Section: Anaesthesiology

Original Research Article

# A COMPARATIVE STUDY OF INTRANASAL DEXMEDETOMIDINE VS INTRANASAL KETAMINE AS A PREMEDICATION FOR PAEDIATRIC PATIENTS

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## Abstract

**Background:** For infants and children who need surgery or other painful or stressful treatments, anaesthesia administration through the intranasal route is preferred. Dexmedetomidine administered intravenously successfully reduces agitation, shivering, and postoperative pain. Ketamine is frequently used in paediatric anaesthesia, which involves hypnosis, potent analgesia, increased sympathetic activity, airway tone preservation, and breathing maintenance. **Aim:** The following study was conducted on paediatric patients having surgery to examine the anxiolytic effects, sedative effects, and hemodynamic stability of intranasal dexmedetomidine and intranasal ketamine as a premedication. **Materials and Methods:** This study included 60 paediatric patients undergoing elective surgery under general anaesthesia and being admitted to the Department of Paediatric Surgery at the Government Thoothukudi Medical College. Group D got dexmedetomidine 1 g/kg body weight as an intranasal spray using Intranasal Mucosal Atomization Device 30 minutes preop, whereas Group K received ketamine 5 mg/kg body weight. Preoperative monitoring included sedation, anxiety, separation score, and hemodynamic indicators. In addition, the negative consequences and intraoperative and postoperative monitoring of hemodynamic parameters were also monitored. **Result:** Compared to the Dexmedetomidine group, the hemodynamic parameters such as heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure are considerably greater in the Ketamine group. Between groups, there were no appreciable differences in the mean respiratory rate or spo2. The Dexmedetomidine group achieved the desired Anxiety Score, Ramsay Sedation score, and Child-Parent Separation score earlier than the Ketamine group. **Conclusion:** As a premedication for paediatric patients having surgery, intranasal dexmedetomidine may be recommended over intranasal ketamine due to its quicker sedative and anxiolytic effects and superior hemodynamic stability.

## INTRODUCTION

Good premedication is necessary for a child's anaesthetic induction to proceed to a successful medical treatment procedure. Most paediatric patients having surgery, as well as diagnostic or interventional treatments, report that the perioperative period is an extremely stressful and distressing experience.[1] Anxiety causes changes in HR and BP, as well as psychological problems and behavioural changes, by stimulating the sympathetic and parasympathetic systems. Premedication with sedatives eases nervousness and speeds the onset of anaesthesia. Anxiety in such patients is exacerbated by parental separation, a lack of comprehension of the need for anaesthesia and surgery, a dread of the operating room, and a fear of injections.[2] Preoperative anxiety and forceful anaesthetic induction are now recognised as avoidable and unethical as they have been associated with postoperative emerging agitation, long-term behavioural alterations, and psychiatric disorders.[3] Children undergoing diagnostic and interventional procedures that call for hemodynamic stability and smooth induction of anaesthesia might especially benefit from the use of sedative premedication, venipuncture, or acceptance of inhalational induction. Pediatric anaesthesia has several


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difficulties because of anxiety and the psychological damage brought on by maternal neglect. Preanesthetic medications for kids should be designed to ease their parents' psychological stress and worry while facilitating anaesthesia's onset without delaying recovery.[4] The best sedative and the pre-eminent way to provide these medications to children have been tested using a variety of substances. In order to avoid adding further stress to the child, premedical medicine must have an appropriate, non-traumatic mode of administration. Midazolam, Dexmedetomidine, Ketamine, Transmucosal Fentanyl, and Meperidine are now the most often used medicines.[5] Midazolam, however, has a risk of respiratory depression. A paediatric patient's optimal sedative premedication should have a quick onset of sedation, little respiratory depression, and quick recovery without having any negative postoperative consequences. However, the intranasal route can meet all optimal administration criteria, including being non-traumatic, well-tolerated, and not requiring the patient's participation.[6] Drops or a mucosal atomization device can be used to provide intranasal medications, and reports have shown that ketamine and dexmedetomidine are equally effective and safe when administered both ways.[7] Numerous studies have demonstrated that giving children sedation and premedication via the intranasal route is successful.[8] Although much research has looked at the effects of various premedication medications, there isn't yet a commonly acknowledged medicine of preference. The best premedication tablet should have a simple and efficient method of administration with negligible or no side effects. Additionally, it ought to function quickly with little impact on cardiovascular stability.[9] A very selective α2-adrenergic agonist is dexmedetomidine. It has a somewhat soothing effect that is dose-dependent and easily arousable. It also relieves pain and reduces anxiety without impairing breathing. Dexmedetomidine can be administered intranasally and is a safe and effective premedication option for kids. Ketamine is an antagonist of the N-methyl-d-aspartate receptor that has a pleasant sedative and analgesic effect. It has negative side effects when used orally as the only premedication, including anxiety and salivation.[10]

