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A randomized controlled trial comparing the efficacy of nebulized dexmedetomidine and nebulized ketamine as premedication in pediatric surgery

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Abstract
Background and Objective: Preoperative anxiety and separation from parents remain persistent challenges for anesthesiologists managing pediatric patients. Dexmedetomidine (DexM), a selective α2-adrenoceptor agonist, exerts sedative and analgesic effects through central nervous system (CNS) pathways. Ketamine (KET), an N-methyl-D-aspartate (NMDA) receptor antagonist, induces sedation and dissociative anesthesia. Aerosolized drug delivery offers a noninvasive, well-tolerated, and cost-effective route with rapid systemic absorption. The present study aimed to compare the sedative efficacy and safety of aerosolized Dexmedetomidine versus aerosolized Ketamine as premedicants prior to general anesthesia in children undergoing elective surgery.
Methods: This prospective, double-blind, randomized controlled trial included 75 pediatric patients (both sexes, aged 3-10 years) classified as American Society of Anesthesiologists (ASA) physical status I or II. All participants were scheduled for elective surgical procedures lasting 30-90 minutes under general anesthesia. Subjects were randomly allocated into three equal groups; Group D (DexM) that received aerosolized Dexmedetomidine 3 µg/kg, Group K (KET) that received aerosolized Ketamine 3 mg/kg, Group C (Control) that received aerosolized normal saline.
Results: After 15 minutes of nebulization, Ramsay sedation scores were comparable between DexM and KET groups. At 30 minutes, DexM achieved significantly higher sedation scores compared to KET. DexM also demonstrated superior parental separation and mask acceptance compared with KET. Heart rate (HR) prior to anesthesia induction was significantly lower in the DexM group versus KET and control groups, indicating greater hemodynamic stability. Recovery and discharge times did not differ significantly among the three groups. Hypersalivation was observed more frequently with Ketamine, while the incidence of other adverse effects (nausea, vomiting, bradycardia, hypotension, or hypoxia) was negligible across all groups.
Conclusion: Aerosolized Dexmedetomidine provides superior preoperative sedation, smoother parental separation, and improved mask acceptance compared to aerosolized Ketamine in pediatric patients, without prolonging recovery or discharge time. It can be considered an effective and well-tolerated premedication option in pediatric anesthesia.

Keywords: Dexmedetomidine, Ketamine, Aerosolized premedication, Pediatric anesthesia, Preoperative anxiety, Sedation

Introduction
Preoperative anxiety and separation from caregivers are distressing experiences for children and often complicate anesthetic induction. Anxiety activates the sympathetic and endocrine systems, resulting in increased heart rate, blood pressure, and cardiac workload. The primary goal of pediatric anesthesiologists is to minimize emotional distress and ensure smooth transition to anesthesia induction [1, 2].

Premedication plays a vital role in reducing anxiety and improving cooperation. An ideal pediatric premedicant should be palatable, fast-acting, reliable, and associated with minimal side effects. Aerosolized drug administration enables efficient absorption through nasal, oral, and respiratory mucosa while being non-invasive and easily accepted by children [3, 4].

Dexmedetomidine, a highly selective α2-adrenergic agonist, produces sedation and analgesia by acting on the locus coeruleus within the brainstem, generating an EEG pattern similar to natural sleep. It is tasteless, colorless, and odorless, and promotes hemodynamic and neurological stability. The bioavailability of aerosolized DexM is approximately 65% via nasal mucosa and 82% via oral mucosa, making it a viable alternative to intranasal routes that may cause local irritation or laryngospasm [4, 5].

Ketamine, on the other hand, is an NMDA receptor antagonist that induces dissociative

anesthesia while maintaining airway reflexes. It provides analgesia, amnesia, and sedation and can be administered through various routes, including intravenous, intramuscular, oral, rectal, intranasal, and aerosolized forms. Aerosolized Ketamine offers rapid onset, safety, and cost-effectiveness, making it suitable for pediatric premedication [5, 6].

