Original Research Article

Comparative analysis of dexmedetomidine, midazolam and propofol for sedation of post operative patients on mechanical ventilation

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Abstract

Background: 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. This study is conducted to know the safety and efficacy of these three drugs- Dexmedetomidine, Midazolam and Propofol for quality of sedation, haemodynamic stability and requirement of supplemental analgesics in post-operative patients who are in mechanical ventilation at Tertiary care Institute of Gujarat. **Material and Methods:** This was single blinded randomized control trial conducted in the Anaesthesia Intensive Care Unit of Medical College and Hospital at Tertiary care Institute of Gujarat for the duration of 1 year on Post-operative patients requiring mechanical ventilator support. This study is carried out in 51 adult patients with Glasgow coma scale score of 9-15, Patients were divided randomly into three groups of 17 each. Group M patients received IV inj. Midazolam loading dose 0.15mg/kg followed by maintenance dose of 0.02-0.1mg/kg/hour. Group P patients received intravenous inj. Propofol loading dose of 1.5mg/kg followed by continuous infusion of 1-6 mg/kg/hr. Group D patients received intravenous inj. Dexmedetomidine loading dose of 1µg/kg followed by maintenance dose of 0.2- 0.5 µg/kg/hr of continuous infusion by infusion pump. Desired depth of sedation was assessed by Ramsay Sedation Score. **Results:** The difference in mean age and ASA status among the three groups are not statistically significant. There is no statistical significance of sex and GCS status of the patients of these three groups. In our study, difference of mean HR at different time interval was not statistically significant. But the fall in Heart Rate is more in Group D and Group M than in Group P. The mean heart rate is less in Group D compared to Group M and Group P after 45 minutes of infusion. In overall Dexmedetomidine Group showed stable RSS score throughout the time interval. **Conclusion:** Difference of mean hemodynamic parameters at different time interval in three drugs was not statistically significant. The Heart Rate of patients at 45 min interval remains lower in Dexmedetomidine Group compared to Midazolam and Propofol Group.

Key Words: Dexmedetomidine, Heart Rate, Midazolam, Propofol

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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] Few factors are necessary for better

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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.[3] 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.[4] Long-term sedation may have serious adverse effects, such as prolonged mechanical ventilation,[5] coma,[6] delirium,[7] delusional memories and posttraumatic stress disorder,[8,9] impaired cognitive function, prolonged hospitalization, increased costs, and mortality. Daily sedation stops, sedation protocols, spontaneous breathing trials and early mobilization, or primary use of opiates without other sedation may help reduce these complications. Current sedatives are problematic in long-term sedation. Benzodiazepines and propofol accumulate unpredictably.[10,11] High-dose or prolonged propofol use may cause potentially fatal propofol infusion syndrome.[12] 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.[13] Dexmedetomidine a α2 adrenoceptors agonist are capable of producing sedation, anxiolysis and analgesia without respiratory depression.[14] These properties make them potentially useful for short duration postoperative ventilation like; neurosurgical patients requiring delayed extubation. This study is conducted to know the safety and efficacy of these three drugs-Dexmedetomidine, Midazolam and Propofol for quality of sedation, haemodynamic stability and requirement of supplemental analgesics in post-operative patients who are in mechanical ventilation at Tertiary care Institute of Gujarat.

MATERIAL AND METHODS

This was single blinded randomized control trial conducted in the Anaesthesia Intensive Care Unit of Medical College and Hospital at Tertiary care Institute of Gujarat for the duration of 1 year on Post-operative patients requiring mechanical ventilator support. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants. 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, and SPO2. In this study 51 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 17 patients. Group M received inj Midazolam loading dose 0.15mg/kg and than 0.1mg/kg/hr infusion. Group P received inj Propofol 1.5mg/kg bolus followed by mg/kg/hr continuous infusion and Group D received inj Dexmedetomidine bolus dose of 1 microgm/kg and infusion at the rate of 0.5 microgm/kg/hr. 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 and RSS was assessed at 0.5,10,15,20,25,30 min and then at 1 hour and 2 hour. All the patients were closely observed for complications like bradycardia and hypotension and managed accordingly if any.

Statistical analysis: The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Table 1: Demographic Profile of Study participants

Variable	Number	Percentage
Gender		
Male	40	78.43
Female	11	21.56
Total	**51**	**100**

RESULT AND 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.[4] Use of BIS monitoring in addition to Ramsay sedation scale (RSS) in our study provided objectivity in monitoring without producing observer bias. Good correlation between responsiveness and BIS levels in healthy volunteers has been described during sedation with isoflurane, midazolam, propofol and dexmedetomidine.[15,16] An equivalent depth of sedation between dexmedetomidine, propofol and midazolam was achieved, with the advantage that the total amount of fentanyl required by the dexmedetomidine group was less. The interaction of α2 -adrenoreceptors and opioids lead to decrease in the dose of fentanyl. The α2 adrenoceptors have an effect on the spinal cord, especially α^2 A and α^2 C as well as modulating the descending noradrenergic pathways leading to 30% to 50% reduction in the requirements of opioids. Our study is in accordance with other studies [17,18] The difference in mean age and ASA status among the three groups are not statistically significant ($p > 0.05$). There is no statistical significance of sex and GCS status of the patients of these three groups ($p>0.05$). These findings are similar to study done by Jakob SM *et al.* (2012)[19] 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.*[20] 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 and P, HR falls more in group D and the mean HR is less in Dexmedetomidine group. Findings of our study is also similar to the study conducted by Esmaoglu *et al.*[20] where they studied 40 patients of eclampsia on mechanical ventilation and their study shows that dexmedetomidine reduces HR more tha Midazolam in first 24 hour. Similar results also obtained by Rashid *et al.*[21] by comparing midazolam, propofol and dexmedetomidine in post-operative eclamptic patients on 2017. Martin *et al.*[22] 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 and 30 min interval it was higher in group P and at 60 min it was higher in group M and these are statistically significant. This finding is similar to the study by Sharma SK *et al.*[23] 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.*[24] 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. 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[25], as the elimination half-life of propofol[26] is approximately three times shorter for dexmedetomidine. Riker *et al.*[27] 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 cooperate without showing irritation. 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.*[28] 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. In a similar study Riker *et al.*[29] concluded that patients receiving dexmedetomidine experience less delirium after extubation. Tripathi M *et al.*[30] 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.

CONCLUSION

Difference of mean hemodynamic parameters at different time interval in three drugs was not statistically significant. The Heart Rate of patients at 45 min interval remains lower in Dexmedetomidine Group compared to Midazolam and Propofol Group. The Ramsay Sedation Score was higher in group M and it was steady in group D. Group D patients were easily arousable and they have tolerated ICU procedures like suctioning, physiotherapy etc better compared to other two groups. There are fewer incidences of post extubation delirium and less requirement of supplementary analgesia in Dexmedetomidine group.

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