

COMPARISON OF DIFFERENT SEDATION PROTOCOLS FOR MECHANICALLY VENTILATED PATIENTS IN TERMS OF SEDATION DEPTH, DURATION OF MECHANICAL VENTILATION AND DELIRIUM RATES

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Abstract

Objective: To compare the different sedation protocols in terms of sedation depth, duration of mechanical ventilation and delirium rates for mechanically ventilated patients managed at a critical unit **Study design:** Comparative Cross-sectional study. **Place and duration of study:** Critical care units of Bahria International Hospital and Safari Hospital. From July 2022 to June 2024. **Methodology:** Patients who were mechanically ventilated at two critical care units were recruited in the study. Before putting them on mechanical ventilation they were randomized by block randomization method into two groups for administration of sedation. Group A received Propofol and Nalbuphine while group B received Midazolam and Nalbuphine. Both the groups were followed up till the need for mechanical ventilation subsided and observed for achievement of adequate sedation depth, duration of mechanical ventilation and occurrence of delirium. **Results:** A total of 60 patients were recruited. Mean age was 31.86 ± 10.79 years. Out of 60, 39 (65%) were male while 21 (35%) were female. Out of two study groups it was revealed that occurrence of delirium was more in Midazolam and Nalbuphine group (p -value=0.006) while achievement of adequate depth of sedation was significantly more in Propofol and Nalbuphine group (p -value<0.001). Duration of mechanical ventilation was significantly more in Midazolam and Nalbuphine group and compare to Propofol and Nalbuphine group (p -value<0.001). **Conclusion:** Sedation protocol consisting of Propofol and Nalbuphine was better than midazolam and Nalbuphine combination with regards to achieving target sedation depth, less duration of mechanical ventilation and having less delirium rates.

INTRODUCTION

Critical care unit is a clinical setting which involves care of severely ill patients from multiple perspectives.¹ Mechanical ventilation is required in huge number of patients managed at critical care unit.

Multiple factors are considered when a patient is prepared for mechanical ventilation.² Studies show that prognosis of patient depends on how smooth the mechanical ventilation is achieved and maintained

during the management of patient in critical care unit.³

Sedation plays a vital role in mechanically ventilated patients for smooth ventilation as well as recovery. If sedation process and maintenance is not smooth; multiple complications can occur in the patients.⁴ Different pharmacological agents have been used to achieve sedation in these patients to get the best results.⁵ Use of combinations of different agents have also been in common clinical practice for sedation of patients who are put on mechanical ventilation.⁶ So far guidelines does not recommend any single agent or one combination so still studies are in progress to find the most appropriate agent for this purpose.

Various medications and combinations of medications have been tried in the past for achieving adequate and beneficial sedation in patients who needed mechanical ventilation. Collins P published a study in Journal of Critical care medicine which recruited patients who required prolonged sedation for mechanical ventilation. He compared Midazolam and Propofol for this purpose and found both the agents effective for it.⁷ Ronan et al. published a similar study and did comparison of Propofol and Midazolam in all the patients who required sedation in intensive care unit. They found both the agents as equally safe and efficacious but quality of sedation was found better with Propofol.⁸ Jacob et al. studied a relatively newer agent Dexmedetomidine for this purpose and compared it with both Midazolam and Propofol. It was revealed that Dexmedetomidine was equally effective as Propofol and Midazolam but had more adverse effects.⁹

Critical care medicine is evolving as a specialty with each passing day as more specialists are getting trained locally. A recent local study was published by Zehra et al. in Pakistan Journal of Medical & Health Sciences regarding comparison of Comparison Dexmedetomidine and Midazolam for purpose of sedation in mechanically ventilated patients of neurosurgery. They found out that Dexmedetomidine was a better option in their patients.¹⁰ Limited local data is available regarding best agent for the said purpose in our population. We therefore planned this study with the rationale to compare the different sedation protocols in terms of sedation depth, duration of mechanical ventilation

and delirium rates for mechanically ventilated patients managed at a critical unit.

Patients and methods

This comparative cross-sectional study was planned and conducted Critical care units of Bahria International Hospital and Safari Hospital from July 2022 to June 2024. Sample size was calculated by using the two groups. Group-I had complications with Midazolam as 47.9% while group-II had complications with Propofol as 14.2%.¹¹ Non probability consecutive sampling technique was used to gather the required sample size for this study and then block randomizations method was used to randomly divide the patients into two equal groups.

Inclusion criteria: Patients of both genders between the age of 18 and 65 years managed at critical care units of both the hospitals and requiring mechanical ventilation were recruited.

Exclusion criteria: Patients whose caregivers did not give consent were not recruited. Those who had history of head injury or neurosurgical procedure were also not recruited in the study. Those who had history of active substance use in recent part were excluded from the study. Those patients who were found allergic to the medications used in the study were also not made part of this study. Those patients who died during mechanical ventilation were not included as well.

Permission from hospital ethics and IREB committee via letter number 154 was obtained before this study was started in the ICU. Informed consent was taken from primary care givers of the patients after giving them all the required details. Patients were divided into two equal groups via block randomization. Group A received Propofol and Nalbuphine while group B received Midazolam and Nalbuphine.

Dose range for Midazolam was 0.1 to 0.5 mg/kg/hr while it was 1 to 6 mg/kg/hr for Propofol.¹² Nalbuphine was given to both the groups along with main agent in standard dose as per guidelines.¹³ Depth of sedation was determined by Richmond Agitation-Sedation Scale (RASS). Target score in our study was -3. Achievement of this or beyond was considered adequate for the patients in our study.¹⁴ Delirium after the mechanical ventilation was over was determined by consultant critical care specialist on the basis of clinical criteria. Patients in both the groups were

followed up to look for and compare depth of sedation, duration of mechanical ventilation and occurrence of delirium.

