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Original Research Article

A Randomised Controlled Study of Dexmedetomidine, Midazolam, and Propofol for Postoperative Sedation in Mechanical Ventilator Patients

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Abstract

Aim: To study 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 Intensive care unit, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India. 45 patients were equality divided into 3 groups, 15 in each groups. Primary variable will be sedation of the patient. Sedation will be 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 response to glabellar tap or loud voice; 6=no response). 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.

Results: The difference in mean age and ASA status among the three groups are not statistically significant (p= 0.29 & p=0.47). There is no statistical significance of sex & GCS status of the patients of these three groups(p= 0.49 & p=0.47). We found mean post sedation delirium was not statistically significant (p=0.078). No statistical significant difference in SBP & DBP among all these groups. There is statistically significant difference in mean RSS at 5 min interval in group D. At 25 & 30 min interval it was higher in group P and at 60 min it was higher in group M and these are statistically significant ($p<0.005$). In our study the mean Opioid at 24th hour is more in Midazolam group and it is significantly less in patients receiving dexmedetomidine. 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 is less in Dexmedetomidine group.

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

Keywords: Dexmedetomidine, midazolam, propofol, sedation.

Introduction

Patients requiring postoperative mechanical ventilation after a major surgical procedure typically have significant anxiety and pain. [1] These patients require sedation to tolerate the tracheal tube and the ventilator, to suppress coughs, to prevent respiratory fighting during intensive care procedures and to prevent psychological complications associated with pain and anxiety. An ideal sedative agent should allow for rapid modification of the sedation level by titration of doses, no depressant effects on the cardiovascular or respiratory systems, cheap, have short duration without cumulative effects, and allow rapid recovery of effective spontaneous respiration after stopping the infusion. [2]

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. [3]

Dexmedetomidine a α2 adrenoceptors agonist is capable of producing sedation, anxiolysis and analgesia without respiratory depression. [4] These properties make them potentially useful for short duration postoperative ventilation like; neurosurgical patients requiring delayed extubation.

Material and methods

This single blinded, open label, randomized control trial conducted in the Intensive careunit, Institute of medical sciences, Banaras hindu University, Varanasi, Uttar Pradesh ,India for 1 year. 45 patients were equality divided into 3 groups, 15 in each groups. Primary variable will be sedation of the patient. Sedation will be 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 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 45 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 15 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<0.005 has been taken as statistically significant.

Results

The difference in mean age and ASA status among the three groups are not statistically significant (p= 0.29 & p=0.47). There is no statistical significance of sex & GCS status of the patients of these three groups (p= 0.49 & p=0.47). We found mean post sedation delirium was not statistically significant (p=0.078). No statistical significant difference in SBP & DBP among all these groups.There is statistically no significant difference in mean RSS between the groups (p<0.005). 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 is less in Dexmedetomidine group.

Table 1. Demographic profile of the patients

	Group D	Group P	Group M	p-value
Age (Yrs)	51.53±7.44	53.1±8.48	52.27±8.04	0.49
Male/Female	12/3	11/4	12/3	0.64
Weight (Kg)	62.87±6.83	60.97+6.43	64.23+6.29	0.17
Duration of Ventilation (hrs)	12.13±3.13	12.96±3.52	12.82±3.20	0.61
Extubation time (Min)	35.38±5.82	26.33±5.12	48.31±7.13	<0.001
RSS	3.52±0.74	3.85±0.99	3.72±0.94	0.31
BIS	68.95±5.80	69.75±6.50	66.58±6.98	0.18
Fentanyl Requirement (mcg/kg/hr)	0.28±0.13	0.52±0.14	0.44±0.14	<0.001

Table 2. The mean of the HR

Time	Group D	Group M	Group P
0 min	101	83	90
5 min	90	82	90
10 min	88	81	88
15min	86	81	87
20 min	83	81	86
25 min	81	81	85
30 min	80	81	84
60 min	79	80	83
3 hr	78	80	84
6 hr	77	79	85
9 hr	86	81	87
12 hr	83	81	86
15 hr	81	81	85
18 hr	80	81	84
21 hr	79	80	83
24 hr	78	80	84
27 hr	86	81	87
30 hr	83	81	86
33 hr	81	81	85
36 hr	80	81	84
39 hr	79	80	83
42 hr	78	80	84

