Original Article

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A Comparative Study used to Evaluate the Quality of Sedation using Dexmedetomidine and Propofol Infusion in Critically Ill Patients Admitted in ICU

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Abstract

Introduction: The ICU environment produces high level of stress, strain and discomfort to the patients with physiochemical, physiological psychological alterations. So adequate level of analgesia and sedation to the patient is necessary for better outcome. We compared a relatively new sedative dexmedetomidine to gold standard sedative propofol with respect to sedation, analgesia, effect on hemodynamic parameters in patients admitted in ICU. *Aims & Objective:* 1. To compare the effectiveness of sedation with dexmedetomidine and propofol in critically ill patient in ICU. 2. To compare haemodynamic and any adverse events observed in both groups. *Method:* To evaluate this Forty (40) patients of ASA grade I to III, aged 18–60 yr, who were admitted in the ICU were divided into two equal groups in a randomized, double blinded fashion. Group A received I.V Dexmedetomidine 1 µg/kg in 10 mints as initial loading dose followed by 0.2-0.7 µg/kg/min. Group B received I.V. propofol 75 µg/kg/min in 10min followed by maintenance dose of 12.5µg/kg/min.The Ramsay sedation scores and hemodynamic (SBP and HR) and respiratory (RR) variables were recorded at baseline, at 10 min, at 30 min, at 1hr and 4hrly for 24 hr. *Observation:* Following parameter will be monitored (1) Quality of sedation using Ramsay sedation score. (2) H.R (3) R.R (4) NIBP (5) Spo_2 (6) Adverse events. *Conclusion:* Dexmedetomidine has excellent sedation for the patient admitted in ICU as compare to Propofol. Dexmedetomidine is a safe sedative agent with patient easily aroused to co-operative without showing irritation. Patients remained hemodynamically stable with minimal depression of cardiovascular system and respiratory functions in Dexmedetomidine group when compared to Propofol group.

Keywords: Dexmedetomidine; Propofol; Sedation; Mechanical Ventilation.

Introduction

The Intensive care unit (ICU) environment produces high level of stress, strain and discomfort to the patients with physiochemical, physiological and psychological alteration resulting in increased morbidity and mortality. Hence, adequate level of analgesia and sedation to the patients is necessary for better outcome.

An ideal sedative should be easy to administer with rapid onset and offset, should have cardio-respiratory stability and should be devoid of toxicity. Despite the mention of many sedative agents in the literature, no agent is near perfect.

The most commonly used drugs are midazolam, propofol and fentanyl. All of these drugs cause respiratory depression [1,2]. Propofol is a very short acting nonopioid sedative-hypnotic agent with rapid onset and offset but with narrow therapeutic index leading to risk of progression into deep sedation. The adverse respiratory profile of benzodiazepines, propofol and opioids, along with the stress response in intensive care, create the need for a sedative that

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can be used safely in ICU in both healthy and high risk patients with limited adverse effect.

Dexmedetomidine is increasingly being used as a sedative both for intubated and non-intubated patient in ICU because of its analgesic properties, co-operative sedation, lack of respiratory depression and its sympatholytic effect. This pharmacologic profile, combined with a very impressive safety margin, has made it an attractive choice for anaesthesiologists and intensivists [3].

This randomized, double-blind, clinical study was designed to compare the effectiveness of sedation, haemodynamic and respiratory parameter with dexmedetomidine and propofol in critically ill patient admitted in ICU.

Aims & Objectives

1 Compare the effectiveness of sedation with dexmedetomidine and propofol in critically ill patient admitted in ICU.

2 There haemodynamic and respiratory parameter

Material & Methods

Forty post-operative patients ASA grade I to III, aged 18–60 yr, who were admitted in the PMCH SURGICAL ICU Planned for elective ventilation for 24hr period enrolled in this randomized, double blind, clinical study.

Exclusion Criteria

Known or suspected allergy to dexmedetomidine or propofol, Severe hepatic or renal disease, Chronic use of α-agonist, Requirement of muscle relaxant, other than for intubation (succinylcholine), Pregnancyor lactation, Severe pulmonary or cardiac disorder, Age <18 yr, History of sleep apnoea, or body weight 50% greater than ideal body weight, Receiving total parenteral nutrition.

