Clinical Investigation

Dexmedetomidine decreases the requirement of ketamine and propofol during burns debridement and dressings

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ABSTRACT

Background and Aims: Dexmedetomidine (Dex), a highly selective α_2-adrenoreceptor agonist, is used for sedation management in various clinical settings and shows anaesthetic-sparing effect. Our aim was to study the effects of Dex on requirements of propofol, ketamine, and intraoperative haemodynamic variations during burns debridement and dressing changes, and compare its effectiveness and safety with combination of ketamine and propofol. **Methods:** Sixty adult patients posted for elective debridement and dressing were included in the study. Thirty patients received Dex (intramuscular) (IM) 1 μg/kg, 1 h before shifting to the operation theatre while the other thirty did not. Anaesthesia was induced with propofol and ketamine followed by adjusted infusion to achieve a Ramsay Sedation Scale score (RSS) of six in all patients. Intraoperatively haemodynamic parameters were recorded at regular intervals of 5, 15, 30, 45, and 60 min. The mean data between the groups were compared by unpaired *t* test and medians by Mann-Whitney U test. Within group analysis was performed by using repeated measures ANOVA. $P < 0.05$ was considered significant. **Results:** The dose requirement of ketamine and propofol in Dex group was significantly lower when compared to control group (100.5 ± 17.58 mg vs. 231.5 ± 60.39 mg ($P < 0.0001$) and 127.7 ± 15.47 mg vs. 254 ± 59.22 mg ($P < 0.0001$) respectively). Additionally, recovery time was lower in the Dex group as compared to the control group, 9.57 ± 1.50 min vs. 11.53 ± 2.56 min ($P = 0.0006$). Haemodynamic variations were also significantly lower in the Dex group as compared to the control group. **Conclusion:** Dexmedetomidine (1 μg/kg IM) reduced the requirement of propofol and ketamine, with more stable intraoperative haemodynamics.

Key words: Burns, dexmedetomidine, drug combinations, debridement and dressing of burns, fentanyl, ketamine, propofol

INTRODUCTION

Patients with burns often present to the operation theatre with different painful conditions that require immediate surgical interventions and anaesthetic agents are needed to provide necessary deep sedation, along with analgesia. Ketamine has been a safe and effective anaesthetic agent for burns dressings with a few limitations such as delayed recovery, emergence phenomenon, and nausea and vomiting.[1] Propofol is also used due to its favourable pharmacokinetics but it lacks the analgesic property intrinsic to ketamine.[2] Fentanyl is added to propofol to compliment the analgesic property. Dexmedetomidine (Dex), a highly selective α_2-adrenoreceptor agonist, is used for sedation in various clinical settings and shows an anaesthetic-sparing effect.[3-7] Studies have shown that concomitant dexmedetomidine use may reduce the requirement of propofol and ketamine, with faster postoperative recovery and more stable intraoperative haemodynamics.[8-12] Hence, we evaluated whether Dex affects the requirement for propofol, ketamine

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and intraoperative haemodynamics during burns debridement and dressing changes, and compared its effectiveness and safety with conventional combination ketamine plus propofol.

METHODS

This prospective, open label study was conducted to assess whether Dex affects the requirement of propofol and ketamine in 60 consenting patients aged between 18-60 years, posted for burns dressing and debridement. Institutional Ethics Committee approved for the study protocol was obtained. Patients were excluded from study with known allergy or contraindications to study drugs, head injury, seizure disorder, and psychological disorders. Written informed consent was obtained from the study participants.

In the Dex group, dexmedetomidine 1 μg/kg IM was given 1 h before induction. The patient was then transferred to the operating room. Monitors (electrocardiography, noninvasive blood pressure (NIBP) and pulse oximeter) were attached and the baseline values were noted.

