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COMPARISON OF PROPOFOL-KETAMINE (KETOFOL) AND PROPOFOL-FENTANYL (FENOFOL) FOR SEDATION, RECOVERY AND HEMODYNAMICS IN PEDIATRIC PATIENTS UNDERGOING BURNS DRESSING CHANGE.

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ABSTRACT

Burn injury is one of the leading cause of hospital admissions that have been associated with long term nervous system morbidity particularly for pediatrics population. Chronic persistent pain have been reported in 52% of the respondents that directs the aim at providing adequate analgesia during burn dressing. Multiple modalities have been used to alleviate the pain, anxiety and stress of burn dressing among pediatric patients. Many such modalities include use of music therapy, use of hypnosis, patient control analgesia and distraction techniques . Multiple intravenous analgesic agents have been studied and recommended to use for burn dressing change such as fentanyl, ketamine, tramadol, midazolam, Dexmedetomidine , morphine and satisfactory results have been achieved. We selected pediatric patients age between 5-12 years, having second degree burn of 5-25% requiring burn dressing change. The patients were divided into two groups to receive propofol-ketamine and porpofol-fentanyl according to their weights. Additional porpofol was given to achieve sedation score of 4 and start the procedure. Thourghout the procedure their sedation score, hemodynamics and any adverse effects were noted. Post procedure their recovery scores were recorded in PACU. We found better and early sedation in ketofol group while fenofol group gave better hemodynamics and recovery of the patients. There were no significant adverse effects in both the groups. we concluded that the combinations propofol- ketamine and propofol- fentanyl are satisfactory sedative agents for change of dressings in pediatric burn patients, however combination of PF is superior to PK group for rapid recovery of patient with better hemodynamic profile.

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INTRODUCTION

Burn injury is one of the leading cause of hospital admissions. It is associated with long term anxiety and pain in pediatric patients. An appropriate sedation regime is extremely important in pediatric burn patient to alleviate its long term effects [1]. Multiple modalities have been used to alleviate the pain, anxiety and stress of burn dressing among pediatric patients. Many such modalities include use of music therapy[2], use of hypnosis[3], patient control analgesia[4] and distraction techniques[5]. Multiple intravenous analgesic agents have been studied and recommended to use for burn dressing change such as fentanyl, ketamine, tramadol, midazolam, Dexmedetomidine , morphine and satisfactory results have been achieved with the aim providing better sedation[6,7]. Multiple routes such as intranasal, oral, intravenous and multiple combinations have also been tried various routes and combinations have also been tried[7,8].

Ketamine is a drug that have been known as complete anaesthetic agents for providing amnesia analgesia and narcosis. It has been found safe and effective agent for painful procedures in pediatrics burn patients[9,10]. Combinations of ketamine and propofol have widely been used to provide sedation and analgesia for short procedure[11].

Among opioids, fentanyl has been popular for its short duration of action and rapid onset[12]. It has been used intranasal, trans mucosal, as an infusion for controlling pain associated with burn as well as in combination with other non-opioid agents[13,14]. Thus different anaesthesia techniques through different routes have been successfully used in pediatric population with satisfying outcomes.

To the best of our knowledge, very limited data is available that compares propofol– ketamine (PK) and propofol– fentanyl (PF) used during burn dressing changes in pediatric patients, particularly at our national level. The popular regime of ketofol is extensively used but limited data and practice is found for fenofol. Therefore, the objective of our study is to compare effects of this TIVA regime that is ketamine and fentanyl with propofol in procedural sedation, time to recover from sedation and hemodynamic effects of drugs on pediatric patients undergoing change of burn wound dressing.

Methodology:

Patients having ASA physical status of I- III, aged between 5-12 years, hospitalized with second degree burns surface ranging between 5 %-25 % were included in the study. Patients who required inotropic support or mechanical ventilation were excluded from the study. The study was performed in the operation theatre of burn unit Civil Hospital Karachi. Patients meeting the inclusion criteria were randomly divided in to two groups, fenofol (PF) and ketofol (PK) by (primary investigator or co-investigator) through coin toss method and were brought to operating room after 6 hours of fasting and without premedication on the day of procedure. After taking patient in operating room the routine monitors were applied for heart rate (HR), noninvasive blood pressures (NIBP), SpO2 and respiratory rate (RR) monitoring and baseline reading were noted by Primary anesthetist. The intravenous line was maintained and half strength dextrose saline was given at 10-15 ml / minute .The study drug solution was prepared by primary investigator or co-investigator who did not participate in drug administration and patient assessment. The drugs was diluted as follow

Ketamine (50milligram/ml ampoule): 1 ml ketamine and 4 ml normal saline, final strength 10mg/ml.