This study was designed to compare the sedative, hemodynamic, and recovery profiles of aerosolized Dexmedetomidine and Ketamine as premedications for pediatric patients undergoing general anesthesia [7, 8].

Materials and Methods

This prospective, double-blind, randomized controlled study was carried out on 75 pediatric patients, aged 3 to 10 years, classified as American Society of Anesthesiologists (ASA) physical status I or II. All participants were scheduled to undergo elective surgical procedures lasting between 30 and 90 minutes under general anesthesia at I-Care Institute of Medical Sciences from December 2017 to November 2018. Prior to enrolment, written informed consent was obtained from the parents or legal guardians of each child.

Exclusion criteria

- Parental refusal to participate
- Presence of respiratory tract infection or distress
- Cardiac disease
- Neurological or physical disability
- Hypersensitivity to study drugs or their constituents
- Nasal abnormalities such as bleeding or masses
- Use of sedatives or anticonvulsant medications
- Other medical condition that could interfere with participation or affect study outcomes

Results

Table 1: Comparison of the study groups with respect to demographic characteristics (n = 75)

Demographic Data	Group D (n = 25)	Group K (n = 25)	Group C (n = 25)	P-value
Age (years)	6.15 ± 3.11	6.23 ± 3.36	5.99 ± 2.1	0.976
Gender				0.819
Male	11 (44%)	9 (36%)	10 (40%)	
Female	14 (56%)	16 (64%)	15 (60%)	
Weight (kg)	20.80 ± 5.28	21.05 ± 6.14	20.65 ± 5.46	0.975
ASA Score				0.920
I	21 (84%)	20 (80%)	19 (76%)	
II	4 (16%)	5 (20%)	6 (24%)	
Type of Surgery				0.985
Cochlear Implant	4 (16%)	3 (12%)	4 (16%)	
Laparoscopic Hernia Repair	5 (20%)	7 (28%)	6 (24%)	
Tonsillectomy	11 (44%)	10 (40%)	10 (40%)	
Duration of Surgery (min)	58.60 ± 18.17	60.85 ± 16.98	67.70 ± 13.82	0.071

Data are presented as mean ± SD or frequency (%). ASA: American Society of Anesthesiologists, group D: Dexmedetomidine, group K: Ketamine, group C: Control.

Table 2: Comparison of the three study groups based on Ramsay sedation scores, parental separation ease, and mask acceptance

Parameter	Group D (n = 25)	Group K (n = 25)	Group C (n = 25)	P-value	Significant Between Groups
Ramsay Sedation Scale (After 15 min)					
Score 1	13 (52.0%)	14 (56.0%)	20 (80.0%)	0.008*	p1 = 0.736p2 = 0.004*p3 = 0.008*
Score 2	12 (48.0%)	11 (44.0%)	5 (20.0%)		
Score 3	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Score 4	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Ramsay Sedation Scale (After 30 min)					
Score 1	3 (12.0%)	9 (36.0%)	20 (80.0%)	0.001*	p1 = 0.026*p2 < 0.001*p3 < 0.001*
Score 2	15 (60.0%)	11 (44.0%)	5 (20.0%)		
Score 3	5 (20.0%)	3 (12.0%)	0 (0.0%)		
Score 4	2 (8.0%)	2 (8.0%)	0 (0.0%)		
Parental Separation and Mask Acceptance				<0.001*	
Excellent	8 (32.0%)	1 (4.0%)	0 (0.0%)		p1 = 0.028*p2 < 0.001*p3 = 0.414
Good	6 (24.0%)	5 (20.0%)	2 (8.0%)		
Fair	9 (36.0%)	12 (48.0%)	11 (44.0%)		
Poor	2 (8.0%)	7 (28.0%)	12 (48.0%)		

Data are presented as frequency (%), * significant as P value < 0.05. group D: Dexmedetomidine, group K: Ketamine, group C: Control.

