Intranasal Dexmedetomidine versus Intranasal Midazolam as Sole Sedative Agents for Pelviabdominal Magnetic Resonance Imaging in Pediatrics: A Randomized Double-Blind Trial

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Abstract

Background: The diagnostic effectiveness of magnetic resonance imaging (MRI) resulted in its growing usage among cases of all ages. Nevertheless, children having MRIs are frequently sedated due to the magnetic field's extremely loud decibel level and to avoid motion artefacts. This research aimed to compare the efficacy and safety of intranasal dexmedetomidine and midazolam in pediatric MRI patients. **Materials and Methods:** This double-blind, randomized clinical trial involved 60 cases aged 2–8 years, both sexes getting elective MRI. Sixty children were randomly allocated into two equal groups, subjects in group D were sedated with 2 µg/kg intranasal dexmedetomidine, whereas group M were sedated with 0.3 mg/kg intranasal midazolam. Successful sedation was considered when the Modified Observer Assessment of Alertness/Sedation Scale < 4. **Results:** The 1st and 2nd dose success rates were significantly higher in group D (80% and 90%) as opposed to group M (46.67% and 63.33%) (P = 0.015 and 0.032, respectively). Sedation onset was significantly faster in group D compared to group M (P = 0.037). Sedation time was significantly prolonged in group D than group M (P = 0.044). MRI satisfaction of operator was significantly higher in group D compared to group M (P = 0.022). **Conclusion:** Intranasal dexmedetomidine provided higher incidence of successful sedation and operator satisfaction with quicker onset and prolonged period of sedation and less adverse events than intranasal midazolam in pediatrics undergoing pelviabdominal MRI.

Keywords: Dexmedetomidine, intranasal, magnetic resonance imaging, midazolam, pediatrics

Introduction

The diagnostic effectiveness of magnetic resonance imaging (MRI) resulted in its growing usage among cases of all ages. Nevertheless, children having MRIs are frequently sedated due to the magnetic field's extremely loud decibel level and to avoid motion artefacts.[1]

Anxiety and fear in children elevate catecholamine concentrations, resulting in hypertension, tachypnea, and tachycardia, as well as greater struggles with parental separation, intravenous access, and sedation induction. Sedation of children undergoing radiological imaging processes has grown more prevalent. The advantages of giving proper procedural sedation incorporate a reduction in parental emotional distress, reduction in anxiety of the patient and emotional trauma, and the facilitation of a procedure's completion.[2]

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A suitable sedative for youngsters ought to have a quick onset and shorter duration of effect, acceptable patient and parenting compliance, predictable outcomes and speedy recovery, and no major adverse effects. The rapid absorption of drugs administered intranasally via means of nose mucosa is achievable, producing a speedy and effective initiation of action, prevention of unpleasant injection, simplicity and predictability, and additionally

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preventing deterioration in the digestive tract and liver first-pass metabolism.[3]

Numerous sedatives have been employed for pediatric sedation. Midazolam and chloral hydrate have been utilized, although they have safety and sedative effectiveness limitations.[4] Midazolam is a commonly prescribed sedative for children due to its anxiolytic, amnesic, sedative, anticonvulsant, hypnotic, and muscle relaxant characteristics. Nevertheless, midazolam has little analgesic effect and is related to respiratory depression risk.[5]

In contrast, the selective 2 agonist dexmedetomidine provides analgesic and sedative effects without the respiratory depression risk and has been utilized in pediatrics as a premedication. Dexmedetomidine has limited impact on hemodynamics or inhibition of respiration and possesses a short half-life. As a unique way of sedation, intranasal dexmedetomidine has been utilized in several clinical evaluations of babies and children. The full bioavailability of dexmedetomidine in children within administration reportedly being 84%. The usage of dexmedetomidine lonely in pediatric sedation delivers proper sedation. Even with congenital heart disease, intranasal dexmedetomidine was effective as sedative in children undergoing transthoracic echocardiography.[6]

Few studies have discussed the comparison between intranasal dexmedetomidine utilization and intranasal utilization of midazolam in radiological procedures as a sole sedative, so we established this study to compare the efficacy and safety of intranasal dexmedetomidine and intranasal midazolam in pediatrics undergoing pelviabdominal MRI.

