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Original Research Article

Comparison of oral midazolam versus oral dexmedetomidine for ease of induction and prevention of emergence delirium in pediatric ENT surgeries under sevoflurane anesthesia: a randomized controlled study

Abinash Panigrahi[1], Kamal Kumar Fotedar[1], Punit Mehta[1], Sanjay Sachdeva[2], Pooja Singh[3]*

[1]Department of Anaesthesiology and Pain Management, Max Superspeciality Hospital, Saket, New Delhi, India
[2]Department of ENT Head and Neck Surgery, Max Superspeciality Hospital, Saket, New Delhi, India
[3]Department of Onco-Anaesthesia, BLK Max Super Speciality Hospital, New Delhi, India

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***Correspondence:**
Dr. Pooja Singh,
E-mail: dr.pooja260887@gmail.com

ABSTRACT

Background: Emergence delirium (ED) is a common and distressing complication in pediatric patients following sevoflurane anesthesia. Preoperative anxiety, rapid anaesthetic emergence and postoperative pain contribute to ED. Midazolam is widely used for premedication but has variable efficacy in preventing ED. Dexmedetomidine, a selective alpha-2 agonist, offers sedative and analgesic properties with minimal respiratory depression. This study compared the efficacy of oral midazolam versus oral dexmedetomidine for ease of induction and prevention of ED in children undergoing ENT surgeries under sevoflurane anesthesia.

Methods: In this prospective, randomized, single-blinded trial, 100 children aged 2–12 years (ASA I–II) scheduled for elective ENT surgeries were assigned to receive either oral midazolam 0.5 mg/kg (Group M) or oral dexmedetomidine 2 µg/kg (Group D) 45 minutes before induction. Preoperative sedation, ease of parental separation, mask acceptance, hemodynamic stability, incidence of ED (assessed using the Pediatric Anesthesia Emergence Delirium (PAED) scale) and recovery profiles were recorded.

Results: Baseline demographics were comparable between groups. Group D demonstrated significantly better preoperative sedation (RSS 3.6 vs 2.8, $p<0.001$), easier parental separation (90% vs 74%, $p=0.03$) and superior mask acceptance (88% vs 70%, $p=0.02$). The incidence of ED was significantly lower in Group D (8%) compared to Group M (26%, $p=0.01$). PACU discharge was earlier in Group D (36.5 vs 42.8 minutes, $p=0.04$). Hemodynamic parameters remained stable in both groups without significant adverse events.

Conclusions: Oral dexmedetomidine provides superior preoperative sedation, smoother induction and significantly reduces emergence delirium compared to oral midazolam in children undergoing ENT surgeries under sevoflurane anesthesia. Dexmedetomidine may be considered a preferred premedication option in pediatric anesthesia practice.

Keywords: Midazolam or administration & dosage, Dexmedetomidine or administration & dosage, Anesthesia, Inhalation, Pediatric anesthesia, Child

INTRODUCTION

Pediatric anesthesia encompasses special considerations that differentiate it significantly from adult anesthesia. The perioperative period in children is complex, requiring meticulous management not only of physiological parameters but also of emotional and psychological needs. Among various complications unique to pediatric anesthesia, emergence delirium (ED) is of particular concern. ED is characterized by a dissociated state of consciousness marked by agitation, crying, thrashing, disorientation and a lack of response to comfort measures. Sevoflurane, a popular inhalational agent owing to its rapid onset and recovery properties, has been particularly

associated with a high incidence of ED.[1] The incidence of ED in children varies widely between 10% to 80%, depending on the type of surgery, anaesthetic agents used, preoperative anxiety levels and pain control.[2,3] Negative postoperative behaviours such as sleep disturbances, separation anxiety, enuresis and temper tantrums have been associated with ED.[4,5]

Midazolam, a benzodiazepine with anxiolytic, amnestic and sedative properties, has been widely utilized as a premedication agent to reduce preoperative anxiety and facilitate smooth induction.[6,7] However, its efficacy in preventing ED has been questioned.[8,9] Dexmedetomidine, a selective alpha-2 adrenergic agonist with sedative, analgesic and sympatholytic properties, offers the advantage of minimal respiratory depression and is gaining attention as a promising agent to mitigate ED.[10,11]

Although previous studies have evaluated intravenous and intranasal dexmedetomidine, limited data exists comparing oral dexmedetomidine and oral midazolam in the pediatric ENT surgical population under sevoflurane anesthesia.[12-15] Therefore, this study was conducted to compare the efficacy of oral midazolam versus oral dexmedetomidine in facilitating ease of induction and prevention of emergence delirium in children undergoing ENT surgeries under sevoflurane anesthesia.

