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COMPARATIVE STUDY BETWEEN DEXMEDETOMIDINE AND PROPOFOL FOR PAIN, AGITATION AND DELIRIUM IN INTENSIVE CARE

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ABSTRACT

Background: Severity of acute medical illness, invasive diagnostic and therapeutic interventions and environmental influences makes the patient prone to pain, agitation and delirium in intensive care units. Several drugs are used for sedation, but it was not clear that whether a single drug is able to address all the three components of pain, agitation and delirium effectively. This study compares dexmedetomidine with propofol in the management of critically- ill patients observing their effect on sedation, pain and delirium scores and other cardio-respiratory parameters. **Material & Methods:** After clearance from institute ethical committee and written informed consent, patients were randomly divided to two groups of thirty each. Group D received dexmedetomidine intravenous infusion in initial dose of 0.5 mcg/kg/hr over 20 minutes followed by 0.1 mcg/kg/hr, while Group P received propofol (0.5 mg/kg/hr). Infusion rate was titrated to achieve target sedation level. RASS(Richmond agitation sedation scale), CAM-ICU(Confusion assessment method- ICU),and CPOT(Critical care pain observation tool) scores were observed for a duration of 24 hours at baseline, 20 minutes after starting the study drug and subsequently at every four hours duration. **Results:** Mean RASS in Group D was significantly lower (-0.23 ± 0.50) than group P (0.57 ± 1.17)]. Mean CPOT was also significantly lower (1.30 ± 0.60) in the group D than group P (2.90 ± 1.32). Delirium was also lower (1/30) in the group D than group P (4/30) but this difference was not statistically significant. **Conclusion:** Both propofol and dexmedetomidine can be used as sedative agent in ICU but dexmedetomidine provides better analgesia and lesser delirium episodes than propofol and thus can be used as sole agent to effectively acts on all the three components pain, agitation and delirium simultaneously.

KEYWORDS: Agitation, delirium, dexmedetomidine, pain, propofol.

INTRODUCTION

Critically- ill patients suffer anxiety, stress and pain due to severity of illness, invasive diagnostic & therapeutic interventions and environmental influences.[1] Endotracheal tubes, invasive arterial BP monitoring, chest tubes, beeping alarms, disrupted day and night cycles, all make the patient prone to experience agitation, pain and delirium in intensive care units (ICU). The 2013 SCCM guidelines stresses on the importance of routine monitoring of pain, agitation and delirium in ICU patients with valid and reliable objective tools and their effective pharmacologic or non-pharmacologic management using appropriate treatment algorithm.[2] Objective monitoring of analgesia and sedation therapy allows patient tailored regimens. These drugs are subject to titration because the dose requirement varies from subject to subject, depending on the pharmacokinetics and the pharmacodynamics of the drug.[3] The SCCM guidelines recommend propofol or dexmedetomidine over benzodiazepines in ICU as first line sedative agents.[2]

Thus, based on the available knowledge it was worth conducting a study that can address the question that whether dexmedetomidine can be the ideal agent that can manage pain, agitation as well as delirium prevalent in the ICU set-up. Also, comparing it with propofol which is frequently used in ICU will be of great help in deciding management protocols in critically-ill patients. This study compares dexmedetomidine with propofol in the management of critically- ill patients observing their effect on sedation, pain and delirium scores and other cardio-respiratory parameters.

MATERIAL AND METHODS

After approval from institutional ethics committee and written informed consent, all patients requiring sedation in ICU with age between 18 to 50 years were included. Thirty patients were enrolled in each group. Patients with

known or suspected allergy to dexmedetomidine or propofol, severe hepatic or renal disease, severe haemodynamic compromise, raised intracranial pressure, stroke or head trauma , pregnant and lactating females, need of muscle relaxant (except for intubation), dyslipidaemias were excluded. During the study period sixty patients were enrolled which were randomly divided to two groups of thirty each. Group D received dexmedetomidine infusion in initial dose of 0.5 mcg/kg/hr followed by dose titrated by 0.1 mcg/kg/hr increase or decrease in infusion rate to achieve target sedation level. The recommended dosing range was 0.2 to 1 mcg/kg/h i.v.[4] Group P received propofol infusion in initial dose of 0.5 mg/kg/hr intravenously which may be increased upto maximum of 5 mg/kg/hr in increments of 0.3 mg/kg/hr every five minutes, until the desired level of sedation is achieved. RASS$^{\alpha}$, CAM-ICU$^{\beta}$ and CPOT$^{\gamma}$ were observed in enrolled patients at starting the respective drug, 20 minutes after infusion then at four-hourly interval subsequently for 24 h. Heart rate, blood-pressure, SpO_2, respiratory rate and ECG lead II were also recorded at same intervals. No muscle relaxants was given during the study period except in some cases where succinylcholine was used for intubation. Rescue analgesia was provided by i.v. tramadol (1 mg/kg body wt.) if the study drug infusion rate was maximum or there was bradycardia or hypotension on dose increment and the CPOT score ≥4.

