ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A RANDOMISED COMPARATIVE STUDY TO EVALUATE THE SAFETY AND EFFICACY OF DEXMEDETOMIDINE VS PROPOFOL FOR SEDATION IN MECHANICALLY VENTILATED PATIENTS.

Anesthesiology

Dr.Tejaswini Jambotkar — Assistant Professor, Lokmanya Tilak Municipal Hospital And Medical College, Sion, Mumbai.

Dr.Kamlesh Gotiwale* — Assistant Professor, Lokmanya Tilak Municipal Hospital And Medical College, Sion, Mumbai. *Corresponding Author

Dr. Bharati Tendolkar — EX.HOD Anaesthesia, Lokmanya Tilak Municipal Hospital And Medical College, Sion, Mumbai.

ABSTRACT

Introduction: The intensive care unit (ICU) environment frequently lends itself to being an unpleasant experience for the critically ill patient.One of the key factors in good patient careis appropriate analgesia and sedation to ensure patient comfort. Traditionally, this has been achieved using benzodiazepines and opioids.The aim of this study was to evaluate and compare FDA approved dexmedetomidine based sedation with the commonly used IV sedative agent in the intensive care unit, namely propofol.

Methodology:A total of 60 postoperative patients expected for 6 to 24 hours on mechanical ventilation were assessed and consent was taken preoperatively. Patients who fulfilled inclusion criteria and exclusion criteria were randomly allocated in group D (Dexmedetomidine) and P (Propofol) according to the computerised randomisation table.Both groups were given infusion for 6 hours or till Ramsay sedation scale(RSS) 3 was reached. Each patient was evaluated hourly for sedation on (RSS), pain on Visual analogue scale(VAS) or Face Rating Scale (FRS) and vital parameters like heart rate, blood pressure, mean arterial pressures (MAP), oxygen saturation were noted for 12 hours.

Results: In our study demographic data was comparable. The results showed that sedation in group D (2.43 + 0.63)and group P (2.77 + 0.43) was comparable. Comparison of pain in both the groups showed VAS score to be significantly less in dexmedetomidine group (P = 0.002) during the infusion. Also, rescue analgesic requirement (fentanyl) was significantly less (P = 0.038) in dexmedetomidine compared to propofol group.Results showed that heart rates were significantly lower (P<0.05) in dexmedetomidine group after the loading dose and also during the maintenance infusion though systolic and diastolic blood pressures, mean arterial pressures and oxygen saturation were similar in both groups.Time to awakening and T- piece respiration was significantly earlier in dexmedetomidine group (P=0.002) compared to propofol. The extubation time was comparatively less in dexmedetomidine group though not statistically significant. The common complication in the study seen was hypotension and bradycardia more in dexmedetomidine group.

Conclusion: Dexmedetomidine is a safe alternative to routinely used drugs with equal depth of sedation compared to propofol in postoperative mechanically ventilated patients with advantage of arousability and better patient co-operation during ICU procedures.Dexmedetomidine has good cardiovascular profile with advantage in patients during stressful episodes but needs monitoring the haemodynamics.

KEYWORDS

Dexmedetomidine, Propofol, Sedation.

INTRODUCTION:

The intensive care unit (ICU) environment frequently lends itself to being an unpleasant experience for the critically ill patient.The patient is exposed to numerous ominous and frightening procedures that are a necessary part of the care process.Due to a critical illness or injury, an ICU patient may experience unpleasant feelings, anxiety, agitation, fear or pain.One of the key factors in good patient careis appropriate analgesia and sedation to ensurepatient comfort.The careful and precise control of sedation therapy may lead to better control of the patient requiring mechanical ventilation support, and reduce the requirement for the use of neuromuscular blocking agents.

Amnesia is probably another useful goal of sedation therapy.Intubated mechanically ventilated patientsin the surgical ICU require sedation to toleratethe tracheal tube and the ventilator, to suppresscough and prevent respiratory fighting duringintensive care procedures such as bronchialsuction, physiotherapy and catheter placement.The maintenance of a normal sleep pattern can help maintain psychological well-being, as well as prevent exhaustion and the loss of a desire to survive.

