimal influence on hemodynamics and respiratory depression. However, Etomidate might cause side effects during anaesthetic induction, such as injection discomfort, phlebitis, hemolysis, and myoclonus. Before inducing of anaesthesia using Etomidate, various opioid agents including sufentany,[6] fentanyl[7] and remifentanil[8] decreased the occurrence of myoclonus.

This study was, therefore, conducted in order to compare the pre-treatment with lignocaine versus dexmedetomidine in deterrence of myoclonus resulting from Etomidate. So far no study has been carried out to compare dexmedetomidine and lignocaine for Etomidate induced myoclonus.

Demographic values were comparable in both the groups. Occurrence of myoclonus in each group, degree of myoclonus in each of the groups were observed at different time intervals.

Dexmedetomidine is an alpha-2 adrenoceptor agonist with a good selectivity. The locus coeruleus, which has one of the largest concentrations of alpha-2A adrenoreceptors in the brain, is where it works. Presynaptic activation of the alpha-2A adrenoreceptors in the locus

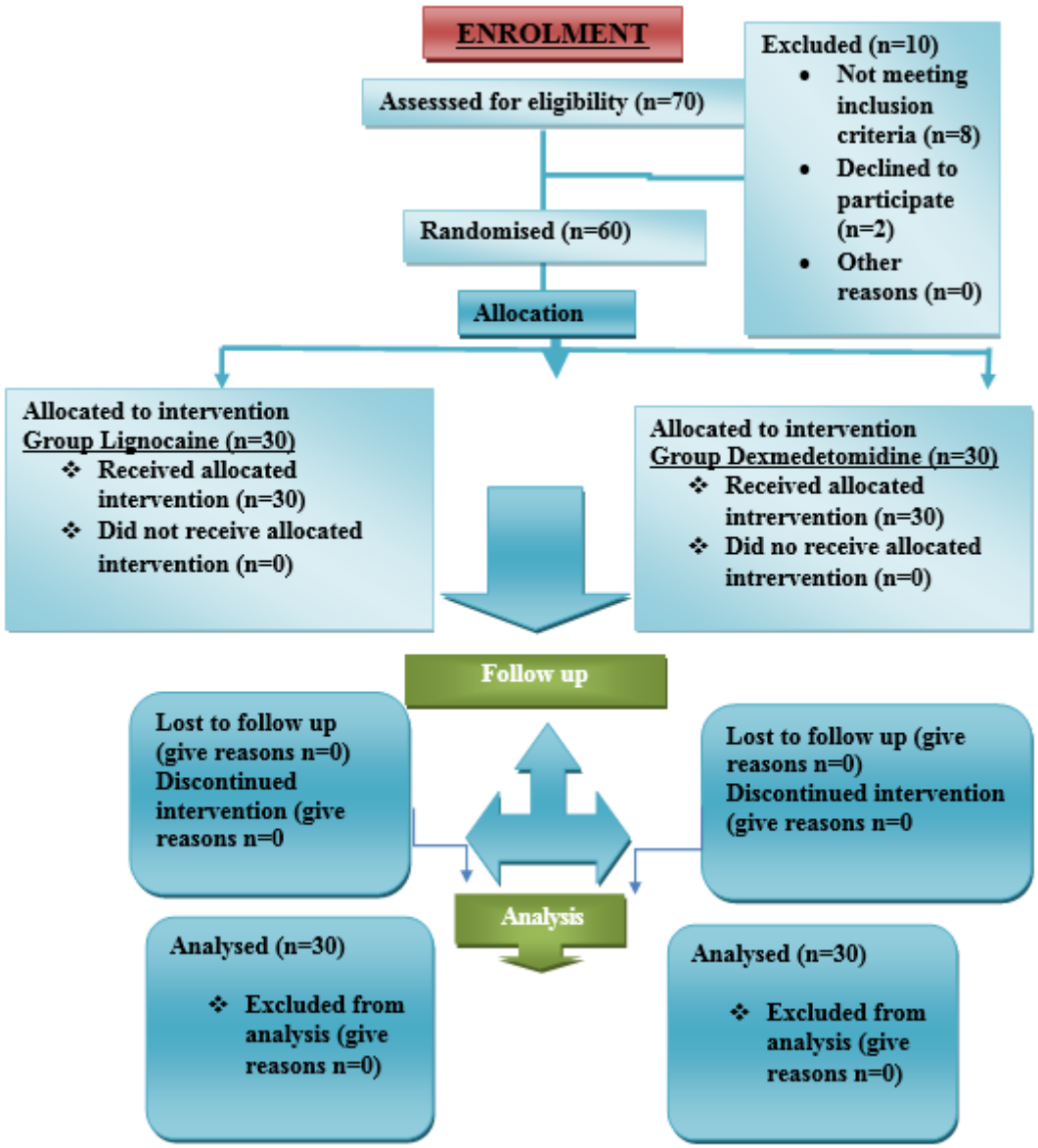

Diagram 1: Consort diagram

coeruleus inhibits the release of norepinephrine resulting in sedative and hypnotic effects. Anxiolysis, analgesia, and sympatholysis with consequences of anaesthetic sparing and no substantial respiratory depression are some of the other pharmacological characteristics. Therefore, dexmedetomidine efficacy in relieving myoclonus may be related to its sedative and analgesic effects.[5]