Patients and Methods

This double-blind randomized parallel trial included 60 boys and girls ages 2–8 years , American Society of Anesthesiologists (ASA) physical status I and II undertaking elective pelviabdominal MRI. The research was done after approval by the Faculty of Medicine's Ethical Committee at Tanta University (32466/11/20) and registration at clinicaltrials.gov (NCT04652661) and the guardians of cases provided informed consent.

The criteria for exclusion were body mass index greater than 30 kg/m^2, sensitivity to dexmedetomidine or midazolam, suspected airway obstruction, infection of the upper respiratory tract, severe liver or kidney disease, pronounced bradycardia, or type 2 atrioventricular block above II-degree, and digoxin or beta blockers administrations.

Randomization and blindness

Sixty children were randomly allocated using a computer-generated sequence and opaque, sealed envelopes into two equal categories. Group D were sedated with 2 µg/kg dexmedetomidine intranasal, group M were sedated with 0.3 mg/kg intranasal midazolam. Observers and accompanying anesthesiologists were blinded to the experimental medication. Drugs were prepared by an additional anesthesiologist who did not participate in the remaining phases of study.

All patients were subjected to regular pre-anesthetic assessment. Children fasted for at least 2 h for clear fluid, 4 h for unclear fluid, and 6 h for solid before sedation. MRI compatible monitor and anesthesia machine were available. Baseline heart rate (HR), pulse, systolic blood pressure (SBP), oxygen saturation (SpO_2), and respiratory rate (RR) were documented.

Magnetic resonance imaging procedure

A guardian placed the child in a supine posture and attended to him. Intranasal medication was dripped into both nostrils by a nurse using a 1-mL syringe. Each child remained in a flat posture for 1–2 min after receiving the medication, whereas the nose alae were massaged gently to encourage absorption via nasal membranes. The anesthesiologists examined the sedation level of the child and recorded HR, SpO_2, SBP, and RR at 5-minute intervals for 30 min after medication supply.

The Modified Observer Assessment of Alertness/Sedation Scale (MOAA/S) was utilized to measure the sedation level of children (adequate sedation was described as an MOAA/S score ≤ 3) around 30 min of first dosage of the sedative. If the MOAA/S score was >3 around 30 min of first dosage of the sedative, a further one-half dosage of the sedative 1 µg/kg intranasal dexmedetomidine and 0.15 mg/kg intranasal midazolam was administered as a "rescue" dosage. If the MRI could not be finished, inhaled sevoflurane was delivered to permit the scan to be finished, that we characterized as sedation failure [Table 1].

Assessments tools

Successful sedation was considered when MOAA/S score of <4 (the patients are quiet and sedated enough to permit intravenous cannulation and MRI scanning without crying or disturbance). The onset of sedation time was described

Table 1: Modified observer's assessment of alertness/sedation scale[22]

Response	Score
Agitated	6
Responds readily to name spoken in normal tone	5
Lethargic response to name spoken in normal tone	4
Responds only after name is called loudly and repeatedly	3
Responds only after mild prodding or shaking	2
Does not respond to mild prodding or shaking	1
Does not respond to a deep stimulus	0

as the interval between application of medication and the effective induction of sedation.

The cases were returned to the sedated recovery zone for continued inspection following the assessment. The definition of the wake-up time is the interval between the introduction of intranasal medication and the child's awakening [a modified Aldrete score (MAS) ≥ 9)]. Patients were discharged when their MAS reached 9.