Surgical incisions, indwelling vascular catheters, endotracheal suctioning, and mechanical ventilation are all potential sources of pain for patients. Pain may result in many adverse events including increased endogenous catecholamine activity, myocardial ischemia, hypermetabolic states, and anxiety.Failure to recognize that pain frequently leads to agitation may result in excessive administration of sedatives. Accordingly, an aggressive approach to managing pain has been strongly recommended by published consensus opinions regarding sedation in the ICU.[1,2] The sequel of severe untreated pain can be long lasting psychological effects on the patient, together with adverse hemodynamic changes. Foremost it is inhumane not to adequately treat pain.

The ideal sedative agent should allow for rapid modification of the sedation level by modifying the dosage titrable and should not have depressor effect on the cardiovascular or respiratory systems.[3] It should be cheap and have short duration without cumulative effects, allowing for rapid recovery of effective spontaneous respiration after interruption of its administration in patients undergoing mechanical ventilation.[4,5]

Assessing adequacy of sedation can be difficult because of its subjective nature. Several objective sedation scales such as the Ramsay Sedation Scale[6] and the Sedation-Agitation Scale [7] have been developed. The Ramsay scoring system is one of the most commonly used scales. The evaluation of sedation adequacy is a bedside manoeuvre. Ideally, one would prefer a patient with all of the indications for sedation outlined above met, yet fully communicative with bedside caregivers. Such a state of sedation correlates with a Ramsay score of 2 or 3.[6,7]

Traditionally, this has been achieved using benzodiazepines and opioids. Previous studies have shown that benzodiazepines may enhance the analgesic effects of opiates, a phenomenon not seen with propofol.Sedation with propofol was more effective in achieving patient ventilator synchrony than that with midazolam. Also, patients sedated with propofol awoke more rapidly and with less variability than those patients sedated with midazolam. Hence propofol is being administered for sedation of patients in the ICU with increasing frequency.[8,9]

Propofol causes systemic vasodilatation which may result in unwanted hypotension, especially in patients who are already hemodynamically compromised. Propofol also causes ventilatory depression, so its use should be restricted in the ICU to patients whose airway is protected by an endotracheal tube and whose ventilation is closely monitored.

Dexmedetomidine is a new, highly selective and potent α 2-adrenoceptor agonist is FDA approved as a sedative agent in intensive care unit patients. As well as offering sedation and anxiolysis, α 2 agonists have analgesic qualities and reduce the stress response to surgery and intensive care procedures.10At therapeutic doses, dexmedetomidine does not cause any significant respiratory depression.[11]

So after studying previous trials we decided to compare propofol - drug with proven better efficacy over routinely used sedatives with dexmedetomidine - newly approved drug for short term sedation with good clinical profile in our study. We compared the sedative effect, analgesic profile, hemodynamic effects, awakening and extubation times of dexmedetomidine with propofol for sedation in ICU patients.

MATERIALS AND METHODS:

STUDY DESIGN: A prospective, randomized, comparative study in age group of 18 - 70 years for postoperative mechanical ventilation.

STUDY APPROVAL: The study was approved by the institutional medical ethics committee and written informed consent was obtained from all patients to be included in the study.

STUDY POPULATION: From January 2011 to September 2012, sixty patients who received mechanical ventilation were enrolled in the study.

RANDOMISATION: A computer generated table of random numbers was prepared allotting equal number of patients in each group.

Sample Size: Total 60 patients were recruited in the study.
30 patients - Inj. Dexmedetomidine
30 patients - Inj. Propofol

Inclusion Criteria:
1. Patients of either sex in age group of 18 - 70 years.
2. Patients requiring postoperative ventilator support.
3. Patients or relatives giving written consent.
4. Patients for major abdominal, thoraco-abdominal, oral surgeries.
5. Patients for emergency surgeries requiring blood transfusion prior to weaning.

Exclusion Criteria:
1. Patients with known hypersensitivity to drugs used in the study.
2. Hemodynamically unstable patients.
3. Pregnant and lactating women.
4. Patients requiring neuromuscular blockers during sedation.
5. Patients requiring epidural drugs during sedation.
6. Patients with grossly deranged liver and kidney functions tests.
7. Patients with airway surgery.

