ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 08 | August - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF INTRAVENOUS SEDATION WITH KETAMINE + PROPOFOL VERSUS KETAMINE + DEXMEDETOMIDINE IN PAEDIATRIC DENTAL PROCEDURES

Anaesthesiology

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ABSTRACT

OBJECTIVE: To assess and compare the sedation levels achieved using two intravenous drug combinations, ketamine + propofol and ketamine + dexmedetomidine , in pediatric dental procedures. **STUDY DESIGN:** Prospective comparative study **MATERIALS AND METHODS:** Forty children satisfying the inclusion criteria were selected and divided into 2 groups of 20 each, group KP and group KD. The study drug was administered once written informed consent was taken, and nil per oral guidelines were followed. Hemodynamic parameters that were continuously monitored throughout the procedures for later comparision were heart rate, blood pressure and oxygen saturation. Sedation was assessed with Modified Ramsay Sedation Score and Houpt Sedation Score and Recovery with Modified Aldrete's Recovery Scale. **RESULTS:** Both the drug combination produced adequate sedation and hemodynamic stability. **CONCLUSION:** Among the two drug combinations, Ketamine + Dexmedetomidine demonstrated greater efficacy compared to Ketamine + Propofol.

KEYWORDS

INTRODUCTION:
Delivering dental care while avoiding any psychological effects on a child is a challenging aspect of paediatric dentistry. Any resistance or uncooperative behaviour from the child can complicate the delivery of safe and effective dental treatment.

The most effective and safe solution for delivering dental treatment is intravenous (IV) sedation.

Commonly used medications for dental sedation include nitrous oxide, midazolam, ketamine, propofol, and dexmedetomidine.

Ketamine, a derivative of phencyclidine, is available as ketamine hydrochloride, which consists of a mixture of two isomers, S and R. It is an effective analgesic that induces a distinctive state of "dissociative anaesthesia." Ketamine offers a broad safety margin, typically preserving the airway's protective reflexes.[1,2] The use of ketamine is restricted by the potential for hallucinations during the postoperative period, though this is less common in children. Subanaesthetic doses (0.5–1.0 mg/kg) of ketamine can offer both sedation and analgesia.

Propofol, chemically known as 2.6-diisopropylphenol, is an intravenous anaesthetic used for both the induction of anaesthesia and procedural sedation. At a dose of 2 mg/kg intravenously, propofol induces general anaesthesia, while subanaesthetic doses (25–50 µg/kg/minute) provide sedation. Additionally, propofol has antiemetic and antipruritic effects. Its recovery is typically fast and of high quality.[3]

Interestingly, a physical combination of ketamine and propofol , commonly referred to as "ketofol," has proven effective for sedation. In this approach, both medications are administered in lower doses.[4]

Dexmedetomidine is a novel centrally acting α2 agonist that delivers sedation and analgesia without causing significant respiratory depression. The sedation it provides resembles certain features of natural sleep. However, dexmedetomidine can affect the cardiovascular system, leading to bradycardia and hypotension, though paradoxically, some patients may also experience hypertension. It has been widely used for sedation across all age groups, including children, and is known for its excellent safety profile.[5]

Ketamine and dexmedetomidine work together synergistically to deliver outstanding sedation while minimizing side effects.[6]

In this study, we evaluated the effectiveness of two different combinations i.e ketamine with propofol and ketamine with dexmedetomidine , in providing sedation for children undergoing dental treatment.

AIM AND OBJECTIVE OF THE STUDY:
To assess and compare the sedation levels achieved using two intravenous drug combinations, ketamine + propofol and ketamine + dexmedetomidine, in paediatric dental procedures.

MATERIALS AND METHODS:
Forty children belonging to the age group 4–8 years of either gender visiting the dental OPD were included in this study. Children considered for the study were, healthy, anxious, and apprehensive children with dental problems, irrespective of socioeconomic status. These children were equally and randomly distributed into two groups.

- Group KP: Ketamine with Propofol
- Group KD: Ketamine with Dexmedetomidine
- The ASA status of the children was determined.