Fentanyl (50 microgram/ml ampoule): 1ml Fentanyl and 4 ml normal saline, final strength 10 microgram/ml.

With above dilution of drug PI and CO PI made two syringes in dose of 1mg/kg for ketamine and 1 mics/kg for fentanyl group.

The Primary anaesthetist was blinded to the sedation regime and was involve procedural sedation, monitoring, patient management and data collection. PK group received 1 mg/kg + 0.5 mg/kg of propofol, and PF group received 1mics/kg of fentanyl +0.5mg of propofol for induction. Ramsey sedation score was recorded after inducing the patient and additional propofol (0.5– 1 mg/kg) was administered to achieve a Ramsey sedation score of 4 and then dressing was started. Throughout the procedure heart rate, systolic and diastolic blood pressures, Oxygen saturation and respiratory rate were recorded every five minute interval. If the patient showed discomfort or increase in heart rate or systolic arterial pressure, despite additional propofol dose, additional bolus of 0.5– 1 mg/kg of ketamine or 0.5– 1 mics/kg of fentanyl was administered in increments OF 1-2 mls. Total doses of propofol , fentanyl and ketamine used for the procedure was recorded. Occurrence of patient movement during the procedure was also assessed and recorded. At the end of procedure, patient was shifted to post anaesthesia care unit (PACU) and patient' s recovery was assessed by using aldrete recovery score at 5 minutes and 10 minutes. Side effects such as nausea, vomiting, respiratory depression and hypoxia was observed and recorded.

Data entry and analysis was done using statistical package of social sciences version 24.Relevant descriptive statistics, frequency, and percentages were computed for qualitative variables like ASA status, gender. Mean and SD were computed for quantitive variables like age, weight, duration of procedure and total burn surface area. Chi square test was applied for categorical data such as ramsey sedation score, aldrete recovery score, adverse effects. Student' s T test was applied for continuous data such as dose of propofol required P-value <0.05 was taken as significant.

RESULTS:

Table 1: Demographic Data.

Variables	Group PF n=25	Group PK n=25	P-Value
Age (Years)	8±1.95	8±1.89	0.999
Weight (kg)	24.92±3.98	25.96±3.07	0.307
Total burn Surface area (%)	12.44±5.1	12.72±3.56	0.855
Male	14(56%)	16(64%)	0.564
Female	11(44%)	9(36%)	
Duration of Surgery (min)	16.8±3.78	16.40±3.39	0.696

Table 2: Comparison of sedation score between groups.

Time	Ramsey Score	Group PF n=25	Group PK n=25	P-Value
5 min	1-3	20(80%)	7(28%)	<0.005
	4	**5(20%)**	**10(40%)**	
	5-6	0(0%)	8(32%)	
10 min	1-3	20(80%)	0(0%)	<0.005
	4	3(12%)	4(16%)	
	5-6	2(8%)	21(84%)	
15 min	1-3	13(52%)	0(0%)	<0.005
	4	12(48%)	7(28%)	
	5-6	0(0%)	18(72%)	
20 min	1-3	1(4%)	0(0%)	<0.005
	4	24(96%)	0(0%)	
	5-6	0(0%)	25(100%)	

Table 3: Total drug consumption and occurrence of movement between groups.

Time		Group PF n=25	Group PK n=25	P-Value
Total Propofol dose(mg/kg)		3.24+-1.42	1.400+-0.611	<0.000
Total ketamine dose (mg/kg)			2.0 +-0.5	
Total fentanyl dose(mg/kg)		1.5+_0.5		
Occurrence of the patients movement	No Movement	2(8%)	10(40%)	0.019
	Mild	19(76%)	14(56%)	
	Gross	4(16%)	1(4%)	

Table 4: Comparison of ALDRETE Recovery score and surgeon Satisfaction between groups.

Time	ALDRETE Recovery Score	Group PF n=25	Group PK n=25	P-Value
5min	1-4	1(4%)	2(8%)	0.0005
	5-7	7(28%)	21(84%)	
	8-10	**17(68%)**	**2(8%)**	
10min	1-4	0(0%)	0(0%)	0.005
	5-7	1(4%)	9(36%)	
	8-10	**24(96%)**	**16(64%)**	
Surgeon Satisfaction	Satisfied	20(80%)	23(92%)	0.417
	Unsatisfied	5(20%)	2(8%)	

The demographics were comparable in terms of age, weight, TBSA, gender and duration of surgery as shown in table 1.

