Original Article

To Compare the Efficacy of Continuous Low-Dose Infusion of Dexmedetomidine & Intermittent Boluses of Dexmedtomidine in Preventing ICU-Induced Delirium

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ABSTRACT

Objective: To compare the efficacy of continuous low-dose infusion of dexmedetomidine and intermittent boluses of dexmedetomidine in preventing ICU-induced delirium.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Critical Care Medicine, PIMS, Islamabad from 1st of September 2022 to 30th of November 2022.

Materials and Methods: 64 patients having RASS score >+2 or <-2, ICDSC score of 4 or greater, and Pre DELERIC score greater than 40% were enrolled through consecutive non-probability sampling. Patients were randomly allocated either to Group A for continuous infusion or Group B for intermittent boluses of dexmedetomidine. Delirium will be screened by the Pre DELERIC tool within 24 hours of admission and the delirium established in patients will be monitored by ICDSC score daily till there's no clinical evidence of delirium. The primary outcome was the efficacy of preventing ICU-induced delirium between the two groups in achieving an ICDSC score of ≤3.

Results: Age ranges from 22 to 75 years with a mean age of 39.81±13.48 years. The male gender was dominant with 42 (65.62%) patients. The treatment outcomes show no significant difference between the two groups regarding the Mean±SD of RASS and ICDSC score. There was no statistically significant difference in the number of patients achieving ICDSC scores of ≤3 between the two groups.

Conclusion: Continuous infusion of dexmedetomidine or its intermittent boluses are equally effective in the treatment of ICU-induced delirium.

Key Words: Critical care unit, Delirium, Dexmedetomidine.

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INTRODUCTION

Delirium is commonly found manifestation but uncommonly monitored in the intensive care unit (ICU) and rarely discussed during rounds as it is considered by the healthcare team present there in ICU that they can't do anything regarding Delirium.[1]

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MATERIALS AND METHODS

This randomized control trial was conducted at the Department of Critical Care Medicine, Pakistan Institute of Medical Sciences, from September 2022 to November 2022.

Inclusion criteria were defined as patients above the age of 18 years and having

Richmond agitation scoring system (RASS) score >+2 or <-2, ICDSC score (Intensive care delirium screening checklist) of 4 or greater, and Pre DELERIC score greater than 40%.

While exclusion criteria were defined as patients having RASS score between +2 and -2, ICDSC score of 3 or less, Pre DELERIC score of less than 40%, hemodynamically unstable patients with hypotension and bradycardia, patients with impaired ventricular function (Ejection Fraction< 30%) and obstetrics patients.

The sample size is calculated with Open Epi software using 95% Confidence Level and power = 80%. Using

efficacy for treating ICU-induced delirium by 33% with continued dexmedetomidine infusion as compared to 5.6% with dexmedetomidine boluses.[9].

Estimated sample size n = 64 (32 in each group)

A total of 64 patients fulfilling the inclusion criteria using consecutive non-probability sampling were randomly allocated either to Group-A (32 patients) for continuous infusion of dexmedetomidine (Continuous infusion of Dexmedetomidine at 0.2 – 1.4 µg/kg/hr) or Group-B (32 patients) for intermittent boluses of dexmedetomidine (Intermittent bolus dosing of 1 µg/kg as bolus over 01 hour three times a day) depending upon their serial number of admission in the ICUs.

In group-A with continuous assessment, monitoring, and consultation with the treating physicians, bedside nursing staff adjusted drug infusion rates as necessary (re-assessing four hourly), aiming to minimize psychomotor agitation and achieve a RASS score of 0. Treatment will be continued for as long as clinically indicated, including following extubation if required, unless any adverse effect developed that would necessitate the drug discontinuation.

In case of agitated delirium not controlled despite adequate treatment with dexmedetomidine and the patient becomes hemodynamically unstable patient would be excluded from the study and rescue therapy with Haloperidol may be prompted as per consultant advice.

The primary outcome was the efficacy of preventing ICU-induced delirium between the two treatment groups in the shape number of patients achieving an ICDSC score of ≤3.

Delirium (Acute confusional state with alternating levels of awareness and fluctuating behavior within 24 hours) will be screened by the Pre DELERIC tool within 24 hours of admission. The delirium established in patients will be monitored by ICDSC (Intensive Care Delirium Screening Checklist) daily till there's no clinical evidence of delirium where a score of 4 will be taken as positive for established delirium. (Annex:1)

Permission for conducting the study was taken from the ethical committee of the Hospital.

Informed consent was taken from all the patient's attendants falling in inclusion criteria.

Data were analyzed using a statistical analysis program, SPSS-26. Frequency and percentage will be computed for qualitative variables like efficacy. Mean ±SD will be presented for quantitative variables like age and ICDSC score. Student t-test was applied to compare efficacy in both groups taking p ≤0.05 as significant.

RESULTS

The age range in this study was from 22 to 75 years with a mean age of 39.81±13.48 years. The male gender was dominant with 42 (65.62%) patients in the overall study population. Group-wise details of patients' demographics were shown in Table-1.

Table No. 1: Details of demographics in both groups. n=64

Demographics		Group-A (n=32)	Group B (n=32)
Age (years)		42.18±12.85	37.43±13.88
Gender	Male Frequency (%)	18 (56.25)	24 (75)
	Female Frequency (%)	14 (43.75)	8 (25)

The clinical details and findings during the stay in ICU were comparable between the 2 groups as shown in Table 2.

