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Original Article

Analgesia for the Change of Dressing in Burn Victims: A Comparison Between Oral Ketamine and Oral Dexmedetomidine

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Abstract

Objective: To compare the efficacy of oral ketamine with oral dexmedetomidine for providing adequate analgesia for change of dressing in burn patients in burn dressing room.

Methods: This randomized controlled trial was carried out in Jinnah Burn and Reconstructive Surgery Center, Lahore, from April 2019 to September 2019 after getting the approval from the Ethical Committee of Jinnah Hospital / Allama Iqbal Medical College, Lahore. 80 patients between 20 to 50 years, with 1st and 2nd degree burns and 20 to 40% of total body surface area involved were allocated in two groups A and B. The patients in group A received oral ketamine at a dose of 5mg/kg in 15 ml of water 30 mins while those in group B received dexmedetomidine, 4 ug/kg orally, in 15 ml of water 30 mins before the start of dressing change. The change of dressing was carried out with continuous vital monitoring. Pain was assessed via visual analogue scale (VAS) and sedation via Ramsay sedation score. All the observations were recorded on the predesigned proforma. SPSS version 21 was used for data analysis.

Result: The baseline mean VAS score of patients in group A was 7.67 ± 0.55 and in group B was 7.70 ± 0.57 (p value = 0.799). Significant decrease in pain score in both groups was noted after 30 mins of drugs administration (p=0.000). Also a significant difference in pain scores was seen between the two groups ($p< 0.05$), with the patients in group A having lower pain scores as compared to patients in group B.

Conclusion: both ketamine and dexmedetomidine provide adequate analgesia for the change of burn dressing when administered orally with ketamine providing better analgesic state as compared to dexmedetomidine.

Key Words: Burn, ketamine, dexmedetomidine, analgesia.

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Introduction

Burns are one the leading causes of injuries inflicted to human body. The damage to the sensory nerve endings leads to considerable pain. The initiation of generalized inflammatory reaction further adds to the insult and compounds the morbidity and mortality.

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In the present days frequent change of dressings is the hallmark of management of burn injuries. This, however, adds on the pain suffered by the burnvictim. Apart from these acute pains, the burn victims develop neuropathic pain later on.[1,2] In the modern era where various options for pain control are available, managing acute burn pain is still a challenging task. Inadequate pain control leads to various deleterious sequels including delayed wound healing, sleep disturbance, anxiety and post traumatic stress disorder.[3]

Ketamine, a phencyclidine derivative, has been well known for its analgesic properties. Apart from NMDA receptors, it acts on other receptors including opioid receptors to modulate pain. Ketamine is successfully used in various burn centers for management of acute pain. However, it comes at the cost of side effects like hallucination, agitation and emergence phenomenon.[3-5]

Dexmedetomidine has emerged as a newer drug providing good sedation and analgesia but with little respiratory depression. However, hypotension and bradycardia are observed with its intravenous use.[5,6]

Oral route of drug administration is a convenient one but studies on the oral use of dexmedetomidine are scarce. This study is thus designed to compare the efficacy of oral ketamine with oral dexmedetomidine for providing adequate analgesia for change of dressing in burn patients at burn dressing room.

Methods

This randomized controlled trial constituting of 80 patients was carried out in Jinnah Burn and Reconstructive Surgery Center, Lahore, from April 2019 to September 2019 after getting the approval from the Ethical Committee of Jinnah Hospital/ Allama Iqbal Medical College, Lahore.

The patients included in the study belonged of American Society of Anaesthesiologist (ASA) class I and II, both male and females having age between 20 to 50 years, with 1st and 2nd degree burns and 20 to 40% of total body surface area involved. Patients having diabetes mellitus, hypertension, ischemic heart disease, compromised renal or hepatic functions, any psychiatric illness or history of allergy to the drugs used in this study were excluded. Patients with electric burn were also not included in the study. Informed consent was taken from all the patients enrolled in this study.

