Open Access

Original Article

Dexmedetomidine Versus Midazolam: Does Choice of Sedatives Effect the Duration of Mechanical Ventilation

Usman Ahmed, Aftab Hussain*, Khursheed Hassan, Zaheer Ud Din, Ahsan Javed***, Faisal Wahid******

Department of Anesthesia, Combined Military Hospital Kharian/National University of Medical Sciences (NUMS) Pakistan, *Department of Anesthesia, Combined Military Hospital Kohat/National University of Medical Sciences (NUMS) Pakistan, **Department of Anesthesia, Combined Military Hospital Rawalakot/National University of Medical Sciences (NUMS) Pakistan, ***Department of Anesthesia, Combined Military Hospital Abbotabad/National University of Medical Sciences (NUMS) Pakistan, ****Department of Anesthesia, Armed Forces Institute of Urology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

***Objective*:** To evaluate Dexmedetomidine and Midazolam in mechanical ventilation regarding the extubation time.
***Study Design*:** Quasi-experimental study.
***Place and Duration of Study*:** Department of Anaesthesia, Combined Military Hospital, Kharian Pakistan, from May to Dec 2019.
***Methodology*:** A total of 88 patients on mechanical ventilator support in ICU were included. In Group-D (Dexmedetomidine), a loading dose of 1 µg/kg Dexmedetomidine over ten minutes was given, and sedation was maintained by continuous infusion at the rate of 0.2–0.6 µg/kg/hr. In Group-M (Midazolam), an intravenous 0.5–1 mg bolus of Midazolam was given over two minutes and maintained by continuous infusion at 10-50 µg /kg/hr; doses were increased incrementally 1–2 mg/hour until desired sedation level was achieved. The Richmond Agitation and Sedation Score assessed the sedation level. The total duration of mechanical ventilation and time from weaning off trial to extubation was recorded.
***Results*:** In this study, the mean duration of mechanical ventilation was 63.07±32.07 hours in Group-D versus 86.14±38.96 hours in Group-M (*p*-value=0.003). The mean extubation time was 25.09±7.33 hours in Group-D versus 30.31±8.37 hours in Group-M (*p*-value =0.002).
***Conclusion*:** This study concluded that Dexmedetomidine is superior Midazolam in providing sedation to mechanically ventilated patients. It reduces the duration of mechanical ventilation and time of extubation.
Keywords: Dexmedetomidine, Extubation, Mechanical ventilation, Midazolam, Sedation.

How to Cite This Article: *Ahmed U, Hussain A, Hassan K, Din ZU, Javed A, Wahid F. Dexmedetomidine Versus Midazolam: Does Choice of Sedatives Effect the Duration of Mechanical Ventilation. Pak Armed Forces Med J 2023; 73(4): 1079-1082. DOI: https://doi.org/10.51253/pafmj.v73i4.8381*

INTRODUCTION

Critically ill patients admitted to Intensive care units (ICU) often require mechanical ventilatory support. In order to reduce this stress response and anxiety; and increase tolerance, sedatives are routinely used in such patients. Sedatives improve patient outcomes.[1] Many sedatives have been used in ICU, but Midazolam and Propofol are the most commonly used sedative agents administered.[2-3] These sedatives are problematic in long-term sedation, for example Midazolam in renal failure cases.[4] Likewise, prolonged Propofol use may cause potentially fatal propofol infusion syndrome.[4] Ventilation-associated pneumonia (VAP) is a grave complication of ventilation, with a reported incidence rate ranging from 7% to 15%.[5]

The sedation with α-2 adrenergic agonists results in a very different pattern of sedation in that the patients are readily arousable, and their cognitive performance is usually preserved.[6] Furthermore, respiratory depression has not been seen with α-2 agonists than with other commonly used sedatives.[7-8] Dexmedetomidine, a new novel agent with analgesic, sympatholytic and sedative properties. Activation of negative feedback receptors in the brain and spinal cord inhibits neuronal firing resulting in analgesia, sedation, bradycardia and hypotension.[9] Literature review showed that Dexmedetomidine scores slightly over commonly used sedative agents such as Propofol and Midazolam by its analgesic properties, reducing the opioid requirements and the associated adverse effects.[10]

The rationale of this study was to find out our experience with Dexmedetomidine in our setup. By evaluating this drug, we can reduce the duration of mechanical ventilation and the health problems associated with prolonged ventilation.

