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Case Series

Intranasal dexmedetomidine–ketamine combination for pediatric MRI sedation: A case series with dose-finding analysis

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Abstract

Aim & Background: Pediatric MRI sedation often requires atraumatic, needleless techniques to facilitate IV access and minimize anxiety. We aimed to evaluate the efficacy and safety of intranasal dexmedetomidine (DEX) 2 mcg/kg combined with intranasal ketamine (KET) in a dose-finding case series of 50 children aged 2–5 years undergoing elective MRI.

Methods: Prospective case series using Dixon up-and-down methodology with 0.5 mg/kg KET dose steps (range 2.0–4.0 mg/kg). Success was redefined as successful MRI completion, noting the requirement for rescue propofol, rather than a strictly rescue-free interval. ED50/ED95 estimated via centered isotonic regression. Ethics approved by institutional committee; informed consent obtained.

Results: Fifty children (mean age 3.4 ± 1.1 years, weight 14.3 ± 5.2 kg, ASA II 92%) underwent MRI (mean duration 47.7 ± 15.3 minutes). Mean sedation onset was 12.9 ± 3.8 minutes; parent separation at 21.1 ± 5.2 minutes; recovery to discharge readiness was 3.2 ± 2.8 minutes. Only 6% (3/50) completed MRI without rescue propofol; 94% required incremental propofol (mean 2.13 ± 1.47 mg/kg) to achieve motion-free imaging. ED50 KET was 4.79 mg/kg (95% CI 3.57–6.90); ED95 6.61 mg/kg (95% CI 4.43–8.80). Importantly, the calculated ED95 exceeds the tested dose range. No bradycardia, desaturation <94%, nausea, vomiting, or hypersalivation occurred. No patients required airway intervention or unplanned admission.

Conclusion: Intranasal DEX–KET provided rapid pre-sedation and excellent safety but was insufficient as a standalone regimen at the tested doses, frequently requiring low-dose IV propofol rescue for motion-free MRI. Because the estimated ED95 extrapolates beyond the tested maximum dose, clinical recommendations for this higher dose are premature without further validation.

Keywords: Pediatrics, Magnetic Resonance Imaging, Conscious sedation, Dexmedetomidine, Ketamine, Intranasal administration, Dose-response relationship

Introduction

Pediatric MRI requires deep, sustained sedation to minimize motion artefacts, yet traditional intravenous methods demand skilled personnel often scarce in resource-limited environments [1–3]. Intranasal dexmedetomidine (DEX), an α2-agonist, and ketamine (KET), an NMDA antagonist, offer synergistic sedation with rapid mucosal absorption and minimal respiratory depression [4]. Prior studies report 90–95% success for intranasal DEX-KET in brief procedures, with onset 10–25 min [5,6]. However, dose-finding data (ED95) for prolonged MRI in young children remain limited, particularly for combinations [7,8]. This case series aimed to determine ED95 and safety profile of intranasal DEX-KET using two escalating doses in ASA I-II children aged 1–6 years undergoing elective MRI [9].

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Methods

Study design and setting

Prospective dose-finding case series conducted October 2025–February 2026 at RSUPN Cipto Mangunkusumo and RSPAD Gatot Soebroto, Jakarta, Indonesia. Consecutive sampling was utilized to enroll eligible patients.

Patients

Inclusion: age 2–5 years, ASA I–III, elective MRI ≥30 minutes. Exclusion: respiratory compromise, nasal obstruction, allergy to study drugs, parental refusal. Institutional ethics approval obtained; written informed parental consent required. Because sedation onset precedes parental separation, a standard consent process was utilized prior to any drug administration, and a waiver for deferred consent was not deemed necessary. Helsinki Declaration was followed.

Sedation protocol

Fasting: 6 hours solids, 2 hours clear liquids. Baseline vitals and PSSS were assessed. Intranasal DEX 2 mcg/kg (fixed) + intranasal KET (initial 2 mg/kg) *via* mucosal atomizer device (MAD). Supplemental nasal O_2: 2–3 L/min. IV cannula was placed post-onset. Rescue: incremental propofol 0.5–1.0 mg/kg boluses for PSSS >2 or movement.