All the patients included in the study were given tab. bromazepam 3mg orally at night time and injection morphine 0.05mg/kg intravenously before the start of change of dressing. Standard NPO protocols were followed. The patients were randomly allocated in two groups, A and B, with 40 patients in each group. The patients in group A received oral ketamine at a dose of 5mg/kg in 15 ml of water 30 mins before the start of dressing change while those in group B received dexmedetomidine, 4 ug/kg orally, in 15 ml of water 30 mins before the procedure. The change of dressing was carried out as per protocol of the burn unit. Continuous vital monitoring i.e. heart rate (HR), non invasive blood pressure (NIBP) and oxygen saturation (SpO_2) via pulse oximeter was carried out throughout the procedure. These haemodynamic parameters were recorded on a pre designed proforma including before the administration of drugs, 5 mins, 30 mins, 60 mins and 120 mins after the drugs administration. Pain was assessed via visual analogue scale (VAS) and sedation via Ramsay sedation score. Any adverse events were also noted and treated accordingly. Any patient requiring rescue analgesia was also noted and treated by giving injection morphine intravenously titrating the dose but not exceeding more than 0.05mg/kg. All the observations were recorded on the predesigned proforma.

Statistical Analysis

The data was analysed using SPSS version 21. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, oxygen saturation, VAS score and sedation were analysed over a period of time using repeated measure ANOVA, with Tukey's method employed as a test of significance. P value < 0.05 was taken as significant. Mean was calculated for quantitative variables like age and body surface area burnt and t-test was used as test of significance with p value <0.05 taken as significant. For qualitative variables like gender, need for rescue analgesia and occurrence of side effects like salivation and delirium frequency, chi square test was used as a test of significance, p value < 0.05 was considered significant.

Table 1: *Physical Characteristics and Base Line Parameters of Two Groups*

Parameters	Group A	Group B	P value
Age (years)	35.o8 + 10.01	34.08+ 9.27	0.899
Gender	Male= 21 Female = 19	Male = 20 Female = 20	0.823
BSA Burn (%age)	29.58+ 6.94	30.12+ 7.15	0.728
SBP (mmHg)	122.63+18.81	123.50+17.51	0.83
DBP (mmHg)	73.75+ 10.36	74.87+ 11.68	0.65
HR (bpm)	99.62+ 12.08	102.70+12.76	0.272
SpO2 (%age)	97.83+ 1.05	97.65+ 1.29	0.55
Sedation (Ramsay scale)	1	1	-
Pain Score (VAS cm)	7.67 + 0.55	7.70 + 0.57	0.799

Results

Both groups were comparable in terms of gender, age, percentage of total body surface area burnt, initial pain score, sedation score and haemodynamic parameters as shown in Table-1.

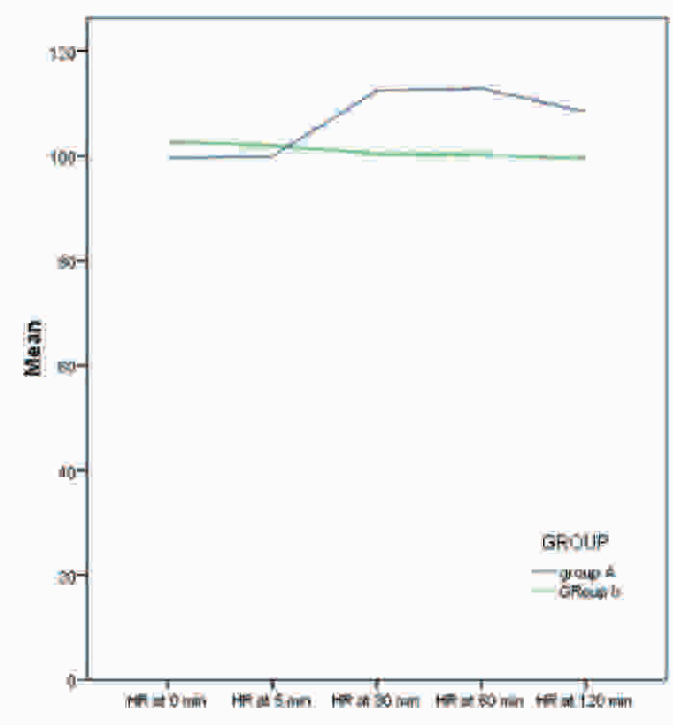
The baseline mean VAS score of patients in group A was 7.67 + 0.55 and in group B was 7.70 + 0.57 with p value of 0.799. Significant decrease in pain score in both groups was noted at 30 mins of drugs administration (p=0.000). Although patients in both groups