Statistical analysis was performed by using the SPSS 23.0. Frequency and percentage were calculated for the qualitative variables in the study. Mean and standard deviation was calculated for the age of the patients included in the study. Pearson chi-square test was used to compare the achievement of adequate sedation and occurrence of delirium in both the groups. Independent t-test was used to compare the mean duration of mechanical ventilation in both the groups. The p-value less than or equal to 0.05 was considered as significant for this study.

Results

A total of 60 patients were recruited. Mean age was 31.86 ± 10.79 years. Table-I summarized the general characteristics of patients who were recruited in this study. Out of 60, 39 (65%) were male while 21 (35%) were female.

Table-II showed the comparison of occurrence of delirium and achievement of adequate depth of sedation. Out of two study groups it was revealed that occurrence of delirium was more in Midazolam and Nalbuphine group (p-value=0.006) while achievement of adequate depth of sedation was significantly more in Propofol and Nalbuphine group (p-value<0.001).

Table-III showed the comparison of duration of mechanical ventilation in two study groups. It was revealed that duration of mechanical ventilation was significantly more in Midazolam and Nalbuphine group and compare to Propofol and Nalbuphine group (p-value<0.001).

Discussion

Critical care is an emerging specialty in our country and local protocols are also under constant evolution. Usually international guidelines are followed with changes made on individual experiences if required. Mechanical ventilation is one of the most commonly performed clinical procedure on patients admitted in critical care unit. Sedating the patient before and during this procedure carries significant importance for smooth mechanical ventilation. Guidelines across the globe suggest different agents for this purpose therefore no set protocols exist in the critical care units and still research is under process to find the

most suitable medication for this purpose. This study was planned with an aim to compare the different sedation protocols in terms of sedation depth, duration of mechanical ventilation and delirium rates for mechanically ventilated patients managed at a critical unit.

A randomized multicenter trial was conducted by Chamorro et al. in which they compared Propofol and Midazolam for sedation of critically ill patients. They revealed that Propofol was as effective as Midazolam in most of the parameters and better in terms of duration and they recommended replacement of benzodiazepines and opiates with Propofol.¹⁵ We used opiate (Nalbuphine) in both the groups but found out that Propofol group was better in all the study parameters as compared to Midazolam group.

A systematic review and meta-analysis of randomized trials published by Jerath et al. which compared use of Volatile Anesthetic Agents with Midazolam or Propofol in patients undergoing mechanical ventilation. They came up with the findings that reduction in extubation time was best in group of patients who were given Propofol as compared to Midazolam or inhalational agents.¹⁶ Propofol emerged as a better agent for sedation in patients with mechanical ventilation in our study participants as well.

Ronan et al. compared Propofol and Midazolam for sedation of patients who underwent mechanical ventilation in critical care unit. It was concluded that Propofol and Midazolam were equally effective for this purpose and quality of sedation was better with Propofol.¹⁷ Our results showed that sedation protocol consisting of Propofol and Nalbuphine was better than midazolam and Nalbuphine combination with regards to achieving target sedation depth, less duration of mechanical ventilation and having less delirium rates.

A post-hoc analysis of DESIRE trial was published in 2022 which concluded that Midazolam was associated with more chances of having delirium and coma and quality of sedation was also not better with Midazolam as compared to Propofol.¹⁸ Our results supported the findings generated in this post-hoc analysis.

Study limitations

Patients were included from two critical care units of private hospitals of one city therefore the findings

could not be generalized. Patients who died during the study were not included in the final analysis therefore mortality could not be compared in both the groups. Randomized controlled trial comparing the two groups would give better results which could be basis for more studies and local guidelines.

Conclusion

Sedation protocol consisting of Propofol and Nalbuphine was better than midazolam and Nalbuphine combination with regards to achieving target sedation depth, less duration of mechanical ventilation and having less delirium rates.

Conflict of interest

No

Acknowledgment

No

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Table-I: Characteristics of Patients put on mechanical ventilation

Study parameters	n(%)
Age (years) Mean $\pm$ SD	31.86 $\pm$ 10.79 years
Gender Male Female	39 (65%) 21 (35%)
Delirium No Yes	47 (78.3%) 13 (21.7%)
Medication used Propofol and Nalbuphine Midazolam and Nalbuphine	30 (50%) 30 (50%)
Indications of Mechanical Ventilation Type-I Respiratory Failure Type-II Respiratory Failure Low GCS Status Epilepticus Others	42 (70%) 12 (20%) 03 (5%) 02 (3.3%) 021 (1.7%)

Table-II: Difference among two groups regarding achieving depth of sedation and post-operative delirium

Parameters	Propofol and Nalbuphine	Midazolam and Nalbuphine	p-value
Achievement of -3 RASS score No Yes	07 (23.3%) 23 (76.7%)	23 (76.7%) 07 (23.3%)	<0.001
Emergence of delirium No Yes	27 (76.7%) 03 (23.3%)	18 (60%) 12 (40%)	0.006

Table-III: Difference among two groups regarding duration of mechanical ventilation

Parameters	Propofol and Nalbuphine	Midazolam and Nalbuphine	p-value
Duration of mechanical ventilation	3.67 $\pm$ 1.26	5.07 $\pm$ 1.08	<0.001