METHODOLOGY

The quasi-experimental study was conducted at the Department of Anaesthesia, Combined Military Hospital, Kharian, from May to December 2019. Approval was sought from the Hospital Ethical Committee

Correspondence: Dr Usman Ahmed, Department of Anesthesia, Combined Military Hospital, Kharian Pakistan
Received: 13 Mar 2022; revision received: 22 Apr 2022; accepted: 25 Apr 2022

(Certificate No. 1103/Adm/Trg). The sample size was calculated with a population meantime of extubation in Midazolam-Group: 95.64 and population meantime of extubation in Dexmedetoidine-Group was 77.86 hours.[11] Non-probability, consecutive sampling was followed.

Inclusion Criteria: Patients of either gender aged between 18 to 60 years who required post-operative mechanical ventilation were selected for the study.

Exclusion Criteria: Patients transferred from other hospitals, patients with anticipated prolonged ventilation and post-CPR patients were excluded from the study.

Written consent was taken from the relatives of every patient. All patients were examined in detail, and all baseline investigations, including haemoglobin levels, total and differential white blood cell counts, platelet count, renal function tests, and serum electrolytes, including Calcium, Potassium and Sodium, were done. Arterial blood gases were done in all patients to monitor the quality of mechanical ventilation and to find any metabolic disturbance if present. Special investigations were performed according to the disease presentation. The choice of sedation was made by a random lottery method. A weaning trial was given when the primary cause for initiating mechanical ventilation was resolved. Patients were extubated after a successful 2-hour Spontaneous Breathing Trial (SBT). SBT was declared successful when patients had adequate Glasgow Coma Scale (GCS >12), maintained adequate tidal volume (4-6 ml/kg), respiratory rate (10-34 breaths/minute), had no hypoxia & hypercarbia and rapid shallow breathing index of less than 105.

In Group- D (Dexmedetomidine), a loading dose of 1 µg/kg Dexmedetomidine over ten minutes was given, and sedation was maintained by continuous infusion at the rate of 0.2–0.6 µg/kg/hr. In Group-M (Midazolam), an intravenous 0.5–1 mg bolus of Midazolam was given over two minutes and maintained by continuous infusion at 10-50 µg /kg/hr; doses were increased incrementally 1-2 mg/hour until desired sedation level was achieved. The sedation level was assessed by the Richmond Agitation and Sedation Score. The total duration of mechanical ventilation and time from weaning off trial to extubation was recorded on a proforma.

The data recorded on performance was transferred to Statistical Package for Social Sciences (SPSS) version 24:0 for statistical analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency & percentages. Independent sample t-test and Chi-square test were applied to explore the inferential statistics. The *p*-value of ≤ 0.05 was taken as significant.

RESULTS

A total of 88 patients were selected for this study and were divided into two equal groups. The age range of the patients selected for this study was from 28 to 60 years, with a mean age of 46.01±8.46 years. Out of 88 patients, 53(60.22%) were male, and 35 (30.88%) were female. In this study, the duration of mechanical ventilation was 18 to 167 hours with a mean value of 74.60±37.33 hours. In Group-D, the mean duration of ventilation was 63.07±32.07 hours, whereas in Group-M, it was 86.14±38.96 hours. The mean time of extubation was 25.09±7.33 hours in Group-D versus 30.31±8.37 hours in Group-M, as shown in Table.

Table: Comparison of the Dexmedetomidine versus Mida-zolam in terms of duration of mechanical ventilation and time of extubation

Outcome	Group-D (n=44)	Group-M (n=44)	*p*-value
	Mean±SD	Mean±SD	
Duration of mechanical ventilation (hours)	63.07±32.07	86.14±38.96	0.003
Time of extubation (hours)	25.09±7.33	30.31±8.37	0.002

DISCUSSION

Patients who undergo major surgery and require post-operative mechanical ventilatory support usually have significant pain and anxiety.[12] Such patients need continuous sedation to withstand the endotracheal tube and the mechanical ventilation, inhibit cough reflex and prevent the psychological complication associated with anxiety and pain. An ideal sedative is cheap and affordable, allowing speedy modification of the sedation levels, having no depressant effect on the respiratory or cardiovascular system & having a short duration of action without any cumulative effect.[13]

