Original Research Article

A Study of Efficacy of Dexmedetomidine and Midazolam for Sedation of Eclamptic Patients on Mechanical Ventilation in ICU

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Abstract

Introduction: Eclamptic patients often land up in Intensive Care Unit (ICU) due to complications or for further postoperative care and frequently need mechanical ventilation. Mechanical ventilation is often associated with patient agitation and reduced tolerance hence requiring sedation to alleviate discomfort and improve patient-ventilator synchrony, and also to facilitate nursing care and improve outcome. It is quite a challenge for optimum care of eclamptic patients in ICU who are usually irritable. Various agents are being used for ICU sedation, such as propofol, midazolam, fentanyl and lately dexmedetomidine. Traditionally, Midazolam has been the most commonly administered sedative drug for ICU patient's worldwide.**Materials and Methods:** The present prospective study comprising of 200 eclamptic pregnant women more than 18 years of age undergoing Lower Segment Caesarean Section for termination of pregnancy under general anaesthesia and requiring postoperative mechanical ventilation in ICU at Department of Medicine, Sheikh Bhikari Medical College, Hazaribag, Kolghati, Jharkhand was planned. The study period was of one year from January 2020 to December 2020. After the approval of the institutional ethical committee, an informed written consent was taken from all patients' first degree relatives. **Results:** Two Hundred patients were enrolled in the study and all completed the study. The demographic data in both the groups were statistically insignificant (Table 1). The difference in mean Ramsay Sedation Scores were statistically insignificant in both groups from 2nd to 24 hours. Haemodynamically, there was decrease in pulse rate in both the groups at all-time intervals and this decrease was significant in group II at 8th, 12th, and 24th hour (p value 0.002) in comparison to group I (Table 3). The drop in mean systolic blood pressure (and mean arterial blood pressure) was statistically significant in group II at 1st hour (p value 0.0041) and remained highly significant at 2nd to 24th hour (p value <0.0001) (Table 4 and table 6 respectively). Similarly, the drop in mean diastolic blood pressure in group II was significant at 1st and 2nd hour and it became highly significant (p value <0.0001) from 4th to 24th hour (Table 5). There were 10 patients each of bradycardia and hypotension in group II.**Conclusion:** In this study, we found that dexmedetomidine is as effective as midazolam for producing and maintaining adequate short-term sedation of mechanically ventilated eclampsia patients and also has good haemodynamic control. The risk of bradycardia and hypotension although higher than traditional sedatives, it may not increase length of hospital stay. Thus, dexmedetomidine could be a safe and efficacious sedative agent in eclamptic patients in ICU.

Keywords: Eclampsia, ICU, dexmedetomidine, midazolam.

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Introduction

Eclamptic patients often land up in Intensive Care Unit (ICU) due to complications or for further postoperative care and frequently need mechanical ventilation. Mechanical ventilation is often associated with patient agitation and reduced tolerance hence requiring sedation to alleviate discomfort and improve patient-ventilator synchrony,[1, 2] and also to facilitate nursing care and improve outcome. It is quite a challenge for optimum care of eclamptic patients in ICU who are usually irritable. Various agents are being used for ICU sedation, such as propofol, midazolam, fentanyl and lately dexmedetomidine. Traditionally, Midazolam has been the most commonly administered sedative drug for ICU patients worldwide[3]. Midazolam is a fast-acting benzodiazepine that rapidly penetrates the central nervous system to produce an onset of sedation in 2 to 2.5 minutes[4].All benzodiazepines reliably cause amnesia, but have no analgesic activity(hence often combined with fentanyl),and produce dose-dependent respiratory depression which is enhanced in combination with opioids. Hence, long-term or high dosage of midazolam in the critically ill patients may lead to over sedation; prolonged mechanical ventilation and longer ICU stay. Dexmedetomidine is a newer sedative used for ICU sedation and has better haemodynamic stability and minimal respiratory depressant effect[5].