In this research, we reported at one minute myoclonus in group II, large majority of patients (90.0%) were myoclonus grade zero, followed by myoclonus grade one (6.7%), myoclonus grade two (3.3%) and no one in myoclonus grade three. However, in group I nearly two-third of patients (60.0%) were myoclonus grade zero, followed by myoclonus grade one (10.0%), myoclonus grade two (13.3%), and myoclonus grade three (16.7%). Dey S & Kumar M[9] observed the large majority of patients who received dexmedetomidine, during the Etomidate treatment, 22 out of 40 (55%) did not had any myoclonus, 14 (35%) had Grade one myoclonus, 4 (10%) had Grade two myoclonus and none of their patients had Grade three myoclonus; The majority of patients who were given midazolam displayed Grade two myoclonus, with 19 of 40 (47.5 percent) having it, followed by 10 (25 percent) had Grade one myoclonus and 6 (15 percent) had Grade three myoclonus. And (12.5%) patients who had Grade zero myoclonus, demonstrated a statistically significant

difference in myoclonus grades among both groups with dexmedetomidine showing a higher efficacy that's rooted for us to choose dexmedetomidine as one of study drugs. Singh AK et al[5] published the tendency of myoclonus was lowest in the group of midazolam (28%), followed by the lignocaine group (44%).

In our study, we waited for ten minutes before administering Etomidate to allow enough time for the pre-treatment drug to act and found that the overall incidence of event of myoclonus in group I was 46% and group II was only 20%. While Xiao-Li Yang[10] reported the myoclonus degree of three groups was significantly different, and their detailed analysis shows that while the number of cases of myoclonus grade zero of 40mg lignocaine group and 20mg lignocaine group was significantly more compared to normal saline group and the total number of cases of myoclonus grade one, grade two and grade three was significantly less than that of the group received normal saline; the number of cases of myoclonus grade zero, grade one, grade two and grade three of 40mg lignocaine group was not significantly distinct from that of 20mg lignocaine group so we have decided to choose a fixed dose of ligocaine (1mg/kg) in our study. Du X et al[11] published that there were substantial variations in the incidence of various grades of myoclonus post Etomidate between the dexmedetomidine-treated and control groups. Mirzak A et al,[2] Doenicke AW et al,[1] Xiao-Li Yang et al,[10] Singh AK et al,[5] Dey S & Kumar M et al[9] have not mentioned the point in time after injection of Etomidate at which myoclonus was observed, whereas in our study at one and two minutes following Etomidate injection, we looked for at the occurrence and extent of myoclonus. We observed that the myoclonus in group II, 80.0% patients were myoclonus grade zero, followed by myoclonus grade one (13.3%), myoclonus grade two (3.3%) and myoclonus grade three (3.3%). However, In group I, 53.3% patients were myoclonus grade zero, followed by myoclonus grade one (10.0%), myoclonus grade two (16.7%), and myoclonus grade three (20.0%). In our study, results concluded significant difference in grades of myoclonus in both the groups. Lang B et al[12] reported the pre-treatment with lidocaine in combination with Etomidate yielded a significantly lower incidence of several grades of myoclonus than with Etomidate alone (incidence of EIM : 11.3% with lidocaine vs 24.3% with saline) supporting our study. Similar to our study Luan HF et al[13] myoclonus intensity among the three batches was statistically significant lower in 0.5 μg/kg dexmedetomidine group and 1.0 mg/kg dexmedetomidine group in relation to isotonic saline group. That is why we chose 0.5 μg/kg dexmedetomidine in our study to avoid inadvertent side effects.