In both Dex and control groups, patients were premedicated with intravenous glycopyrrolate 0.2 mg, ramosetron 0.3 mg, and fentanyl, 2 μg/kg. All patients were administered bolus dose of ketamine 0.5 mg/kg and propofol 1 mg/kg I.V. in separate syringes. Then the patients received an infusion of 1 mg/kg/h of Ketamine and 100 μg/kg/min of propofol for maintenance in separate i.v lines. The propofol plus ketamine infusion was adjusted to achieve a Ramsay Sedation Scale score (RSS) of 6. As soon as the desired level of sedation was achieved, an appropriate size of laryngeal mask airway (LMA) was inserted and patients were maintained on spontaneous respiration. If patients showed increase in the heart rate, blood pressure, respiratory rate, or body movement on initiation of the surgical procedure was considered as inadequate anaesthesia / analgesia and managed by administering bolus dose of ketamine, 0.25 mg/kg or propofol 0.25 mg/kg through an infusion pump. Blood pressure and heart rate were measured just after placing LMA and at a regular interval of 5, 15, 30, 45, and 60 min.

The study drug infusion was discontinued at the end of the surgical procedure, and total drug consumption was noted. The recovery time (i.e. the time from discontinuation of infusion of the study drug and achievement of RSS score of 3) was also noted. Patients were discharged from the recovery room after attaining an Aldrete Recovery Scale Score of 9/ [as the aldrete score is cosidered to be standard for discharge from recovery room].

Statistical analysis was performed using graph pad prism (Version-4) year 2008.The categorical data were expressed as frequencies and percentages and continuous variables were expressed as mean, median and standard deviation. The categorical variables between the groups were compared using Chi-square test. The mean data between the groups was compared by unpaired *t* test and Medians by Mann-Whitney U test. Within group analysis was performed by using repeated measures ANOVA. $P < 0.05$ was considered significant. A sample of 30 patients per group was required to demonstrate an estimated reduction in dose of ketamine and propofol in both the groups, with 99% power to detect the difference and two-sided alpha error of 0.05.

RESULTS

There was no statistically significant difference in the demographic and clinical characteristics among the two groups [Table 1]. The mean dose of ketamine used in Dex group was significantly less (100.5 ± 17.58 mg) whereas it was 231.5 ± 60.39 mg in the control group ($P < 0.0001$). Similarly, mean dose of propofol in Dex and control groups were 127.7 ± 15.47 mg and 254 ± 59.22 mg respectively ($P < 0.0001$) [Figure 1].

Table 1: Demographic and clinical characteristics

	Dexmedetomidine plus ketamine+ propofol *N*=30	Ketamine+ propofol *N*=30	*P* value
Age (year)	33.67±8.79	32.52±8.84	
Gender (M/F)	8/22	6/24	
Median % of burns	45	42.50	0.88
Ketamine (mg)	100.5±17.58	231.5±60.39	<0.0001
Propofol (mg)	127.7±15.47	254±59.22	<0.0001
Recovery time (min)	9.57±1.50	11.53±2.56	0.0006

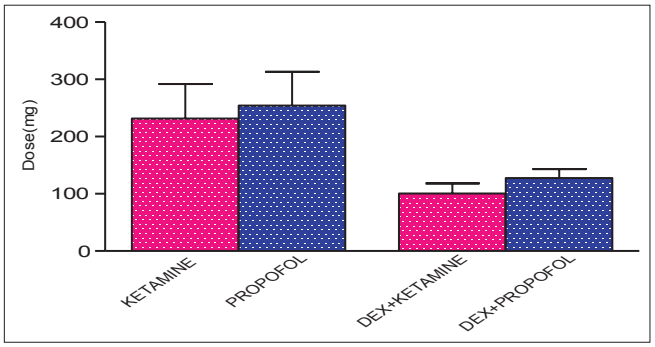

Figure 1: Comparison of dose requirement of ketamine and propofol with and without Dexmedetomidine

Time to recovery was 9.57 ± 1.50 min in the Dex group which was significantly lower than in the control group 11.53 ± 2.56 min ($P = 0.0006$) [Figure 2].

In can be noticed from Table 2 that in dexmedetomidine group HR, SBP, and DBP varied from 74.23 ± 6.76 to 80.47 ± 9.54 beats/min, 114.8 ± 12.6 to 118.9 ± 5.9 mm Hg and 80.17 ± 8.02 to 76.90 ± 7.16 mm Hg, respectively, whereas in control group HR, SBP, and DBP varied from 97.80 ± 17.70 to 85.60 ± 19.87 beats/min, 137.60 ± 14.33 to 129.37 ± 9.98 mm Hg and 93.60 ± 9.68 to 85.67 ± 9.46 mm Hg [Figures 3 and 4] starting from 0 min to 60 min.