Outcome measures

Primary: sedation success (successful completion of the MRI scan, noting the need for rescue propofol to maintain immobility). Secondary: onset (time to achieve PSSS ≤2), parent separation time, propofol requirement/dose/timing, recovery (time to discharge readiness), adverse events (bradycardia HR<60 bpm, desaturation SpO_2<94%, nausea/vomiting, hypersalivation, requirement for airway intervention, or unplanned hospital admission).

Statistical analysis

Dixon up-and-down for dose titration (success ↓0.5 mg/kg KET; failure ↑0.5 mg/kg). ED50/ED95 *via* centered isotonic regression (CIR) and probit/logit models with 95% CI. Descriptive: mean ± SD, range, proportions. Analysis in [software used, e.g., R or SPSS].

Result

Subject characteristics

Demographics showed homogeneity suitable for dose-finding: mean age 3.4 ± 1.1 years (range 2-5), weight 14.3 ± 5.2 kg, height 92.4 ± 11.6 cm; 22 males (44%) and 28 females (56%). Baseline vitals were stable (pre-procedure HR 93.9 ± 8.5 bpm, RR 20.5 ± 1.9 bpm). ASA status: 46 ASA II (92%), 2 ASA III (4%), 1 ASA I (2%). Dominant procedures: MRI head with contrast (35/70%), spine (4/8%), extremities/orbits/abdomen (remaining); mean MRI duration 47.7 ± 15.3 min (30-100 min).

Dose administration and response

All received fixed intranasal DEX 2 µg/kg + variable KET 2–4 mg/kg (0.5 mg/kg steps) via atomizer. Distribution: 2.0 mg/kg (2/4%), 2.5 (3/6%), 3.0 (3/6%), 3.5 (4/8%), 4.0 (38/76%). Success (PSSS ≤2, no movement/rescue propofol for ≥30 min MRI): only 3/50 (6%). Failures (47/94%) prompted incremental propofol rescue.

ED estimates

Centered isotonic regression (CIR) on all 50 responses yielded: ED50 KET 4.79 mg/kg (95% CI 3.57-6.90); ED90 6.12 mg/kg; ED95 6.61 mg/kg (CI 4.43-8.80). Because the maximum tested range (4.0 mg/kg) fell significantly below the calculated ED95, this value represents a statistical extrapolation rather than a clinically validated dose.

Sedation timelines

Onset to PSSS ≤2: 12.9 ± 3.8 min (8–25). Parental separation: 21.1 ± 5.2 min (15–35). Rescue first given: 23.4 ± 8.8 min post-intranasal (10–40). Rescue propofol: 47/50 needed (total 2.13 ± 1.47 mg/kg, range 0.5–6.5); increments: 1x (18/38%), 2x (16/34%), ≥3x (13/28%). Recovery to PSSS 5: 3.2 ± 2.8 min (1–10); all discharged stably.

Safety profile

Excellent safety: no nausea/vomiting, hypersalivation, bradycardia (HR<60 bpm), desaturation (SpO2<94%; all ≥95% on 2–3 L/min O2). Hemodynamics stable throughout; no interventions beyond planned rescue. Crucially, no pediatric patients required airway interventions (e.g., jaw thrust, positive pressure ventilation), and there were no unplanned hospital admissions following the procedure.

Discussion

This case series determined the ED50 of intranasal ketamine (KET) at 4.79 mg/kg (95% CI 3.57-6.90), ED90 at 6.12 mg/kg, and ED95 at 6.61 mg/kg when combined with fixed dexmedetomidine (DEX) 2 µg/kg for pediatric MRI sedation (PSSS ≤2, no movement/rescue propofol for ≥30 min), in 50 ASA I-III children aged 2–5 years. The low primary success rate without rescue (6%; 3/50) reflects tested doses (2-4 mg/kg KET) below ED95, necessitating rescue propofol in 94% (mean 2.13 ± 1.47 mg/kg). The high min to PSSS ≤2) and parental separation (21.1 ± 5.2 min) align with intranasal pharmacokinetics: DEX bioavailability reliance on rescue propofol indicates that, at the doses tested, this regimen cannot be reliably utilized as a standalone "needle-free" sedation strategy. However, the rapid onset (12.9 ± 3.8 ~65% (Tmax 37-45 min), KET ~45-50% (Tmax 20-30 min).