INCLUSION CRITERIA:
- Children requiring any comprehensive dental treatment such as restorations, extractions, pulp therapy, etc
- Children with ASA I or II physical status.

EXCLUSION CRITERIA:
- Children requiring major surgical procedures.
- Children requiring dental procedures of more than 45 minutes duration.
- Children who are differently abled.

Written informed consent for dental procedures under conscious sedation were taken from each parent/guardian. The NPO guidelines followed were: the child could not consume clear fluids 2hrs before and solid fluids 6hrs before surgery.

Vital signs (heart rate, oxygen saturation, and blood pressure) were recorded as follows:

Before premedication, after 15 minutes of premedication, before sedating the patient, every 5 minutes of the procedure, after the procedure. Electrocardiogram was continuously monitored in all patients.

All children were premedicated with oral midazolam (0.5mg/kg) 30 minutes prior to the procedure. 22-gauge iv cannula was secured.

Group KP: received propofol 1 mg/kg and ketamine 1 mg/kg over a period of 2–3 minutes.

Group KD: received dexmedetomidine 1 µg/kg and ketamine 1 mg/kg over a period of 2–3 minutes.

Top-up doses of ketamine were given whenever required , 5 mg/dose . All patients were administered supplemental oxygen through nasal prongs throughout the procedure. Once adequately sedated the dental procedure was started.

Adequate sedation was considered to be acheived when there was–

- Absence of eyelash reflex
- Relaxation of the jaw
- Modified Ramsay Sedation Score of 3 or 4.

Vital signs were monitored at 5 minute intervals in the post operative room till the time of discharge. Modified Aldrete's Recovery scale was used to record recovery of each patient.[9]

According to this system, criteria for discharge is a minimum total score of 8.

Each patient was monitored & vital signs were noted every 15 minutes up until discharge. If the Aldrete's scale was low, observation was continued.

CRITERIA FOR DISCHARGE WERE:

- Stable vital signs (room air oxygen saturation >97%, and heart rate above 80 mm hg and below 120 mm hg)
- Maintained airway patency with respiratory rate >12 minute
- Oriented to time, place and person
- Hydrated adequately
- Ability to sit unaided & also ambulate
- Parent/guardian accompanying the child.

All the data were statistically analyzed by chi-square test and student-t test.

Table 1: Modified Ramsay sedation score[12]

Score	*Characteristics*
1	Awake and alert, minimal or no cognitive impairment
2	Awake but tranquil, purposeful responses to verbal commands at conversation level
3	Appears asleep, purposeful responses to verbal commands at conversation level
4	Asleep, purposeful responses to verbal commands at conversation level but at louder than usual conversation level or requiring light glabellar tap
5	Asleep, sluggish purposeful responses only to verbal commands or strong glabellar tap
6	Asleep, sluggish purposeful responses only to painful stimuli
7	Asleep, reflex withdrawal to painful stimuli only (no purposeful response)
8	Unresponsive to external stimuli, including pain

Table 2: Sedation score by Houpt et al.[13]

Score	*Rating scale*
(A) Sleep	
4	Awake, but responsive
3	Drowsy, disoriented
2	Asleep, easily aroused
1	Asleep, difficult to arouse
(B) Movement	
4	No movement
3	Intermittent movement affecting treatment
2	Continuous movement affecting treatment
1	Violent movement that interrupted or prevented the treatment
(C) Crying	
4	No crying
3	Intermittent crying
2	Continuous crying
1	Hysterical crying
Overall behavior	
6	Excellent, no disruption
5	Very good, limited disruption
4	Good, some difficulty
3	Fair, much difficulty but treatment done
2	Poor, partial treatment done
1	Aborted

Table 3: Modified Aldrete's recovery scale[14]

Score	*Rating scale*
Activity: ability to move voluntarily or on command	
2	4 extremities
1	2 extremities
0	0 extremity
Respiration	
2	Able to breathe deeply and cough freely
1	Dyspnea, shallow or limited breathing
0	Apneic
Circulation	
2	BP ± 20 mm of pre-PSA level
1	BP ± 20—50 mm of pre-PSA level
0	BP ± 50 mm of pre-PSA level
Consciousness	
2	Fully awake
1	Arousal on calling
0	No response
Color	
2	Normal
1	Pale, dusky, blotchy
0	Cyanotic