Table 2: *Comparison of Sedation Score of Two Study Groups*

	Group	Mean	Std. Deviation	N
sedation score at 0 min	Group A	1.00	.000	40
	Group B	1.00	.000	40
	Total	1.00	.000	80
sedation score at 5 min	Group A	1.00	.000	40
	Group B	1.00	.000	40
	Total	1.00	.000	80
sedation score at 30 min	Group A	2.00	.000	40
	Group B	2.00	.000	40
	Total	2.00	.000	80
sedation score at 60 min	Group A	2.75	.439	40
	Group B	2.00	.000	40
	Total	2.38	.487	80
sedation score at 120 min	Group A	2.92	.267	40
	Group B	2.00	.000	40
	Total	2.46	.502	80

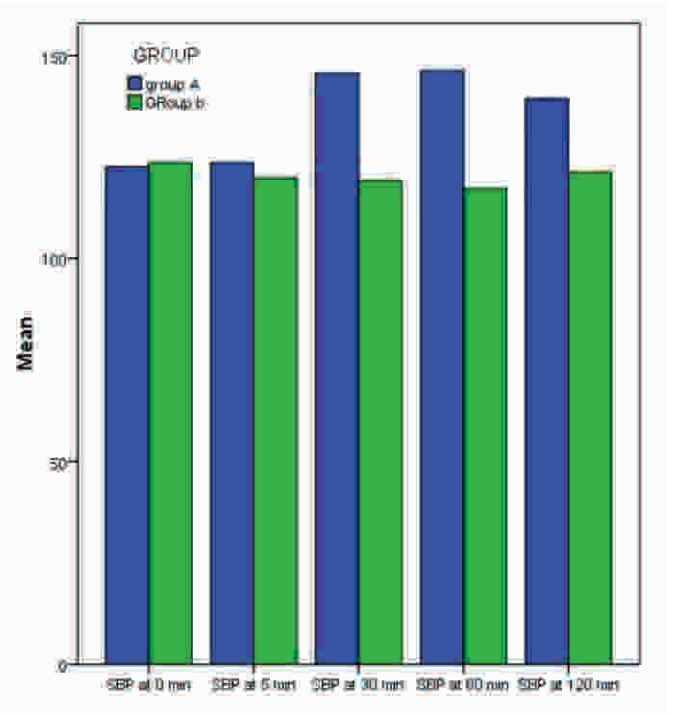
displayed significant pain relief, but a significant difference in pain scores was seen between the two groups as well ($p< 0.05$), with the patients in group A having lower pain scores and hence better analgesia as compared to patients in group B.

In both groups the baseline sedation score was 1 and at 30 mins it was 2. After 30 mins the sedation score in group A gradually increased whereas no change of score was seen in group B. (Table-2).