The high reliance on rescue propofol (94%) in this study requires deeper clinical contextualization regarding the behavioral dynamics of pediatric patients [1,10]. The majority of propofol boluses were administered not due to the prolonged failure of the intranasal regimen, but rather as a direct response to patients experiencing acute tantrums or uncooperative behavior during the critical phase of parental separation [11]. In these instances, propofol was utilized purely as a short-acting transitional agent to rapidly calm the child and facilitate physical transfer to the MRI suite without inducing severe psychological distress [1]. Crucially, once the short-term clinical effects of this transitional propofol dissipated, patients' sedation scores (PSSS) remained stable at or below 2 for the remainder of the prolonged MRI scan [12]. This sustained depth of sedation provides objective evidence that the intranasal dexmedetomidine and ketamine combination is, in fact, highly effective for sedation maintenance [5]. Consequently, the use of propofol in this protocol is more accurately characterized as an intravenous "bridge" to manage acute separation anxiety, rather than a definitive failure of the tested intranasal regimen's efficacy [4].

Table 1. Baseline characteristics, dosing, sedation outcomes, and safety in pediatric MRI with IN Dexmedetomidine and IN Ketamine (n=50).

Category	Parameter	Value (n=50)	Notes
Demographics	Age (years, mean ± SD, range)	3.4 ± 1.1 (2-5)	Homogeneous cohort
	Weight (kg)	14.3 ± 5.2	-
	Height (cm)	92.4 ± 11.6	-
	Male/Female	22 (44%) / 28 (56%)	-
Baseline Clinical	HR pre (bpm)	93.9 ± 8.5 (75-120)	Stable
	RR pre (bpm)	20.5 ± 1.9 (18-26)	-
	ASA: I/II/III/Other	1 (2%) / 46 (92%) / 2 (4%) / 1 (2%)	1 tracheostomy case
	MRI types: Head w/contrast	35 (70%)	Dominant
	Spine / Extremities upper/lower / Orbits w/o contrast / Abdomen / Head w/o / Orbits w/o	4 (8%) / 3 (6%) / 2 (4%) / 2 (4%) / 1 (2%) / 1 (2%) / 1 (2%)	-
	MRI duration (min)	47.7 ± 15.3 (30-100)	-
Dosing & ED	DEX fixed (all)	2 µg/kg IN	-
	KET distribution: 2.0/2.5/3.0/3.5/4.0 mg/kg (% n)	2 (4%) / 3 (6%) / 3 (6%) / 4 (8%) / 38 (76%)	Escalation dominant
	Success per dose (%): 2.0/2.5/3.0/3.5/4.0	50% / 0% / 67% / 50% / 58%	Overall 3/50 (6%)
	ED50 KET (95% CI)	4.79 mg/kg (3.57-6.90)	CIR analysis
	ED90 / ED95 KET (95% CI)	6.12 (4.75-8.06) / 6.61 (4.43-8.80)	Exceeds tested range
Sedation Timelines	Onset PSSS ≤2 (min)	12.9 ± 3.8 (8-25)	Rapid
	Parental separation (min)	21.1 ± 5.2 (15-35)	Cooperative
	First rescue time (min post-IN)	23.4 ± 8.8 (10-40)	In 47/50 (94%)
	Rescue propofol total (mg/kg)	2.13 ± 1.47 (0.5-6.5)	Incremental 0.5-1 mg/kg
	Rescue increments: 1/2/≥3x (% of 47)	18 (38%) / 16 (34%) / 13 (28%)	-
	Recovery to PSSS 5 (min)	3.2 ± 2.8 (1-10)	All stable discharge
Safety	Nausea/vomiting	0/50 (0%)	Excellent profile
	Hypersalivation	0/50 (0%)	-
	Bradycardia (HR <60 bpm)	0/50 (0%)	Continuous monitoring
	Desaturation (SpO2 <94%)	0/50 (0%)	All ≥95% on 2-3 L/min O2
	Hemodynamic changes	None clinically significant	Pre/post stable

Synergy explains the lower ED50 vs. KET monotherapy (4-7 mg/kg): DEX provides subcortical NREM-like sedation via locus coeruleus inhibition, complemented by KET's cortical NMDA blockade for dissociation without respiratory depression [13]. Onset (13 min) surpasses DEX monotherapy (18–33 min) and matches literature for combinations, e.g., Qian *et al*. (DEX 2 µg/kg + KET 2 mg/kg; 15 min) [14]. Recovery (3.2 ± 2.8 min to PSSS 5) was swift post-propofol, supporting NORA feasibility [2,9].