All adverse events were recorded. The minimal adverse reactions include the following: (1) bradycardia, defined as an HR slowing of over twenty percent of the usual rate modified for age under sedation, requires pharmaceutical approach (managed with IV atropine); (2) a considerable drop in oxygen saturation, characterized by a SpO_2 below 90% and the necessity for oxygen supplements; (3) obstruction of the upper respiratory system (open airway; reversible with oxygen supply); (4) postoperative nausea and vomiting (PONV; tilt the head of the youngster to one side while you remove vomit from his or her mouth); (5) a delay in recovery, described as duration of sedation recovery more than 2 h; and rash. Emergency airway intervention constituted the significant adverse effects (tracheal intubation or the insertion of airway assistance, like larynx or oropharynx masks); laryngospasm (stimulation of laryngeal notch, lidocaine up to intubation was done); reflux aspiration (suctioning, oxygen supplementation and even intubation was done); severe arrhythmia (treated according to the type of arrythmia).

The primary outcome was the incidence of successful sedation. The secondary outcomes were the onset time of sedation, adverse effects, and operator satisfaction.

Sample size calculation

G*Power 3.1.9.2 performed the sample size calculation (Universitat Kiel, Kiel, Germany). The sample size was computed according to the incidence of successful sedation (our primary outcome). It is expected to increase by 40% with higher dose of dexmedetomidine than midazolam according to a previous study,[7] 0.05 α error, 80% study power, 1:1 group ratio, and two patients were recruited to each group to compensate drop out. Therefore, we included 60 patients.

Statistical analysis

Statistical Package for the Social Sciences v26.0 (IBM, Chicago, Illinois) was used for statistical analysis. The distributional normality of the data was tested using the Shapiro-Wilks test and histograms. Using an unpaired student *t* test, quantitative data reported as mean and standard deviation were analyzed. Using the Mann–Whitney test, the median and interquartile range (IQR) of nonparametric quantitative data were analyzed. When applicable, qualitative variables were expressed as frequency and percentage (percent) and analyzed with the Chi-square or Fisher's exact test. A two-tailed *P* value of 0.05 or less was considered statistically significant. A two-tailed *P*-value of 0.05 or less was judged statistically significant.

Results

In this trial, eligibility was tested for 89 patients. 60 patients were recruited to two groups. of equal size. All allocated patients were followed up and analyzed [Figure 1]. Patients' demographic data and MRI duration were comparable between both groups as seen in Table 2.

The first and second dose success rates were higher significantly in group D (80% and 90% (than group M (46.67% and 63.33%) (P = 0.015 and 0.032 respectively). Sedation onset was significantly faster in group D compared to group M (P = 0.037). Sedation time was significantly prolonged in group D versus group M (P = 0.044).

MRI operator satisfaction [Table 3] was significantly in group D versus group M (P = 0.022). Moreover, HR and SBP were significantly lower in group D compared to group M at 10 min, 15 min, 20 min, 25 min, and 30 min while were insignificantly different at baseline and 5 min. Respiratory rate and oxygenation were similar between both groups [Figure 2], as well as the incidence of bradycardia, PONV, and hypotension were matched between both groups [Table 4].

Discussion

MRI is extremely sensitive to motion; thus, the participant must remain motionless during the scan. The pre-operative phase is an extremely stressful time for the majority of surgical patients, particularly pediatric cases.[8] Anesthetic drugs used for MRI on juvenile patients should have minimal side effects and provide rapid induction and recovery of anesthesia.[9] Intranasal medication is a generally noninvasive, convenient, and simple method of administration that accelerates the initiation of action and minimizes first-pass metabolism.[10] Premedication aids in resolving these obstacles, showing midazolam being the most often used medication. Midazolam and dexmedetomidine are efficient sedatives among these premedication. When administered as a premedication in children, midazolam offers a variety of favorable outcomes: Sedation, vomiting restriction, short duration and rapid onset of effect.[11] However, it is linked to respiratory depression and a higher frequency of postoperative behavioral abnormalities, hiccups, and paradoxical behaviors.[12] Dexmedetomidine is anti-shivering and analgesic does not produce respiratory depression.[13]