After approval by hospital ethical committee, informed consent was taken for the study. The patients were be allocated by computer-generated random numbers into two groups each comprising of 20 patients. The random allocation sequence is concealed in opaque, sealed envelopes until a group was assigned. In patients randomized to the dexmedetomidine group (Group I), an initial loading dose of dexmedetomidine (1μg/kg) was infused IV for 10 minutes followed by 0.2 – 0.7 μg /kg/hour.In patients randomized to the propofol group(Group II), an initial loading dose of propofol (75 μg /kg/min) was infused for 10 minutes followed by maintenance dose of 12.5 – 75 μg /kg/min.The evaluation of quality of sedation was based on a six point Ramsay Sedation Score (RSS) 4 and according to the sedation level infusion dose was decreased to one half or increased to twice to maintain the adequate sedation score of 2 to 4 of Ramsay scale. Pain was considered as the 1st cause of inadequate analgesia/sedation. Any increase in 20% heart rate/ MAP will be treated with bolus dose of morphine at 0.05mg/kg dose before increasing the dose of dexmedetomidine or propofol The Ramsay sedation scores and hemodynamic (SBP and HR) and respiratory (RR) variables were recorded at baseline, at 10 min, at 30 min, at 1hr and 4th hrly for 24 hrs. Patient were ventilated mechanically with oxygen enriched air. The sedative infusion was discontinued in preparation for extubation when patient was cardiovascularly stable, normothermic and with PO2 of 80-110 mm Hg on an FiO2 of less than 40%. Once spontaneous respiration has been established with pressure support < 10 cm H2O, a tidal volume of > 6 ml/kg, respiratory rate > 10 breaths/minute but < 20 breaths/minute, extubation was undertaken. Extuabtion time was defined as the time from cessation of sedation infusion to extubation heart rate, arterial pressure, central venous pressure and oxygen saturation were monitored continuously. Venous samples were taken for all routine haematological and biochemical profiles immediately on arrival to intensive care unit, and then at 24 and 48 hours. Cardiovascular and respiratory adverse events were defined as a change in arterial pressure of > 40% from baseline, bradycardia < 50bpm, tachyarrhytmia and a respiratory rate <8 or > 25 breaths/minute after extubation.

The evaluation of quality of sedation was based on a six point Ramsay Sedation Score (RSS) [4] and according to the sedation level infusion dose was decreased to one half or increased to twice to maintain the adequate sedation score of 2 to 4 of Ramsay scale.

Pain was considered as the 1st cause of inadequate analgesia/sedation. Any increase in 20% heart rate/ MAP will be treated with low dose of tramadol 5 mg/kg before increasing the dose of dexmedetomidine or propofol. My observation period was approximately 24 hrs.

The Ramsay sedation scores and hemodynamic (SBP and HR) and respiratory (RR) variables were recorded at baseline, at 10 min, at 30 min, at 1hr and 4th hrly for 24 hrs.

Statistical Analysis

Data are presented as mean ± SD and percentage as appropriate. Statistical analyses was performed by Fisher's exact test and chi-square test for nominal data. Where it was found significant, randomised block analysis of variance (ANOVA) was done for each group and't' test for each point was done for comparison between the groups. 'P' value <0.05 was considered statistically significant.

Observation & Results

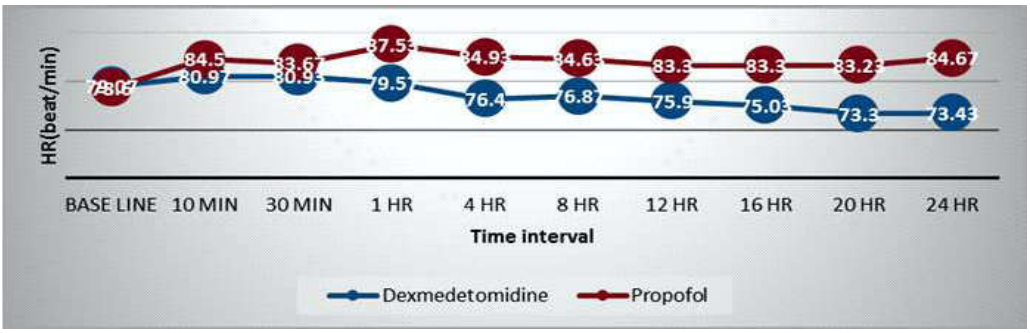
Demographics

Forty patients were entered into this study.The two groups were comparable with respect to the following variables; age, sex, weight, ASA status, and duration of surgery (*P*>0.05).

