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ORIGINAL ARTICLE

Effect of Pretreatment of Lignocaine Versus Midazolam in the Prevention of Etomidate Induced Myoclonus

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ABSTRACT

Background: The myoclonus after induction of anesthesia with etomidate can lead to increased risk of regurgitation and aspiration. We conducted this study to compare the effectiveness of midazolam and lidocaine for the prevention of etomidate induced myoclonus.

Methodology: This randomized controlled trial was done in the Department of Anesthesiology and Intensive Care, Holy Family Hospital, Rawalpindi from January-June 2015 after approval of hospital ethical committee. Informed consent (written) was taken from 224 patients. Patients were allocated into 2 equal groups randomly with the help of computer-generated numbers. Two minutes after induction with etomidate, Group A got 1 ml of 2% lidocaine, and one ml (1 mg) of midazolam was given to Group B. Myoclonus was evaluated in the following one minute, after which 0.5 mg/kg of succinylcholine was given to the patient to facilitate endotracheal intubation.

Time of onset of induction was marked by loss of eyelash reflex. Myoclonus was recorded at 20, 40, and 60 seconds. Drug was found to be effective if there was no myoclonus within one minute of etomidate induction. Analysis of data was done using SPSS 17.

Results: Lignocaine was effective in preventing myoclonus in 55.40% of patients and Midazolam prevented it in 69.60%. The variation between the results of the groups was found significant statistically. (P< 0.05)

Conclusion: Both midazolam and lignocaine are effective in preventing the occurrence of myoclonus associated with etomidate. However, midazolam is the more effective of the two drugs.

Keywords: Etomidate, Lignocaine, Midazolam, Myoclonus

Authors' Contribution:
[1]Conception; Literature research; manuscript design and drafting; [2,3] Critical analysis and manuscript review; [4]Data analysis; Manuscript Editing.

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Article info:
Received: June 12, 2021
Accepted: December 2, 2022

Cite this article. Batool F, Shah A A, Lodhi S, Zahir J. Effect Of Pretreatment Of Lignocaine Versus Midazolam In The Prevention Of Etomidate Induced Myoclonus. J Islamabad Med Dental Coll. 2022;11(4): 211-215
DOI: https://doi.org/10.35787/jimdc.v11i4.661

Funding Source: Nil
Conflict of Interest: Nil

Introduction

Choice of induction agent is important owing to pharmacodynamics and patients' physiological condition.[1] Although there are concerns with myoclonus and adrenocortical suppression, Etomidate is still one of the commonly used agents. For the prevention of myoclonic jerks, other used agents include benzodiazepine, lignocaine, midazolam and rocuronium etc.[2] However there is still debate over the effectiveness of these medicines.[3] The incidence of myoclonus is 50-80% in unpremeditated patients following the induction dose of etomidate.[4]

Myoclonus jerks increase the danger of regurgitation and aspiration.[5] Thus the prevention of these jerks is a major concern for the patient safety.

Lidocaine is a member of amide family of local anaesthetics.[6] Lidocaine acts by binding to the voltage gated Na channels present in the neuron.[7] Midazolam is part of the benzodiazepine group and produces sedation.[8]Other effects include anti-seizure activity, anxiolysis and amnesia.[9] Drug which is short acting, with no effect on respiration and hemodynamics would be considered ideal in this case.[10]

Singh KA et al studied the effectiveness of lidocaine and midazolam as compared to placebo for the avoiding etomidate induced myoclonus. There results indicated 44% incidence with lidocaine, 28% with midazolam and 76% with placebo.[11]

After the literature review, no research was found to be done in the Asian population, therefore this study was conducted which will help to establish the better modality for the myoclonus prevention.

Methodology

This randomized control trial was performed in the Department of Anesthesiology and Intensive care at Holy Family Hospital, Rawalpindi. The study duration was 6 months between 01-01-2015 till 30-06-2015. American Society of Anesthesiology -I and II patients aged between 20-45 years who were admitted for elective surgical procedures were included in the study. Patients having drug allergies, pregnant patients or those with any neurological disease were not included in the study.

After ethical committee's approval and obtaining informed written consent, 112 patients [11] were recruited according to the inclusion criteria, using WHO sample size calculator. Preoperative anesthesia assessment was done a day before surgery. Patients were prepared by fasting and allocated to the study groups using computer generated numbers.

Group A got one ml of 2 % lidocaine, 120 seconds prior to the administration of etomidate while Group B got one ml (One mg) of midazolam, 120 sec prior to induction. The preparation of medication was done in coded syringes. Etomidate (0.3 mg/kg) was administered by team members who were blinded to group allocations of the patients.

In operating room, crystalloid infusion was initiated using lactated ringers, and ASA standard monitoring was initiated. Heart rate, BP, oxygen saturation, and rate of respiration were recorded and taken as baseline readings. Pre-oxygenation was done with 100% oxygen for all patients for 3 minutes. The time when eyelash reflex was lost, was marked as onset of induction. Additional dose of etomidate was given if necessary. After induction with etomidate, the researchers waited for 60 seconds to observe for any sign of myoclonus after which succinyl choline was administered for endotracheal intubation. Vital charting was done every minute for the first five minutes, every 5 minutes for the next fifteen minutes then at 15 minutes interval till the end of surgery. Maintenance of anesthesia was done with isoflurane and for muscle relaxation atracurium was used.

Recorded data analysis was done using the SPSS version 17. For quantitative variables (weight, BMI and age) mean ± SD calculation was done. Chi-square test was done for comparison of myoclonus frequency in the two groups, p-value less than 0.05 was considered statistically significant.