Dexmedetomidine is a highly selective α2-adrenergic receptor agonist.

In contrast to other sedative hypnotic agents, dexmedetomidine also has adequate analgesic effect and may induce a sedative state similar to physiologic sleep by acting on α2 receptors in the locus coeruleus[6].Various studies regarding the efficacy of midazolam and dexmedetomidine for sedation of critically ill patients in ICU have been done globally[3,7]. The studies comparing efficacy of midazolam and dexmedetomidine for sedation in eclamptic patients requiring mechanical ventilation in ICU are minimal[7].

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The aim of this clinical study was to compare the efficacy of dexmedetomidine and midazolam for sedation of eclamptic patients on mechanical ventilation in ICU so that a near ideal sedative agent for eclamptic patients could be determined.

Materials and Methods

The present prospective study comprising of 200 eclamptic pregnant women more than 18 years of age undergoing Lower Segment Caesarean Section for termination of pregnancy under general anaesthesia and requiring postoperative mechanical ventilation in ICU at Department of Medicine, Sheikh Bhikari Medical College, Hazaribag, Kolghati, Jharkhand was planned. The study period was of one year from January 2020 to December 2020. After the approval of the institutional ethical committee, an informed written consent was taken from all patients' first degree relatives.

200 postoperative patients (LSCS for termination of pregnancy under GA) were selected and distributed randomly into two groups of 100 each (By paper chits prepared in a box) who were sedated either by IV midazolam or dexmedetomidine immediately after admission in the ICU. The exclusion criteria were patients with baseline HR< 60 bpm, those with hypovolaemia and SBP < 90 mm of Hg, those with Mobitz type 2 and 3rddegree heart block, those with pre-existing comorbidities like cardiac, hepatic, pulmonary, neurological, endocrine or renal diseases, patients with past history of chronic hypertension, those developing Haemolysis, Elevated Liver enzymes and low platelets (HELLP syndrome), having allergy to the study drugs, history of drug abuse, use of antipsychotic or sedative medications. Group I received loading dose of 0.05 mg/kg of midazolam over 10 minutes followed by maintenance dose of 0.1 mg/kg/hour (50 mg of midazolam made to 50 mL with 0.9% NaCl and connected to syringe infusion pump was used). Group II received loading dose of 1 µg/kg of dexmedetomidine over 10 minutes followed by maintenance dose of 0.5µg/kg/hour (200 µg of dexmedetomidine made to 50 mL with 0.9% NaCl and connected to syringe infusion pump was used). The drug combinations were prepared by an anesthesiologist not involved in patient monitoring and followup. Vital parameters -Invasive blood pressure (IBP), oxygen saturation (SpO2), heart rate (HR) and electrocardiography (ECG) of all patients were monitored in the ICU. All patients received $MgSO_4$ 2g every 4th hourly for 24 hours and rest of the treatment was as per our standard ICU protocol. The Ramsay Sedation Score was assessed hourly with target sedation of 2-3. Visual analogue scale (VAS 0 -10) was assessed hourly and every patient received injection fentanyl IV 1 µg/kg if VAS >4. Patients with mean arterial pressure (MAP) > 130 mmHg were administered Inj. Labetalol 20 mg bolus as antihypertensive and if response was inadequate it was repeated as per guidelines. Patients were continuously observed for any episode of convulsion and were treated with injection thiopentone. Side effects like hypotension if systolic blood pressure (SBP<90 mmHg), hypertension if mean arterial pressure (MAP>130 mmHg), tachycardia if HR>100 bpm, bradycardia if HR<60 bpm and level 4 sedation were observed and treated in both groups. All parameters and observations were recorded by two anaesthesiologists on rotation basis not involved in preparation of the study drugs. The mode of mechanical ventilation was synchronised intermittent mandatory ventilation (SIMV) and pressure support (PS) in all patients and gradual weaning and extubation was done as per our standard ICU guidelines.