Saad *et al*.[14] compared intranasal dexmedetomidine to midazolam as a pre-anesthetic medicine in children and found that pre-medicated children with dexmedetomidine

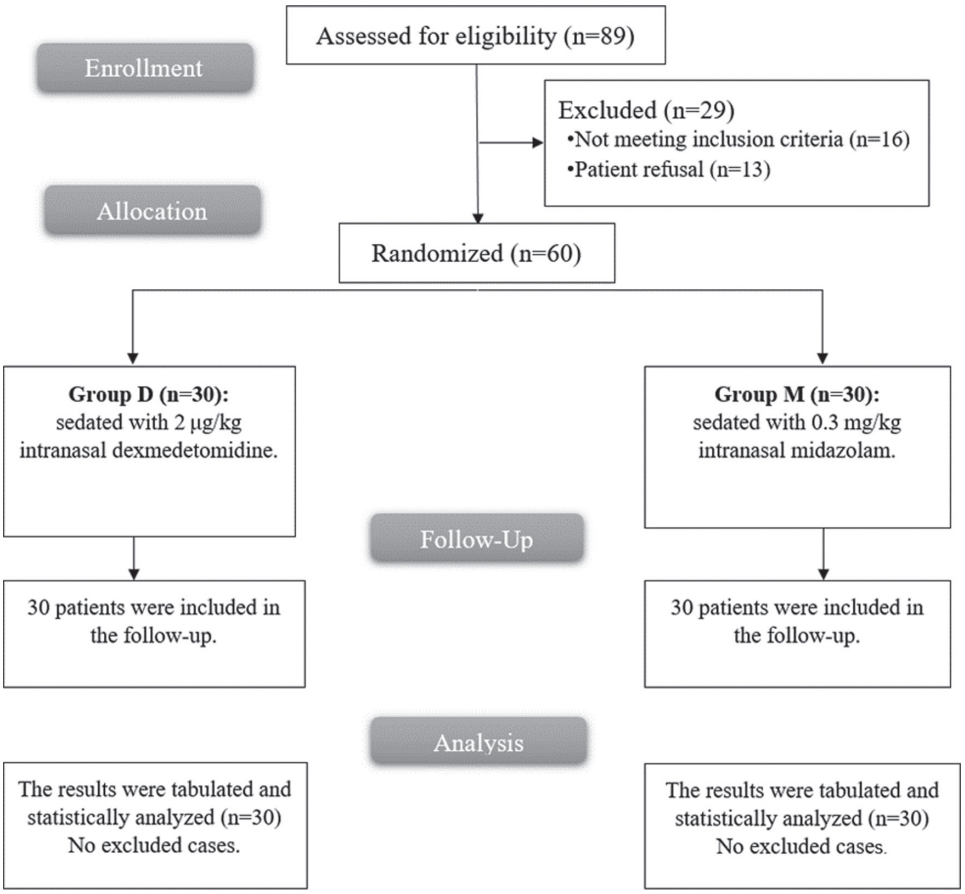

Figure 1: Consort flow diagram of the enrolled participants through each stage of the trial

Table 2: Patient characteristics in the studied groups

		Group D (n = 30)	Group M (n = 30)	P value
Age (years)		4.87 ± 1.81	4.93 ± 2.1	0.896
BMI (kg/m^2)		13.37 ± 3.4	13.43 ± 4	0.954
Sex	Male	18 (60.0%)	16 (53.33%)	0.749
	Female	12 (40.0%)	14 (46.67%)	
ASA physical status	I	24 (60%)	22 (53.33%)	0.761
	II	6 (40%)	8 (46.67%)	
Duration of MRI (min)		40.87 ± 7.26	42.17 ± 7.80	0.367

D: dexmedetomidine, M: midazolam, BMI: body mass index, ASA: American Society of Anesthesiologists, MRI: magnetic resonance imaging

Data presented as mean ± SD and frequency (%)

had reducing sedation scores (MOAA/S), reduced anxiety, simplified parental separation, improved mask acceptability, but they showed that intranasal midazolam induces sedation more rapidly than dexmedetomidine.