METHODS

This randomized, prospective, single-blinded study was conducted at the Department of Anaesthesiology and Department of ENT Head and Neck Surgery at Max Super Speciality Hospital, Saket, New Delhi, from November 2016 to October 2017 after obtaining approval from the Institutional Ethics Committee. Informed written consent was obtained from the parents or legal guardians of all participants.

One hundred children aged 2 to 12 years, classified as ASA physical status I or II, scheduled for elective ENT surgeries of less than two hours' duration under sevoflurane anesthesia were enrolled. Children with neuropsychiatric disorders, cognitive impairments, chronic sedative or analgesic use, seizure disorders, allergy to study drugs or anticipated difficult airway were excluded.

Participants were randomized into two groups of 50 each. Group M received oral midazolam 0.5 mg/kg, while Group D received oral dexmedetomidine 2 µg/kg.[16,17] Injectable preparations of both drugs were mixed with clear apple juice. Premedication was administered 45 minutes before induction. Baseline hemodynamic parameters were recorded. Preoperative sedation was assessed using Ramsay Sedation Scale (RSS).[18] Ease of parental separation was evaluated using the Parental Separation Anxiety Scale (PSAS). Mask acceptance during inhalational induction with sevoflurane was assessed using the mask acceptance scale (MAS).[19,20] Anesthesia induction was achieved using 5–8% sevoflurane in oxygen via a face mask. After securing intravenous access, glycopyrrolate, fentanyl and atracurium were administered. Anesthesia was maintained with 1–1.5% sevoflurane and 50% nitrous oxide in oxygen. Emergence delirium was assessed using the Pediatric Anesthesia Emergence Delirium (PAED) scale at 0, 1, 5 and 15 minutes after arrival in the PACU.[21,22] A PAED score≥10 was considered indicative of ED. Rescue medication with fentanyl 0.5 µg/kg was administered if ED was unresponsive to parental comforting.

Secondary outcomes included time to extubation, time to discharge from PACU and postoperative rescue analgesia requirement. Data were analyzed using SPSS v20.

RESULTS

Demographic variables including age, weight, gender distribution and type of surgery were comparable between the two groups as shown in Table 1. The level of preoperative sedation was significantly better in Group D. The mean Ramsay Sedation Scale score was 3.6±0.5 in Group D compared to 2.8±0.7 in Group M ($p<0.001$). Parental separation was significantly smoother in Group D. Acceptable separation occurred in 90% of children in Group D and 74% in Group M ($p=0.03$). Similarly, mask acceptance was better in Group D, where 88% of children demonstrated calm or slightly anxious behavior compared to 70% in Group M ($p=0.02$). These data are shown in Table 1.

Emergence delirium was significantly reduced in Group D. The incidence of ED, defined as a PAED score≥10, was 8% in Group D compared to 26% in Group M ($p=0.01$). The mean PAED score at 5 minutes post-arrival in PACU was significantly lower in Group D (6.2±2.1) than in Group M (9.1±3.5) as depicted in figure 2. Most episodes of ED resolved spontaneously within 15 minutes. Children experiencing ED required rescue fentanyl more frequently in Group M.