RESULTS

The data was analyzed using SPSS version 20. Baseline demographics among the two groups and mean baseline readings of pulse, systolic and diastolic BP, respiratory rate, spO_2, RASS, CPOT and CAM-ICU is shown in Table 1.

Table 1: Demographics and baseline characteristics.

Variable	Dexmedetomidine	Propofol	'p' Value
Weight (Kg)	69.27 ± 10.66	68.87 ± 9.26	0.877
Sex (M:F)	11:4	23:7	0.776
Age (years)	47.03 ± 18.16	42.30 ± 13.41	0.256
Pulse (beats/min)	87.00 ± 13.86	94.93 ± 17.58	0.057
Systolic BP(mm Hg)	129.10 ± 14.29	124.73 ± 14.76	0.249
Diastolic BP (mm Hg)	76.23 ± 10.92	78.87 ± 7.29	0.276
spO_2 (%)	84.30 ± 2.53	85.07 ± 2.23	0.218
Resp rate (breath/min)	20.87 ± 4.36	18.93 ± 4.98	0.115
RASS	1.37 ± 1.19	1.07 ± 1.78	0.446
CPOT	2.70 ± 1.29	2.87 ± 1.28	0.617
CAM-ICU (present: absent)	1:4	1:5	0.753

There was no intergroup statistically significant variation in the baseline features or the demographic profile. The patients enrolled in the study were admitted for respiratory failure arising due to various aetiologies. Majority of the patients had acute exacerbation of COPD in both the groups, 56.67% in the dexmedetomidine group and 43.33% in the propofol group. The diagnoses has been tabulated in Table 2.

Table 2: Case- Distribution.

Diagnosis	Dexmedetomidine (number/percentage)	Propofol (number/ percentage)
COPD(acute exacerbation)	17/56.67	13/43.33
ARDS	2/6.67	2/6.67
Pulmonary Edema	0/0	3/10
Acute asthmatic attack	4/13.33	6/20
ARF in ILD	1/3.33	2/6.67
Pneumonia	6/20	4/13.33

Both dexmedetomidine and propofol were efficient to provide adequate sedation as the mean RASS was within target sedation score (RASS= 0/1). Mean RASS in group D was significantly lower than group P. Mean CPOT was also significantly lower in group D than group P). Greater prevalence of pain in the propofol group was also evident from the fact that inj. tramadol was used in 6 patients in the propofol group as add- on analgesia while none in the dexmedetomidine group. Prevalence of delirium was also lower (1/30) in the dexmedetomidine group than the propofol group (4/30) but this difference was not statistically significant (Table 3).

Table 3: Observations.

Observation	Dexmedetomidine	Propofol	'p' value
RASS	-0.23 ± 0.50	0.57 ± 1.17	0.001
CPOT	1.30 ± 0.60	2.90 ± 1.32	0.000
CAM-ICU(absent/present)	29/1	26/4	0.207

Decrease in pulse and BP was noted in both the groups 20 minutes after initiating the infusion but greater decrease was seen in the propofol group than the dexmedetomidine group. Pulse and diastolic BP was not significantly lowered in the propofol group, but decrease in systolic BP was significantly more in the propofol group. The haemodynamic variations are shown in Table 4.

Table 4: Haemodynamic alterations.

Observation	Dexmedetomidine			Propofol			
	baseline	After 20 min	Percentage change	baseline	After 20 min	Percentage change	'p' value for change after 20 min in two groups
pulse	87.00 ± 13.86	79.53 ± 12.40	-8.58 %	94.93 ± 17.58	84.80 ± 17.19	-10.67 %	0.179
Systolic BP	129.10 ± 14.29	121.60 ± 13.92	-5.80 %	124.73 ± 14.76	111.13 ± 14.20	-10.90 %	0.006
Diastolic BP	76.23 ± 10.92	71.93 ± 9.61	-5.64 %	78.87 ± 7.29	73.73 ± 7.66	-6.51%	0.426

There was no significant variation in respiratory rate and oxygen saturation among the two groups. Arrhythmia episodes were observed in none of the patients of either group.