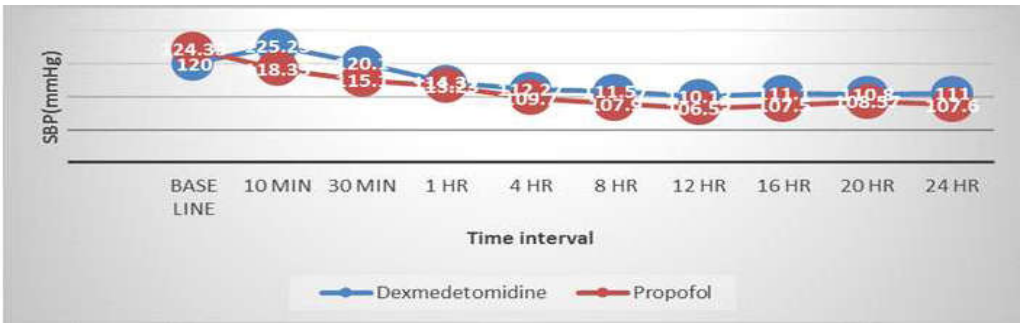
Heart Rate

In the present study, there is drop in the Pulse rate at 10 minutes to 4hr in the Dexmedetomidine group, with mean pulse rate at 10 minutes of 80.97 (SD: 12.88) and at 4hr mean was 76.40 (SD: 12.61) when compared to Propofol group.

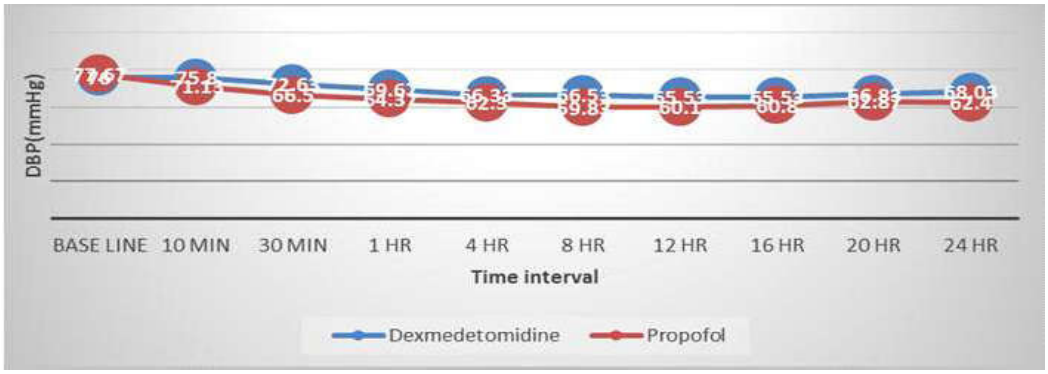
There is drop in SBP (mmHg) in the Dexmedetomidine and propofol Group with mean at 30 min 120.10 (SD: 14.30) in Dexmedetomidine group and 115.10 (SD: 14.77) in the Propofol group with p value of 0.2836 and At 1hr 114. 37(SD: 14.17) in the Dexmedetomidine group and mean of 113.23 (SD: 15.29) in Propofol group with p value of 0.8081 respectively.



