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To Evaluate the effect of Dexmedetomidine Pretreatment on Myoclonus during Anaesthetic Induction with Etomidate

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Abstract
Etomidate is frequently used nowadays as an inducing agent in patients with compromised cardiovascular function, but it leads to undesirable side effects like myoclonus during induction. Several drugs have been considered before induction to reduce the incidence of myoclonus. This prospective, randomized double blinded study was aimed to compare the effect of dexmedetomidine (DEX) pretreatment on the incidence and severity of etomidate-induced myoclonus. 100 patients undergoing elective surgical procedures were randomly allocated to two groups for i.v. administration of 1.0 µg/kg DEX in 100 mL isotonic saline (group D) and 100 mL isotonic saline (group NS) 10 minutes prior to induction. All groups subsequently received 0.3 mg/kg etomidate by intravenous injection. The incidence and severity of myoclonus were recorded for 1 min after etomidate administration and the incidence of cardiovascular adverse effects were also recorded. The incidence of myoclonus was 38% was in group D and 70% in group NS. The severity of myoclonus was graded as mild, moderate and severe. In group D and group NS number of patients who had mild, moderate and severe myoclonus were 10,5,4 and 11,15,9 respectively. It was concluded that pretreatment with 1.0 µg/kg DEX significantly reduced the incidence and severity of etomidate-induced myoclonus during anesthetic induction.

Keywords: *Dexmedetomidine; Etomidate; Myoclonus.*

Introduction

An ideal inducing agent for general anaesthesia should have smooth induction, good haemodynamic stability, minimal respiratory and other side effects and rapid clearance. Etomidate, an imidazole derivative has unique properties like hemodynamic stability, favorable toxicity profile and pharmacokinetics enabling rapid recovery after a single dose[1]. Etomidate is also preferred in patients with respiratory and airway disease, intracranial hypertension and in patients with shock[2].

However, it has two well known and disturbing side effects, injection pain and myoclonus apart from nausea and vomiting. Injection pain has been minimized by a new lipid formulation of Etomidate[3]. However, suppression of myoclonus continues to be a clinical problem as a common

side effect of Etomidate administration during induction of anesthesia. The incidence of myoclonus has been reported to be as high as 50-80 %[4].The consequences of this side effect can be serious in non fasted emergency patients, patients with open eye injuries, or patients with limited cardiovascular reserves[5]. In addition, during the jerky movements ECG leads can become detac-hed. It should be noted that ECG leads detachment during myoclonic movements leads to delay of monitoring and success of early intervention[6].

The neurologic mechanism of myoclonic activity after etomidate administration is not clear. Some studies suggested that it may be a kind of seizure activity[6]. A study that investigated EEG alterations in patients with etomidate induced myoclonus stressed the correlation between myoclonus and the increase in delta waves on EEG recordings, and it was not a typical seizure.Other studies suggested that myoclonus aft -er etomidate administration is a result of subcorti-cal disinhibition like that of restless leg during sleep and does not happen from epileptic focus. An unsynchronized onset of etomidate induces fas t depression of the cortex, resulting in temporary disinhibition of the subcortex resulting in inducing the myoclonic movement[7, 8].

A number of drugs have been investigated to redu ce the rate and intensity of this adverse effect.Vari ous drugs are premedicated to reduce myoclonic jerks induced by etomidate like midazolam[9], opioids[10], magnesium sulphate[11], rocoronium[12]. Dexmedetomidine is among the new agents tried as premedicants to reduce myoclonus. Dexmedetomidine, an α2-adrenoceptor agonist having analgesic and anxiolytic activity, is widely used for anesthesia and intensive care[13].Though mechanism is still not very clear, it has been recently tried to reduce the incidence and severity of myoclonus due to its anxiolytic properties and by subcortical inhibition.

This study was primarily aimed to see the efficacy of dexmedetomidine in reducing the incidence and severity of myoclonus prior to etomidate induction.

Materials and Methods

This randomized, double blind, prospective study was performed on 100 cases in the department of anesthesiology, Sardar Patel Medical College and Associated Group of Hospitals Bikaner after obtaining the ethical committee clearance. Hundred adult patients of either sex between age group 18 to 60 years belonging to ASA grade 1 or ASA grade 2 were included in study. They were randomized into 2 groups of 50 patients each and an effort was made that the group do not significantly differ with respect to age, weight and height.

