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Original Research Article

Open Label Randomized Comparative Assessment of Dexmedetomidine, Midazolam and Propofol for Sedation of Post Operative Patients on Mechanical Ventilation

Anshu Kumari[1], Sumit Kumar Singh[2], Priyanka Awasthi[3]

[1]Senior Resident, Department of Anaesthesiology, Indira Gandhi institute of Medical sciences, Patna, Bihar, India

[2]Senior Resident, Department of Anaesthesiology, Indira Gandhi institute of Medical sciences, Patna, Bihar, India

[3]Senior Resident, Department of Anaesthesiology, Indira Gandhi institute of Medical sciences, Patna, Bihar, India

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Corresponding Author: Dr. Sumit Kumar Singh

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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 at Department of Anesthesiology for 1 year. 60 patients were equality divided into 3 groups, 20 in each groups. Primary variable will be sedation of the patient.

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 statistical 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 neurosurgical mechanically ventilated patients with good hemodynamic stability and extubation time as rapid as propofol.

Keywords: Dexmedetomidine, Midazolam, Propofol, Sedation.

Introduction

Mechanical ventilation is a life-sustaining therapy for the treatment of patients with acute respiratory failure and indeed the advent of its use heralded the dawn of modern intensive care units. Many patients require ventilator support for respiratory insufficiency or abnormal Arterial Blood Gas. The critically ill surgical patients in the ICU experienced discomfort due to endotracheal intubation and mechanical ventilation, intermittent physiotherapy, tracheal suction and also experience pain due to surgical procedure. Moreover noise produced by the monitoring and support system, lighting in the ICU surrounding are not pleasant rather it is enhancing the adverse reactions requiring adequate sedation. [1]

Few factors are necessary for better ICU practice like adequate sedation & analgesia which will reduce anxiety and improve the tolerance of the patient on ventilation, reduce fighting against ventilation and also it will increase metabolic and cardiac stability. Practice of ICU sedation has been changed remarkably now a days. Deep sedation is no longer practiced as it increases ICU stay and morbidity on the other hand inadequate sedation result in anxiety, agitation and stressful experiences. An ideal sedative should provide a rapid onset, a rapid recovery, have low profile to accumulate, leaving no withdrawal effects, should be easily titratable and should not disturb hemodynamic stability. [2]

Patients requiring postoperative mechanical ventilation after a major surgical procedure typically have significant anxiety and pain. [3] 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. [4] Few factors are necessary for better ICU practice like adequate sedation and analgesia which will reduce anxiety and improve the tolerance of the patient on ventilation, reduce fighting against ventilation and also it will increase metabolic and cardiac stability. Practice of ICU sedation has been changed remarkably now a days. Deep sedation is no longer practiced as it increases ICU stay and morbidity on the other hand inadequate sedation result in anxiety, agitation and stressful experiences. An ideal sedative should provide a rapid onset, a rapid recovery, have low profile to accumulate, leaving no withdrawal effects, should be easily titratable and should not disturb hemodynamic stability. [5] Sedation in intensive care patients is assumed to reduce discomfort from care interventions, increase tolerance of mechanical ventilation, prevent accidental removal of instrumentation, and reduce metabolic demands during cardiovascular and respiratory instability. [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.

Materials and Methods

This single blinded, open label, randomized control trial conducted at department of Anesthesiology, IGIMS, Patna, Bihar, India for 1 year. 60 patients were equality divided into 3 groups, 20 in each groups. Primary variable will be sedation of the patient. 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 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

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
BIS	67.93+5.84	68.72±6.54	66.54±6.94	0.12
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
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.

Discussion

Many sedative agents are in use in different ICU setup. Propofol is most commonly used in ICU as sedative agent due to its rapid onset & offset and shot duration of action but few factors which limit the use of propofol are haemodynamic unstability

like hypotension and bradycardia and lack of analgesic action. [10] Benzodiazepine mainly Midazolam is another commonly used gamma aminobutyric acid inhibitor 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 statistical 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 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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