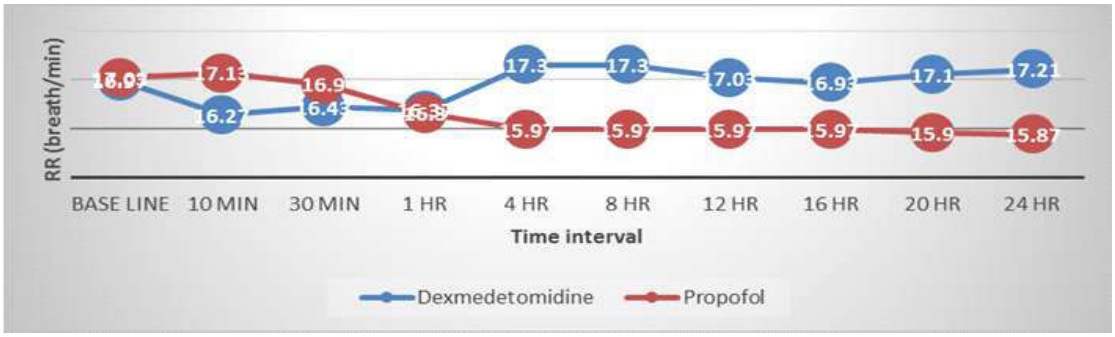
Graph 1: Line Graph showing HR in Dexmedetomidine and Propofol group



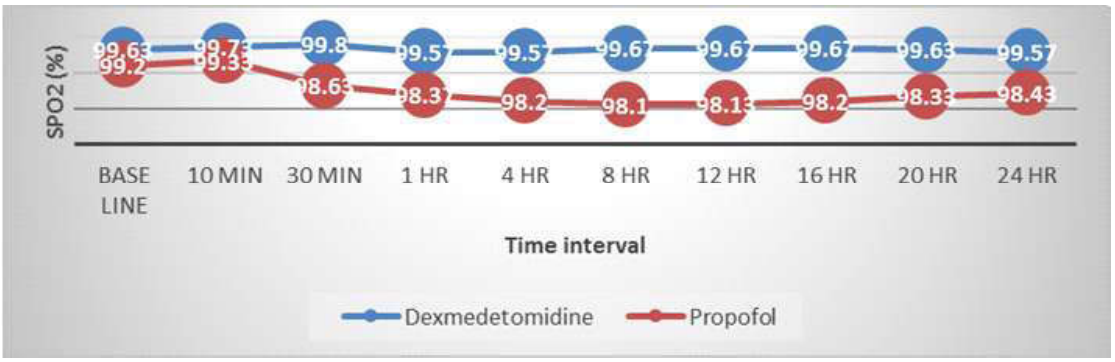
Graph 2: Line Graph showing Systolic Blood Pressure (mmHg) in Dexmedetomidine and Propofol Group



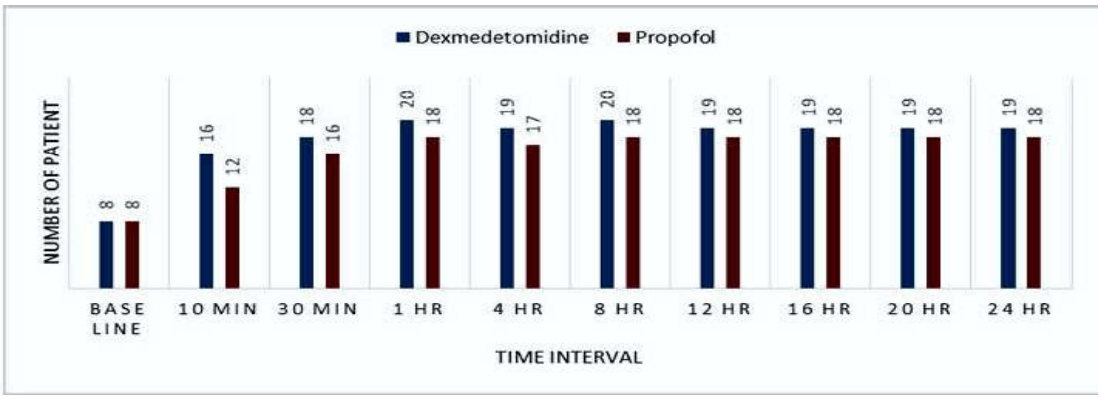
Graph 3: Line Graph showing diastolic Blood Pressure (mmHg) in Dexmedetomidine and Propofol



Graph 4: Line chart showing Respiratory Rate (per minute) in the Dexmedetomidine and Propofol Group



Graph 5: Line graph showing SpO2 (%) in Dexmedetomidine and Propofol Group



Graph 6: Histogram showing the number of patients who were optimal sedation at different time period

There is drop in DBP (mmHg) in the dexmedetomidine and Propofol Group with mean at 10 min 75.80 (SD: 10.09) in dexmedetomidine group and 71.13 (SD: 11.83) in the propofol group with p value of 0.1872 and at 1hr 69.67 (SD: 8.20) in the dexmedetomidine group and mean of 64.37 (SD: 12.23) in propofol group with p value of 0.1157 respectively.