Table No. 2: Clinical Findings of Patients n=64

Clinical details of patients	Group-A (n=32)	Group B (n=32)	p-value
BMI (Kg/m2)	24.84±2.73	24.71±2.67	0.84
Days of ventilation	3.56±1.75	4.87±4.84	0.15
Pre Deleric score	53.65±7.54	54.56±6.82	0.61

The treatment outcomes show no significant difference between 2 groups regarding the Mean±SD of RASS, ICDSC score, and the number of patients achieving ICDSC score of ≤3 as shown in Table 3.

Table No. 3: Details of Demographics and clinical parameters in both groups n=64

Treatment Outcomes	Group-A (n=32)	Group B (n=32)	p-value
RASS (Mean±SD)	1.84±1.22	2.25±1.07	0.15
ICD SC Score (Mean±SD)	2.25±0.91	2.06±1.24	0.48
Number of patients with ICD SC Score 3 or less n (%)	26 (81.25)	24 (75%)	0.36

Agitated delirium was not controlled despite adequate treatment with dexmedetomidine in 5 patients in Group-A and 7 patients in Group B and these hemodynamically unstable patients were excluded from the study. Rescue therapy with haloperidol was prompted as per the consultant's advice.

DISCUSSION

Dexmedetomidine has been found to be more effective and safer compared to conventional treatment options for the treatment of delirium and agitation in ICU patients.

Different dose regimen has been employed in different studies to evaluate the dose with maximum benefit and good safety profile for the patients.

Rodriguez K in their retrospective review mentioned the lowest dose of dexmedetomidine as 0.2 (0.1-0.3), the highest dose of 2.4 (2.1-2.5) while an average dose of 1.6 (1.2-2.1) µg/kg/hr used in the study and compared them for their efficacy and safety profiles. The study results concluded that doses above 1.5 mcg/kg/hr although safe but not more effective in achieving and maintaining the levels of sedation.[15]

Gu Y et al. in a placebo-controlled trial studied different doses of dexmedetomidine on the dose requirements of propofol for loss of consciousness. Different dose groups of dexmedetomidine were 0.5 µg·kg− 1 and 1.0 µg·kg− 1 infusion and the results showed that both doses were equally effective in reducing the dose of propofol.[16]

Su X et al. studied the low-dose dexmedetomidine (iv 0.1 µg/kg per h), starting from the admission to ICU up to 8 hours postoperatively, as prophylactic to decrease delirium after surgery in elderly patients aged 65 years or above. In this randomized controlled study against a placebo primary endpoint was set as the incidence of delirium assessed twice a day. The incidence of postoperative delirium was significantly low in the dexmedetomidine group compared to the placebo group (9% Vs 23%, p=0.000). The treatment was also safe with no increased incidences of hypertension, hypotension tachycardia, or bradycardia.[17]

Skrobik Y determined the efficacy of dexmedetomidine to prevent nocturnal delirium and to improve sleep quality in critically ill patients. They used IV 0.2 mg/kg/h dose of dexmedetomidine which was titrated up by 0.1 mg /kg/h every 15 minutes until they achieved RASS score of 21. The maximum dose used was 0.7 mg/kg/h. The result of this double-blind placebo controlled trial was that 80% of the patients remained free of delirium with dexmedetomidine compared to 54% with placebo (P = 0.006) during their ICU stay. The researchers concluded that the low doses of dexmedetomidine given at night minimize the incidence of delirium in critically ill patients.[18]

The latest review published in 2022 discussed dexmedetomidine for providing sedation and minimizing the risk of delirium due to a unique mode of action. The dose of the drug was mentioned as a bolus dose of 1 mcg/kg for 10 min and then continuous infusion at starting 0.1mcg/kg/hr. The conclusion of the review mentions dexmedetomidine as providing sedation, managing symptoms of delirium and offering primary analgesia, and controlling the adverse effects related to other medications.[19]

The mean age of patients in our study was 39.81±13.48 years with an age range from 22 to 75 years. The male gender was dominant with 42 (65.62%) patients in the overall study population. The other parameters like BMI, days of ventilation, and Pre DELERIC score were comparable among the two groups. The Mean±SD of the RASS score was 1.84±1.22 in Group-A while 2.25±1.07 in Group B (p-value=0.15). The Mean±SD of the ICD SC Score was found as 2.25±0.91 in Group-A and 2.06±1.24 in Group B (p-value=0.48). There was no significant difference between Group-A and Group B regarding primary outcome i.e. efficacy of preventing ICU-induced delirium assessed through a number of patients achieving ICDSC scores of ≤3, as 26 (81.25%) patients in Group-A and 24 (75%) patients in Group-B were free of delirium.

No previous study has used the dosage regimen used in our study however the results of our study are similar in efficacy with both doses in preventing ICU-induced delirium as shared with different doses of the drug in studies discussed above.[15,16,17,18,19] Both continuous low-dose infusions of dexmedetomidine (Continuous infusion at 0.2 – 1.4 µg/kg/hr) and intermittent boluses of dexmedetomidine (1 µg/kg as a bolus over 01 hours three times a day) are equally effective in preventing ICU induced delirium.

The major limitation of our study is the small number of patients enrolled in this study so future studies with a larger number of patients will be helpful in comparing the efficacy of dexmedetomidine with either continuous low dose or intermittent boluses.

CONCLUSION

Continuous infusion of dexmedetomidine or its intermittent boluses is equally effective in the treatment of ICU-induced delirium. Hence in settings where continuous infusions aren't available or expensive to afford, intermittent boluses can be used as an option to treat delirium.

Author's Contribution:

Concept & Design of Study:	Sadia Imran
Drafting:	Usman ul Haq, Imran ul Haq
Data Analysis:	Muhammad Ali, Muhammad Fareed Azam, Mahjabeen
Revisiting Critically:	Sadia Imran, Usman ul Haq
Final Approval of version:	Sadia Imran

Conflict of Interest: The study has no conflict of interest to declare by any author.

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