Original Research Article

A comparative study of dexmedetomidine propofol and midazolam with respect to changes in heart rate and blood pressure after sedation at tertiary health care centre

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Abstract

Background: Sedation is frequently required as a component of compassionate care in these patients. Use of sedation is important to help achieve the right balance between sleep and wakefulness; the correct balance is essential for incorporating physical activity and patients cooperation in the plan of care. Other goals of adequate sedation include optimizing safety for patients and caregivers, facilitating mechanical ventilation, reducing anxiety and delirium, inducing sleep, and, ultimately, providing comfort and safety. In present study, we compared the sedative and analgesic properties of dexmedetomidine with those of the commonly used i.v. sedative agent propofol and midazolam with respect to Changes in Heart rate and Blood pressure after sedation in ICU at tertiary health care centre. **Material and Methods-** This study was randomized. open label trial conducted in the ICU in patients >18 years of age, who required immediate sedation as to permit the initiation and tolerance of mechanical ventilation. Patient enrolled in the study divided into three groups (dexmedetomidine, propofol and midazolam). 30 patients allocated for each group. **Results:** According to age distribution most common age group in dexmedetomidine, propofol and midazolam group was 31-45 years (40 %), 18-30 years (40 %) and 46-60 years (36 %) respectively. Mean ± SD in age group in dexmedetomidine, propofol and midazolam group was 37.03 ± 12.75 years, 36.7 ± 12.18 years and 37.9 ± 12.48 years respectively. Male predominance was noted, in all groups. A statistically significant difference was present among the groups During sedation, From stoppage of sedation of extubation and At extubation. There is no significant difference present among the groups in baseline pulse rate and from extubation to ICU discharge. **Conclusion:** Dexmedetomidine is a satisfactory agent for sedation in ICU. There was no significant difference in time to ICU discharge in all the three groups. There was significant difference in the heart rate of the patients during sedation. Lower heart rate was seen in dexmedetomidine receiving patients. Blood pressure and respiratory rate were lower in dexmedetomidine and propofol group though it's not statistically significant.
Keywords: IV sedation; Dexmedetomidine, Propofol; Midazolam; SBP; DBP; Heart rate; Respiratory rate

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INTRODUCTION

Patients in ICU are exposed to a variety of noxious stimuli including pain after surgery, frequent venepuncture and discomfort from the presence of an endotracheal tube. Sedation is frequently required as a component of compassionate care in these patients. Promotion of rest and sleep in critically ill patients facilitates healing.

Use of sedation is important to help achieve the right balance between sleep and wakefulness; the correct balance is essential for incorporating physical activity and patients cooperation in the plan of care. Other goals of

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adequate sedation include optimizing safety for patients and caregivers, facilitating mechanical ventilation, reducing anxiety and delirium, inducing sleep, and, ultimately, providing comfort and safety.

Inadequate sedative techniques may adversely affect morbidity and even mortality in the intensive care unit (ICU), and the search for the ideal sedative agent continues. The ideal agent should satisfy the physician's desire for an effective, safe, titratable, cheap and rapidly acting drug that has both sedative and analgesic properties, and should also prevent anxieties and unpleasant memories for the patient.

In present study, we compared the sedative and analgesic properties of dexmedetomidine with those of the commonly used i.v. sedative agent propofol and midazolam with respect to Changes in Heart rate and Blood pressure after sedation in ICU at tertiary health care centre.

MATERIAL AND METHODS

After approval from ethical committee and written informed consent of the patient, 90 patients were recruited for the study. This study was randomized. open label trial conducted in the ICU in Basaveshwar Teaching and General Hospital, Kalaburagi. Assessment as to whether patients would require sedation for short term (<24 hr), medium term (>24 to <72 hr) or long term >72hr) mechanical ventilation on admission to ICU was done. Patients stratified by predicted sedation time while receiving mechanical ventilation, were randomized and were entered into trial.