Groups	Drugs & Doses	No. of Patients
Group D	1μg/kg dexmedetomidine pretreatment with etomidate induction at 0.3 mg/kg	50
Group NS	100 ml saline pretreatment with etomidate induction at 0.3 mg/kg	50

After complete pre-anaesthetic assessment, the procedure was explained to the patients and written informed consent was taken one day before surgery.

Patient with known allergy to the drugs used in thestudy, with significant cardiac, respiratory, hepaticor renal dysfunction, an anticipated difficult airway, hypotension, history of seizure disorder, presence of primary and secondary steroid deficiency or on steroid medication were excluded from study.

The patients were shifted to the operating room with all aseptic precautions. Patients were kept NPO 8 hours prior to surgery. An intravenous line was secured. Then standard monitoring and recording of non invasive B.P., pulse rate, oxygen saturation, ECG and respiratory rate before induction of anaesthesia.

Premedication with Inj. Glycopyrrolate 0.2 mg was done. Ringer lactate was infused at a rate of 4-6 ml/min. Before anaesthesia induction in group D, 1.0 μg/kg dexmedetomidine in 100 mL isotonic saline was infused over 10 minutes. In group NS, 100 ml isotonic saline was infused over 10 minutes. When the infusion was completed 0.3 mg/kg etomidate was injected intravenously over

a period of 1 min. Patients were observed continuously for myoclonus for 1 min by a physician who was blinded to all group treatments. Myoclonic movements were defined as involuntary short muscle contractions leading to short observable movements in parts of the body. The intensity of myoclonus was graded as 0, no myoclonus; 1, mild myoclonus (short movements of a body segment, e.g., a finger or a wrist only) 2, moderate myoclonus (mild movements of two different muscles, e.g., face and leg) ; and 3, severe myoclonus (intense clonic movements in two or more muscle groups, e.g., fast adduction of a limb).

After administration of etomidate and evaluation o f myoclonus, all patients were injected with 2 µg/ kg fentanyl. One minute after the end of etomidate injection, muscle relaxation was achieved with 0.08 mg/kg vecuronium and endotracheal intubation was performed after another 2 minutes. Following etomidate injection, mask ventilation with 100% O_2 was carried out until intubation.

In both the groups myoclonus, haemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, oxygen saturation) were recorded before and after premedication,before and after induction and intubation.

Maintenance anesthesia was provided by sevoflur ane with 50% oxygen and nitrous oxide (N2O) in 1:1 ratio, and Vecuronium 0.02 mg/kg as per need with controlled ventilation. Intraoperative hemodynamics parameter (heart rate, systolic blood pressure, diastolic blood pressure) were recorded every 10 minute for first hour of surgery then every 15 min till the end of surgery.

After completion of surgical procedure reversal of neuromuscular blockade was achieved with Inj. Neostigmine (40µg/kg) and Inj. Glycopyrrolate (5µg/kg) and extubation was done when adequate muscle power, regular spontaneous respiration and cough reflex was present.

Complications like nausea, vomiting, hypotension, bradycardia, respiratory depression, agitation and arrhythmia were observed.

Patient were observed for 2 hours in PACU (post anaesthesia care unit) for any postoperative complications like nausea, vomiting, hypotension, bradycardia, respiratory depression, agitation, arrhythmia. Any complication that occurs, was treated with appropriate measures.

All the data was filled up in the proforma attached and statistical analysis were performed using SPSS software to draw conclusions. Students t-test and chi- square test was used in drawing conclusions and statistical significance.

Results

Demographic characteristics

DEMOGRAPHICS	GROUP D	GROUP NS
AGE	43.72± 13.12	43.12±13.4
SEX(M/F)	13/37	08/42
WEIGHT	63.32 ±6.56	61.42 ±5.80

Data as reported as mean ±SD or number for n = 50 patients/ group. There were statistically insignificant. (p value >0.05)

