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A clinical comparative assessment of dexmedetomidine, midazolam and propofol for sedation of post operative patients on mechanical ventilation

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ABSTRACT

Aim: The aim of the present study was to assess the Comparison of Dexmedetomidine, midazolam and propofol for sedation of post operative patients on mechanical ventilation.

Methods: This single blinded, open label, randomized control trial conducted in the Department of Anaesthesia for 1 year. 90 patients were equality divided into 3 groups, 30 in each group.

Results: The difference in demographic profile among the three groups was not statistically significant. In our study we found that difference of mean HR at different time interval was not statistically significant but compared to group M & P, HR falls more in group D and the mean HR was less in Dexmedetomidine group. No statistically significant difference in SBP & DBP among all these groups.

Conclusion: Dexmedetomidine is safer and equally effective agent compared to propofol and midazolam for sedation of mechanically ventilated patients with good hemodynamic stability and extubation time as rapid as propofol. Dexmedetomidine also reduced postoperative fentanyl requirements.

Keywords: Dexmedetomidine, midazolam, propofol, sedation

1. INTRODUCTION

Patients admitted to the ICU are usually in need of invasive and uncomfortable interventions such as mechanical ventilation. To reduce anxiety, increase tolerance, and improve outcomes of such interventions, sedation is common practice.[1] Traditionally, sedative agents

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administered in the ICU are g-aminobutyric receptor agonists (GABA) which include the benzodiazepines (usually midazolam) and propofol.[2]Optimum sedation is vital in striking a balance between providing pain relief and maintaining patient calm while preventing over-sedation and unnecessarily lengthy ICU stays.[3]

Many protocols advise daily sedation interruptions to assess the level of sedative in the patient and to avoid oversedation.[4]Dexmedetomidine has been studied as an alternative to traditional GABA-based sedation in the ICU. As a selective a2-receptor agonist, it acts at the locus coeruleus and spinal cord to exert anxiolytic and sedative effects without respiratory depression.[5] Furthermore, there is evidence to suggest that administration of dexmedetomidine instead of standard sedatives (propofol or midazolam) in a critical care setting significantly reduces the incidence of delirium.[6]

High-dose or prolonged propofol use may cause potentially fatal propofol infusion syndrome.[7]Commonly used agents include benzodiazepines, propofol, short acting opioids like remifentanil and dexmedetomidine. Although opioids are useful for treatment of postoperative pain, they alone cannot be appropriate for sedation for postoperative mechanically ventilated patients.[8] Dexmedetomidine a α2 adrenoceptors agonist are capable of producing sedation, anxiolysis and analgesia without respiratory depression.[9]These properties make them potentially useful for short duration postoperative ventilation like; neurosurgical patients requiring delayed extubation.

The aim of the present study was to assess the Comparison of Dexmedetomidine, midazolam and propofol for sedation of post operative patients on mechanical ventilation.

2. MATERIALS AND METHODS

This single blinded, open label, randomized control trial conducted in the Department of Anaesthesia for 1 year. 90 patients were equality divided into 3 groups, 30 in each group.

Inclusion and Exclusion Criteria

Patients with 20 to 65 years of age, ASA grade I to III, undergoing elective neurosurgical procedure and expected to require postoperative ventilator support were included. Exclusion criteria included significant hepatic, renal, or neurologic impairment, second or third degree heart block, history of use of long-term benzodiazepine, opioids, and a known allergy to any of the study drug, gross obesity (over 50% above ideal body weight) and known or suspected pregnancy.

The Standard anaesthetic technique for the perioperative period included midazolam 0.04 mg/kg, fentanyl 2 mcg/kg and thiopental sodium 5 mg/kg body weight for induction followed by vecuronium 0.15 mg/kg body weight for facilitation of tracheal intubation. Maintenance of anaesthesia was done with oxygen: nitrous oxide (O2:N2O; 33:66), isoflurane, intermittent boluses of vecuronium and fentanyl. At the end of the surgical procedure, neuromuscular blockade was not reversed and patients shifted to the neurological ICU for elective ventilation. Ventilated was commenced with synchronized intermittent mechanical ventilation (SIMV) with pressure support mode. On arrival in the ICU, patients were allocated randomly into three groups of 30 with the help of a computer-generated table of random numbers to receive i.v. infusions of dexmedetomidine, propofol or midazolam whilst being mechanically ventilated. Drug infusions were prepared by personnel not involved in the study or the patient's care. All patients received short acting fentanyl infusions (5mcg/ml). The infusion rate was adjusted by the ICU doctor as required by the patient to relieve pain. No muscle relaxants were given during the study period.

Sedation was assessed by Ramsay Sedation Score. (1=agitated; 2 = cooperative, tranquil; 3=responds to verbal command; 4=brisk response to loud voice or glabellar tap; 5 = sluggish

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response to glabellar tap or loud voice; 6=no response). Secondary variable will be depth of analgesia achieved and hemodynamic stability which will be assessed by Heart Rate, Blood Pressure, Respiratory Rate, SPO2. In this study 90 patients were chosen with GCS 9- 15 who are on post-operative mechanical ventilation and they were divided randomly into three groups each group has total 30 patients.