Inclusion criteria

- Patients >18 years of age
- Patients who require immediate sedation as to permit the initiation and tolerance of mechanical ventilation.

Exclusion criteria

- Known or suspected allergy or intolerance to dexmeditomedine, propofol or midazolam.
- Pregnancy.
- Head injury
- Patient currently treated with or been treated with alpha-2 agonist and blockers.
- Status epilepticus.
- Coma due to cerebrovascular accidents or unknown etiology.
- Acute unstable angina.
- Acute myocardial infarction.

Patient enrolled in the study divided into three groups. There are 30 patients allocated for each group.

GROUP 1: Patient randomized in dexmedetomidine group received a loading dose of dexmedetomidine 0.5 to 1 mcg/kg over 10 minutes followed by a maintenance infusion of 0.1 to 1 mcg/kg/hr. The rate of the maintenance was subsequently titrated to achieve a target Ramsay sedation score that was specified for each for each patient response to therapy.

GROUP 2: Patients randomized to the propofol group received a loading dose of 0.5 to 1mg/kg then an infusion of 25 to 75 mcg/kg/min was adjusted to achieve the target Ramsay sedation score. As for the propofol group in situations in which rapid control of sedation was required an infusion bolus could be administered.

GROUP 3: Patients randomized in midazolam group received an infusion of 0.012 to 0.024 mg/kg/hr adjusted to achieve the target Ramsay sedation score. Situations in which rapid control of sedation was required an infusion bolus could be administered.

Only tramadol 1mg/kg was given to patients of all the three groups as analgesic agent.

Measurement Scales

The Ramsay sedation score was used to quantitate the desired degree of sedation, specified at the regular intervals and adjusted as the patient's condition (i.e. recovery or deterioration) dictated. Patients were maintained at Ramsay sedation score of >2 by adjustments to the sedative regimens. Patients receiving muscle relaxants and sedation were given a Ramsay sedation score of 6. The Ramsay sedation score (target and actual) was recorded hourly for the first 72 hours or up to the time of discharge from ICU if this occurred prior to 72 hours. After 72 hours, it was recorded as the patient's condition or infusion rate was altered. Time to tracheal extubation, time to ICU discharge and requirements of reintubation were recorded. A record of vital signs was maintained every 20 minute for 40 minutes, then every 6 hour for 48 hours following extubation or until ICU discharge, whichever comes first. Decisions as to when a patient was ready for a trial of extubation or for discharge from the ICU were left to the attending intensivists.

Ramsay sedation scale to judge sedation level in critically ill patients.

Awake	Asleep
Anxious and / or agitated	Quiescent with brisk response to light glabellar tap or Loud auditory stimulus
Cooperative, oriented and tranquil	Sluggish response to light glabellar tap or loud auditory stimulus.
Response to command	No response

Complications which occurred as a result of patient's conditions, mechanical ventilation or infusion of sedative agent were recorded in all the three groups. All statistical analyses were performed using INSTAT for windows. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Data was expressed as either mean and standard deviation or numbers and percentages. All the data were compared with One way Analysis of Variance (ANOVA).

RESULTS

30 patients each were randomly allocated to dexmedetomidine, propofol and midazolam group. According to age distribution most common age group in dexmedetomidine, propofol and midazolam group was 31-45 years (40 %), 18-30 years (40 %) and 46-60 years (36 %) respectively. Mean ± SD in age group in dexmedetomidine, propofol and midazolam group was 37.03 ± 12.75 years, 36.7 ± 12.18 years and 37.9 ± 12.48 years respectively.

Table 1: Age Distribution

Age (yrs)	Dexmedetomidine		Propofol		Midazolam	
	No	%	No	%	No	%
18-30	8	26	12	40	9	30
31-45	12	40	9	30	10	34
46-60	10	34	9	30	11	36
Mean ± SD (yrs)	37.03 ± 12.75		36.7 ± 12.18		37.9 ± 12.48	

Male predominance was noted, in all groups (dexmedetomidine, propofol and midazolam). M : F Ration for Dexmedetomidine was 1.3 : 1, M : F ratio for propofol was 1.5: 1 and M: F ratio for midazolam was 1.4: 1. Total M:F ratio was 1.3 : 1.