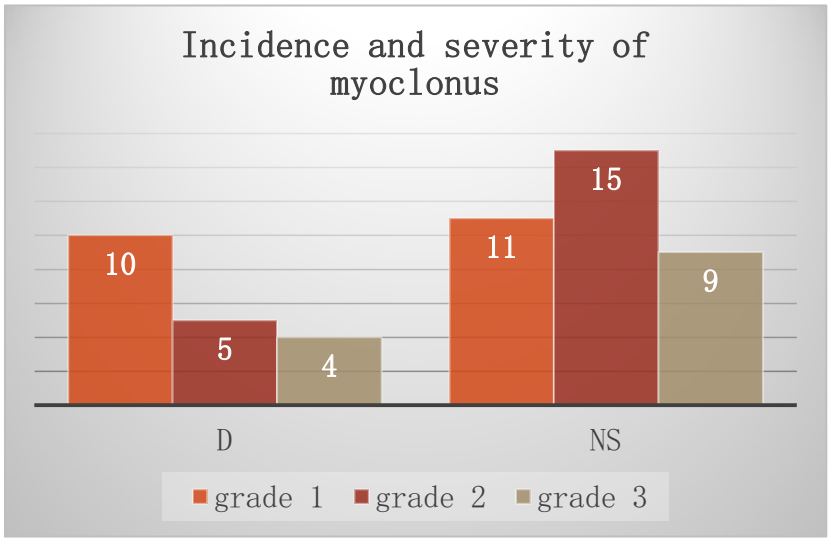
There were no significant differences among the 3 groups with regard to age, gender, weight, or AS A class.

MYOCLONUS	Mild		Moderate		Severe			
Group	Number of Patients	%	Number of Patients	%	Number of Patients	%	Total	
Group D	10	20%	5	10%	4	8%	19	38%
Group NS	11	22%	15	30%	9	18%	35	70%

Table showing incidence and severity of myoclonus

Myoclonus	Group D	Group NS	P value
Mean ±SD	0.7± 1.00	1.36± 1.09	0.001

The total percentage of myoclonus in NS group was 70% whereas it was 38 % in group D. The results remained statistically significant. (p value = 0.001)



Comparison between complications in dexmedetomidine and normal saline group

GROUP	Low blood pressure	Sinus bradycardia	PONV
GROUP D	4 (8%)	6 (12%)	10 (20%)
GROUP NS	2 (4%)	1 (2%)	12 (24 %)

Data reported as number or number and percentage =50 patients in each group.

P value >.05 in each in each group for each category

This suggested that there was no significant difference in the complications among the groups.

Discussion

Etomidate fulfills the requirement as an induction agent with stable cardiovascular and respiratory profile. But it comes with the side effects like myoclonus on induction. The consequences of this side effect can be serious.

In agreement with previous literature the use of Etomidate was found to be associated with higher incidence of myoclonus activity and upto 70 to 80 % in non premedicated patients.

Myoclonus was observed in 35 patients out of 50 (70%) in NS group. Out of them 11 (22%) had mild, 15(30%) moderate and 9 (18%) had severe myoclonus. Whereas in group D where 1µg/kg dexmedetomidine was given as premedication before induction with Etomidate, the incidence of myoclonus was 38%. 10 patients (20%) had mild myoclonus, 5(10%) had moderate and 4(8%) had severe myoclonus.

The results demonstrate that premedication with1µg/kg Dexmedetomidine reduces the incidence and intensity of myoclonus.

The results of our study correlates with study of Mizrak A et al (2010)[14] They concluded that premedication with Dexmedetomidine (0.5µg/kg) and thiopentone (1 mg/kg) are effective in reducing the incidence and severity of myoclonus induced by Etomidate.

Nevriye Salman et al (2013)[15] concluded that Dexmedetomidine (0.5 µg/kg) and midazolam (0.25 mg/kg) both are effective in reducing the myoclonus induced by etomidate induction but midazolam had respiratory depression.

H.F.Laun et al (2014)[16] documented that pretreatment with 0.5 and 1.0 µg/kg Dexmedetomidine significantly reduced the incidence of etomidate induced myoclonus during anesthetic induction but Dexmedetomidine with 1.0 µg/kg was associated with more side effects like bradycardia.

Limitations

Our study design had some limitation. The first is that we did not measure plasma cortisol and

adrenocorticotropic hormone levels. It has been well known that adrenocortical suppression is one of the most important adverse effects of Etomidate. Although Etomidate causes adrenocortical suppression, a single injection to induce anaesthesia will only produce a transient and clinically insignificant interference with adrenocortical function. Other limitation is that the study was conducted on a single center with small group of patients with normal LV function which will truly not reflect for very old age patient with relatively unstable haemodynamic.

Conclusion

According to our study, patients given pretreatment with 1 µg/kg Dexmedetomidine 10 minutes prior to induction with Etomidate could significantly reduce the incidence and severity of myoclonus without significant complications as compared to group NS in which pretreatment was done with Normal Saline as control group. So these characteristics indicate that Dexmedetomidine can be safely used as premedication prior to Etomidate for reduction in Etomidate induced myoclonus.