Group M: Midazolam loading dose 0.04 mg/kg over 15 minutes, followed by maintenance infusion at a rate of 0.08 mg/kg/h

Group P: Propofol loading dose 1mg/kg over 15 minutes, followed by maintenance infusion at a rate of 1-3 mg/kg/h

Group D: Dexmedetomidine loading dose

1 mcg/kg over 15 minutes, followed by maintenance infusion at a rate of 0.4-0.7 mcg/kg/h

If any patients need analgesia, inj fentanyl has been used to supplement it. Desired depth of sedation was assessed by Ramsay Sedation Score. All of them received those study drugs as bolus first at 0 hour and then continuous infusion for at least 48 hours to keep RSS within 2-3. Ventilator mode was set SIMV, Tidal Volume 7-8 ml/kg. HR, SBP, DBP, RR, SPO2 & RSS were assessed at 0.5,10,15,20,25,30 min, 60 min and then 3 hourly till 48 hrs. All the patients were closely observed for complications like bradycardia and hypotension and managed accordingly if any.

Statistically analysis

All results are measured in Mean±SD & ANOVA test has been used for independent variables with normal distribution. SPSS 24.0 has been used for data analysis. $P<0.05$ has been taken as statistically significant.

3. RESULTS

Table 1: Demographic profile of the patients

Parameters	**Group D**	**Group P**	**Group M**	**p-value**
Age(Yrs)	50.58±8.42	52.8±8.32	53.27±8.03	0.44
Male/Female	15/5	14/6	16/4	0.68
Weight(Kg)	63.77±6.84	60.94+6.44	65.25+6.24	0.12
Duration of Ventilation(Hrs)	12.14±3.14	12.88±3.56	12.80±3.22	0.64
Extubation time(Min)	34.36±5.75	27.33±5.15	47.33±7.13	<0.001
RSS	3.56+0.73	3.84±0.98	3.75±0.96	0.34
Fentanyl Requirement (mcg/kg/hr)	0.26±0.14	0.54±0.16	0.46±0.14	<0.001

The difference in demographic profile among the three groups was not statistically significant.

Table 2: The mean of the HR

Time	Group D	Group M	Group P
0 min	102	85	91
5 min	92	83	90
10 min	89	82	89
15min	88	82	86
20 min	84	82	85
25 min	83	82	84
30 min	82	81	83
60 min	78	80	82
3 hr	77	79	83

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6 hr	76	78	84
9 hr	84	82	86
12 hr	85	82	86
15 hr	82	82	84
18 hr	79	81	83
21 hr	78	80	82
24 hr	76	80	85
27 hr	84	83	89
30 hr	81	82	87
33 hr	80	82	86
36 hr	79	82	85
39 hr	78	81	84
42 hr	77	81	85

In our study we found that difference of mean HR at different time interval was not statistically significant but compared to group M & P, HR falls more in group D and the mean HR was less in Dexmedetomidine group.

Table 3: The mean of the SBP and DBP with time

Time	Group D	Group M	Group P
0 min	135	131	129
5 min	131	129	126
10 min	126	125	123
15min	121	119	118
20 min	116	114	114
25 min	115	114	114
30 min	114	115	115
60 min	111	114	114
3 hr	110	115	115
6 hr	110	114	112
9 hr	121	119	118
12 hr	116	114	114
15 hr	113	115	114
18 hr	121	120	119
21 hr	116	115	114
24 hr	115	114	115
27 hr	112	113	114
30 hr	111	114	115
33 hr	121	118	118
36 hr	116	115	114
39 hr	115	112	114
42 hr	112	114	115
45 hr	111	115	115
48 hr	110	113	114

No statistical significant difference in SBP & DBP among all these groups.

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4. DISCUSSION

Many sedative agents are in use in different ICU setups. Propofol is most commonly used in ICU as a sedative agent due to its rapid onset & offset and shot duration of action but few factors which limit the use of propofol are haemodynamic instability like hypotension and bradycardia and lack of analgesic action.[10]Benzodiazepine mainly Midazolam is another commonly used gamma aminobutyric acid agonist having rapid action also frequently used for ICU sedation. Dexmedetomidine is a potent alpha 2 adrenoceptor agonist. Dexmedetomidine is good sedative and also it reduces the need for opioid as it has good analgesic property.[11]

The difference in demographic profile among the three groups was not statistically significant. These findings are similar to study done by Jakob SM et al (2012)12 where they find no statistical significance Sex, Age and GCS score between their three groups (P>0.05).In the study in 2018 Elgebaly AS et al[13]also found no difference in age and BMI in both groups. In our study we found that difference of mean HR at different time interval was not statistically significant but compared to group M & P, HR falls more in group D and the mean HR was less in Dexmedetomidine group. In another similar study Elgebaly AS et al[13] also found that Mean Arterial Pressure is lower in Propofol group. The HR was lower in Group D patients then Group P and Group M. As per their inference dexmedetomidine is safe & effective sedative agent for mechanically ventilated patients after cardiac surgery. Martin et al[14] found that occurrence of bradycardia and hypotension is more in patients who received dexmedetomidine. No statistically significant difference in SBP & DBP among all these groups. In a study Conti G et al[15] in 2016 calculated the asynchrony index (AI) by tracing electrical activity of diaphragm, airflow etc, and they opined that AI was lower in dexmedetomidine group from 2 hour onwards than propofol group. So, they concluded that dexmedetomidine provide better patient ventilator synchrony than propofol. In a similar study Riker et al[16] concluded that patients receiving dexmedetomidine experience less delirium after extubation. Tripathi Met al[17] conducted a study on 2017 comparing dexmedetomidine and midazolam and found that patients receiving dexmedetomidine infusion for sedation have quick extubation time.

5. CONCLUSION

Dexmedetomidine is safer and equally effective agent compared to propofol and midazolam for sedation of mechanically ventilated patients with good hemodynamic stability and extubation time as rapid as propofol.

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