**Aim**

The study's primary goal was to compare and contrast the sedative, anxiolytic, and hemodynamic stabilising effects of intranasal dexmedetomidine and ketamine in paediatric patients having surgery.

## MATERIALS AND METHODS

A randomised, double-blind trial was conducted at the Department of Anaesthesiology, Government Thoothukudi Medical College, for 18 months (December 2019 to May 2021). The study included 60 paediatric patients receiving elective surgery under general anaesthesia at the Department of Paediatric Surgery at Government Thoothukudi Medical College. Patients who met the inclusion criteria after the pre-anaesthesia evaluation were recruited. Institutional Ethical Committee approval and informed written consent were obtained before the study's start.

**Inclusion Criteria**

The study included patients aged 2-10 of both genders following American Society of Anesthesiologists (ASA) physical status I and II.

**Exclusion Criteria**

The study did not include children with a history of Upper airway disease- Respiratory tract infections, o CNS dysfunction, cardiovascular dysfunction or gastrointestinal disorders that may affect drug absorption. Also, those with known allergies to the studied drugs refused to take the premedication, and those who fell within Children's physical status ASA Classes III and IV and with any intranasal pathology or children with any congenital anomaly were not included in this study. Preanesthetic check-ups, including a detailed history and thorough general physical examination of the patient, were carried out a day before surgery and recorded. In addition, all children were investigated preoperatively for Haemoglobin: (gm%), Platelet count (lakh/mm3), Bleeding and clotting times, RFT- blood urea & serum creatinine, ECG and Chest X-ray (All patients were kept nil by mouth: light meal or formula feeds were given up to 6 hours before induction; breast milk up to 4 hours and clear fluids up to 2 hours before induction). Boyle's machine was checked. Appropriate size endotracheal tube, working laryngoscope-size 0,1 and 2 Millers blades and size 1, 2 and 3 Macintosh blades, Jackson Rees circuit with 1, 2 and 3 size masks, stylet and working suction apparatus was kept ready before the procedure. In addition, emergency drug trays consisting of atropine, adrenaline, ephedrine and dopamine were kept ready. Patients were allocated randomly based on a computer-generated table in a double-blinded fashion into two equal groups (30 in each group). Group K (n = 30): The patients were given intranasal ketamine -5mg/kg body weight as a nasal spray with an intranasal mucosal atomization device 30 minutes before surgery. Group D (n = 30): The patients were given intranasal dexmedetomidine 1 µg/kg body weight as a nasal spray with an intranasal mucosal atomization device 30 minutes before surgery. Intranasal drugs were delivered with nasal mucosal atomizer into both nostrils using a 2 ml syringe with the child in the recumbent position, and the plunger was pushed. Heart rate, blood pressure, respiratory rate, oxygen saturation levels, sedation, and anxiety levels are noted at the time of administration of premedication and then monitored continuously. Readings were recorded every 5min until the patient attained a sedation score of 5. Once the sedation score of 5 was achieved, the child was transferred to the operating room. Any side effects


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such as hypotension, bradycardia, hypoxemia, apnoea, nasal irritation, vomiting, itching, or others were looked for. Then, the child was taken inside the operating theatre. General Anaesthesia was administered. After the child had undergone surgery under general anaesthesia, the child was extubated after suctioning the oral cavity and return of protective reflexes and after adequate neuromuscular recovery and regular respiratory rate were achieved. When a Numerical variable is compared with the Ketamine and Dexmedetomidine groups, an independent t-test is used. When a Categorical Variable is compared with the Ketamine and Dexmedetomidine groups, the variables are represented in tables and bar diagrams. For the test of significance, the chi-square test is used. P-values less than 0.05 were considered statistically significant.