DISCUSSION

Importance of sedation for the management of critically-ill patients has been widely recognized across the world. The present study compared dexmedetomidine with propofol for prevention of pain agitation and delirium in ICU patients. This study found that both dexmedetomidine and propofol are equally efficient in producing adequate sedation, within the target range of RASS= 0/-1. This finding corroborates the SCCM 2013 recommendation that both dexmedetomidine and propofol can be used as first- line agents for ICU sedation.[2]

Pain score (CPOT) was higher in propofol group compared to those treated with dexmedetomidine. Also, use of supplemental analgesia by i.v. tramadol was more (6 patients) in propofol group compared to none in the dexmedetomidine group. Similar observations were made in previous studies which showed the analgesic potency of dexmedetomidine. Dexmedetomidine has notable effects to increase the potency or reduce requirement of analgesics as an adjunctive as observed by Ohtani et al and Arain et al in two different studies made in post-operative patients[6,7] However, it is not evident that dexmedetomidine has consistent and dose-dependent analgesia against various nociceptive stimuli such as for post- operative pain, because the present study included the patients with respiratory failure with no obvious painful foci.

Incidence of delirium was higher in the propofol group, four out of thirty patients were diagnosed to be positive for delirium using the CAM- ICU tool during the observation period as compared to one out of thirty in the dexmedetomidine group. It was similar to the findings of previous studies where the incidence of delirium in the dexmedetomidine group was significantly lower than either the midazolam or propofol groups. This finding is similar to the previous observations as in MENDS trial or SEDCOM study, where dexmedetomidine use was associated with lesser delirium episodes.[8,9] One study compared dexmedetomidine to haloperidol and observed that dexmedetomidine perhaps have a therapeutic potential on delirium, as well as on prevention.[10,11] But, in the present study this difference was not statistically significant. In this study, even the propofol group did not witness statistically significant increase in delirium episodes which is similar to previous observations that suggest that the short-term administration of the GABA-ergic agent, propofol, permits normal recovery after a period of sleep deprivation, indicating similarities between propofol induced hypnosis and sleep.[12] However, there are studies that contradict the fact and report delirium incidences with propofol.[13,14,15]

Regarding the respiratory parameters, no group showed respiratory depression or apnea episodes and oxygen saturation remained within acceptable range (with or without use of supplemental oxygenation). This finding is in contradiction to previous literature that suggest that propofol have respiratory depression as a side- effect.[16] However it supports the fact that dexmedetomidine have minimal respiratory depression.[17]

Both the groups witnessed fall in pulse rate and blood pressure suggesting that both the drugs have depressant effect on the cardio- vascular system.[18,19,20] Decrease in pulse rate and diastolic BP was not significant in both the groups, however the propofol group witnessed significantly greater decrease in mean systolic BP 20

minutes after starting the drug infusion. During the observation period of 24 hours, propofol group evidenced statistically significant lowering in mean systolic BP as compared to the dexmedetomidine group while mean pulse rate and diastolic BP was significantly lesser in the dexmedetomidine group compared to the propofol group. No patient in either group observed arrhythmic events. No patient in either group witnessed severe bradycardia (pulse rate less than 50/ min) or severe hypotension (systolic BP less than 90 mm Hg). This observation is contradictory to previous assumptions that both propofol and dexmedtomidine are notorious for their cardio- vascular depressant effect as one study by Barr et al, showed that in 17% of patients' hypotension was the cause of discontinuation of propofol infusion.[21] Studies done by other researchers led to many controversial results. In a direct comparison of propofol to dexmedetomidine, Heard et al,[22] found higher SBP with dexmedetomidine. In a similar study, Koroglu et al,[23] detected no BP change, while Mason et al,[24] observed hypotension associated with the administration of i. v. dexmedetomidine during pediatric MRI procedures.

However, observations made in present study corroborate the fact that abolition of loading dose with higher per kg body weight doses can lead to lesser incidences of bradycardia and hypotension. However the sample size in this study is a limiting factor and this hypothesis need to be tested with larger study sample.

Thus, this study helps a lot to prove the assumption that dexmedetomidine can be safely and effectively used in ICU for the management of critically- ill patients. Dexmedetomidine provides adequate sedation and analgesia and decreases delirium episodes during the hospital stay. Incidences of hemodynamic as well as respiratory depression are much less with its use, and it can be used safely without any apprehension.

CONCLUSION

This study concluded that, both propofol & dexmedetomidine can be used as sedative agent in ICU and both of them are not associated with increased incidences of delirium. Dexmedetomidine provides good analgesia and reduces adjunctive analgesic requirement while propofol is a poor analgesic. Thus, dexmedetomidine is the agent which can be used alone to treat pain, agitation & delirium in ICU.