Results

The mean age of the participants in group A was 30.61± 0.66 years and 30.16 ± 0.56 years in group B. The mean weight was 62.64 ± 0.30 kg and 61.75 ± 0.22 kg in groups A and B respectively. The mean BMI of group A was 21.87 ± 0.16 and 21.93 ± 0.15 in group B.

Midazolam was effective in preventing etomidate-induced myoclonus in 69.60% whereas lignocaine was effective in 55.40% patients. The difference was statistically significant with a p-value of 0.027 (Table I).

TABLE I: Comparison of frequency of myoclonus between Group A (Lignocaine group) and Group B (Midazolam group) (n=112)

	Myoclonus within 60 seconds of Etomidate induction				
	Present		**Absent**		
	Count	Percentage	Count	percentage	P-Value
Group A	50	44.60	62	55.40	.027
Group B	34	30.40	78	69.60	

Group A- Lignocaine **Group B Midazolam**

Discussion

Various studies are available in the literature which explored the use of various agents for the prevention of myoclonus after induction with etomidate. Ghodki PS et al [5] explored the use of dexmedetomidine and magnesium, they found that magnesium was more efficacious. However, the use of magnesium has been associated with increased duration effects of muscle relaxants, hence may prolong the duration of anesthesia. Zhu Y et al [9] conducted a meta-analysis in 2018 and put forward their conclusion in favor of lignocaine. They considered eight studies which concluded that lignocaine was significantly efficacious in prevention of myoclonus however still they wanted more good quality studies on the subject for a conclusive opinion. Jayasingh SC et al [10] in their study compared various doses of lignocaine, they concluded that at the dose of 1 mg/kg or 1.5 mg/kg, lignocaine provided a statistically significant reduction in myoclonus. They also put forward that lignocaine was nearly the ideal agent for the purpose as it had minimal cardiac effects and also that it did not prolong the duration of anesthesia. An RCT conducted by Kahlon A Singh and colleagues found that lignocaine and midazolam were effective in preventing the frequency and severity of etomidate induced myoclonus.[11]

In our study, done at the Holy family hospital, we also compared the effect of lignocaine and midazolam in prevention of myoclonus with etomidate. Our results indicated that midazolam was more effective as compared to lignocaine. Myoclonus incidence was 44.60% in lignocaine group whereas it was 30.40% in midazolam group. Furthermore, the intensity and frequency were much lower in female group than male population (p=0.04)

In a randomized control study, Schwarzkopf and colleagues [12] compared the efficacy of (0.015mg/kg) midazolam with etomidate 0.05 mg/kg and placebo. Patients who were premedicated with midazolam (oral), were divided randomly into 3 equal groups: etomidate IV 0.05 mg/kg, midazolam IV 0.015 mg/kg, or IV normal saline (placebo). Etomidate 0.3 mg/kg IV was administered after 90 seconds of premedication. Induction was done with sufentanil & rocuronium after 1 minute of the onset of hypnosis. Grading of Myoclonic movements was done on a scale of zero to three. The results showed that the incidence of myoclonic movements in the placebo group was significantly lower as compared to patients who were premedicated with midazolam . Myoclonus incidence is 20% in their study which is not comparable to our study (33.40%) possibly

because the sample size used in their study was small as compared to our study.

Clinicians have been experimenting with other medications as well, Swaminathan V et al in their study concluded that the prevalence of Etomidate-induced myoclonus was significantly decreased in patients who were pre-treated with dexmedetomidine as compared with lignocaine.[13] Ghodki et al compared dexmedetomidine and Magnesium. They found magnesium is superior to dexmedetomidine in decreasing not only the incidence but also the severity of myoclonus.[14]

Srivastava et al worked with pregabalin, their observation was that giving 150 mg pregabalin in the morning of IV induction with etomidate, reduced the incidence and the severity of myoclonus but incidence of sedation was more.[15] Zhang KD et al used pretreatment with opioids and etomidate itself. According to them, both were safe and effective for making induction of anesthesia safer by preventing the myoclonus associated with etomidate.[16]

Similarly, Hüter et al [17] found the same results using low dose midazolam (0.015mg/kg) 3 minutes before etomidate induction in elective cardioversion patients. Forty patients were included in their study, and all belonged to ASA-III & IV. Myoclonic movements and sedation were recorded on a scale between zero and three. 2 patients (10%) had myoclonic movements in the midazolam group, whereas 10 out of 20 patients (50%) received the placebo experienced such movements (P 0.006). There were no other significant differences between the two groups; particularly, there was no difference in the time of recovery following etomidate. The frequency of myoclonus is only 10% as compared to our results which is 30%, this is a big difference and can be due to many reasons. Firstly, our study has a much bigger sample size, hence making it more representative. Secondly, their study was conducted on ASA III and IV patients whereas we included only ASA I and II patients. Moreover, the time difference between pretreatment was different.

Myoclonus is a disturbing side effect associated with etomidate induction.[18] Midazolam (1mg) was found to be more useful in preventing myoclonus and it is recommended to use it prophylactically before etomidate induction, based on our study findings. The limitation of our study is that we did not analyze any drug-related side effects, extubation, and recovery times. Also, we only observed frequency of myoclonus and not the severity.

Conclusion

Both midazolam and lignocaine are effective in preventing the occurrence of myoclonus associated with etomidate. However, midazolam is the more effective of the two drugs.

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