Methodology Details:
A total of 60 postoperative patients expected for 6 to 24 hours on mechanical ventilation were assessed and consent was taken preoperatively. The patients included were:

1. Patients undergoing major surgeries for oral or abdominal carcinomas.

2. Patients with large upper abdominal or thoracic incisions for elective ventilation for 10-12 hours.

3. Patients for emergency surgery with preoperative and intraoperative blood loss requiring adequate blood and blood products transfusion before weaning.

During the surgery - After premedication, Anaesthesia was induced with Inj. Propofol 2mg/kg in graded doses till loss of consciousness.Anaesthesia was maintained on inhalational anaesthetics like isoflurane or desflurane and neuromuscular blocker namely, vecuronium. Analgesia was given initially using Inj. Fentanyl 2 mcg/kg and later 0.5-1 mcg/kg, Inj. Paracetamol 1g, Inj. Diclofenac 75mg intravenously. No long acting opioids were used intraoperatively. At the end of surgery neuromuscular blockade was reversed with Inj. Glycopyrollate 0.008mg/kg and Inj. Neostigmine 0.06mg/kg. After oropharyngeal and endotracheal suction, patients were shifted with endotracheal tube in situ in the intensive care unit.

After the surgery - On arrival of patient in the intensive care unit, patients were put on advanced ventilators with volume control mode.Monitors like cardioscope, pulse oximeter, blood pressure were attached. Patients who fulfilled inclusion criteria and exclusion criteria were randomly allocated in group D and P according to the computerised randomisation table. Each patient was evaluated for pain on Visual analogue scale(VAS) or Face Rating Scale (FRS) and sedation on Ramsay sedation scale(RSS). Pre-sedation vital parameters like heart rate, blood pressure, MAP, oxygen saturation, general and systemic examination were noted.

Group D was given Inj. Dexmedetomidine 1mcg/kg intravenous loading dose over 10 minutes followed by 0.2-0.7mcg/kg/hour infusion.

Group P was given Inj. Propofol 1mg/kg intravenous loading dose over 10 minutes followed by 1mg/kg/hour infusion. Both groups were given infusion for 6 hours or RSS 3 was reached. Patients were monitored hourly for pulse(P), BP(systolic, diastolic), mean arterial pressures(MAP), oxygen saturation(Spo2), Pain(VAS or Face Rating Scale), sedation(RSS).

If sedation was inadequate (RSS<3) rescue sedation with midazolam 0.5-1mg was given as required. During sedation, if required, rescue analgesia was given with Inj. Fentanyl 1mcg/kg as per VAS score >4. Total number of rescue sedation and analgesic doses were noted.

After stoppage of infusion hourly monitoring of patient's vital parameters like heart rate, blood pressure, MAP, oxygen saturation, VAS score, RSS was continued for next 6 hours. As per patient's breathing efforts, awakening and hemodynamic response patients were gradually weaned to pressure support ventilation and later to T-piece with oxygen at 5 litres/min. Awakening was defined as patient with spontaneous eye opening and obeying verbal commands. Awake patients maintaining oxygen saturation on T- piece, breath rate between 12-18 breaths/min, taking deep breaths and maintaining heart rate and blood pressure within normal range were extubated. Time from stoppage of infusion till extubation was noted.

During the study complications if any, like hypotension, bradycardia were noted and treated with IV fluids, Inj. Ephedrine in graded doses as and when required. Infusion was stopped between the study in those patients in whom complications were resistant to treatment.

Ramsay Sedation Scale [1]
1 Patient is anxious and agitated or restless, or both
2 Patient is co-operative, oriented, and tranquil
3 Patient responds to commands only
4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5 Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.

Statistical Analysis:
Sample size
The two groups were compared with each other in terms of age, weight and sex. The statistical test used was Unpaired Student's t test for age and weight . For qualitative data like the sex of the patient and type of surgery, the statistical test employed was Pearson Chi–square test .

The hourly values of hemodynamic parameters like heart rate, systolic and diastolic blood pressure, mean arterial pressure and oxygen saturation were compared in each group with the values at the time of loading dose using Paired t test. The comparison of these parameters in two groups was done using Unpaired t test. The baseline parameters were compared using unpaired t test.