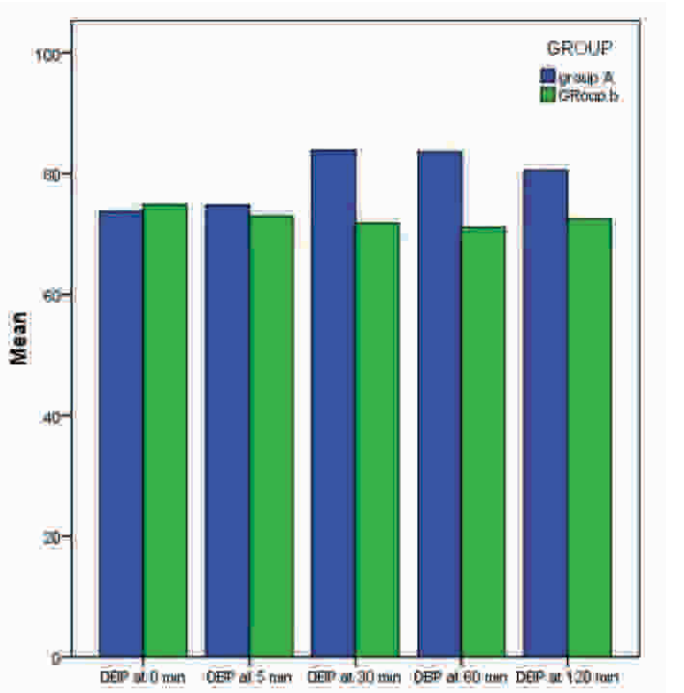


Graph-1: *Comparison of Mean Heart Rate of Two Groups*

Significant changes were noted in SBP, DBP and HR in both groups over time ($p < 0.05$). It was observed that the changes were significant between two groups as well, with these parameters showing a rising trend in group A while a decreasing trend in group B. (Graphs- 1,2,3,)



Graph-2: *Comparison of Mean Systolic Blood Pressure of Two Groups*



Graph-3: *Comparison of Mean Diastolic Blood Pressure of Two Groups*

Mean oxygen saturation at the time zero in group A was 97.83% + 1.05 and in group B was 97.65% + 1.29 with p value = 0.51. No significance difference in oxygen saturation was seen between the two groups at any point of time. No patient in any of the two groups had fall of oxygen saturation below 90% (Table-3).

7 out of 40 patients in group B (17.5%) needed rescue analgesia while none in group A needed it. In group A, 12 patients (30%) had delirium and 15 patients (37.5%) had excessive salivation while there was no case of delirium or excessive salivation in group B.

Table 3: *Oxygen Saturation of Two Groups Over Time*

	Group	Mean	Std. Deviation	N	P value between groups
Saturation at 0 min	Group A	97.83	1.059	40	
	Group B	97.65	1.292	40	0.510
	Total	97.74	1.177	80	
Saturation at 5 min	Group A	98.00	.906	40	
	Group B	97.92	1.047	40	
	Total	97.96	.974	80	0.733
Saturation at 30 min	Group A	96.80	1.305	40	
	Group B	96.95	1.260	40	0.602
	Total	96.87	1.277	80	
Saturation at 60 min	Group A	96.97	1.209	40	
	Group B	97.07	1.207	40	
	Total	97.02	1.201	80	0.712
Saturation at 120 min	Group A	97.50	1.155	40	
	Group B	97.52	1.154	40	0.923
	Total	97.51	1.147	80	

Discussion

Burn injuries are considered one of the most debilitating of acute injuries. The degree of pain endured depends upon the thickness of burns and the area involved. It must be kept in mind that the full thickness burn in which even the sensory nerve endings carrying the nociceptive stimuli are damaged, are frequently surrounded by the areas of superficial burns which are much painful. Also different individuals have different threshold of pain. Hence the pain experienced by patients having similar burn injuries may also vary. Apart from the baseline pain suffered by the patients due to burn, the procedures carried out to accelerate the healing like frequent dressing changes, debridement and graftings further add to the acute pain suffered by the burn victims.[1-3]

Ketamine is being used as an anaesthetic for over fifty years now with the unique characteristic of producing dissociative anaesthesia. It is also an excellent analgesic agent even at subanaesthetic doses. It produces analgesia by acting as an antagonist at N-methyl-D-aspartate (NMDA) receptors. It not only blocks the channel by plugging the pore but also decreases the frequency of channel opening. However, NMDA antagonism is not the only mechanism which is responsible for the analgesic effects of ketamine.[4,7] Various other mechanisms have been proposed which confers ketamine its analgesic property. These include Serotonin reuptake inhibition, partial agonistic effect at opioid receptors and interaction at GABA, cholinergic and dopaminergic receptors.[4,7-9] Such is the quality of analgesia conferred by ketamine that it is now being used in emergency for the management of acute pain and also for chronic pain management[10] including the opioid resistant pain.[4] Due to its excellent analgesic profile, ketamine has been used for the change of burn dressings and graftings in burn victims for long time now.[7] Recent studies have shown that ketamine also possess anti-depressant effect[4,7,11], a property which could be of additional benefit for the burn patients in whom the element of depression is not uncommon.[12] Ketamine can be given by various routes including intravenous which has 100% bioavailability, intramuscular with 93% bioavailability, oral, intranasal, rectal, subcutaneous, transdermal andepidural.[4,7,13] The bioavailability of orally administered ketamine is low, around 16% to 25%. However much higher plasma levels of norketamine, a metabolite of ketamine, were seen when oral route is used for ketamine administration.[4,5,11] Ketamine causes minimal respiratory depression. Upper airway reflexes are usually maintained.[7,8] Some of the common side effects includes hallucination, delirium, excessive salivation, raised ICP, hypertension and tachycardia.[4,7,9]

