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Original Article

Comparison of Propofol and Midazolam for Sedation in Intensive Care Unit

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ABSTRACT

Objective: To compare the relative efficacy and extubation time by using Propofol and Midazolam for patients requiring sedation in intensive care unit.
Study Design: Quasi experimental study.
Place and Duration of Study: Intensive Care Unit, Department of Anesthesia, Combined Military Hospital Multan, Pakistan from Jan to Jul 2023.
Methodology: Sixty-two (n=62) patients fulfilling the inclusion criteria were incorporated in the study, the were divided in two group of 31 each. Group-P was infused Propofol at the dosage of 0.05mg/kg/min whereas Group-M received Midazolam as 0.1mg/kg/hour. Standard monitoring was used in both groups. End points included efficacy of sedation (RASS +1 to -2), time taken for extubation after stoppage of sedative drugs.
Results: Patients in both the groups were comparable in terms of mean age in years 45.17±14.42 and 44.40±13.56 with p value 0.83. Mean time in minutes taken for extubation was 80.40±21.35 and 92.23±22.61 (*p*-0.042) for Propofol and Midazolam group respectively. Richmond agitation sedation score (RASS) scores of 90% (n=27 patients) and 73.3% (n=22 patients) of the patients remained in desired limits in Propofol and Midazolam groups respectively.
Conclusion: Propofol and Midazolam demonstrated efficacy in sedating ICU patients and different profiles regarding safety. The choice of sedative to be individualized, considering the patient's clinical status and the desired sedation goals.

Keywords: ICU, Sedation, Propofol, Midazolam, RASS, Anxiety.

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INTRODUCTION

In the intensive care unit(ICU), sedation is crucial to promoting anxiety management, preventing materi al loss and unintentional extubation, and enhancing pa tient-ventilator synchrony.
However, using too many of these drugs raises mortali ty and morbidity, necessitating a balanced approach.[1] It is concluded in the recent guidelines that the frequency of tracheostomies and the duration of time it took to extubate adult patients in the ICU were strongly correlated with sedation.[2,3]

The pain, agitation, delirium, immobility and sleep disturbance (PADIS) guidelines do not classify Benzodiazepines as standard care, yet they are frequently used.[4] Compared to short-lasting sedatives like Propofol and Dexmedetomidine, both long and short acting Benzodiazepines specifically, Lorazepam and Midazolam are linked to patients who experience high levels of sedation.[5] Propofol sedation compared to Midazolam resulted in lower catecholamine doses, lower mortality, and lower rates of bleeding, according to a recent observational cohort study.[6] Propofol and low sedation are not advised in some therapeutic circumstances, such as when patients require several days of intense sedation.[7] Additionally, Propofol has a lower time to extubation in comparison to Midazolam in mechanically ventilated patients.[8] The selection of sedatives can influence the results following mechanical breathing in the intensive care unit due to the unique features of each medication; yet, there is no agreement on the sedation regimen, leading to significant variability.[9]

We set out to perform a study to evaluate the effects of using a non-Benzodiazepine medicine; Propofol in comparison to a Benzodiazepine drug; Midazolam, in adult patients admitted in the ICU because patients admitted to the ICU are frequently sedated with either treatment.

METHODOLOGY

This was a prospective quasi experimental study conducted in Intensive care unit, Department of Anesthesia, Combined Military Hospital, Multan. From Jan 2023 to Jul 2023 after seeking approval from the hospital ethical committee (vide letter no 13/Trg/91/2023 dated 1st Jan 2023).

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Inclusion Criteria: Postoperative patients of both the genders aged between 18 years to 50 years requiring sedation along with mechanical ventilation, who were hemodynamically stable were included.

Exclusion Criteria: Critically ill with no promising prognosis depicted by sequential organ failure assessment score and those patients who died in their ICU stay or those allergic to any of the two drugs (propofol /midazolam) were excluded.

Sample size was calculated using WHO sample size calculator using reference parameter as mean time for extubation 94.47±6.11 minutes and 91.91±3.94 minutes for Midazolam and Propofol group respectively.[8] Confidence interval (two sided) was kept at 95%, power of study 78% while ratio of sample size as 1. Convenient consecutive sampling technique was used, and a total of 62 patients were selected for study, 31 for each group as shown in patient flow diagram Figure below.

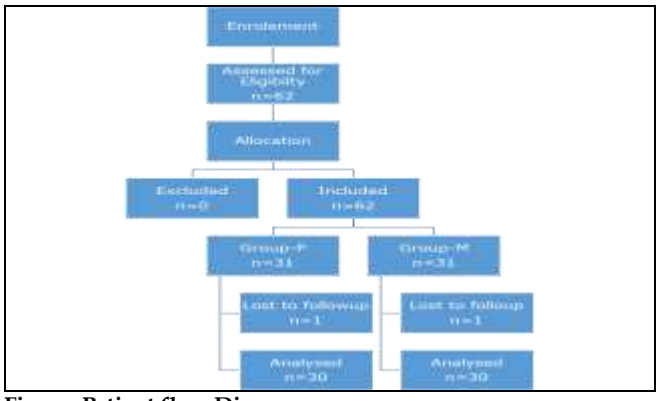

Figure: Patient flow Diagram

All the patients were monitored as per standard protocols, continuous pulse oximetry, electro-cardiography and noninvasive blood pressure monitoring every 10-15 minutes or as required. Patients were divided in two groups, Group-M and P for Midazolam and Propofol respectively. Group-M was infused with Midazolam at infusion rate of 0.1mg/kg/hour and Group-P was infused with Propofol at infusion rate of 0.05mg/kg/min. The infusion rates were adjusted targeting Mean arterial blood pressure ≥65mmhg and Richmond Agitation Sedation Score (RASS) +1 to -2.