Statistical Analysis: The sample size was calculated considering power of test as 80%, confidence interval of 95%, ratio of sample size (between group II and group I) as one. For this study, it was expected that the difference observed in mean between two groups was ten. SPSS version 21 was used to perform statistical analysis. The data were expressed in mean ± standard deviation (Range). Statistical analysis was done using student t test, paired for intra group and unpaired for intergroup comparisons. A value of $p<0.05$ was considered to be statistically significant while $p<0.001$ was considered highly statistically significant.

Results

Two Hundred patients were enrolled in the study and all completed the study. The demographic data in both the groups were statistically insignificant (Table 1). The difference in mean Ramsay Sedation Scores were statistically insignificant in both groups from 2nd to 24 hours. Haemodynamically, there was decrease in pulse rate in both the groups at all-time intervals and this decrease was significant in group II at 8th, 12th, and 24th hour (p value 0.002) in comparison to group I (Table 3). The drop in mean systolic blood pressure (and mean arterial blood pressure) was statistically significant in group II at 1st hour (p value 0.0041) and remained highly significant at 2nd to 24th hour (p value <0.0001) (Table 4 and table 6 respectively). Similarly, the drop in mean diastolic blood pressure in group II was significant at 1stand 2ndhour and it became highly significant (p value <0.0001) from 4th to 24th hour (Table 5). There were 10 patients each of bradycardia and hypotension in group II.

Table 1: Showing Patient Characteristics in Both Groups

No of patients 100 each		
	Group I	**Group II**
Mean age (Years)	20.85±2.08	20.84±2.23
Weight (Kg)	52.19±3.86	53.48±2.67
Height (cm)	160.12±3.51	162.16±2.57

Table 2: Comparison of Ramsay Sedation Score in Both Groups

Time	**Group I**	**Group II**	**t' value**	**P' value**
Pre-drug	1±0	1±0		
1 hr	1.97±0.28	2.25±0.42	3.73	0.0003
2 hr	2.17±0.37	2.2±0.40	0.52	0.60
4 hr	2.19±0.36	2.23±0.42	0.74	0.45
8 hr	2.47±0.47	2.52±0.48	0.40	0.68
12 hr	2.7±0.46	2.64±0.48	0.41	0.67
24 hr	2.09±0.26	2.18±0.36	1.51	0.1

Table 3:Statistical Analysis of Mean PR per minute in Both Groups

Time	**Mean PR/Minute**		**t value**	**p value**
	Group I	**Group II**		
Pre-drug	118.23±14.27	120.13±22.15	0.61	0.521
1 hr	111.18±15.37	110.52±17.56	0.20	0.812
2 hr	106.25±15.37	101.52±17.65	1.35	0.18
4 hr	101.27±14.87	95.12±18.75	1.76	0.076

8 hr	95.47±16.24	84.45±19.32	3.02	0.002
12 hr	90.37±15.98	78.79±14.59	3.80	0.002
24 hr	89.19±14.15	77.12±12.15	4.53	<0.0001

Table 4: Comparison of mean SBP in both groups

Time	Mean PR/Minute		t value	p value
	Group I	Group II		
Pre-drug	151.57±16.20	145.23±15.13	1.08	0.276
1 hr	144.70±17.67	134.46±15.25	2.93	0.0042
2 hr	140.51±17.45	123.43±17.52	4.65	<0.0001
4 hr	137.18±18.63	111.25±14.26	7.42	<0.0001
8 hr	130.52±22.67	109.25±15.26	5.45	<0.0001
12 hr	129.12±16.13	109.24±12.63	6.78	<0.0001
24 hr	127.43±20.15	109.52±11.10	5.42	<0.0001

Table 5:Comparison of Mean DBP in Both Groups

Time	Mean PR/Minute		t value	p value
	Group I	Group II		
Pre-drug	93.35±12.02	91.53±11.80	0.85	0.3850
1 hr	90.16±13.56	83.89±10.32	2.46	0.0146
2 hr	85.30±12.30	77.56±11.91	3.19	0.0019
4 hr	83.54±12.60	74.03±12.10	3.75	0.0003
8 hr	85.80±13.12	74.12±12.10	4.27	<0.0001
12 hr	82.90±10.12	72.10±8.58	5.38	<0.0001
24 hr	82.67±11.31	72.16±8.84	5.25	<0.0001