Sedation and pain were compared in two groups using MannWhittneytest.In all the parameters, P< 0.05 was considered to be significant.

RESULTS:
In our study 60 patients who received postoperative mechanical ventilation for 10-12 hours were recruited. It was a comparative study where patients were randomly allocated in Group D who received Inj. Dexmedetomidine and Group P received Inj. Propofol according to the computer generated randomisation table. Both groups received initial

loading dose over 10 minutes and infusion for 6 hours.

The demographic data, type of surgery in both groups were found comparable.

In patients of each group baseline parameters like heart rate (HR), Blood pressure (SBP,DBP), Mean arterial pressure (MAP), Oxygen saturation (SPO2), Pain on Visual analogue scale (VAS) scale and Sedation on Ramsay sedation scale (RSS) were studied and found to be comparable .

Heart rate in dexmedetomidine group showed significantly lower heart rates after loading dose and during infusion. The difference was statistically significant (P<0.01) between two groups Comparison of systolic, diastolic blood pressure, mean arterial pressure and oxygen saturation respectively in between groups D and P showed both groups were comparable but there was no statistically significant difference between two groups.

VAS score was significantly less (P= 0.002) in Dexmedetomidine group (1.43 + 0.90) compared to propofol group (1.90 + 0.76) after loading dose and also for first three hours during the infusion .

Comparison of Ramsay sedation score (RSS) for sedation in two groups was analysed using MannWhitney test showed sedation with propofol (2.77 + 0.43) to be significantly greater compared to dexmedetomidine (2.43 + 0.63) after loading dose and 1 hour of infusion . Later during the infusion depth of sedation as compared by RSS was similar and thus comparable.

Both groups were comparable but requirement of rescue analgesia was significantly higher (P= 0.038) in propofol group compared to dexmedetomidine .

Dexmedetomidine group showed significantly faster awakening (56.33 + 28.28 min) than propofol (78.00 + 23.33) and T- piece insertion (P=0.002) compared to Propofol group. Though extubation was earlier in Dexmedetomidine group but the difference was not statistically significant.

The difference was not statistically significant though more in dexmedetomidine group.

DISCUSSION:

Patients subjected to major and ultra-major surgical procedures may require short periods of postoperative mechanical ventilator support, especially those operated for upper abdominal surgeries, prolonged operative time and morbidly obese patients. The characteristic feature of sedation, together with a concomitant opioid sparing effect, may decrease the length of time spent on a ventilator, length of stay in ICU, and prevalence and duration of delirium, as the evidence shown from several comparative studies.[12,13,14] The aim of this study was to evaluate and compare dexmedetomidine based sedation with the commonly used IV sedative agent in the intensive care unit, namely propofol.

In our study we did not mask the tested drug because the physical appearance of propofol (formulated in a white lipid emulsion) is different from dexmedetomidine (clear liquid) and any leakage of solution would unmask the study drug. Also, when bolus infusions for acute agitation need to be administered, knowledge of the treatment groups would prevent potentially hazardous hemodynamic changes through appropriate drug infusion rates.

Sedation and Analgesia:

Sedation score after loading dose and at first hour of infusion was significantly greater in the propofol group showed deeper sedation and less communicability with the patients than the other group. Also, the need of rescue sedation was more in dexmedetomidine group though the difference in two groups was not statistically significant. But it is difficult to quantify the arousability, cooperation of the patient and thus ease in management in the dexmedetomidine group which reflects only mild cognitive impairment with the drug. In our study comparison of pain in both the groups showed VAS score to be significantly less in dexmedetomidine group (P=0.002) during the infusion. Also, rescue analgesic requirement (fentanyl) was significantly less (P=0.038) in dexmedetomidine compared to propofol group which can be attributed to its central analgesic property. These findings in our study were consistent with other studies also.

YahyaShehabi et al [15] studied clinical applications of dexmedetomidine in ICU and demonstrated that dexmedetomidine cannot be used to achieve deep sedation or to control acutely agitated or combative patients; therefore additional and rescue conventional sedatives may be required in some patients. Thus this study supported our use of rescue sedation (midazolam) more in dexmedetomidine group.