45 hr	77	79	85
48 hr	86	81	87

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

Time	Group D	Group M	Group P
0 min	133	130	128
5 min	130	128	126
10 min	125	124	122
15min	120	119	117
20 min	115	114	114
25 min	114	114	114
30 min	113	114	114
60 min	112	114	114
3 hr	111	114	114
6 hr	111	114	112
9 hr	120	119	117
12 hr	115	114	114
15 hr	114	114	114
18 hr	120	119	117
21 hr	115	114	114
24 hr	114	114	114
27 hr	113	114	114
30 hr	112	114	114
33 hr	120	119	117
36 hr	115	114	114
39 hr	114	114	114
42 hr	113	114	114
45 hr	112	114	114
48 hr	111	114	114

Discussion

The inadequate sedative technique may adversely affect morbidity and even mortality in the ICU. In addition, the sedative drug used can modulate the neuroendocrine stress and the inflammatory response to surgery, which is more important in improving recovery. Recent studies suggest that long term administration of those drugs might be associated with significant risks and adverse effects. [2] The difference in mean age and ASA status among the three groups are not statistically significant (p= 0.29 & p=0.47). There is no statistical significance of sex & GCS status of the patients of these three groups (p= 0.49 & p=0.47). These findings are similar to study done by Jakob SM et al (2012) [5,6] where they find no statistical significance Sex, Age and GCS score between their three groups (P>0.05).

In their study in 2018 Elgebaly AS et al.6also found no difference in age and BMI in both groups. The extubation times were similar and rapid with the use of dexmedetomidine and propofol both compared to midazolam. Although, a longer extubation time would have predicted with dexmedetomidine from volunteer pharmacokinetic data [7], as the elimination half-life of propofolis approximately three times shorter (30-60 min for propofol vs 100-150 min) for dexmedetomidine. [8] In our study similar extubation time may be due to the less dose of fentanyl in dexmedetomidine group. Riker et al., [9] also found that

extubation time was significantly shortened in patients sedated with dexmedetomidine compared with those receiving midazolam. Despite ventilation and intubation, patients sedated with dexmedetomidine could be easily aroused to co- operate without showing irritation.

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 is less in Dexmedetomidine group. No statistical significant difference in SBP & DBP among all these groups.

Findings of our study is also similar to the study conducted by Esmaoglu et al.10 where they studied 40 patients of eclampsia on mechanical ventilation and their study shows that dexmedetomidine reduces HR more Midazolam in first 24 hour.

Similar results also obtained by Rashid et al. [11] by comparing midazolam, propofol and dexmedetomidine in post-operative eclamptic patients in 2017.

In another similar study Elgebaly AS et al. [6] 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. [12] found that occurrence of bradycardia and hypotension is more in patients who received dexmedetomidine. In our study also one patient of dexmedetomidine group developed bradycardia after dexmedetomidine infusion.

There is statistically significant difference in mean RSS at 5 min interval in group D. At 25- & 30-min interval it was higher in group P and at 60 min it was higher in group M and these are statistically significant ($p<0.005$).

This finding is similar to the study by Sharma SK et al. [13] where they found that the Ramsay Sedation Score was comparable, and it maintained at a mean score of 2-3 at most time intervals in both group I (Midazolam) and Group II (Dexmedetomidine).

In a study Conti G et al. [14] 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 our study the mean Opioid at 24th hour is more in Midazolam group and it is significantly less in patients receiving dexmedetomidine

Herr et al. [15] also found that morphine required four times more in patients receiving propofol compared to patients receiving dexmedetomidine.

We found mean post sedation delirium was not statistically significant ($p=0.078$). In a similar study Riker et al. [16] concluded that patients receiving dexmedetomidine experience less delirium after extubation. Tripathi M et al. [17] conducted a study on 2017 comparing dexmedetomidine and midazolam and found that patients receiving dexmedetomidine infusion for sedation have quick extubation time and comparatively less duration of ICU stay. [18]

Conclusion

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

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