Furthermore, Abdelmoneim *et al.*[15] found that effective and safe use of dexmedetomidine intranasally as a pre-anesthetic drug in children receiving simple fracture repair congenital heart abnormalities. This was attributed to the fact that premedication with intranasal dexmedetomidine, children reported reduced sedation ratings (MOAA/S scale) and simplified parental separation versus children who were pre-medicated with intranasal midazolam.

Olgun *et al.*[16] found that due to the rate of sedative processes that are successfully completed without requiring a rescue medication, intranasal dexmedetomidine is an excellent agent for sedating newborns undergoing MRI (except the repetition of dexmedetomidine). Another study[17] also found that dexmedetomidine administered intranasally was preferable than midazolam as an antianxiety, with a reduced anxiety score 30 and 45 min before surgery.

However, in conflict with our findings, Akin *et al.*[18] stated that there was no indication of a difference in sedation or anxiety scores across groups upon parental separation when they compared intranasal midazolam (0.2 mg/kg) and dexmedetomidine (1 µg/kg).

Our findings are also similar to another study[19] that found the mean HR and blood pressure (BP) reduced significantly at 30 min after (1 µg/kg) intranasal dexmedetomidine, as compared to that in children who received (0.5 mg/kg) midazolam intranasally. Also, a study[17] found that intranasal dexmedetomidine (1 µg/kg) lead to statistically significant but clinically insignificant reductions in HR and BP at 10, 20, and 30 min after administration compared to midazolam. Sun *et al.*[20] also

Table 3: Success rate and onset of sedation in the studied groups

		Group D (n = 30)	Group M (n = 30)	P value
Success rate of 1st dose		24 (80%)	14 (46.67%)	0.015*
success rate of 2nd dose		27 (90%)	19 (63.33%)	0.032*
Successful sedation score		1.5 (1–3)	4 (1.25–5)	0.01*
Onset of sedation (min)		8.10 ± 4.45	12.1 ± 8.07	0.037*
Successful sedation time (min)		38.21 ± 7.29	33.58 ± 7.83	0.044*
MRI operator satisfaction	Very satisfied	15 (50.0%)	6 (20%)	0.022*
	Satisfied	9 (30.0%)	8 (26.67%)	
	Neither satisfied nor unsatisfied	3 (10%)	2 (6.67%)	
	Dissatisfied	1 (3.33%)	3 (10%)	
	Unsatisfied	2 (6.67%)	11 (36.67%)	

D: dexmedetomidine, M: midazolam, MRI: magnetic resonance imaging

Data presented as mean ± SD or median [IQR], frequency (%)