Hussein Agameya et al [16] compared dexmedetomidine and propofol in 20 patients and showed both agents produced almost equivalent depth of sedation in both groups using bispectral index scale with non-significant statistical difference. In spite of this, dexmedetomidine group patients showed more co-operative behaviour of patients with ICU staff.

SamiaElbaradie et al [17] compared propofol and dexmedetomidine and showed despite ventilation and intubation, patients sedated with dexmedetomidine could be easily aroused to co-operate without showing irritation although an equivalent depth of sedation between dexmedetomidine and propofol was achieved, with the advantage that the fentanyl requirement was reduced by over 54% in patients who received dexmedetomidine.

Venn RM et al [18] in comparison to propofol found opioid requirement was reduced by 50% with dexmedetomidine even with equal depth of sedation. Also observed that postoperative analgesic requirements were reduced by 50% in cardiac patients, and the need for rescue midazolam for sedation was diminished by 80%.

Herr DL and colleagues [19] compared dexmedetomidine and propofol based sedation in post coronary artery bypass grafting ICU sedation and stated that only 28% of the dexmedetomidine patients required morphine for pain relief while ventilated versus 69% of propofol based patients (P< 0.001). Propofol patients required 4 times the mean dose of morphine while in the ICU.

Shah PN et al[27] compared dexmedetomidine and propofol in 30 mechanically ventilated patients for 24 hours and concluded that though sedation was comparable in both groups but requirement of analgesia was higher in propofol group.

Haemodynamics :

In our study results showed that heart rates were significantly lower in dexmedetomidine group after the loading dose and also during the maintenance infusion though systolic and diastolic blood pressures, mean arterial pressures and oxygen saturation were similar in both groups. Other studies also support this hemodynamic profile of dexmedetomidine.[20,21,22] Vasodilation which manifests as reduction in arterial pressures is a feature of both propofol and dexmedetomidine [20]. So equipotent doses of both the drugs were used and showed equivalent reduction in arterial pressures.

Venn and colleagues [23] compared dexmedetomidine with propofol in 20 adults expected to require artificial ventilation. They also found no differences in arterial pressures between groups, but heart rate was significantly lower in the dexmedetomidine group.

Elbaradie and colleagues [17] studied 60 patients for postoperative sedation and showed that the mean values of heart rate during sedation with dexmedetomidine were significantly lower compared with the propofol group, but did not need intervention. There was no intergroup statistically significant difference in mean arterial pressures. No patient in both groups needed inotropic support. But, hypotension and bradycardia occurred in the dexmedetomidine group as confirmed from other studies in volunteers 220 and surgical ICU patients.[23]

Eike Martin et al [24] studied dexmedetomidine for sedation in 401 post-surgical patients found that majority of dexmedetomidine patients maintained blood pressures within normal range, without rebound but hypotension and bradycardia occurred more frequently in this group.

Awakening and Extubation :

Dexmedetomidine produces a state of sympatholysis, optimal analgesia, easy arousability and less respiratory depression as compared to the standard drugs used in ICU patients.[16,25] Our study also confirmed similar findings of dexmedetomidine.

In our study after stoppage of the drugs, time to awakening and T- piece respiration was significantly earlier in dexmedetomidine group (P =

0.002) compared to propofol which can be related to only mild cognitive impairment seen with dexmedetomidine. The extubation time was comparatively less in dexmedetomidine group though not statistically significant.The lower heart rates seen in the dexmedetomidine group during extubation were beneficial in patients to avoid stress precipitated cardiac events.

Also dexmedetomidine group showed more alertness and co-operation during ventilator support and more rapid and easy extubation (P = 0.7), but these changes were statistically non-significant in study by Agameya et al [16] and Shah et al [27].

Elbaradie and colleagues [17] in their study showed that the extubation time were comparable in both groups but the significantly lower heart rate seen with the dexmedetomidine group compared with the propofol group may lower the stressful ICU episode, in particular over the extubation periods. Other studies by Wan LJ et al[26] and Venn et al[23] also confirmed similar findings.