The primary end points were efficacy of sedation which was assessed by RASS score, time taken for extubation after stopping the sedative agent and mortality in both the groups. Other parameters recorded were, gender, age, weight and ASA status. RASS score was measured for each patient senior resident anesthetist on duty, who was not part of the study.

Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 25. Numerical variables like time for extubation, age and weight were expressed as Mean±SD. Categorical data like efficacy of sedation, mortality rate, gender and ASA status were presented as frequency and percentage. Independent sample t-test was used to compare the differences between the two groups (Propofol and Midazolam) in terms of continuous and normal distributed variable's outcome.A *p*-value less than 0.05 was considered as significant.

RESULTS

Out of the total 62 patients included in the study 60 completed the study.

Mean age of patients in years was 45.17±14.42 and 44.40±13.56 in Groups-P and M respectively with *p*-value 0.83. Comparative profile of both groups in terms of weight, gender and ASA status is shown in Table-I.

Table-I: Demographic Profile Comparison Among Groups (n=60)

Variables		Group-P Propofol (n=30)	Group-M Midazolam (n=30)	*p*-value
Gender	Male	18(60%)	16(53.33%)	-
	Female	12(40%)	14(46.67%)	-
ASA Status	I	0	0	-
	II	18(60%)	15(50%)	-
	III	12(40%)	15(50%)	-
	IV	0	0	-
Age (years)		45.17±14.42	44.40±13.56	0.833
Weight (Kg)		68.56±7.30	69.6±7.24	0.583

ASA: American society of Anesthesiologists

All patients fell in category of ASA II and III. Mean time taken for extubation in Propofol group was 80.40±21.35 and comparison of both groups in this regard is given in Table-II.

Table-II: Comparison of Extubation Time Among Groups(n=60)

Parameter	Study Groups		*p*-value
	Group-P Propofol (n=30)	Group-M Midazolam (n=30)	
Time taken for Extubation (minutes)	80.40±21.35	92.23±22.61	0.042

Of the 60 patients in both groups RASS scores of 49 and 11 remained within and out of desired limits.

Detailed comparison of the two groups in terms of RASS scores is given in Table-III.

Table-III: Pain scores (RASS) Comparison Groups Crosstabulation (n=60)

Parameter		Groups		Total
		Propofol (n=30)	Midazolam (n=30)	
RASS scores	Within Limits	27(90.0%)	22(73.3%)	49
	Out of Limits	3(10.0%)	8(26.7%)	11

RASS: Richmond Agitation Sedation Score

Richmond agitation sedation score (RASS) scores of 90% (27 patients) and 73.3% (n=22 patients) of the patients remained in desired limits in Propofol and Midazolam groups respectively.

DISCUSSION

The findings of our study demonstrated that both Propofol and Midazolam have equal efficacy in sedating ICU patients but different profiles regarding safety. Propofol has a rapid onset and short half-life, which provides quick sedation and allows easy titration and fast recovery.[10] On the other hand, Midazolam, due to its longer half-life, provides a more prolonged sedative effect. However, this can also lead to over sedation and a longer period of recovery.[11]

Both Propofol and Midazolam have been considered relatively safe for sedation in the ICU. Nonetheless, they present different safety profiles. Propofol has been associated with propofol infusion syndrome (PRIS), a potentially fatal condition characterized by metabolic acidosis, cardiac failure, rhabdomyolysis, and renal failure. However, PRIS is rare and usually associated with high-dose or prolonged infusions.[12] Midazolam, being a Benzodiazepine, can lead to a risk of delirium, which has been associated with longer ICU stays and increased mortality.[13]

In this study we compared the relative efficacy and extubation time for Propofol and Midazolam group. It was found that Propofol is more effective in achieving and maintaining light sedation, shorter time of extubation along with lesser mortality which is in accordance with a detailed review conducted by Opdenekkar et al, which suggests that Propofol may facilitate a faster weaning process and shorter duration of mechanical ventilation compared to Midazolam.[14]

Hu et al conducted a calibrated trial on 17410 patients and they found out that those patients who were not given sedation, when required, had a greater rate of mortality. They also found out that hospital stay and extubation time of Propofol group was shorter when compared with Midazolam but Dexmedetomidine was better than both of these drugs.[15] Another study by Hughes et al. shows that results in patients who got Dexmedetomidine did not differ from results in patients who received Propofol among mechanically ventilated people with sepsis who were being treated with suggested light-sedation methods.[16]

Jiang *et al*., conducted a study on patients of myocardial infarction who needed mechanical ventilation and sedation. They used Propofol and Midazolam for respective group and found out that Propofol was linked to shorter extubation time and lesser stay in the critical care unit. These results are in accordance with our study.[17]

Similarly, another study by Sun *et al*., on 4188 patients concluded that 28-day mortality in Propofol group was 25.5% whereas in Midazolam group it turned out to be 30.8%.[18]

Contrary to our results a meta-analysis of four trials revealed that when used to produce sedation for patients with severe traumatic brain injury, there are no significant differences between Propofol and Midazolam.[19]

Likewise, another study showed, for long-term sedation of critically sick mechanically ventilated patients, the sequential administration of Midazolam and Propofol was a safe and effective sedation procedure with higher clinical effectiveness and a better cost-benefit ratio than Midazolam or Propofol administered alone.[20]

CONCLUSION

Both propofol and midazolam have demonstrated efficacy in sedating ICU patients and different profiles regarding safety. The choice of sedative has to be individualized, considering the patient's clinical status and the desired sedation goals.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MAA & A: Data acquisition, critical review, approval of the final version to be published.

MS & SMW: Conception, study design, drafting the manuscript, approval of the final version to be published.

MAA & MA: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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