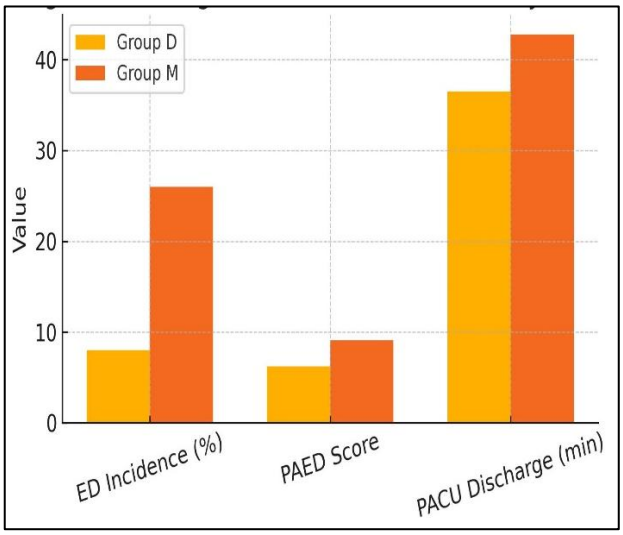

Figure 1: Emergence delirium and recover metrics.

Hemodynamic parameters remained within acceptable clinical ranges throughout the perioperative period. Group D exhibited lower heart rates compared to Group M post-induction and post-extubation ($p<0.05$), but no bradycardia requiring intervention was observed. Mean arterial pressures were stable without significant intergroup differences. The mean time to extubation was 9.4±2.1 minutes in Group M and 9.8±2.4 minutes in Group D ($p=0.47$). However, time to discharge from PACU was significantly shorter in Group D (36.5±7.2 minutes) compared to Group M (42.8±8.5 minutes) ($p=0.04$). Intraoperative fentanyl requirements were slightly lower in Group D, although this did not reach statistical significance. No major adverse events such as hypotension, desaturation, nausea, vomiting or delayed emergence were observed in either group.

Table 1: Baseline demographic and clinical characteristics.

Variable	Group D (n=50)	Group M (n=50)	P value
Age (in years)	5.6±1.2	5.5±1.3	0.72
Weight (kg)	17.3±3.5	17.6±3.2	0.65
Height (cm)	108.4±6.8	107.9±7.2	0.78
Gender (M/F)	28/22	30/20	0.68
ASA grade I / II	34/16	33/17	0.84
Type of surgery	ENT (100%)	ENT (100%)	-

Values are expressed as Mean±SD or count. ENT surgeries included adenotonsillectomy, myringotomy, and FESS. Group D: Dexemdetomidine, Group M: Midazolam.

Table 2: Results including sedation and acceptance parameters.

Outcome	Group D	Group M	P value
Ramsay sedation score (Mean±SD)	3.6±0.5	2.8±0.7	<0.001
Acceptable parental separation (%)	90%	74%	0.03
Calm/slightly anxious mask acceptance (%)	88%	70%	0.02
Time to extubation (min)	9.8±2.4	9.4±2.1	0.47
Intraop fentanyl use	Slightly Lower	-	NS
Hemodynamics	Stable, Lower HR	Stable	<0.05

Group D: Dexemdetomidine, Group M: Midazolam

DISCUSSION

This randomized controlled study demonstrates that oral dexmedetomidine at a dose of 2 µg/kg provides superior outcomes compared to oral midazolam at 0.5 mg/kg in pediatric patients undergoing ENT surgeries under sevoflurane anesthesia. Children premedicated with dexmedetomidine exhibited better preoperative sedation, easier parental separation, improved mask acceptance, lower incidence and severity of emergence delirium and faster PACU recovery.[35]