Bibliography

1. Ruth WJ, Burton JH, Bock AJ. Intravenou s etomidate for procedural sedation in eme rgency department patients. Acad Emerg Med 2001; 8: 13-18, doi: 10.1111/j.1553-2 712.2001.
2. Moss E, Powell D, Gibson RM, McDowall DG. Effects of etomidate on intracranial pressure and cerebral perfusion pressure. Br J Anaesth 1979; 51:347-51.
3. Doenicke A, Roizen MF, Nebauer AE, Ku gler A, Hoernecke R, Beger-Hintzen H. A comparison of two formulations for etomidate, 2-hydroxypropyl-beta-cyclodex trin (HPCD) and propylene glycol. Anesth Analg 1994; 79: 933-939, doi: 10.1213/00000539-199411000-00020
4. Doenicke AW, Roizen MF, Kugler J, Kroll H, Foss J, Ostwald P. Reducing myoclonu s after etomidate.Anesthesiology 1999; 90: 113-119, doi: 10.1097/00000542-1999010 00-00017. [Links]
5. Hueter L, Schwarzkopf K, Simon M, Bredl e D, Fritz H. Pretreatment with sufentanil e duces myoclonus after etomidate. Acta Anaesthesiol Scand 2003; 47: 482-484, doi: 10.1034/j.1399-6576.20 03.00081
6. Van Keulen SG,Burton JH. Myoclonus associated with etomidate for ED procedural sedation and analgesia. Am J Emerg Med 2003:21:556-558.
7. Reddy RV, Moorthy SS, Dierdorf SF, Deitch RD, Jr, Link L. Excitatory effects and electroencephalographic correlation of etomidate, thiopental, methohexital, and propofol. Anesth Analg. 1993;77:1008–1011. [PubMed]
8. Modica PA, Tempelhoff R, White PF. Pro- and anticonvulsant effects of anesthetics (part I) Anesth Analg. 1990;70:303–315
9. Schwarzkopf KR, Hueter L, Simon M, Fritz HG. Midazolam pretreatment reduces etomidate-induced myoclonic movements. Anaesth Intensive Care 2003; 31: 18-20.
10. Hueter L, Schwarzkopf K, Simon M, Bredle D, Fritz H. Pretreatment with sufentanil reduces myoclonus after etomidate. Acta anaesthesiologica-scandinavica. 2003 Apr 1;47(4):482-4.
11. Guler A, Satilmis T, Akinci SB, Celebioglu B, Kanbak M. Magnesium sulfate pretreatment reduces myoclonus after etomidate. Anesthesia & Analgesia. 2005 Sep 1;101(3):705-9.
12. Choi JM, Choi IC, Jeong YB, Kim TH, Ha hm KD. Pretreatment of rocuronium reduc es the frequency and severity of etomidate induced myoclonus. J Clin Anesth 2008; 2 0: 601-604, doi: 10.1016/j.jclinane.2008.0 6.010
13. Ramsay MA, Newman KB, Leeper B, Ha mman BL, Hebeler RF Jr, Henry AC, et al. Dexmedetomidine

infusion for analgesia up to 48 hours after l ung surgery performed by lateral thoracoto my. Proc (Bayl Univ Med Cent) 2014; 27: 3-10.

14. Wujtewicz M, Maciejewski D, Misiolek H , Fijalkowska A, Gaszynski T, Knapik P, e t al. Use of dexmedetomidine in the adult intensive care unit. Anaesthesiol Intensive Ther 2013; 45: 235-240, doi: 10.5603/ AIT.2013.0045.
15. Salman N, Gurbuz HA, Oguzalp H, Ucar HI, Yorgancıoglu C, Sekerci S. Comparison of dexmedetomidine and midazolam in prevention of myoclonus occurring due to etomidate in coronary bypass surgery. Journal-Cardiovascular Surgery. 2013;1(3):52-6.
16. Mizrak A, Koruk S, Bilgi M, Kocamer B, Erkutlu I, Ganidagli S, Oner U. Pretreatment with dexmedetomidine or thiopental decreases myoclonus after etomidate: a randomized, double-blind controlled trial. Journal of Surgical Research. 2010 Mar 31;159(1):e11-6.
17. Luan HF, Zhao ZB, Feng JY, Cui JZ, Zhang XB, Zhu P, Zhang YH. Prevention of etomidate-induced myoclonus during anesthetic induction by pretreatment with dexmedetomidine. Brazilian Journal of Medical and Biological Research. 2015 Feb;48(2):186-90.