DISCUSSION

Dexmedetomidine, by activating pre and postsynaptic α2-receptors of sympathetic system produces vasodilatation.By acting on postsynaptic α2-receptors of vascular smooth muscle cells it produces vasoconstriction. It thereby, shows a biphasic, dose-dependent response on blood pressure and heart rate, characterized by an initial short-term increase in BP followed by a longer lasting reduction in BP and HR.[13-16] Most previous investigations have proven the cardiovascular depressive effects of IM Dex at a dose of 2.5 μg/kg, which increases the incidence of hypotension and bradycardia.[3,17-19] However, Virkkila *et al.* showed that IM Dex 1 μg/kg produced sedation and a reduction of intraocular pressure with minimal haemodynamic side effects when given as premedication before cataract surgery under regional anaesthesia.[20] According to Markku *et al.* IM Dex provides complete bioavailability and needs less preoperative monitoring as compared to IV Dex.[21] Also, Scheinin *et al.* showed that the intramuscular doses resulted in linearly dose-related plasma concentrations of dexmedetomidine;[19] henceforth, clearance and half-life remains constant irrespective of its plasma concentration. For all these reasons we evaluated the effect of 1.0 μg/kg IM Dex on the requirement for supplemental propofol and ketamine during anaesthesia for burns debridement and dressing changes.

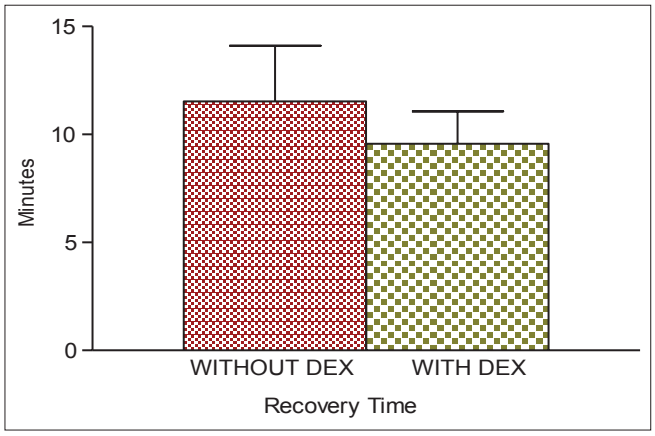

Figure 2: Comparison of recovery time with or without Dexmedetomidine

Despite the limited data, the advantage of adding dexmedetomidine with ketamine is that both balance the haemodynamic and adverse effects of each other. Dexmedetomidine may decrease the incidence of tachycardia, hypertension, salivation, and emergence phenomena from ketamine, while ketamine may prevent the bradycardia and hypotension of dexmedetomidine.[22,23] Additionally, ketamine as part of the sedation induction may speed the onset of sedation and eliminate the slow onset time of IM Dex.[23-26]

In our study, IM Dex reduced the amount of adjuvant propofol and ketamine needed to maintain a RSS score of 6 and provided more stable haemodynamics without Compromising postoperative recovery. These results are consistent with previous investigations showing a 30-50% reduction in the propofol requirement with concomitant use of Dex in adolescent patients and healthy volunteers.[4,5] The sedative effect of Dex is mediated through the locus ceruleus in the brain stem, where Dex decreases sympathetic outflow and

Table 2: Haemodynamic variables between dex group and control group

Time	Dexmedetomidine			Control		
Min	HR beats/min	SBP mm Hg	DBP mm Hg	HR beats/min	SBP mm Hg	DBP mm Hg
0	74.23±6.76	114.8±12.6	80.17±8.02	97.80±17.70	137.60±14.33	93.60±9.68
5	78.67±7.03	122.8±11.3	78.03±8.65	97.03±17.52	135.53±12.30	87.80±18.68
15	83.93±13.21	119.5±10.9	77.27±10.87	94.63±18.55	133.13±11.17	88.40±9.33
30	83.73±13.03	117.0±11.9	77.27±9.02	93.90±18.86	131.90±15.23	86.57±8.57
45	83.13±13.06	119.2±8.6	77.70±8.18	89.90±15.84	133.43±12.95	85.77±8.82
60	80.47±9.54	118.9±5.9	76.90±7.16	85.60±19.87	129.37±9.98	85.67±9.46
P value	<0.0001	0.02	0.14	0.0003	0.15	0.01