Table 3: Comparison of the three study groups with respect to recovery time, discharge time, and incidence of complications

Parameter	Group D (n = 25)	Group K (n = 25)	Group C (n = 25)	P-value
Recovery Time (min)	8.55 ± 3.39	8.25 ± 2.89	8.40 ± 3.39	0.936
Discharge Time (min)	42.9 ± 8.66	32.45 ± 10.22	31.9 ± 9.09	0.792
Complications				
Nausea	0 (0%)	0 (0%)	0 (0%)	—

Vomiting	0 (0%)	0 (0%)	0 (0%)	—
Hypotension	0 (0%)	0 (0%)	0 (0%)	—
Hypertension	0 (0%)	0 (0%)	0 (0%)	—
Tachycardia	0 (0%)	0 (0%)	0 (0%)	—
Bradycardia	0 (0%)	0 (0%)	0 (0%)	—
Hypoxia	0 (0%)	0 (0%)	0 (0%)	—
Salivation	0 (0%)	5 (20%)	0 (0%)	0.029*

Data are presented as mean ± SD or frequency (%), * significant as p-value < 0.05. group D: Dexmedetomidine, group K: Ketamine, group C: Control.

Discussion

Preoperative anxiety in children represents a multifaceted clinical concern that can significantly impact not only the patient but also parents and perioperative staff if not managed appropriately. The present study was designed to evaluate the effectiveness of aerosolized dexmedetomidine (DexM) and ketamine (KET) in achieving an optimal level of conscious sedation, thereby alleviating anxiety during parental separation and improving mask acceptance during induction of anesthesia [9, 10].

The primary endpoint of this study was to assess the sedative efficacy of both agents using the Ramsay Sedation Scale at 15 and 30 minutes following nebulization. Secondary outcomes included evaluation of mask acceptance, hemodynamic stability, and the ease of parental separation [10, 11].

Various pharmacologic agents have been explored as premedications in pediatric anesthesia with varying degrees of success. An ideal premedicant should have a rapid onset, short duration, ease of administration, high patient acceptability, and minimal adverse effects [12, 13].

Zanaty et al. demonstrated that the combination of DexM (1 µg/kg) with KET (1 mg/kg) produced deeper sedation than either agent alone in pediatric dental procedures. This discrepancy may be attributed to the synergistic interaction between the two drugs and differences in the sedation scale employed, as their study utilized the Modified Observer's Assessment of Alertness/Sedation Scale, whereas the present study applied the Ramsay Sedation Scale [14].

With respect to hemodynamic parameters, the current results concur with *Zanaty et al.*, who reported a significant reduction in heart rate following nebulized DexM (2 µg/kg) compared with KET (2 mg/kg) or their combination in pediatric dental patients. Similar to our observations, *Bhat et al.* found no significant intergroup variation in mean arterial pressure (MAP) when comparing intranasal DexM (1 µg/kg) alone and in combination with KET (2 mg/kg) in children undergoing minor elective surgeries [15, 16].

However, *Zanaty et al.* reported improved outcomes with the DexM-KET combination, which may reflect the synergistic pharmacodynamic effect of combined dosing, their use of different concentrations, and a narrower age range than in the present study. *Zanaty et al.* reported a shorter recovery and discharge time with the DexM-KET combination, possibly due to lower doses of each agent in combination producing effective sedation with more rapid clearance [14].

In terms of adverse events, hypersalivation and coughing were more common in the KET group (four cases) compared with the DexM and control groups, whereas no instances of nausea, vomiting, hypotension, hypertension, tachycardia, bradycardia, or hypoxia were reported in any group [15].

Limitations of the study were the use of a facemask during nebulization may have resulted in variable drug delivery due to incomplete seal; a mouthpiece could provide more consistent dosing, Parent satisfaction, analgesia, sedation onset, and peak sedation levels were not evaluated, the relatively small sample size warrants further large-scale trials to confirm these findings [16].

Conclusion

Aerosolized dexmedetomidine can be used with advantage versus aerosolized Ketamine for preoperative sedation in pediatric surgeries.

Conflict of interest: None.

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