RESULTS:

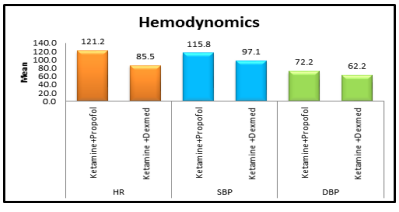
The comparison between the two groups KP and KD was done by statistical analysis using IBM SPSS Statistics for Windows, Version 29.0.(Armonk, NY: IBM Corp) with the help of Chi-square test and Student t test. The ketamine–propofol combination was compared with ketamine–dexmedetomidine for changes in heart rate, blood pressure, and oxygen saturation.

- The p value was found to be highly significant (<0.001) for heart rate. The heart rate was significantly high in KP group throughout the procedure compared to KD group.
- The p value for systolic blood pressure was <0.001 and for diastolic blood pressure was also <0.001, which suggested the highly significant difference between the two groups KP and KD. The KP group showed higher blood pressure than the other group.
- The changes in oxygen saturation between the two groups was insignificant with a p value of >0.05. The saturation was maintained above 95% throughout the procedure in both the groups.

Table 1:Hemodynamics

	Groups	N	Mean	SD	t-value	p-value
HR	Ketamine+Propofol	10	121.2	9.1	9.688	0.0005 **
	Ketamine +Dexmed	10	85.5	7.2		
SBP	Ketamine+Propofol	10	115.8	2.9	13.749	0.0005 **
	Ketamine +Dexmed	10	97.1	3.1		
DBP	Ketamine+Propofol	10	72.2	3.4	5.077	0.0005 **
	Ketamine +Dexmed	10	62.2	5.2		
** Highly Statistical Significance at p < 0.01 level						

Figure 1: Hemodynamics



- The Modified Ramsay sedation score (MRS) was recorded and compared at three different time intervals,

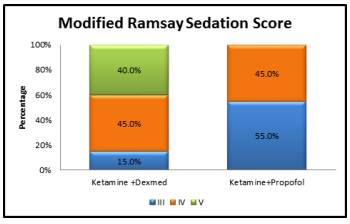
a) immediately after the delivery of drug,
b) after 5 minutes of delivery of drug,
c) at the end of the procedure.

MRS score between the two groups KP and KD, immediately after the delivery of drug, was similar. At 5 minutes of the delivery of the drug, the difference between the two groups was highly significant with p value of <0.001. The quality of sedation was better in KD group. Also, the MRS score at the end of the procedure was similar in both the groups.

Table 2:Modified Ramsay sedation score (MRS)

			Groups		Total	2 - value	p-value
			Ketamine +Dexmed	Ketamine +Propofol			
Score	3	Count	3	11	14	12.571	0.002**
		%	15.0%	55.0%	35.0%		
	4	Count	9	9	18		
		%	45.0%	45.0%	45.0%		
	5	Count	8	0	8		
		%	40.0%	0.0%	20.0%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

Figure 2: Modified Ramsay sedation score after the treatment



- Houpt et al. sedation score was also recorded at three time intervals similar to MRS score. The Houpt sedation score has four subcategories: SLEEP, CRYING, MOVEMENT, AND OVERALL SCORE. All the categories were assessed at three different time intervals.

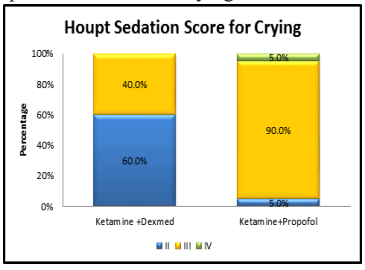
Houpt score for crying and movement showed no statistically significant difference between the two groups KP and KD, whereas the score for sleep showed statistically significant difference between the two groups KP and KD immediately after the delivery of the drug with the p value of 0.007 . The children showed better quality of sedation in KD group. Thereafter, there was no difference between the scores after 5 minutes of drug delivery or at the end of the procedure