HR - Heart rate, SBP - Systolic blood pressure, DBP - Diastolic blood pressure, Dex - Dexmedetomidine

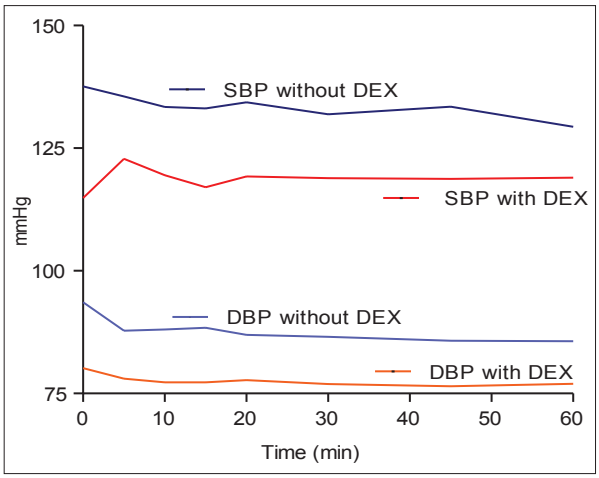

Figure 3: Comparison of changes in blood pressure between two groups

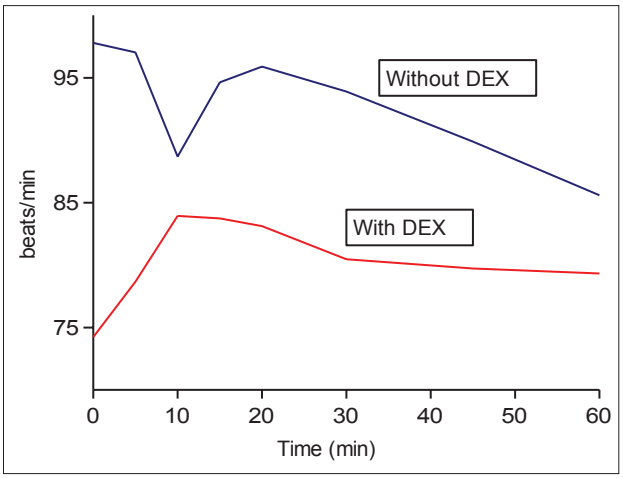

Figure 4: Comparison of changes in pulse rate between two groups

increases parasympathetic outflow.[6,27-29] Though Dex, propofol. and ketamine act at different centres of the brain, they show synergism with respect to their sedative effects.

Previous studies showed a possible delay in recovery from propofol anaesthesia with the concomitant use of Dex, probably due to its quite long duration of action.[5,7,18,30] However, such findings of prolongation of extubation or recovery time profiles were not observed in the present study. Dex, by its propofol sparing effect, may be beneficial for reducing the propofol dosage and avoiding adverse effects such as myocardial depression, metabolic acidosis, impaired platelet aggregation, and extended recovery caused by prolonged and large-dose administration of propofol.[31-37]

According to our study, IM dexmedetomidine use does not cause any significant haemodynamic changes. However, we observed a transient increase in BP immediately after shifting the patient inside the operation theatre may be due to patients anxiety and it came down to normal level after giving fentanyl and midazolam premedication. A more constant stable haemodynamics observed during anesthesia induction, surgical incision and throughout the procedure. A significant change in haemodynamics was observed in the control group. There is decreased consumption of propofol and ketamine because of sedo-analgesic, anaesthetic-sparing effect of dexmedetomidine.

Bispectral index could have been a better monitor for assessing awareness and sedation but could not be used due to non-availability. Clinical changes in the heart rate and blood pressure that are nonspecific were used as signs of increased nociception during our study.

CONCLUSION

Dexmedetomidine (1 μg/kg IM dose) is a good anaesthetic adjuvant that decreases the requirement of propofol and ketamine during burns debridement and dressings, attenuates sympathoadrenal response, maintains stable intraoperative haemodynamics and adequate duration of analgesia, and also has an excellent recovery profile.

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