Table 6: Comparison of Mean MAP in Both Groups

Time	Mean PR/Minute		t value	p value
	Group I	Group II		
Pre-drug	114.76±12.21	111.56±10.57	1.43	0.150
1 hr	110.84±14.24	102.32±10.56	3.30	0.0012
2 hr	106.25±11.24	94.14±12.15	5.10	<0.0001
4 hr	104.86±12.39	88.24±10.70	6.76	<0.0001
8 hr	102.49±14.20	88.12±13.24	5.14	<0.0001
12 hr	101.36±11.79	86.57±9.35	6.90	<0.0001
24 hr	100.32±9.61	87.50±12.34	5.10	<0.0001

Table 7: Side-effects among Two Drugs used

Side effects	Group I	Group II
Bradycardia	1	10
Hypotension	0	10
Level 4 sedation	0	0

Discussion

The eclamptic patients often need to be mechanically ventilated in the ICU postoperatively after LSCS. Sedation in ICU is of paramount importance in such patients. The goals and standards for analgesia cum sedation of mechanically ventilated ICU patients have undergone considerable changes in the past few years. While excessively deep levels of sedation resulted in increased morbidity due to prolongation of mechanical ventilation and ICU stay, on the other hand inadequate sedation increased the risk of accidental extubation and other adverse events. The goal of sedation in ICU in present scenario is to have a calm, but arousable patient, with stable haemodynamics[8]. Midazolam continues to be the most commonly administered sedative drug for ICU patients worldwide, including our hospital. On the other hand, dexmedetomidine is a newer, effective and safe sedative agent finding its way into the ICU. In our study, the study groups were comparable in all patient characteristics (Table 1). On comparison of Ramsay Sedation Score, both Group I and group II had mean Ramsay Sedation Score of 1±0 before starting the study drug and was maintained at a mean score of 2 at most times in both groups. On statistical evaluation, it was found that the p value was highly significant at 1st hour but by 2nd to 24th hour it was not significant (p value >0.05), meaning that both group I and group II are comparable in sedation levels (Table 2). Riker et al (2009), Jacob et al (2012), Adams et al (2013), S. Gupta et al (2015) observed no statistically significant difference between dexmedetomidine and midazolam regarding levels of sedation with the two study drugs[3,8-10].A meta-analysis by Jen A. Tan et al observed that dexmedetomidine was associated with increased risk of bradycardia and hypotension.

It was observed that 3 patients (6%) in group I needed antihypertensive drug (IV labetalol) while it was not required in group II. Esmaogluet al in 2009 observed that in patients who were given dexmedetomidine only few required nitroglycerin and nitroprusside as compared to midazolam[7].It was observed that 1 patient (2%) of group II had convulsion episode whereas it was not observed among group I patients. Comparing the ICU stay in hours in both group I and group II, it was observed that group I had mean duration of 39 hours whereas that of group II was 38.48 hours and were almost comparable. Also a study by Stephen M Jacob et al (2012) observed that length of ICU stay was similar in both dexmedetomidine and midazolam groups[6].In this study, we found that dexmedetomidine is as effective as midazolam for producing and maintaining adequate short-term sedation of mechanically ventilated eclampsia patients and also has good haemodynamic control[10].

Conclusion

In this study, we found that dexmedetomidine is as effective as midazolam for producing and maintaining adequate short-term sedation of mechanically ventilated eclampsia patients and also has good haemodynamic control.The risk of bradycardia and hypotension although higher than traditional sedatives, it may not increase length of hospital stay. Thus, dexmedetomidine could be a safe and efficacious sedative agent in eclamptic patients in ICU.

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