Table 3: Houpt sedation score for crying

Crosstab for Houpt sedation score for crying immediately after the delivery of drugs

			Groups		Total	2 - value	p-value
			Ketamine +Dexmed	Ketamine +Propofol			
Score	2	Count	12	1	13	14.154	0.001**
		%	60.0%	5.0%	32.5%		
	3	Count	8	18	26		
		%	40.0%	90.0%	65.0%		
	4	Count	0	1	1		
		%	0.0%	5.0%	2.5%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

Figure 3: Houpt sedation score for crying

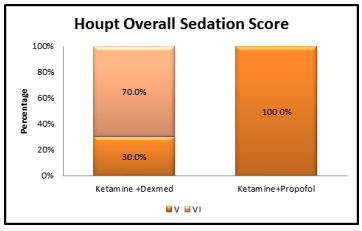


The overall Houpt et al. sedation score between the two groups KP and KD, immediately after the delivery of drug, was similar. The p value on comparison between the two groups for overall Houpt et al. sedation score immediately after the delivery of drug was insignificant , after the delivery of the drug was also insignificant but was highly significant at the end of the procedure with a value of <0.001. The graphs represent the comparison between the groups.

Table 4: Houpt overall sedation

			Groups		Total	2 - value	p-value
			Ketamine +Dexmed	Ketamine +Propofol			
Score	5	Count	6	20	26	21.538	0.0005**
		%	30.0%	100.0%	65.0%		
	6	Count	14	0	14		
		%	70.0%	0.0%	35.0%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0 %		
** Highly Statistical Significance at p < 0.01 level							

Figure 4: Houput overall sedation after treatment

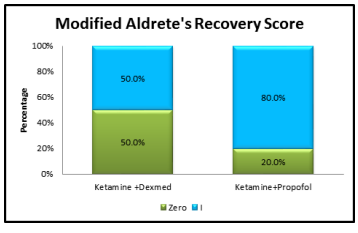


- The Modified Aldrete's recovery scale was measured at the end of the procedure to assess the recovery status of the patient. The scale measures activity, respiration, circulation, consciousness, and colour. Student t test between the two groups showed insignificant difference in the recovery scale with p value of >0.05 for all the components of Modified Aldrete's recovery scale.

Table 5: Modified Aldrete's recovery scale for consciousness—comparison. between the two groups

			Groups		Total	2 - value	p-value
			Ketamine +Dexmed	Ketamine+ Propofol			
Score	0	Count	10	4	14	3.956	0.096 #
		%	50.0%	20.0%	35.0%		
	1	Count	10	16	26		
		%	50.0%	80.0%	65.0%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0%		
# No Statistical Significance at p > 0.05 level							

Figure 5: Modified Aldrete's Recovery Score



DISCUSSION:

Children vary in their levels of cooperation; some are cooperative, while others are not. When a child does not cooperate, it negatively impacts both the quality and duration of their treatment, which can have lasting repercussions for both the child and the parent. Managing uncooperative children in a dental setting can be quite challenging.

Pharmacological techniques are well-suited for providing pain-free dental care. These methods of behaviour management encompass various levels of sedation (often referred as "conscious sedation") as well as general anaesthesia. The selection of the appropriate technique depends on several factors, including the patient's needs, the dental environment, and the preferences of the dental professionals.[10]

Different levels of sedation i.e minimal, moderate, and deep, come with varying risks of complications, necessitating different degrees of monitoring. Although many drugs or drug combinations

can induce sedation, each has unique clinical effects, making it crucial to understand the safety profile of each drug or combination. Sedative drugs can impair airway protective reflexes and alter hemodynamic status, potentially leading to serious complications such as airway obstruction, hypoxia, aspiration, and delayed recovery.

Preliminary research indicates that midazolam is an effective premedication for children when given intramuscularly, rectally, intranasally, or orally. Intravenous sedation, however, offers a quicker onset and superior quality of sedation. To administer IV sedation, a venous cannula is required, which also aids in managing potential complications.