Complications:

The numerous adverse cardiovascular events seen previously with the loading infusion of dexmedetomidine were not seen in this study [20], due to reduction of the loading infusion dose (1mcg/kg). The common complication in the study seen was hypotension and bradycardia more in dexmedetomidine group was treated with IV fluids, Inj. Ephedrine in graded doses. No patient needed inotropic support. But infusion was stopped in one patient of the dexmedetomidine group due to resistant hypotension.

Elbaradie et al [17] also found hypotension and bradycardia occurred more in dexmedetomidine group but intervention was not needed in any of the study groups.

Adverse cardiovascular events (hypotension ± bradycardia) were nearly all confined to the initial loading infusion of dexmedetomidine in a study by Venn et al.

Though these complications were seen with dexmedetomidine group but they were usually well tolerated in healthy adults.[22]

CONCLUSION:

In our study similar to the previous studies, dexmedetomidine showed equivalent depth of sedation in comparison to propofol with better arousability and patient co-operation. Also, reduced need of analgesia, optimal clinical profile and early weaning and extubation makes it a better choice for sedation in post-operative mechanically ventilated patients.

Comparison of Heart rate in groups D and P using unpaired T test and within the group with the baseline using Paired T test. Both groups were comparable. Heart rate in dexmedetomidine group showed significantly lower heart rates after loading dose and during infusion. The difference was statistically significant between two groups.

COMPARISON OF HEART RATE

PR (per min)	Group D			Paired P value	Group P			Paired P value	P value D vs P
	N	Mean	S.D.		N	Mean	S.D.		
Loading dose	30	70.40	13.33	< 0.001	30	77.63	11.95	0.000	**0.031**
1 hour	30	69.30	13.02	< 0.001	30	76.50	11.52	0.000	**0.027**
2 hour	29	65.17	17.71	< 0.001	30	75.57	11.02	0.000	**0.008**
3 hour	29	63.83	18.42	< 0.001	30	74.23	11.03	0.000	**0.010**
4 hour	29	63.33	19.20	< 0.001	30	73.37	10.66	0.000	**0.015**
5 hour	29	62.07	18.16	< 0.001	30	73.10	9.70	0.000	**0.005**
6 hour	29	61.90	17.82	< 0.001	30	72.33	8.88	0.000	**0.006**
7 hour	29	71.52	12.97	0.000	30	73.13	8.62	0.000	0.574
8 hour	29	71.93	13.12	0.000	30	74.13	9.08	0.000	0.455
9 hour	29	71.93	11.79	0.000	30	74.27	8.92	0.000	0.393
10 hour	29	73.21	11.41	0.000	30	75.07	8.98	0.000	0.489
11 hour	29	73.83	13.80	0.000	30	75.10	9.24	0.000	0.678
12 hour	29	74.59	14.18	0.000	30	75.87	9.75	0.000	0.687

Mean arterial pressure respectively in between groups D and P using unpaired T test and within the group with the baseline using Paired T test. Both groups are comparable but there is no statistically significant difference between two groups with respect to these variables.

COMPARISON OF MEAN ARTERIAL PRESSURE (MAP)

MAP (mmHg)	Group D			Paired P value	Group P			Paired P value	P value D v/s P
	N	Mean	S.D.		N	Mean	S.D.		
Loading	30	87.03	9.47	0.000	30	85.90	7.00	0.000	0.600
1 hour	30	86.90	11.74	0.000	30	85.50	10.04	0.000	0.621
2 hour	30	82.43	18.03	0.000	30	84.00	8.80	0.000	0.670
3 hour	30	80.33	17.25	0.000	30	82.87	10.28	0.000	0.492
4 hour	30	80.80	17.51	0.000	30	82.37	8.60	0.000	0.662
5 hour	30	81.07	17.08	0.000	30	81.97	7.28	0.000	0.792
6 hour	30	80.47	16.85	0.000	30	81.83	7.61	0.000	0.687
7 hour	30	78.00	21.57	0.000	30	80.93	11.62	0.000	0.515
8 hour	30	81.17	17.04	0.000	30	83.80	7.68	0.000	0.443
9 hour	30	80.97	17.47	0.000	30	84.40	8.55	0.000	0.338
10 hour	30	82.87	17.65	0.000	30	84.43	7.37	0.000	0.655
11 hour	30	83.17	17.31	0.000	30	85.70	8.69	0.000	0.477
12 hour	30	110.97	148.03	0.568	30	86.13	7.79	0.000	0.363