Table 2: Sex Distribution

Sex	Dexmedetomidine		Propofol		Midazolam	
	No	%	No	%	No	%
Male	17	56	18	60	16	54
Female	13	44	12	40	14	46
Total	30		30		30	

P value is calculated by one way analysis of variance (ANOVA). in all three groups in not statistically significant. (P > 0.05). A statistically significant difference was present among the groups During sedation, From stoppage of sedation of extubation and At extubation. There is no significant difference present among the groups in baseline pulse rate and from extubation to ICU discharge.

Table 3: Mean Changes in Pulse Rate

	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine (Mean ± SD)	92.00 ± 3.7	78.26 ± 4.97	83 ± 2.56	84.7 ± 2.27	89.21 ± 0.75
Propofol (Mean ± SD)	92.26 ± 3.55	85.66 ± 3.02	92.33 ± 1.74	94.23 ± 1.47	92.49 ± 0.84
Midazolam (Mean ± SD)	92.6 ± 3.64	84.93 ± 2.21	93.86 ± 1.814	94.4 ± 1.32	92.45 ± 0.85
P value	>0.05	<0.0001	<0.0001	<0.0001	>0.05

The difference in respiratory rate was not significant at baseline, during sedation, from stoppage of sedation to extubation and extubation to ICU discharge.

Table 4: Mean Changes in Respiratory Rate

Drugs	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine (Mean ± SD)	18.83 ± 1.36	13.93 ± 0.78	14.5 ± 0.5	14.46 ± 0.5	14.6 ± 0.56
Propofol (Mean ± SD)	18.46 ± 2.36	14 ± 0.83	14.56 ± 0.5	14.5 ± 0.5	14.5 ± 0.50
Midazolam (Mean ± SD)	18.56 ± 1.04	13.93 ± 0.78	14.53 ± 0.5	14.56 ± 0.5	14.53 ± 0.50
P value	>0.05	>0.05	>0.05	>0.05	>0.05

At all times the difference is systolic blood pressure among all the three groups calculated by ANOVA test is not statistically significant (P > 0.05).

Table 5: Mean Changes in Systolic Blood Pressure

Drugs	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine (Mean ± SD)	132.7 ± 11.1	121.6 ± 8.61	125.8 ± 8.88	126.9 ± 9.47	119.8 ± 9.5
Propofol (Mean ± SD)	134.8 ± 11.5	118.8 ± 10.1	127.4 ± 10.09	128.2 ± 10.10	121.4 ± 9.26
Midazolam (Mean ± SD)	134.3 ± 15.2	123.6 ± 8.79	126.9 ± 9.74	128.4 ± 8.78	122.9 ± 9.17
P value	>0.05	>0.05	>0.05	>0.05	>0.05

At all times the difference is dystolic blood pressure among all the three groups calculated by ANOVA test is not statistically significant (P > 0.05).

Table 6: Mean Changes in Diastolic Blood Pressure

	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine (Mean ± SD)	77.87 ± 8.40	73.56 ± 7.40	74.89 ± 7.26	74.23 ± 6.96	76.22 ± 6.01
Propofol (Mean ± SD)	76.32 ± 7.56	70.75 ± 7.56	74.98 ± 6.47	73.23 ± 7.14	75.04 ± 6.90
Midazolam (Mean ± SD)	75.98 ± 8.03	73.99 ± 7.48	74.67 ± 6.95	75.33 ± 7.36	74.44 ± 6.09
P value	>0.05	>0.05	>0.05	>0.05	>0.05

At all times difference in mean blood pressure among all the three groups calculated by ANOVA test is not statistically significant (P > 0.05).