In our study, midazolam was used as a common premedication across both groups due to its minimal risk of respiratory depression and excellent safety profile. Midazolam offers anxiolytic, amnesic (anterograde amnesia), sedative, and anticonvulsant effects. Ketamine was chosen for its effective analgesic properties at sub-anaesthetic doses (1 mg/kg). Propofol was administered at a sub-anaesthetic dose to induce sedation. In one group (the KP group), ketamine and propofol were combined, each at a dose of 1 mg/kg.[3,4]

Dexmedetomidine, a newer centrally acting α2 agonist, was included for its ability to provide sedation and analgesia with minimal respiratory depression. The combination of ketamine and dexmedetomidine (1 mg/kg and 1 µg/kg, respectively) was used in the KD group, as their synergistic effects offer excellent sedation with fewer side effects.[5,6]

In dental procedures, local anaesthetic (LA) is initially administered, which can cause pain and stress. Thus, the goal is to achieve optimal sedation and anxiolysis during the injection of the LA.

The heart rate in the KP group was notably higher, aligning with the results of Kramer and Ganzberg's study.[12] The KP group exhibited the highest heart rate, likely due to ketamine's stimulating effect on the cardiovascular system. This occurred despite the inclusion of propofol, which typically causes bradycardia; however, the low dose of propofol used in this study may explain this outcome.[6] Conversely, the KD group showed a significantly lower heart rate compared to the other groups. This reduction is attributed to dexmedetomidine's cardiovascular effects, which counteract ketamine's stimulatory and psychological effects, thereby mitigating its central nervous system impact.[13]

Our findings, which mirror those of Canpolat, indicate that no cardio-stimulatory effects of ketamine were observed in children receiving the dexmedetomidine-ketamine combination.[14]

The systolic blood pressure was notably higher in the KP group compared to the KD group, a finding consistent with Canpolat et al.'s study. This increase in the KP group can be attributed to the cardio-stimulatory effects of ketamine. In contrast, the KD group had lower systolic blood pressure, primarily due to the depressant effects of dexmedetomidine.[6]

There was a statistically significant difference in sedation levels, as measured by the Modified Ramsay Sedation Score, 5 minutes after drug administration. The sedation quality was superior in the KD group compared to the KP group. However, in both groups, recovery was delayed by the end of the procedure. These results are consistent with the findings of Canpolat et al.[6]

The Houpt sedation scores for movement and crying were similar between the groups and were not statistically significant. However, there was a significant difference in the Houpt sedation score for sleep immediately after drug administration (p-value 0.007). The KD group achieved better sedation (Score of 5) compared to the KP group. Although the overall behavior scores were not statistically significant, children in the KD group displayed calmer and more controlled behaviour than those in the KP group.

The Modified Aldrete's Recovery Scale was assessed at the end of the procedure, evaluating activity, respiration, circulation, consciousness, and colour. No significant difference was observed between the two groups.

It was observed that KP and KD group had delayed recovery. In all, 80% of children from KP group showed the score of 1, i.e., arousal on calling. The remaining 20% showed a score of 0, i.e., no response.

In the KD group,50 % of the children had a score of 1, while the remaining 50% had a score of 0. The KD group experienced a longer recovery time of approximately 45 minutes to 1 hour compared to the KP group, though this difference was not statistically significant. Additionally, both the KP and KD groups received extra doses of ketamine (5 mg), which may have contributed to a slightly extended recovery period. These results are consistent with the findings reported by Canpolat.[6]

The absence of any unusual psychological behaviour in those who received ketamine (KP and KD groups) might be attributed to the mitigating effects of propofol or dexmedetomidine on ketamine's adverse psychological effects. Similar results have been reported in previous studies by Badrinath et al.[14]

CONCLUSION:

Both ketamine combined with propofol and ketamine combined with dexmedetomidine offer effective sedation and adequate analgesia. When evaluating the overall sedation levels, perioperative adverse effects, recovery patterns, and any interruptions during treatment, it can be concluded that the ketamine-dexmedetomidine combination delivers more satisfactory and higher-quality sedation for paediatric dental procedures. Ultimately, the selection of drug combinations, dosages, and administration routes should be determined by the dentist and anaesthesiologist based on their clinical judgment.

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