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Comparison of dexmedetomidine versus midazolam in weaning from mechanical ventilation and length of stay in ICU.

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ABSTRACT… Objectives: To compare the role of dexmedetomidine versus midazolam as sedative in facilitating early mechanical ventilation weaning thereby decreasing ICU cost. **Study Design:** Randomized Controlled trial. **Setting:** Surgical ICU of Lahore General Hospital, Lahore. **Period:** December 2018 to July 2019. **Material & Methods:** Total of 60 adult postoperative patients (30 in each group) who required mechanical ventilation in the surgical ICU for minimum 24 hours postoperatively after major pelvi-abdominal operations were included. Patients of group "A" and "B" received midazolam infusion 20-100 mcg/kg/hr & dexmedetomidine infusion 0.2-0.7 µg/kg/hr respectively while being mechanically ventilated. The degree of sedation was measured by using the Richmond agitation sedation score (RASS) every 6 hourly. Extubation time (i.e. time from termination of drug to extubation) was recorded. The time of ICU length of stay was also recorded **Results:** Mean age of patients was 41.97 ±10.21 and 42.57±10.93 years in group-A and B, respectively. In group-A 18 patients (60%) and in group-B 16 patients (53.0%) were male while 12 patients (40%) in group-A and 14 patients (47.0%) were females. A significant decrease in extubation time was observed in Group-B when compared with the Group-A (p=0.046) along with odds ratio 0.938 while no significant relationship could be proved between length of stay at ICU between two groups. **Conclusion:** Dexmedetomidine is more favourable than midazolam for sedation in intensive care patients by facilitating early exubation and decreasing the duration of invasive ventilation while no significant relationship could be proved in two groups between length of stay in intensive care unit.

Key words: Dexmedetomedine, Midazolam, Mechanical Ventilation, Sedation, Weaning.

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INTRODUCTION

Sedation has fundamental role in care of mechanically ventilated critical patients and encompasses a wide range of control of symptoms that vary among patients during their stay in intensive care unit.[1] In critically ill patients, anxiety and pain add to stress response which is present in these patients.[2] If not relieved it may progress to severe agitation and patient may take out lifesaving equipments. In the later life, these events may lead to posttraumatic stress disorder (PTSD).[2]

Thus sedation and analgesia are provided in intensive care units to decrease stress response and ensure patient safety and comfort.[2]

An ideal sedative agent should not be a respiratory depressant, must not have any adverse effects on hemodynamics, titratable to sedation level and must have rapid recovery for weaning purposes.[3]

Weaning from mechanical ventilation is studied for many years and includes skills as well as thorough knowledge .Weaning can be simple in few patients but it may be difficult in others and may lead to prolonged weaning.[4] As associated mechanical ventilation complications, one must try to wean from mechanical ventilation as early as underlying cause is towards resolving side and spontaneous breathing can be maintained by patient. Weaning failure is an important concern because it may end in increased morbidity, prolonged hospital stay, increased cost and mortality.[5]

Common sedatives which are used in intensive care are midazolam, propofol, and dexmedetomidine. The overuse of these drugs can be unfavourable for weaning.[6] So the goal of treatment is to keep the patient cooperative and calm by using minimum amount of sedation.[6]

Dexmedetomidine is a relatively new drug used for short-term sedation in intensive care units. It is a useful sedative drug with hemodynamic stability and efficient analgesic properties without respiratory drive depression facilitating early weaning.[7]

The objective of the study was to compare role of dexmedetomidine versus midazolam as sedative in facilitating mechanical ventilation weaning thereby decreasing ICU cost and preventing ventilator associated complications.

MATERIAL & METHODS

This randomized controlled clinical trial study was conducted in surgical ICU of Lahore General Hospital from December 2018 to July 2019. After seeking permission from the hospital ethical committee, 60 adult postoperative patients who will be requiring mechanical ventilation in ICU for minimum 24 hours postoperatively were included. The sample size of 60 (30 in each group) was calculated at 95% confidence interval and 80% power of test and taking expected mean time of extubation of 60.73± 3.33 in dexmedetomidine group and 101.40±4.72 in midazolam group.[3]

Inclusion criteria was 20 to 60 years old male and female. Patients requiring mechanical ventilation after prolonged major pelvi-abdominal operations and requiring sedation for 24 to 48 hours in surgical ICU. Major operations are Whipple's operation, radical cystectomy, partial gastrectomy and partial or total colectomy.

The exclusion criteria are patients age < 20 years and >60 years, patients with co-morbid diseases like hepatorenal or cardiac dysfunction, patients with neurological diseases, gastrointestinal bleed clotting disorders, pregnant or lactating mothers and those allergic to midazolam or dexmedetomidine.

The intubated patients with inclusive criteria were received to the SICU and were mechanically ventilated with synchronized intermittent mandatory ventilation (SIMV) mode. An informed written consent was obtained from legal attendants and patients were randomly divided into two groups when they were able to open their eyes following command. Randomization was done using random number generator software. Group 'A' received IV midazolam infusion 20-100 mcg/kg/hr while being mechanically ventilated.

Patients in group 'B' received dexmedetomidine infusion at a rate of 0.2-0.7 µg/kg/hr.

The ICU resident (level 4 PG) measured the degree of sedation using the Richmond agitation sedation score (RASS) 6 hourly. To maintain the level of sedation within acceptable range (RASS -2 to 0), the rate of infusion of drugs was adjusted accordingly by 10 % decrease or increase in infusion rate. No patient was given any muscle relaxant in the study period. An awakening trial was given daily and patient was extubated when awake and responsive fulfilling the weaning criteria.