Table 2 is showing comparison of ramsey sedation scores at 5, 10, 15 and 20 minutes between the groups and showing significant results. At 5 minute, 40% of patients in group PK had desired sedation score of 4 while only 20% in PF group had score of 4 (P value <0.005). We found deeper levels of sedation (5 and 6) in PK group at 10, 15 and 20 mint (84%, 72% and 100 % respectively) (table 3). In fenofol group, total dose of propofol used to achieve desired sedation scorey of 4 was significantly higher with average requiring 3.24 mg per kg and 1.4 mg/kg in ketofol group.

Despite of more propofol consumption, we found only 2 patient with deeper sedation of 5, 6 at 10 minutes. The desired level of sedation was achieved gradually in 96% of patients over the period of 20 minutes

Table 3 shows statistical significant difference in recovery scores at 5 and 10 minutes with early recovery in propofol-fentanyl group as compare to propofol-ketamine group. The recovery score of 8-10 at 5 and 10 minute in PF group was 68 % and 96% while in PK group it was 8% and 64% respectively in table 4. Surgeons were equally satisfied in carrying out the procedure in both the groups however the fenofol group showed occurrence of patient movement but only a few lead to withholding of procedure.

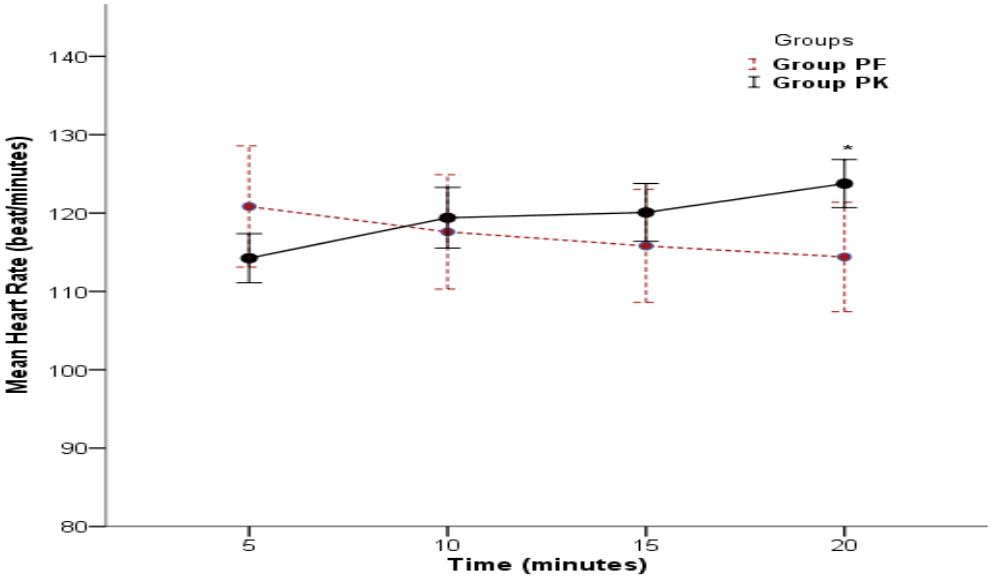

Figure 1: Comparison of mean heart rate of patients between groups.