REFERENCES

1. Sessler CN, Varney K. Patient-focused sedation and analgesia in the ICU. Chest, 2008; 133: 552-65.
2. Barr J, Fraser GL, Puntillo K, Ely EW, Gélinas C, Dasta JF et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med., 2013; 41: 263–306.
3. Riggi G, Glass M. Update on the management and monitoring of deep analgesia and sedation in the intensive care unit. AACN Adv Crit Care, 2013; 24: 101-7.
4. Shagufta Naaz, Erum Ozai. Dexmedetomidine in Current Anaesthesia Practice- A Review. J Clin Diagn Res., 2014; 8: GE01–GE04.
5. Ohtani N, Yasui Y, Watanabe D, Kitamura M, Shoji K, Masaki E. Perioperative infusion of dexmedetomidine at a high dose reduces postoperative analgesic requirements: a randomized control trial. J Anesth, 2011; 25: 872-8.
6. Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesth Analg, 2004; 98: 153-8.
7. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F et al; SEDCOM (Safety and Efficacy of Dexmedetomidine Compared With Midazolam) Study Group. Dexmedetomidine vs midazolam for sedation of critically ill patients. JAMA, 2009; 301: 489-99.
8. Pandharipande PP, Pun BT, Herr DL, Maze M, Girard TD, Miller RR et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. JAMA, 2007; 298: 2644-53.
9. Reade MC, O'Sullivan K, Bates S, Goldsmith D, Ainslie WR, Bellomo R. Dexmedetomidine vs. haloperidol in delirious, agitated, intubated patients: a randomised open-label trial. Crit Care., 2009; 13: R75.
10. Maldonado JR, Wysong A, van der Starre PJ, Block T, Miller C, Reitz BA. Dexmedetomidine and the reduction of postoperative delirium after cardiac surgery. Psychosomatics, 2009; 50: 206-17.
11. Tung A, Bergmann BM, Herrera S, Cao D, Mendelson WB. Recovery from sleep deprivation occurs during propofol anesthesia. Anesthesiology, 2004; 100: 1419-26.
12. Gadalla F, Spencer J. Prolonged delirium after propofol. Can J Anaesth, 1996; 43: 877.
13. Robinson DA. Abreaction on recovery from propofol anaesthesia. Anaesthesia, 1989; 44: 364.
14. Brown KE, Mirrakhimov AE, Yeddula K, Kwatra MM. Propofol and the risk of delirium: exploring the anticholinergic properties of propofol. Med Hypotheses, 2013; 81: 536-9.
15. Diedrich DA, Brown DR: Analytic reviews: propofol infusion syndrome in the ICU. J Intensive Care Med., 2011; 26: 59-72.
16. Hsu YW, Cortinez LI, Robertson KM, et al. Dexmedetomidine pharmacodynamics: part I: crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology, 2004; 101: 1066-76.
17. Peck TE, Hill SA, Williams M. Pharmacology for Anaesthesia and Intensive care, 2nd Edn. Greenwich Medical Media Ltd, 2003.
18. Devlin JW, Roberts RJ: Pharmacology of commonly used analgesics and sedatives in the ICU:

benzodiazepines, propofol, and opioids: Crit Care Clin., 2009; 25: 431-49.
19. Veselis RA, Pryor KO, Reinsel RA, Li Y, Mehta M, Johnson R Jr. Propofol and midazolam inhibit conscious memory processes very soon after encoding: an event-related potential study of familiarity and recollection in volunteers. Anesthesiology, 2009; 110: 295-312.
20. Barr J, Egan TD, Sandoval NF, Zomorodi K, Cohane C, Gambus PL et al. Propofol dosing regimens for ICU sedation based upon an integrated pharmacokinetic-pharmacodynamic model. Anesthesiology, 2001; 95: 324–33.
21. Heard C, Burrows F, Johnson K, Joshi P, Houck J, Lerman J. A comparison of dexmedetomidine midazolam with propofol for maintenance of anesthesia in children undergoing magnetic resonance imaging. Anesth Analg, 2008; 107: 1832–9.
22. Koroglu A, Demirbilek S, Teksan H, Sagir O, But AK, Ersoy MO. Sedative, haemodynamic and respiratory effects of dexmedetomidine in children undergoing magnetic resonance imaging examination: preliminary results. Br J Anaesth, 2005; 94: 821-4.
23. Mason KP, Zurakowski D, Zgleszewski SE, et al. High dose dexmedetomidine as the sole sedative for pediatric MRI. Paediatr Anaesth, 2008; 18: 403-11.