We observed that the overall incidence of EIM was significantly lower in the group II (only 20.0%) than in the group I (46.7%). Dey & Kumar M[9] presented the tendency of myoclonus in patients who received dexmedetomidine as a pre-treatment was substantially lower than in those who received midazolam. Miao S et al[14] reported the dexmedetomidine a significant 38% reduction in the number of patients who experienced EIM 26% vs 64%. In addition, the severity of myoclonus in the dexmedetomidine group was way lower than in the placebo group. Singh AK et al[5] mentioned the incidence of myoclonus in control group was 76%, whereas patients pre-medicated with midazolam or lignocaine showed 28% and 44% incidence, respectively. Gultop et al[3] examined the effects of pre-treatment with 2 percent lignocaine (1 ml) and saline, given 30 seconds before getting induced with Etomidate, and found that the lignocaine group had 56.6 percent myoclonus compared to 83 percent in the saline group supporting our study,

Mizrak A et al[2] reported the in 34% patients in dexmedetomidine group. They reported the extent of myoclonus was graded as mild in 16.0%, moderate in 3.0%, and severe in 13.0% patients in dexmedetomidine group. Luan HF et al[13] reported the isotonic saline group (63.3%), 0.5 mg/kg dexmedetomidine group (36.7%), and 1.0 mg/kg dexmedetomidine (30.0%) occurrence of myoclonus among the groups. Mizrak A et al[2] reported the dexmedetomidine (0.5 mg/kg) and thiopental (1.0 mg/kg) were shown to lower the act of myoclonus from 64% to 34% and 36%, respectively. Guler A et al[15] reported that magnesium sulphate (2.48 mmol) decreased myoclonus incidence from 72% in the placebo group to 24% in the magnesium sulphate group. The usage of fentanyl and midazolam together led in a 15.7 percent EIM rate. In a study by Prakash S et al[16] they reported that in the groups Fentanyl, Midazolam, and Fentanyl and Midazolam, moderate or severe myoclonus occurred in 32.9 percent, 64.3 percent, and 8.6 percent, respectively. Ghodki PS & Shetye NN et al[17] reported a significant difference in its incidence in all three factions (Normal saline, magnesium and dexmedetomidine group).

In the current study we observed that the myoclonus at 1^{st} minute it was group II (10.0%) and group I (40.0%); while at 2nd minute incidence in both the groups increased; among group II (20.0%) and group I (46.7%) had myoclonus. After the first minute of Etomidate administration, roughly half of the incidents occur. To capture the real incidence of myoclonus in both the pre-medicated and non-medicated groups, a 2-minute observation time was selected. Singh AK et al[5] reported the 1 mg midazolam and 1 ml of 2% lignocaine decrease the incident rate and intensity of myoclonus due to Etomidate. However, midazolam was more efficient than lignocaine. Gupta P & Gupta M[18] reported there was a statistically significant difference in the incidence of severe myoclonus at one minute between groups normal saline, 0.5 mg/kg lignocaine, 1 mg/kg lignocaine, and 1.5 mg/kg lignocaine. Similarly, at two minutes, there was

a statistically significant decrease in the event of severe myoclonus was observed among 1.5 mg/kg, 1 mg/kg, 0.5 mg/kg lignocaine groups andnormal saline groups. Rajkumari R et al[19] reported that myoclonus was found in 34 individuals (68%) in control group who received normal saline and 15 patients (30%) in the 1 mg/kg lidocaine group at one minute. There was a statistically significant reduction in the occurrence of myoclonus at one minute when comparing the 1 mg/kg lidocaine group to the normal saline group. In the normal saline and 1 mg/kg lidocaine groups, two minutes myoclonus was found in 32 patients (64%) and 19 patients (38%) respectively. There was a statistically significant reduction in the incidence of event of myoclonus at two minutes when comparing the 1 mg/kg lidocaine group to the normal saline group. Dey S & Kumar M[9] reported the incidence of Etomidate-induced myoclonus was significantly dropped in the number of patients who received dexmedetomidine as a pre-treatment in contrast to midazolam.

7. Limitation

The main limitation of this study was a single centre and small sample size. The other limitation of the present study was that we used only single fixed doses of dexmedetomidine and lignocaine to evaluate its effect on myoclonus due to Etomidate and there was no control group as it causes myoclonus to the patient after induction. The study cohort, namely ASA I/II patients, does not reflect the optimum population for whom Etomidate is the preferred induction drug.

8. Conclusion

We conclude that the prevalence of Etomidate-induced myoclonus was significantly decreased in patients who were pre-treated with dexmedetomidine in comparison with lignocaine. In our study, 46.7% patients in lignocaine group developed Myoclonus; but 20.0% in dexmedetomidine group shows the myoclonus.

In compared to lignocaine, the prevalence of Etomidate-induced myoclonus was substantially lower among patients who received pre-treatment with dexmedetomidine. So dexmedetomidine can be a promising drug in preventing EIM, however more extensive studies are required.

9. Source of Funding

None.

10. Conflict of Interest

The authors declare no conflict of interest.

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Author biography

Vigneshwaran Swaminathan, Resident https://orcid.org/0000-0002-4344-6833

Mohd Khalik, Assistant Professor

Neeharika Arora, Professor

Pallavi Ahluwalia, Professor

Akash Gupta, Associate Professor

Ankur Garg, Assistant Professor

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