Table 7: Mean Changes in Mean Blood Pressure

Drugs	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine (Mean ± SD)	96.21 ± 5.98	89.23 ± 6.11	89.78 ± 6.07	90.11 ± 7.46	89.98 ± 4.69
Propofol (Mean ± SD)	95.56 ± 6.85	86.86 ± 5.48	86.21 ± 4.38	87.73 ± 5.27	88.78 ± 5.69
Midazolam (Mean ± SD)	95.11 ± 7.91	90.99 ± 6.49	90.54 ± 6.17	90.11 ± 6.11	89.99 ± 5.42
P value	>0.05	>0.05	>0.05	>0.05	>0.05

At all times the difference in SPO_2, blood pressure among all the three groups calculated by ANOVA test is not statistically significant (P>0.05).

Table 8: Mean Changes in SpO_2

Drugs	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine (Mean ± SD)	98.33 ± 0.95	98.78 ± 0.68	98.21 ± 0.71	98.99 ± 0.64	98.11 ± 0.63
Propofol (Mean ± SD)	97.6 ± 1.08	98.21 ± 0.58	98.34 ± 0.66	98.22 ± 0.63	98.1 ± 0.63
Midazolam (Mean ± SD)	96.99 ± 0.93	97.1 ± 0.62	98.34 ± 0.63	98.21 ± 0.60	98.85 ± 0.66
P value	>0.05	>0.05	>0.05	>0.05	>0.05

The mean time (hours) from cessation of sedation to extubation for dexmedetomidine is 7.4 hours, for propofol is 5.6 hours and for midazolam is 16.9 hours. P-value of dexmedetomidine, propofol and midazolam group is <0.001, which is statistically significant. Cessation of sedation to ICU discharge for dexmedetomidine its 83 hours for propofol is 92 hours and for midazolam it is 78 hours. p value calculated by ANOVA test among all the three groups is >0.05 which is statistically not significant.

DISCUSSION

This study was considered to assess the efficacy of dexmedetomidine with propofol and midazolam, IV sedation agents regularly used in ICU in terms of changes in vitals, duration of extubation ICU discharge and complications. The patients in this study were of gynaecological and obstetrical cases, emergency laprotomy cases, trauma cases, post-operative routine