COMPARISON OF PAIN SCALE (VAS)

Pain (VAS)	Group D			Group P			Test Mann Whitney	
	N	Mean	S.D.	N	Mean	S.D.	Z value	P value
Loading	30	1.43	0.90	30	1.90	0.76	2.122	**0.034**
1 hour	30	1.30	1.02	9	2.33	0.87	3.150	**0.002**
2 hour	30	0.83	0.53	9	2.67	1.50	3.917	**0.000**
3 hour	30	0.77	0.57	9	3.33	1.22	4.433	**0.000**
4 hour	2	1.50	0.71	9	2.44	0.53	1.532	0.126
5 hour	2	1.50	0.71	9	2.44	1.01	1.179	0.239
6 hour	2	2.50	0.71	9	2.11	0.78	0.589	0.556
7 hour	2	4.00	2.83	9	1.89	0.78	1.179	0.239
8 hour	2	3.00	1.41	9	2.44	1.59	0.707	0.480
9 hour	2	3.00	0.00	9	1.89	0.93	1.650	0.099
10 hour	2	3.00	0.00	9	1.67	1.00	1.650	0.099
11 hour	2	2.00	0.00	9	1.56	0.73	0.943	0.346
12 hour	2	2.00	0.00	9	1.67	0.71	0.707	0.480

Comparison of pain in both the groups on Visual analogue scale using MannWhitney test. VAS score was significantly less ($p< 0.05$) in Dexmedetomidine group (1.43 ± 0.90) compared to propofol group (1.90 ± 0.76) after loading dose and also for first three hours during the infusion.

COMPARISON OF SEDATION ON RSS

RSS	Group D			Group P			MannWhitney Test	
	N	Mean	S.D.	N	Mean	S.D.	Z value	P value
Loading dose	30	2.43	0.63	30	2.77	0.43	2.230	0.026
1 hr	30	2.73	0.45	30	2.97	0.18	2.510	0.012
2 hr	30	2.87	0.35	30	2.97	0.18	1.390	0.165
3 hr	30	2.97	0.18	30	2.97	0.18	0.000	1.000
4 hr	30	2.97	0.18	30	2.93	0.25	0.587	0.557
5 hr	30	2.90	0.31	30	2.80	0.41	1.076	0.282
6 hr	30	2.63	0.49	30	2.90	0.31	1.421	0.115
7 hr	21	2.38	0.50	29	2.52	0.51	0.945	0.345
8 hr	14	2.07	0.27	23	2.09	0.29	0.166	0.869
9 hr	11	2.00	0.00	7	2.00	0.00		
10 hr	6	2.00	0.00	2	2.00	0.00		
11 hr	4	2.00	0.00	1	2.00		0.000	1.000
12 hr	4	2.00	0.00	1	2.00		0.000	1.000

Comparison of Ramsay sedation score (RSS) for sedation. Data was analysed using MannWhitney test shows sedation with propofol (2.77 ± 0.43) to be significantly greater compared to dexmedetomidine (2.43 ± 0.63) after loading dose and 1 hour of infusion. Later during the infusion depth of sedation as compared by RSS were similar and thus comparable.

REFERENCES:

1. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 2002; 30:119–141.
2. Shapiro BA, Warren J, Egol AB, Greenbaum DM, Jacobi J, Nasraway SA, et al. Practice parameters for intravenous analgesia and sedation for adult patients in the intensive care unit: an executive summary. Crit Care Med 1995; 23:1596–1600.
3. Osborne RJ, Joel SP, Slevin ML. Morphine intoxication in renal failure: the role of morphine-6-glucoronide. BMJ 1986; 292: 1548-1549.
4. Grounds RM, Lalor JM, Lumley J, Royston D, Morgan M. Propofol infusion for sedation in the in the ICU: a preliminary report. BMJ 1987; 294: 397-400.
5. Atkenhead AR, Willats SM, Park G. Comparison of propofol and midazolam for