Dexmedetomidine is a relatively newer drug in the world of medicine. This highly selective centrally acting alpha-2 adrenergic agonist has sedative, amnestic, anxiolytic and analgesic properties. The sedation produced by dexmedetomidine is unique in the sense that it resembles natural sleep. Patients remain calm, lightly sedated and easily arousable.[14-16] Apart from intravenous route of administration which has the highest bioavailablity, this drug can be administered via intranasal, sublingual and oral route. However, the bioavailability after oral administration is low due to high first-pass metabolism.[14] Dexmedetomidine

provides analgesia by acting on adrenergic receptors, thereby, having an opioid sparing effect. Due to the provision of stable haemodynamics, sedative, anxiolytic and analgesic properties, this drug is increasingly used for premedication and also in post operative period to provide analgesia. Despite shorter elimination half-life, the analgesic effect was observed to last for up to 24 hours.[17] Dexmedetomidine is becoming popular for sedation in ICU for mechanically ventilated patients. Patients get more natural sleep, are less delirious, have better pain relief and are extubated earlier with shorter ICU stay.[14,16] Common adverse effects associated with the use of dexmeditomidine includes a fall in blood pressure especially in frail patients and bradycardia. Patients may also experience heart blocks, dry mouth, pulmonary edema, lactic acidosis and paresthesia.[14] However; these adverse effects are minimally seen with the oral use of dexmeditomidine.[18]

The results of our study show that both ketamine and dexmedetomidine provide effective analgesia for the dressing change in burn patients when administered orally. Analgesia provided by ketamine is significantly more as compared to dexmedetomidine. However, the patients receiving ketamine had experienced increase in the HR, BP, excessive salivation and delirium. These changes were not seen with the use of dexmedetomidine. Similar results were seen in the study conducted by Kundra et al.[5] Ravipati et al used intra muscular dexmeditomidine as premedication for the dressing change and grafting in burn patients. Their results showed dexmedetomidine reduces the requirement of ketamine and propofol ($p< 0.0001$) and provides better haemodymanic state.[19]

Norambuena et al. concluded in their study that orally administered midazolam combined with ketamine provides better analgesia as compared to the combination of midazolam, codeine and acetaminophen for burn dressing and other related procedures in paediatric population.[20]

Although dexmedetomidine has been used in infusion form for sedation and analgesia in burn victims in ICU but studies regarding its use as an analgesic for burn dressing change and that too in oral form are scarce.

Our study data shows that dexmedetomidine is orally effective for providing analgesia in burn patients. This route of administration will help to overcome the problems of parenteral administration of this drug and improved patient compliance.

Conclusion

The study showed that both ketamine and dexmeditomidine provide adequate analgesia for the change of burn dressing when administered orally with ketamine providing better analgesic state as compared to dexmedetomidine. 17.5% patients who received dexmedetomidine needed rescue analgesia. However, side effects like excessive salivation and delirium seen with the use of ketamine (37.5% and 30% respectively) were not seen with the dexmeditomidine. Also dexmeditomidine provided better haemodynamic profile as compared to ketamine which causes tachycardia and hypertension; conditions detrimental for cardiac patients.

Conflict of Interest: None

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Authors Contribution

SF: Conceptionlization of Project
SF,RL,AF: Data Collection
RL,SF,AW: Literature Search
RL: Statistical Analysis
SF: Drafting, Revision
SF,RL: Writing of Manuscript