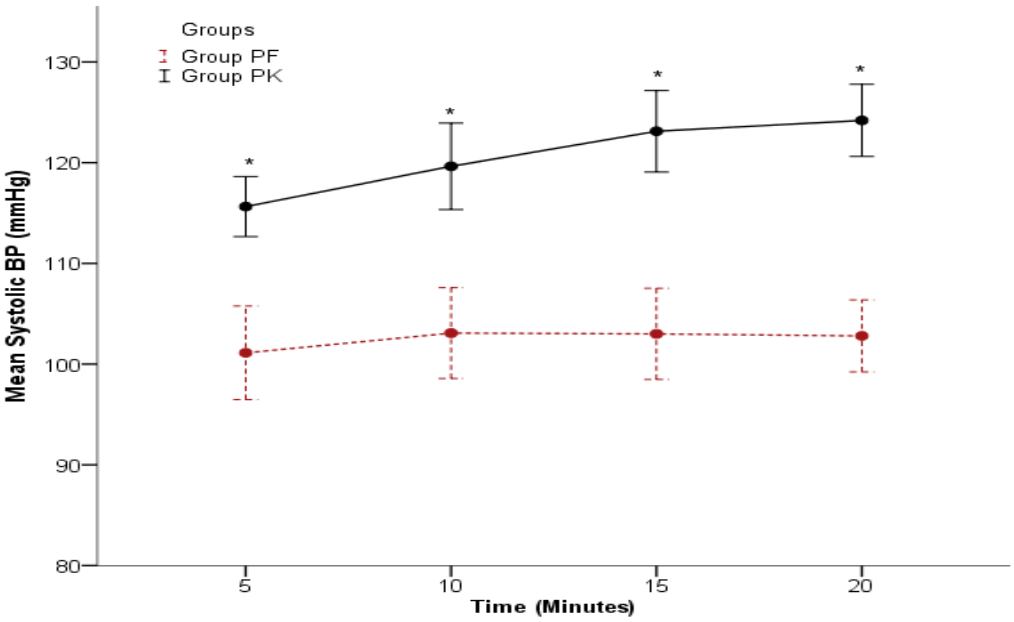

Figure 2: Comparison of mean systolic blood pressure of patients between groups.

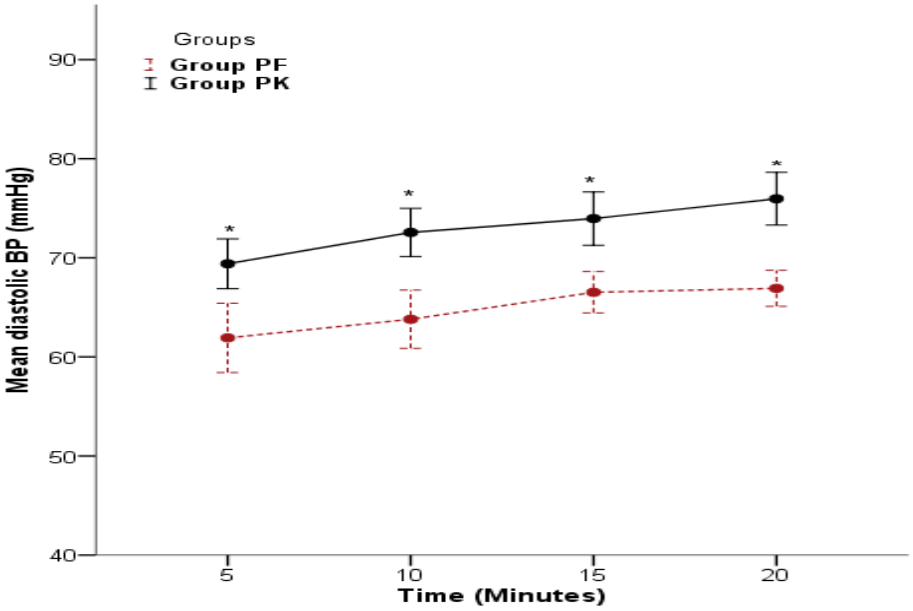

Figure 3: Comparison of mean Diastolic blood pressure of patients between groups.

Mean heart rate were compared in both groups at every 5 minute time points. The difference was significant at 20 minutes with mean heart rate of 114.40 (standard deviation 16.924) in fenofol group and 123.7 (std deviation 7.4) in ketofol group (P value = 0.015). Figure 1

Mean systolic blood pressures were compared and found significant at 5 minute, 10minutes, 15minutes and 20 minutes between the groups (P-value 0.005 for each point of time). Figure 2

Mean diastolic blood pressures were also compared and found significant at 5 minute, 10minutes, 15minutes and 20 minutes between the groups (P-value <0.01). Figure 3

Therefore, group fenofol had better hemodynamics than group ketofol. It showed greater fall in mean systolic and diastolic blood pressures.

Two patients in propofol-fentanyl group desaturated up to 90%SpO_2 that required jaw adjustment during the procedure. There were no episodes of respiratory depression, laryngospasm or nausea vomit or emergence reaction in either group during or after the procedure. Rate of hypoxia was 4% cases and rate of hypoxia was not statically significant between group PF vs. group PK [8% vs. 0% p=0.490]

DISCUSSION

Dressing change is essential procedure for all degrees of burn injury as it leads to good wound healing. Although it is a short procedure but still requires a challenging anaesthetic technique keeping in account good sedation and anaelgesia as well as early patient' s recovery[15].Pediatric case for burn dressing change are not so uncommon, pain and anxiety are two main factors burn patients face for long duration of time after their injury and these concerns are more challenging to control in pediatric population[16]. Thus it is essential that a drug or a combination of drug be present and used which leads to adequate sedation, has duration according to procedure period, provide good recovery status and better hemodynamic. Combinations commonly used are propofol and low-dose ketamine (ketofol) or propofol with opioids[17,18]Although propofol and low-dose ketamine (ketofol) or propofol with opioids (fenofol) have been used in various procedures, there is scarcity of their use in pediatric patients undergoing burns dressing.