## RESULTS

The subjects were divided into two groups: Group K received intranasal ketamine (5 mg/kg body weight) 30 minutes before surgery via nasal spray with an intranasal mucosal atomization device, and Group D received intranasal dexmedetomidine (1 g/kg body weight) 30 minutes before surgery via nasal spray with an intranasal mucosal atomization device. Demographic data, including age, weight, and sex, were comparable in the two groups [Table 1].

**Table 1: Demographic data of patients included in both groups**

| Demographic data | | Group K (N = 30) | Group D (N = 30) | P-value |
|---|---|---|---|---|
| Age | | 5.12 ± 2.41 | 5.48 ± 2.49 | 0.564 |
| Sex | Male (44 -73.33%) | 23 (76.66%) | 21 (70%) | 0.56 |
| | Female (16 - 26.66%) | 7 (23.33%) | 9 (30%) | |
| Weight | | 14.95± 2.69 | 15.17 ± 3.68 | 0.094 |

In comparison to Group D's mean age of 5.48 (± 2.49), which was lower by 0.37 but not statistically significant, Group K's mean age was 5.12 (± 2.41). Regarding gender, Group K had 76.66% male children and 23.33% female children, compared to Group D's 70% male and 30% female composition. However, the difference was not statistically significant ($p > 0.05$). The mean Weight (kg) among Group K was 14.95 (±2.69) which is lower by 0.22 but not statistically significant compared to 15.17 (± 3.68) in Group D [Table 1]

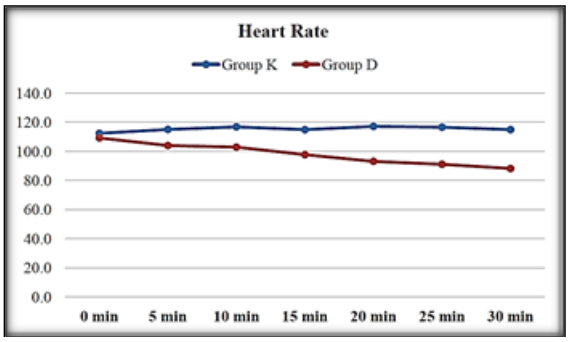


**Figure 1: Comparison of Heart rate of patients among two groups**

Compared to 109.2 (± 10.77) in Group D, the mean HR at 0 min in Group K was 112.33 (± 7.3), which is higher by 3.13 but not statistically significant. At all-time points, children who received ketamine had considerably greater heart rates than children who received dexmedetomidine [Figure 1]. The mean SBP at 0 min in Group K was 125.37 (± 12.57), statistically significant and higher by 8.77 compared to Group D's mean SBP of 116.6 (± 12.6). In comparison to Group D's mean SBP at 30 minutes, which was 96.87 (± 11.15), Group K's mean SBP at that time was 126.73 (± 15.1), a difference of 29.87 and statistical significance [Table 2]. During the procedure, the Ketamine group's mean SBP was substantially greater than the Dexmedetomidine group's [Table 2]. There were no appreciable differences in the mean DBP at 0 min between the groups. During the operation, the Ketamine group's mean DBP and MAP were substantially greater than the Dexmedetomidine group's [Table 2]. There was no statistical significance among baseline RR between the groups. Except for the first 30 minutes, when the Ketamine group's respiratory rate was much greater than the other groups, the mean respiratory rate was not statistically different.

**Table 2: Hemodynamic changes and oxygen saturation levels**

| Parameters | Groups | | P-value |
|---|---|---|---|
| | K | D | |
| Mean Arterial Pressure | | | |
| 0 min | 99.93 ± 8.06 | 85.57 ± 13.59 | 0.001 |
| 5 min | 100.10 ± 7.18 | 81.20 ± 11.15 | 0.001 |
| 10 min | 95.10 ± 9.77 | 76.33 ± 10.25 | 0.001 |
| 15 min | 97.77 ± 12.65 | 72.80 ± 7.89 | 0.001 |
| 20 min | 99.97 ± 11.12 | 72.33 ± 8.94 | 0.001 |
| 25 min | 95.57 ± 13.29 | 69.77 ± 8.68 | 0.001 |
| 30 min | 96.90 ±12.01 | 68.77 ± 7.92 | 0.001 |

Throughout the operation, there was no discernible difference in the mean SpO2 between the groups [Table 2].