cases, aspiration pneumonia cases, COPD cases. In present study, patients receiving dexmedetomidine have significantly lower heart rate compare to propofol and midazolam, During sedation mean pulse rate in dexmedetomidine group was 77.54±9.34, in propofol group 89.34±10.1 and for midazolam group 90.23± 10.7. During sedation with dexmedetomidine, propofol and midazolam p value is <0.001 which is highly significant. Atikenhead AR *et al.*.[1] concluded that desired level of sedation was achieved easily in most patients in both groups. There were slight falls in arterial pressure, but there were no significant differences between the groups. Heart rate was lower in patients who received propofol. When the infusion was discontinued, there was less variability, in recovery of consciousness In patients who had received propofol. In a subgroup of patients, weaning from mechanical ventilation was achieved significantly faster after discontinuation of propofol than of midazolam. Grounds RM *et al.*.[2] concluded that propofol infusion allowed rapid and accurate control of the level, of sedation which was satisfactory for longer than with midazolam, Patients given propofol recovered significantly more rapidly from their sedation once they had fulfilled the criteria for weaning from artificial ventilation and as a result spent a significantly shorter time attached to a ventilator. There were no serious complications in either group. Above findings are in accordance with present study where significant difference is present in weaning the patient from mechanical ventilator after stoppage of sedation. Midazolam took longer time in weaning. Barrientos-Vega R *et al.*.[3] noted that in critically ill patients sedated with midazolam or propofol over prolonged periods, midazolam and propofol were equally effective as sedative agents. However, despite remarkable differences in the cost of sedation with these two agents, the economic profile is more favorable for propofol than for midazolam due to a shorter weaning time associated with propofol administration. So dexmedetomidine infusion leads to reduction in heart rate during sedation an it is statistically significant when compared with propofol and midazolam. Hoy SM *et al.*.[4] concluded that intravenous dexmedetomidine is generally well tolerated when utilized in mechanically ventilated patients in an intensive care setting and for procedural sedation in non-intubated patients. While dexmedetomidine is associated with hypotension and, bradycardia, both usually resolve without intervention. Eren G *et al.*.[5] concluded that dexmedetomidine was as effective as higher doses of midazolam in sedation. The hemodynamic and respiratory effects were minimal. Although dexmedetomidine caused significant decrease in the blood pressure and heart rate, it probably just normalized increased levels caused by preoperative stress. Ebert TJ *et al.*.[6] The initial dose of dexmedetomidine decreased catecholamines 45-76% and eliminated the norepinephrine increase leads to reduction in heart rate. Subsequent higher doses increased sedation, all pressures, and calculated vascular resistance, and resulted in significant decreases in heart rate cardiac output, and stroke volume. Venn RM *et al.*.[7] who demonstrated statistically significant reduction in pulse rate in patients receiving dexmedetomidine infusion in the ICU. After discontinuation of sedation heart rate were initially lower in patients receiving dexmedetomidine, but after a return to baseline in these patients there were no difference among the groups (P ~ 0.15). All of the above studies showing that dexmedetomidine infusion leads to reduction is heart rate which is in accordance with present study. During the sedation with dexmedetomidine, propofol and midazolam there was no significant effect on respiratory rate was noted (p> 0.05). Hoy SM *et al.*.[4] concluded that intravenous dexmedetomidine is generally well tolerated when utilized in mechanically ventilated patients in an intensive care setting and for procedural sedation in non-intubated patients. It is not associated with respiratory depression. Arterial pressures were reduced in dexmedetomidine, propofol and midazolam sedation. The difference in arterial pressure between all the three groups during sedation was found to be statistically not significant (p > 0.05). Esko Ruokonen *et al.*. noted that propofol alone decreased mean arterial pressure and cardiac index; heart rate was increased. Myocardial blood flow and myocardial oxygen consumption were decreased by 26% and 31%, respectively. This result is in accordance of my study where arterial pressure reduced during propofol sedation. Ebert TJ *et al.*.[8] concluded that dexmedetomidine decreased catecholamines 45-76% and eliminated the norepinephrine increase. Catecholamine suppression persisted in subsequent infusions. The first two doses of dexmedetomidine increased sedation 38 and 65%, and lowered mean arterial pressure by 13%, but did not change central venous pressure or pulmonary artery pressure. The mean SpO_2 in all the three groups during sedation, from cessation of sedation to extubation at extubation and from extubation to ICU discharge, were comparable in dexmedetomidine, propofol and midazolam groups and there was statistically significant difference found, (p> 0.05). In this study chest complications (nosocomial pneumonia, barotraumas) were the most common complication noted. 18% patients in dexmedetomidine groups, 25.4% patients in propofol group, 21% patients in midazolam group had chest complications. These findings were in accordance to Goodman NW *et al.*.[9] studied the ventilatory effects of propofol infusion and concluded that it leads to more chest complications. Bradycardia occurred in 7.5% patients receiving dexmedetomidine and the time of loading of the drug. This finding was in accordance with

Eren G *et al.*.[5] also noted that dexmedetomidine cause bradycardia. None of the complications were statistically significant.

CONCLUSION

Dexmedetomidine is a satisfactory agent for sedation in ICU. There was no significant difference in time to ICU discharge in all the three groups. There was significant difference in the heart rate of the patients during sedation. Lower heart rate was seen in dexmedetomidine receiving patients. Blood pressure and respiratory rate were lower in dexmedetomidine and propofol group though it's not statistically significant.

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