The present study showed that the propofol- ketamine and propofol – fentanyl combinations both were effective for deep sedation during dressing change in pediatrics burn patients. However, patients in the group PF had more propofol consumption to achieve the desired level of sedation. Propofol is a drug of choice for sedation in short procedures. Behzad et al in their research on lumpectomy used the above combinations for quality of sedation and similar to our study found that the PF group had lower level of sedation[19]. Akin et al compared the two drug combination for sedation during biopsy and found that these combinations are comparable in providing deep sedationwhich is contrary to our result[20]. In a recent study conducted by Shweta et al on combinations for sedation in examination under anaesthesia, they found that propofol combined with either fentanyl or ketamine reduces its total dose of consumption and similar to our study the total dose of propofol used in fenofol group was higher than ketofol[21]. Like our study dose of propofol used in fenofol group was more in a study conducted on short orthopeadic procedures in which Hemodynamic variable were similarly decreased in fenofol group but contrary to our study sedation and recovery times were more in fenofol group[22]. A study was conducted by Tosun et al on upper GI endoscopy they found that dose required for adequate sedation in propofol fentanyl group was significantly higher than propofol Ketamine group similar to our study[23] but it was contrary to the other study done for burn dressing change[7].

In current study, the recovery scores of both group' s patient were different, with fenofol group acquiring early recovery in post anaesthesia care unit. Like our study, an RCT done on women undergoing tubal ligation with above combination found that recovery was significantly prolong in ketofol group and concluded that fenofol combination provide faster recovery[24]. Ketamine when combined with propofol and dexmedetomidine in pediatric burn dressing change showed prolong recovery time in PK group similar to our study[25]. Results were also in line with study conducted by Seol et al on ketofol and propofol with opiod showing similar prolong recovery in ketofol group[26]. In a study conducted by Bajwa et al, two drug combinations of TIVA using propofol– ketamine and propofol– fentanyl were studied for the induction, maintenance and recovery characteristics in order to find the ideal anaesthetic agent. Similar to our study they found early wakefulness in PF group and no major adverse effects of the drugs [27].

Owing to the sympathomimetic activity of ketamine, we don' t found comparable results in both groups interms of hemodynamics with higher mean heart rate and blood pressure in PK group. There is abundance of literature showing hemodynamic differences in both the groups. Similar to our study, BARADARI et al studied the hemodynamic response to laryngoscopy and intubation and found better hemodynamics in fenofol group[28]. Tuncali et al used various combinations for sedation during colonoscopy and also showed similar hemodynamic profile[29]. Ramdev B et al compared TIVA techniques using same drug regime of ketofol and fenofol. Similar to our study, They found significant fall in pulse rate and blood pressure on induction with fenofol compared to ketofol, however they returned to baseline values postoperatively[30]. Another study conducted by Sandhya et al comparing the hemodynamic variables in short elective surgeries of less than 30 minutes using the above regimes. Contrary to our study, they found no significant differences in recovery characteristics of the pateints and also found comparable hemodynamics in both group[31].

From the above discussion we found that Propofol combined with either ketamine or fentanyl provides effective sedation for burn dressing change. The propofol combination with ketamine although providing good sedation but can prolong recovery time in pediatric patients. the propofol– fentanyl combination provides faster recovery with better hemodynamics.

CONCLUSION

The combinations propofol- ketamine and propofol- fentanyl are known sedative agents and both provide satisfactory sedation in pediatric burn patients. However, procedures like burn dressing change are relatively short and are associated with fluctuations in hemodynamics. Quick recovery and stable hemodynamics are needed to safely discharge patient from PACU. Therefore combination of PF is found to be superior to PK group for burn dressing change owing to rapid recovery of patient with better hemodynamic profile. However this study is single centered. More extensive research is needed in this area to set proper standards for pediatric sedation and recovery.

Authors' Statements

Competing Interests

The authors declare no conflict of interest

Authors contribution:

Dr Anum Mughal and Dr Sana Urooj did manuscript writing. Dr jamil akhtar, dr basher sheikh and dr hanya javaid did critical review and finalized the article.

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Abbreviations:

PK	=	propofol-ketamine,
PF	=	propofol-fentanyl,
PACU	=	post anaesthesia care unit,
TIVA	=	total intravenous anaesthesia.

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