Sedative agents commonly used in ICUs include Midazolam, Propofol, Dexmedetomidine and short-acting opioids like Remifentsanil. Although opioids play a vital role in managing post-operative pain, they cannot be given solely for sedation in patients who require mechanical ventilation.[14] Dexmedetomidine is an α-2 adrenergic receptor agonist. It can produce anxiolysis, analgesia and sedation without producing any respiratory depression.[15]

We conducted this study to compare Dexmedetomidine versus Midazolam in mechanical ventilation

in terms of duration of mechanical ventilation and time of extubation. In this study, the mean duration of ventilation was 63.07±32.07 hours, whereas, in Group-M, it was 86.14±38.96 hours; the mean time of extubation was 25.09±7.33 hours in Group-D versus 30.31±8.37 hours in Group-M with a *p*-value of 0.002. In a study, a significant difference in extubation time in both the groups was observed with results of Dexmedetomidine (21±6.44h) and Midazolam (30.4±10.62 h) with a *p*-value 0.008.8 In another study of similar type, conducted by Riker *et al*.[16] compared Midazolam and Dexmedetomidine used for sedation in patients who were mechanically ventilated. Their study concluded that comparable sedation levels could be achieved with both drugs. However, patients given Dexmedetomidine had fewer episodes of hypertension and tachycardia, experienced less delirium, and spent less time on ventilators. Bradycardia was the most noted side effect of Dexmedetomidine. They observed that the median extubation time in Dexmedetomidine-Group was 1.9 days lesser, and the stay in ICU was 1.7 days lesser compared to Midazolam-Group.

A conducted by Siobal *et al*.[17] observed in their study that Dexmedetomidine maintains an adequate sedation level without any adverse hemodynamic or respiratory depression. Hence, it facilitates early extubation in patients with agitation who were difficult to wean off. A meta-analysis carried out by Tan *et al*. analyzed 24 trials in which 2419 critically ill patients from eleven different countries were involved. It was observed in this meta-analysis that a substantial heterogeneousness prevailed in studies pooled for this meta-analysis, but limited evidence proposes that Dexmedetomidine may result in a reduction in stay ICU.[18]

A study conducted by Shahabi *et al*.[19] observed that patients who received Dexmedetomidine infusion for sedation required supplemental sedatives to attain desired sedation level. On the contrary, we did not face this problem. A local study conducted by Shamim *et al*.[20] in the ICU of Liaquat National Hospital Karachi concluded that Dexmedetomidine was successful in achieving light sedation, which resulted in better tolerance of the endotracheal tube and helped in weaning off from the ventilator. Dexmedetomidine also helped in reducing the ICU stay of the patients.

CONCLUSION

This study concluded that Dexmedetomidine is superior Midazolam in providing sedation to mechanically ventilated patients. It reduces the duration of mechanical ventilation and time of extubation. Therefore, Dexmedetomidine should be in ICU patients on mechanical ventilation to reduce the duration of mechanical ventilatory support and time of extubation.

Conflict of Interest: None.

Authors' Contribution

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

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

KH: & ZUD: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AJ: & FW: Critical review, data acquisition, drafting the manuscript, 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.