Respiratory rate (in minutes) is maintained in bothGroup Iand Group II. The change in respiratory rate was similar in both the groups and was not found to be statistically significant. the RR values in the group I were significantly increased (P<0.05) compared with baseline values, while there was significant reduction in the RR in the group II (P<0.05) compared with baseline values. RR values in the group I were significantly higher than those in the group II during the sedation period (P<0.05).

Though the fall in SpO2 is significant between two groups, clinically it is maintained above (>95%) in both the Dexmedetomidine and Propofol Groups.

Patients showing acceptable Ramsay sedation score 2 – 5.

More number of patients in dexmedetomidine group had acceptable sedation compared to propofol group. However, patients in propofol group tended to have excessive sedation more often than patients

in dexmedetomidine group. This was found to be statistically significant (p=0.039).

Side effects-The incidence of dry mouth, nausea, vomiting and oxygen supplementation were similar between the study groups. Deep sedation causing hypotension, bradycardia, or respiratory depression (SpO2 _92%) was not encountered in any patient.

Discussion

The intensive care environment is stressful for the patient who experience anxiety, pain and inability to sleep. It is the moral responsibilityof the physician attending these patients to appropriately manage these aspects as relief of pain and anxiety is often neglected while efforts are mostly focused on immediate life threatening events.

We study the effect of continuous infusion of dexmedetomidine and propofol on fourty postoperative patients who were mechanically ventilated for a duration of 24 hours.

Alpha 2-adrenoceptor agonists are being increasingly used in anaesthesia and critical care as they not only decrease sympathetic tone and attenuate the stress responses to anesthesia and surgery; but also cause sedation and analgesia. They are also used as adjuvant during regional anesthesia. Dexmedetomidine is the most recent agent in this group approved by FDA in 1999 for use in humans for analgesia and sedation.

In our study there was no difference between the groups in patient characteristics and other demographic data.

Quality of Sedation

Venn RM, Ball J, et al [15] in 2000 studied dexmedetomidinefor sedation in medical ICU. They concluded that dexmedetomidine provides safe, titrate sedation with cardiovascular stability for critically medical patients requiring artificial ventilation.

R. M. Venn and R. M. Grounds [19] in 2001 compared dexmedetomidine and propofol for sedation in the ICU. He concluded dexmedetomidine appears to be a safe and acceptable ICU sedative agent when both the clinician and patient perceptive are considered. Depth of sedation and cardiovascular response similar in both group but patient receiving dexmedetomidine do not increase their heart rate. These properties combined with analgesic qualities and lack of respiratory depression seen with dexmedetomidine, have advantage in patient of myocardial ischemia.

Samia Elbaradie et al [20] in 2004 Compare Dexmedetomidine vs Propofol for short term sedation of postoperative mechanically ventilated patients in ICU. He concluded that dexmedetomidine is a safe sedative agent with patients easily aroused to co-operate without showing irritation. Dexmedetomidine significantly reduced the requirement for fentanyl analgesia.

Azrina Md Ralib, Saedah Ali et al [21] in 2007 compare Dexmedetomidine and propofol for sedation in the cardiothoracic ICU. He concluded Dexmedetomidine is comparable to propofol in the provision of sedation and its effect on haemodynamic and respiratory parameters. However, it has added advantages in the provision of analgesia and causes a significant reduction in heart rate.

Sessler CN, Varney K. [22] in 2008 Patient focused sedation and analgesia in the ICU in postoperative and trauma patient has been shown to decrease opiate use and to facilitate extubation in patient who have failed previous ventilator weaning attempts due to severe agitation.