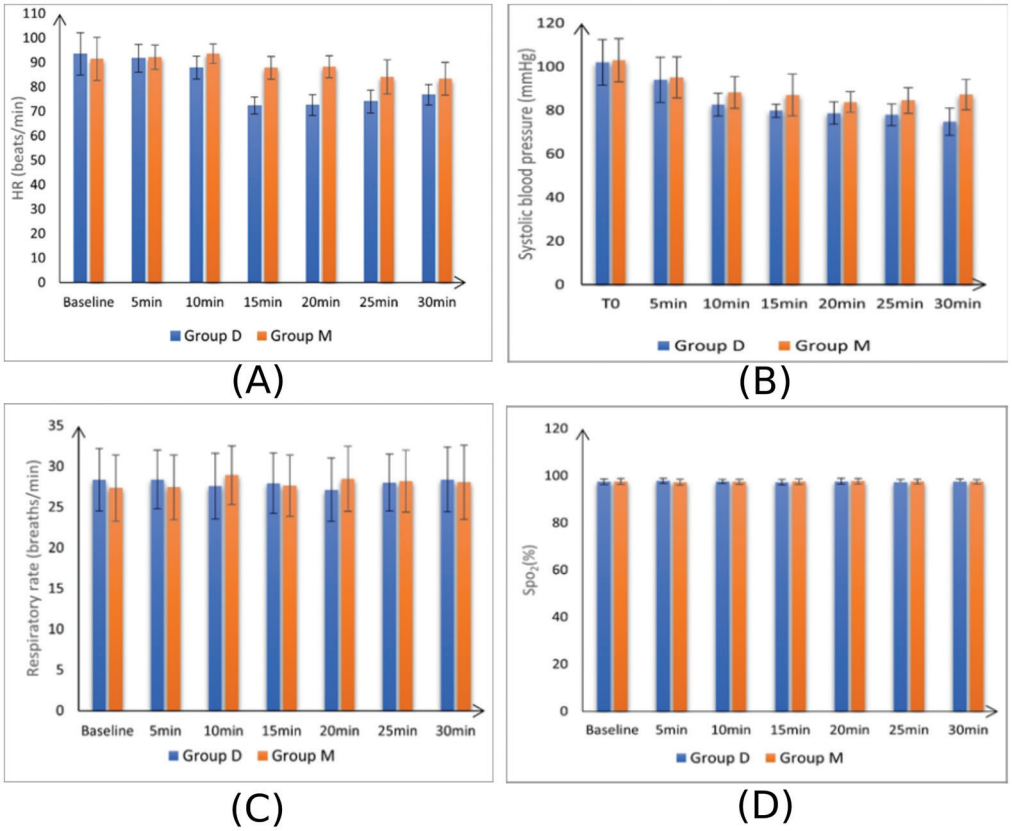

Figure 2: Heart rate (HR) (A), systolic blood pressure (B), respiratory rate (C), and SpO_2 (D) of the studied groups

Table 4: Adverse effects in the studied groups

	Group D (n = 30)	Group M (n = 30)	P value
PONV	5 (16.67%)	9 (30%)	0.359
Bradycardia	7 (23.33%)	2 (6.67%)	0.145
Desaturation	2 (6.67%)	4 (13.33%)	0.670

D: dexmedetomidine, M: midazolam, PONV: postoperative nausea and vomiting

Data presented as frequency (%)

found that dexmedetomidine premedication reduced SBP, mean BP and HR and prolonged the onset of sedation relative to midazolam.

In our study adverse effects as (PONV, bradycardia, hypotension), were matched between both groups. Moreover, a study[21] found that all procedures were completed without any complications so intranasal Dexmedetomidine is an useful drug regimen for who need sedated for an MRI.

This study imposed some limitations. Our sample size is relatively limited to demonstrate that this sedative regimen does not result in infrequent but major adverse effects. This duration may be insufficient for dexmedetomidine, and for some children, the medicine may have yet to take action. If we had waited longer, it is probable that

we would have observed stronger sedative effects in the intranasal dexmedetomidine group.

Conclusion

Intranasal dexmedetomidine provided higher incidence of successful sedation and operator satisfaction with quicker onset and prolonged duration of sedation and less adverse effects than intranasal midazolam in pediatrics undergoing pelviabdominal MRI. Consequently, it can be used successfully and safely as the only sedative drug in children undergoing MRI.

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Nothing to declare.

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Conflicts of interest

There are no conflicts of interest.

Author contributions

Each author took part in the idea and design of the research. Preparation of materials, gathering and analysis of data were carried out by Taysser M. Abdelraheem and Amira M. Abdelsamad. The initial draught of the manuscript has been written by Taysser M. Abdelraheem, and all authors provided feedback on earlier versions of the manuscript. All authors reviewed and approved the final manuscript.

Ethical approval and protocol registration

The study was done after approval by the Faculty of Medicine's Ethical Committee at Tanta University (32466/11/20) and registration at clinicaltrials.gov (NCT04652661) and the guardians of cases provided informed consent.

Availability of data and material

The datasets utilized and/or analyzed for this work are accessible as MS Excel files (.xlsx) from the corresponding author upon reasonable request.

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