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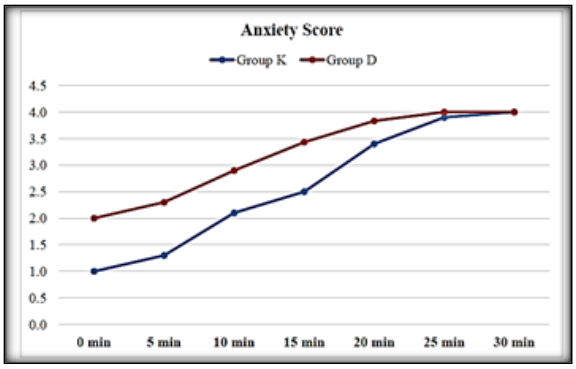


**Figure 2: Anxiety score**

The anxiety scores differed statistically significantly from baseline time to 20 min, increasing from 1 to 3.40(±0.50) and 2 (±0.69) to 3.83 (±0.38), respectively, in groups K and D (Figure 2). The mean Anxiety Score at 30 min among Group K was 4 (± 0), which is equal compared to 4 (± 0) in Group D and hence no difference. The anxiety score of 4 was attained earlier in the dexmedetomidine group compared to the ketamine group [Figure 2].

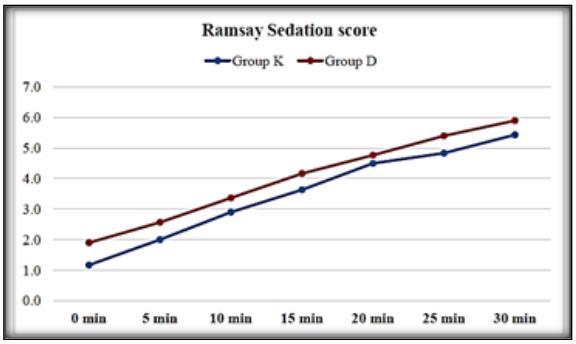


**Figure 3: Ramsay Sedation score**

Ramsay sedation score differed statistically among the groups from 0 to 15 mins, increasing from 1.17 (±0.38) to 3.63 (±0.49) and 1.9 ± (0.31) to 4.17 (±0.65), respectively, in groups K and D (Figure 3). The scores at 25 and 30 mins were also statistically significant. Ramsay sedation score of 5 was attained earlier in the dexmedetomidine group compared to the ketamine group.

**Table 3: Child-Parent separation scores at 0 to 30 min**

| Child-Parent Separation score | Group K | | | | Group D | | | | P-value |
|---|---|---|---|---|---|---|---|---|---|
| | Poor | Good | Fair | Excellent | Poor | Good | Fair | Excellent | |
| 0 min | 30 (100%) | 0 | 0 | . | 24 (80%) | 4 (13.33%) | 2 (6.66%) | . | 0.012 |
| 5 min | 30 (100%) | 0 | 0 | . | 6 (20%) | 21 (70%) | 3 (10%) | . | 0.001 |
| 10 min | 6 (20%) | 24 (80%) | 0 | . | 1 (3.33%) | 7 (23.33%) | 22 (73.33%) | . | 0.001 |
| 15 min | . | 21 (70%) | 9 (30%) | 0 | . | 2 (6.66%) | 19 (63.33%) | 9 (30%) | 0.001 |
| 20 min | . | 0 | 26 (86.66%) | 4 (13.33%) | . | 1 (3.33%) | 6 (20%) | 23 (76.66%) | 0.001 |
| 25 min | . | . | 12 (40%) | 18 (60%) | . | . | 1 (3.33%) | 29 (96.66%) | 0.001 |
| 30 min | . | . | . | 30 (100%) | . | . | . | 30 (100%) | . |

Comparing the Child–Parent Separation score at 0 min between the groups, Group K had a higher proportion of Poor with 100%, followed by Good and fair with 0%, compared to Group D, which had a higher proportion of Poor with 80% followed by Good with 13.33% and least in Fair with 6.66%. The difference in Child–Parent Separation score at 0 min distribution between Group K and Group D was statistically significant ($p < 0.05$) [Table 3]. Comparing the Child–Parent Separation score at 30 min between the groups, 100% of Group K and 100% of Group D had Excellent scores and hence no difference. The child-parent separation score of excellent was attained earlier in the dexmedetomidine group compared to the ketamine group.