In our study significant number of patients in dexmedetomidine group had acceptable sedation compared to propofol group and patients in propofol group tended to have excessive sedation more often than patients in dexmedetomidine group. These findings suggest that dexmedetomidine may provide advantages over propofol as a sedative drug in ICU.

Patients in dexmedetomidine group was shown in the results. This showed that dexmedetomidine showed conscious sedation. This was not seen in propofol group. This is clinically important when a rapid recover from sedation is necessary to assess neurologic functions which suggests that dexmedetomidine demonstrates excellent attributes for an anaesthetic.

Jalowiecki et al [8] evaluated the ability of dexmedetomidine to provide analgesia and sedation for outpatient colonoscopy.

In contrast to our study, they suggested that the use of dexmedetomidine to provide analgesia/ sedation for colonoscopy is limited by its distressing side effects, profound hemodynamic instability and a complicated administration regimen. Our study differed in that, for both the dexmedetomidine and propofol group did not show hemodynamic instability or any distressing side effects that required any treatment.

Cardiovascular and Respiratory Parameter

Patients in both the groups of our study had decreased blood pressure compared to baseline However, this decrease in BP did not require treatment in either group.

In addition Patients receiving propofol had significantly decreased blood preasure levels compared to dexmedetomidine groups. Similarly various studies have demonstrated a powerful inhibitory effect of propofol on sympathetic outflow [9]. Dexmedetomidine also is known to decrease sympathetic outflow and circulating catecholamine levels and would therefore be expected to cause decreases of MAP similar to those of propofol [10,11]. However, larger doses of dexmedetomidine have a direct effect at the postsynaptic vascular smooth muscle to cause vasoconstriction, and it is possible that the sympathoinhibitory effects of dexmedetomidine were slightly opposed by direct α_2-mediated vasoconstriction [12]. In contrast, propofol has no direct effects on vascular smooth muscle [13]. The present study demonstrated decrease in HR compared to baseline in both the groups. In other studies also dexmedetomidine has been associated with decreases in HR, in part because of the sympatholytic effects of this drug, but also because of a vagal mimetic effect [14].

Anecdotal reports describe incidents of respiratory depression during infusions of propofol for sedation. However, in the present study, patients receiving propofol did not have significant respiratory depression.

This preservation of respiratory function may be related to the study design that did not include a bolus dose of propofol at sedation administration and the close monitoring and frequent patient queries by independent observers in the ICU. Dexmedetomidine has not been associated with respiratory depression despite oftentimes profound levels of sedation [10,15].

In our Study also there was preservation of respiratory function with the use of dexmedetomidine. Hsu et al [16] have reported a significant increase in RR with dexmedetomidine, whereas Belleville et al [17] reported a significant decrease in RR. This discrepancy may result from the physiologic reactions due to arousal phenomenon. This discrepancy could also have resulted from the fact that boluses were used in the study of Belleville et al., whereas Hsu et al [16] used infusions that resulted in sustained and higher dexmedetomidine concentrations.

Undesirable Effects and Complications

Klement et al (1991) [18] studied the effects of concentration and diluents in producing pain on injection of Propofol. He concluded that the intensity of pain after i.v injection of Propofol was related to its free aqueous concentration. In our study 20% of the patients had pain on injection, 5% of patients had nausea, and vomiting and 20% patient require oxygen supplementation in Propofol group. However, 20% of the patient complain dry mouth and 5% require oxygen supplementation in Dexmedetomidine group.

Conclusions

It is concluded that,

1. Both dexmedetomidine and propofol were effective in providing adequate level of sedation. Dexmedetomidine, at the doses used in this study, had a significant advantage over propofol in terms of haemodynamic stability and acceptable sedation at most of the time with rapid onset and recovery parameters. However, weaning from mechanical ventilation was significantly better in Dexmedetomidine than propofol sedation. Patient in Dexmedetomidine group had a shorter duration on SIMV mode of ventilation and were wean more rapidly than in propofol group.
2. Patients remained hemodynamically stable with minimal depression of cardiovascular system and respiratory functions, and also with less amnesic effects in Dexmedetomidine group when compared to Propofol group. Propofol treated patient tended to remain in excessive sedation on more number of occasion than Dexmedetomidine treated patient.
3. There were minimal undesirable side effects in both the group.

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