sedation in critically ill patients. Lancet 1989; 2: 704-709.
6. Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with alphalaxone-alphadolone. BMJ 1974; 3:656–659.
7. Riker RR, Picard JT, Fraser GL. Prospective evaluation of the Sedation-Agitation Scale for adult critically ill patients. Crit Care Med 1999; 27:1325–1329.
8. McKeage K., Perry CM. Propofol: A Review of its Use in Intensive Care Sedation of Adults. CNS Drugs2003;17Suppl 4: 235-272 Rowe
9. K, FletcherS. Sedation in the intensive care unit. ContinEducAnaesthCrit Care Pain 2008; 8 Suppl2: 50-55.
10. Hayashi Y, Maze M. Alpha-2 adrenoceptor agonists and anaesthesia. BJA 1993; 71: 108-118.
11. Belleville JP, Ward DS, Bloor BC. Ventilatory effects of dexmedetomidine in humans. Anesthesiology 1990; 73: A1167 Riker RR
12. , Shehabi Y, Bokesch PM et al.Dexmedetomidinevs midazolam for sedation of critically ill patients: a randomized trial.JAMA 2009;301(5):489-99. Jakob SM
13. Ruokonen E, Grounds RM, Sarapohja T, Garratt C, Pocock SJ et al. Dexmedetomidinevs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA 2012;307(11):1151-60. Yu SB
14. Dexmedetomidine sedation in ICU. Korean J Anesthesiol. 2012; 62(5): 405-11.
15. ShehabiY, BothaJA, Ernest Det al; Clinical application, the use of dexmedetomidine in intensive care sedation; Crit Care & Shock 2010; 13:40-50
16. AgameyaHM,.MostafaAA, HassanAA.Sedation for mechanically ventilated postoperative patients in the intensive care unit: comparative study between propofol and dexmedetomidine. Alexandria Journal of Anaesthesia and Intensive Care2005;8Suppl 2: 20
17. ElbaradieS; Faten H,SolymanAH.Dexmedetomidine vs. Propofol for Short-Term Sedation of Postoperative Mechanically Ventilated Patients. Journalof the Egyptian Nat. Cancer Inst., 2004; 16Suppl 3:153-158.
18. VennM, BallJ, SteeleA, Newman PJ and GroundsRM. Dexmedetomidine for sedation in the medical ICU. Critical Care 2000; 4 Suppl 1:192 Herr DL
19. Sum-Ping ST, England M. ICU sedation after coronary artery bypass graft surgery: dexmedetomidine-based versus propofol-based sedation regimens. J CardiothoracVascAnesth. 2003;17(5):576-84
20. Venn RM, Bradshaw CJ, Spencer R, Grounds RM et al. Preliminary UK experience of dexmedetomidine, a novel agent for postoperative sedation in the intensive care unit. Anaesthesia 1999;54:1136-1142.
21. GertlerR, BrownHC, MitchellDH, SilviusEN. Dexmedetomidine: a novel sedative-analgesic agent. BUMC Proceedings 2001; 14:13-21
22. VennM, BallJ, SteeleA, Newman PJ,GroundsRM. Dexmedetomidine for sedation in the medical ICU. Critical Care 2000; 4Suppl 1:192
23. Venn RM and Grounds RM. Comparison between dexmedetomidine and Propofol for sedation in intensive care unit: patients and clinicians perceptives. Br J Anaesth 2001; 87(5): 684-90. Martin
24. E, RamsayG, MantzJ. The Role of the α2-Adrenoceptor Agonist Dexmedetomidine in Postsurgical Sedation in the Intensive Care Unit. J Intensive Care Med. 2003;18Suppl 1: 29-41
25. OstermannME, KeenanSP, SeiferlingRA.SibbaldWJ. Sedation in the Intensive Care Unit A Systematic Review. JAMA. 2000;283:1451-1459 Wan LJ
26. Huang QQ, Yue JX, Lin L, Li SH. Comparison of sedative effect of dexmedetomidine and midazolam for post-operative patients undergoing mechanical ventilation in surgical intensive care unit. Zhongguo Wei Zhong Bing JiJiu Yi Xue. 2011;23(9):543-6.
27. Shah PN, Dongre V, Patil V et al. Comparison of post-operative ICU sedation between dexmedetomidine and propofol in Indian population. Indian J Crit Care Med 2014;18:291-6