## DISCUSSION

Preoperative anxiety relief, successful parental separation, and a seamless induction of anaesthesia are the main objectives of premedication in paediatric anaesthesia. Children who experience anxiety during the perioperative phase may react aggressively, have more anguish, delay the onset of anaesthesia, experience more pain after surgery, exhibit postoperative behavioural abnormalities, or become agitated. Dexmedetomidine administered intravenously successfully reduces agitation, shivering, and postoperative pain. Ketamine is frequently used in paediatric anaesthesia, which involves hypnosis, potent analgesia, increased sympathetic activity, airway tone preservation, and breathing maintenance. Our study included children of both gender between ages 2-7 separated equally into groups K and D. However, age, gender differences, and weight of patients between the groups were not statistically significant; hence these characteristics cannot play a confounding effect in determining the benefit of anaesthetics used under study. A likely perplex in the association of demographic factors towards analysing the


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premedication effects of intranasal dexmedetomidine, midazolam and ketamine for children undergoing bone marrow biopsy and aspirate was reported by Mostafa and Morsy.[12] The preoperative conditions among patients, such as haemodynamic stability and respiratory rates, were analysed and compared between groups K and D. Heart rate and blood pressure, inclusive of systolic, diastolic and mean arterial BPs at 30 min, was significantly lower in group D compared to group K. Significant changes in hemodynamic parameters might be attributable to greater sedation intensity. Many studies have previously demonstrated that changes in heart rate, respiration rate, and blood pressure in groups of children given Dexmedetomidine and Ketamine after 30 minutes might be connected with sedation intensities.[12,13] As the previous studies indicated, there was also a significant change in respiratory rates at 30 min in our study, with a relatively lower RR observed in group D. 12, 13 We, however, did not find any statistical differences in SPO2 values between the groups. Similar insignificance in SPO2 values at 30 min between groups D and midazolam was reported.[14] Ramsay scores were used to analyse the sedation rate.[15] It was evident that the dexmedetomidine group achieved a Ramsay sedation score of 5 faster than the ketamine group. The significantly reduced hemodynamical factors could also affirm this in group D. A likely dominance of dexmedetomidine in the faster achievement of sedation based on Ramsay score was reported earlier by Abdellatif and Ibrahim.[16] This could also be associated with the reduction in anxiety levels of children significantly effective in group D than those in group K. The dexmedetomidine group achieved an exceptional child-parent separation of 'excellent' score faster than the ketamine group. Geetha et al. observed, similarly to our study, that the administration of dexmedetomidine gave a rapid onset of adequate sedation, with excellent parental separation and a speedier and more clear-headed recovery.[17] Our study indicated dominance in dexmedetomidine performance, indicating it to be more efficient in sedating earlier with a higher intensity and providing an exceptional hemodynamic and parental separation score. A similarity in the supremacy of dexmedetomidine in sedative performances over ketamine was reported in various studies. Bhat et al. reported that intranasal dexmedetomidine had a high success rate, good parental separation, good sedation, and low emerging anxiety.[18] In research that evaluated the premedication effects of Intranasal Dexmedetomidine, midazolam, and ketamine, a likely dominance of dexmedetomidine with favourable sedative rates and child behaviour was reported.[12]

Our study had low measurement, interviewer, allocation, and confounding bias because it was double-blinded and randomised. However, there were significant connections between problems and sample size. A lack of attention to these medications' economic feasibility and long-term consequences on behavioural changes may have limited our study. Further research with a larger sample size will reveal the exact nature of the difficulties and unfavourable side effects

## CONCLUSION

Finally, we discovered that ketamine and dexmedetomidine caused enough sedation with minimal adverse effects. However, because of its early anxiolytic effects, sedative effects, and superior hemodynamic stability, intranasal dexmedetomidine may be chosen over intranasal ketamine as a premedication in paediatric patients having surgery. As a result, we choose dexmedetomidine over ketamine and dexmedetomidine because of its effectiveness and safety.

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