Demographic data i.e. gender, age and weight was recorded for the patients. Standard monitoring of all patients was done as per ICU protocols. Extubation time was also recorded which was considered as the time from termination of sedative agent to event of extubation. It was taken as the end point of study. The length of ICU stay was also recorded. Patient who maintained effective spontaneous breathing for 24 hours after extubation was considered as successful weaning and those who needed reintubation were excluded from the study.

RESULTS

Statistical analysis and presentation of study was performed using mean and standard deviation, the chi-square as well as the logistic regression by SPSS V23. Chi-square describes that there is only relationship between dexmedetomidine and exubation time; therefore keeping in view the required hypothesis, logistic regression was applied. A significant decrease in extubation time

was observed in Group-B when compared with the Group-A (p=0.046) along with odds ratio 0.938 which indicates that there is an inverse relationship between dexmedetomidine and early exubation; that means the hypothesis is approved i.e. dexmedetomidine is more favourable than midazolam for sedation in intensive care patients by facilitating early exubation. As far as the length of stay at hospital is concerned, it is not showing any significant relationship with the type of drug.

DISCUSSION

In this study, dexmedetomidine seemed to decrease the mechanical ventilation duration when compared with midazolam. It is also associated with better communication of patient with staff as well.

Diminishing the period on mechanical ventilation decreases the risk of ventilator related complications such as delirium, pneumonia and stress ulcers and therefore has major cost implications.[8]

Extubation time is always longer with deep sedation and is directly related with increased mortality. Conversely, it is seen that calmness during mechanical ventilation can be accomplished with light sedation.[9]

Parameter	Mean±Sd		χ^2	P-Value
	Group A	Group B		
Age	41.97±10.21	42.57±10.93	16.86	0.951
Height(ft)	5.33±1.2	5.45±1.12	0.73	0.787
Weight(kg)	59.97±10.28	60.83±10.26	20.6	0.805
Extubation time(min)	91.30±15.53	70.2± 18.3	33.01	0.046
Length of stay(hrs)	80.4±10.737	67.33±10.33	29.26	0.210

Table-I. Demographic Data.

Gender / Surgery	Group A		Group B		Chi Square	
	n	%	n	%	χ^2	P-Value
Male	18	60	16	53	1.067	0.302
Female	12	40	14	47		
Total/ hemicolectomy	5	41.7	7	58.3	0.714	0.870
Partial gastrectomy	10	55.6	8	44.4		
Radical cystectomy	4	44.4	5	55.6		
Whipples operation	11	52.4	10	47.6		

Table-II. Comparison between groups regarding gender & type of surgery.

RASS (HR)	χ^2	P-Value
RASS 0	4.062	0.398
RASS 6	2.688	0.611
RASS 12	0.310	0.958
RASS 18	1.433	0.838
RASS 24	0.436	0.979
RASS 30	3.750	0.441
RASS 36	1.836	0.766
RASS 42	1.608	0.807
RASS 48	3.172	0.530

Table-III. Statistical analysis regarding RASS.

Recent guidelines have promoted a modification of intensive care unit sedation practices and the taking up of sedation strategies based on non-benzodiazepine sedatives that is either propofol or dexmedetomidine to improve outcomes in adult ICU patients who are mechanically ventilated.[9]

All patients of intensive care unit who are on mechanical ventilation require sedation to tolerate endotracheal tube, to facilitate mechanical ventilation, for various invasive procedures, repeated suctioning, to relieve anxiety and to blunt excessive metabolic and hemodynamic responses.[10] These patients typically have noteworthy anxiety and agony.[2] However, continuing lighter levels of sedation in these patients result in better outcomes.[11]

Dexmedetomidine has become accepted sedative drug in ICU as its sedation is calm, patients are responsive on command and it does not cause any respiratory drive depression or any agitation thus making possible early weaning from ventilator and decreasing overall ICU costs.[12] Dexmedetomidine is also recommended in delirious mechanically ventilated patients who have distress prohibiting extubation.[13]

Sedation vacation is act of titrating the dose of sedative to keep the patient comfortable and agitation free as well as keeping the dose at lowest possible rate.[14] The ideal level of sedation however differs according to the disease and treatment needs of the individual patient.[15] The patient agitation can be easily controlled on dexmedetomidine and as it does not depress the respiratory centre, patient can be extubated even on the continuous infusion of dexmedetomidine.[14]

Sedatives that work through γ-aminobutyric acid pathways like benzodiazepines and opioids badly affect the respiratory drive and may also cause patient ventilator asynchrony prolonging the time of mechanical ventilation. On the other hand, alpha2-agonists have favourable effect on respiratory drive facilitating early extubation.[16] As compared to clonidine, dexmedetomidine has eight times more affinity for alpha-2 adrenoceptors and it also decreases the plasma catecholamines levels reducing overall stress response.[17] Dexmedetomidine also decreases the requirement of opioids for analgesia which may cause neurocognitive disorders.[18] It is possible that its analgesic effects are responsible of decreasing incidence of delirium.[19] The alpha 2 receptor stimulation by dexmedetomidine in the brain prevents neuronal firing thus decreasing heart rate and blood pressure and increasing the sedation.[20]

This study coincides with work done by Nabila M and colleagues who stated that dexmedetomidine has benefit clinically as compared to midazolam in terms of early extubation and hence it can be used as an efficient and safe drug for sedation to facilitate early extubation in intensive care units.[3]

CONCLUSION

We conclude that in comparison to midazolam, dexmedetomidine is more favourable than midazolam for sedation in intensive care patients by facilitating early exubation and decreasing the duration of invasive ventilation while no significant relationship could be proved between length of stay in intensive care unit and type of drug. This could be explored in future in the larger data set of patients.

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1	Afia Arshed Dodhy	Corresponding author, Data collection, Literature review, Write up, Analysis of data result & conclusion.