Emergence delirium is a well-recognized phenomenon following sevoflurane anesthesia, attributed to the agent's rapid offset kinetics and its effects on cortical and subcortical brain structures responsible for arousal and perception.[1-3] Rapid emergence can lead to a mismatch between the recovery of consciousness and cognitive processing, resulting in dissociation, agitation and restlessness. Midazolam has been traditionally used to reduce preoperative anxiety, but its role in preventing ED remains controversial.[6-9] Some studies report paradoxical reactions with midazolam, further exacerbating agitation on emergence.[8,9] Dexmedetomidine offers a unique advantage due to its pharmacological profile. As a highly selective alpha-2 adrenergic agonist, dexmedetomidine produces sedation by inhibiting norepinephrine release at the locus coeruleus, promoting a state similar to natural sleep.[23,24] This sedation is associated with minimal respiratory depression, making it safer than traditional sedatives like benzodiazepines or opioids in pediatric patients.[23] Our findings are consistent with earlier studies that demonstrated a reduced incidence of emergence delirium when dexmedetomidine was administered intravenously or intranasally prior to surgery.[25,26] Moreover, dexmedetomidine's analgesic properties reduce nociceptive stimuli that may contribute to postoperative agitation.[27,28] Importantly, hemodynamic parameters in our study remained stable in both groups, although lower heart rates were noted in the dexmedetomidine group post-induction and emergence, consistent with its known sympatholytic effects.[29,30]

However, no episodes of clinically significant bradycardia or hypotension were observed.[30] A low incidence of emergence agitation and delirium with dexmedetomidine has also been reported previously in other studies.[31-33] A meta-analysis by Blaudszun et al, showed that perioperative systemic alpha-2 agonists significantly decreased postoperative opioid requirements and pain scores.[34,35] Although the oral bioavailability of dexmedetomidine is relatively low (~16%), higher dosing (2 µg/kg) effectively compensated for this and achieved meaningful clinical benefits without notable side effects.[36]

The Ramsay Sedation Scores were significantly higher in the dexmedetomidine group, correlating with easier parental separation and better mask acceptance.[24,25] These are critical aspects of pediatric anesthesia, as traumatic separation or stressful induction may have lasting psychological effects on children.[37] Improved sedation quality helps in achieving a smoother transition into anesthesia, decreasing emotional distress for both the child and the parents.[38]

A key finding of our study was the substantially lower incidence of ED in the dexmedetomidine group (8% vs. 26%).[27,28] Previous studies have reported ED rates as high as 80% following sevoflurane anesthesia without preventive measures.[4,5] This striking reduction emphasizes the effectiveness of dexmedetomidine as a prophylactic agent against ED.[39] Additionally, children in the dexmedetomidine group had significantly shorter PACU stays.[32] A faster recovery not only improves turnover in busy surgical centers but also enhances parental satisfaction and reduces hospital resource utilization.[40] These operational benefits, coupled with clinical advantages, make oral dexmedetomidine a valuable agent in pediatric anesthesia protocols.

There are important clinical implications of our study. Oral dexmedetomidine, being a non-invasive route of administration, is well-tolerated by children and parents and can easily be incorporated into preoperative workflows. It offers an attractive alternative especially in settings where intravenous access is challenging or where minimizing preoperative procedural anxiety is a priority.

However, our study is not without limitations. Firstly, the study was conducted at a single center, which may limit the generalizability of the findings. Secondly, the use of oral dexmedetomidine in a commercially approved oral formulation is currently not widespread and, in our study, an injectable preparation was administered orally, mixed with apple juice.

Although this method has been validated in other studies, pharmacokinetic variations may exist. Thirdly, the study was single-blinded; although the assessors were blinded to group allocation, true double blinding was not feasible. Finally, we did not perform long-term behavioral follow-up to assess whether the reduction in ED translated into improved postoperative psychological outcomes.

Future research should focus on multicentre randomized trials comparing oral dexmedetomidine with other emerging agents such as intranasal dexmedetomidine, clonidine or newer sedatives like dexmedetomidine analogs. Studies assessing the cost-effectiveness of dexmedetomidine use and its impact on parental satisfaction and hospital throughput would further strengthen the case for its routine incorporation into pediatric anesthesia practice. Moreover, exploration of optimal dosing strategies, considering oral bioavailability and evaluating pharmacodynamic profiles in various age groups would refine its usage protocols.

CONCLUSION

In conclusion, oral dexmedetomidine at a dose of 2 µg/kg is superior to oral midazolam 0.5 mg/kg in facilitating smoother induction and recovery in pediatric patients undergoing ENT surgeries under sevoflurane anesthesia. It significantly reduces emergence delirium, improves preoperative and intraoperative conditions and accelerates postoperative recovery without major adverse effects.

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