REFERENCES

1. Nassar AP, Zampieri FG, Salluh JI. Organizational factors associated with target sedation on the first 48 h of mechanical ventilation: an analysis of checklist-ICU database. Crit Care 2019; 23(1): 34-36. https://doi.org/10.1186/s13054-019-2323-y.
2. Garcia R, Salluh JI, Andrade TR, Farah D, Da Silva PS, Bastos DF, et al. A systematic review and meta-analysis of propofol versus Midazolam sedation in adult intensive care (ICU) patients. J Crit Care 2021; 64(1): 91-99. https://doi.org/10.1016/j.jcrc.2021.04.1
3. Gersonde F, Eisend S, Haake N, Kunze T. Physicochemical compatibility and emulsion stability of propofol with commonly used analgesics and sedatives in an intensive care unit. Eur J Hosp Pharm 2016; 24(5): 293-303. https://doi.org/10.1136/2016
4. Tse AH, Ling L, Lee A, Joynt GM. Altered pharmacokinetics in prolonged infusions of sedatives and analgesics among adult critically ill patients: A systematic review. Clin Ther 2018; 40(9): 1598-1615.e2. https://doi.org/10.1016/j.clinthera.2018.07.021
5. Hemphill S, McMenamin L, Bellamy MC, Hopkins PM. Propofol infusion syndrome: A structured literature review and analysis of published case reports. Br J Anaesth 2019; 122(4): 448-459. https://doi.org/10.1016/j.bja.2018.12.025
6. Guillamet CV, Kollef MH. Is Zero Ventilator-Associated Pneumonia Achievable? Practical Approaches to Ventilator-Associated Pneumonia Prevention. Clin Chest Med 2018; 39(4): 809-822. https://doi.org/10.1016/j.ccm.2018.08.004
7. Nguyen V, Tiemann D, Park E, Salehi A. Alpha-2 Agonists. Anesthesiol Clin 2017; 35(2): 233-245. https://doi.org/10.1016/j.anclin.2017.01.009.
8. Cruickshank M, Henderson L, MacLennan G, Fraser C, Campbell M, Blackwood B, et al. Alpha-2 agonists for sedation of mechanically ventilated adults in intensive care units: a systematic review. Health Technol Assess 2016; 20(25): 1-117. https://doi.org/10.3310/hta20250
9. Lee S. Dexmedetomidine: Present and future directions. Korean J Anesthesiol 2019; 72(4): 323-330. https://doi.org/10.4097/kja.19259
10. Adams R, Brown GT, Davidson M, Fisher E, Mathisen J, Thomson G, et al. Efficacy of Dexmedetomidine compared with Midazolam for sedation in adult intensive care patients: a

systematic review. Br J Anaesth 2013; 111(5): 703-710. https://doi.org/10.1093/bja/aet194
11. Tripathi M, Kumar V, Kalashetty MB, Malviya D, Bais PS, Sanjeev OP, et al. Comparison of Dexmedetomidine and Midazolam for sedation in mechanically ventilated patients guided by bispectral index and sedation-agitation scale. Anesth Essays Res 2017; 11(4): 828-833. https://doi.org/10.4103/aer.aer_48_17
12. Weinrib AZ, Azam MA, Birnie KA, Burns LC, Clarke H, Katz J, et al. The psychology of chronic post-surgical pain: New frontiers in risk factor identification, prevention and management. Br J Pain 2017; 11(4): 169-177. https://doi.org/10.1177/204946371
13. Devlin JW, Roberts RJ. Pharmacology of commonly used analgesics and sedatives in the ICU: benzodiazepines, propofol, and opioids. Anesthesiol Clin 2011; 29(4): 567–585. https://doi.org/10.1016/j.anclin.2011.09.001
14. Martyn JAJ, Mao J, Bittner EA. Opioid Tolerance in Critical Illness. N Engl J Med 2019; 380(4): 365-378. https:// doi.org/10.1056/NEJMra1800222.
15. Silva-Jr JM, Katayama HT, Nogueira FA, Moura TB, Alves TL, De Oliveira BW, et al. Comparison of Dexmedetomidine and benzodiazepine for intraoperative sedation in elderly patients: A randomized clinical trial. Reg Anesth Pain Med 2019; 44(3): 319-324. https://doi.org/10.1136/rapm-2018-100120
16. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs Midazolam for sedation of critically ill patients: a randomized trial. JAMA 2009; 301(5): 489–499. https://doi.org/10.1001/jama.2009.56
17. Siobal MS, Kallet RH, Kivett VA, Tang JF. Use of Dexmedetomidine to facilitate extubation in surgical intensive-care-unit patients who failed previous weaning attempts following prolonged mechanical ventilation: A pilot study. Respir Care 2006; 51(5): 492-496.
18. Tan JA, Ho KM. Use of Dexmedetomidine as a sedative and analgesic agent in critically ill adult patients: A meta-analysis. Intensive Care Med 2010; 36(1): 926-939. https://doi.org/10.1007/s00134-010-1877-6
19. Shahabi Y, Howe BD, Bellomo R, Arabi YM, Bailey M, Bass FE ,et al. Early Sedation with Dexmedetomidine in Critically Ill Patients. N Engl J Med 2019; 380(1): 2506-2517. https://doi.org/10.1056/nejmoa1904710
20. Shamim K, Anum L, Irfan A, Misbah S, Moomal Z, Madiha M, et al. Use of Dexmedetomidine in intubated and non-intubated patients of critical care and its outcome. Trends Anaesth Crit Care 2020; 35(1): 51-54. https://doi.org/10.1016/j.tacc.2020.