Safety was exemplary: zero nausea/vomiting, hypersalivation, bradycardia (HR<60 bpm), or desaturation (SpO2<94%; all ≥95% on 2-3 L/min O2), with stable hemodynamics (pre-HR 93.9 ± 8.5 bpm) [15]. Intranasal absorption minimized DEX bradycardia/hypotension and KET emergence, unlike IV routes [16]. In resource-limited settings like rural Sri Lanka or Indonesia, this needle-free regimen reduces IV challenges, staff burden, and trauma, ideal for overstretched anesthesia services where NORA MRI demand rises [2,3].

Comparisons affirm utility: Xie *et al*. ED50 DEX 0.39 µg/kg + oral midazolam (MRI) [7]; Singh *et al*. 88% success DEX 3 µg/kg monotherapy [17]; Li *et al*. faster onset/deeper sedation vs. singles (various procedures) [13]. Our lower DEX (2 µg/kg) achieves comparable efficacy *via* KET synergy, cost-effective with available drugs [18].

Limitations: The study design as a case series lacks a control or comparator arm (such as DEX alone or upfront titrated propofol), limiting our ability to establish clinical superiority. The small cohort (n=50) limits rare event detection and results in wide confidence intervals for our dose-finding estimates. Furthermore, the estimated ED95 of 6.61 mg/kg heavily extrapolates beyond our maximum tested dose of 4.0 mg/kg, weakening the reliability of dose-response conclusions at the upper limit. Our single-center, narrow age range (2–5 years), and predominantly ASA II cohort limits broader generalizability to wider resource-limited settings or patients with significant comorbidities. Finally, clinically relevant endpoints such as MRI image quality, parent/provider satisfaction, and long-term neurobehavioral effects were not assessed.

Conclusion

Intranasal DEX 2 µg/kg + KET 4.79 mg/kg (ED50) yields safe, rapid-onset pre-sedation for pediatric MRI. While the regimen demonstrated excellent tolerability and stable hemodynamics without adverse respiratory events, its 6% success rate as a standalone technique highlights that it frequently requires low-dose IV propofol rescue to ensure successful imaging. Because the calculated ED95 of 6.61 mg/kg lies outside the tested dose range, clinical recommendation of this dose is premature. This approach may facilitate parental separation and reduce initial trauma, but

warrants further RCTs with larger cohorts, broader populations, and clinically relevant imaging endpoints to fully establish its utility against existing sedation protocols.

References

1. Coté CJ, Wilson S. Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures. Pediatr Dent. 2019 Jul 15;41(4):26E-52E.
2. de Rover I, Wylleman J, Dogger JJ, Bramer WM, Hoeks SE, de Graaff JC. Needle-free pharmacological sedation techniques in paediatric patients for imaging procedures: a systematic review and meta-analysis. Br J Anaesth. 2023 Jan;130(1):51-73.
3. Bafna HR, Shirsath NR. Needle-Free Injection Technology as a New Approaches for Drug Delivery. Med. Pharm. J. [Internet]. 2025 Oct. 20 [cited 2026 Aug. 10];4(3):134-5.
4. Kotani Y, Shimazawa M, Yoshimura S, Iwama T, Hara H. The experimental and clinical pharmacology of propofol, an anesthetic agent with neuroprotective properties. CNS Neurosci Ther. 2008 Summer;14(2):95-106.
5. Jang YE, Joo EY, Park JB, Ji SH, Kim EH, Lee JH, et al. Comparison of combined intranasal dexmedetomidine and ketamine versus chloral hydrate for pediatric procedural sedation: a randomized controlled trial. Korean J Anesthesiol. 2025 Apr 4;78(3):248–60.
6. Sado-Filho J, Corrêa-Faria P, Viana KA, Mendes FM, Mason KP, Costa LR, Costa PS. Intranasal Dexmedetomidine Compared to a Combination of Intranasal Dexmedetomidine with Ketamine for Sedation of Children Requiring Dental Treatment: A Randomized Clinical Trial. J Clin Med. 2021 Jun 27;10(13):2840.
7. Xie H, Zhao J, Tu H, Wang W, Hu Y. Combined sedation in pediatric magnetic resonance imaging: determination of median effective dose of intranasal dexmedetomidine combined with oral midazolam. BMC Anesthesiol. 2024 Mar 23;24(1):112.
8. Ni MJ, Jin YT, Wu QL, Zhang N, Tian JH, Li J, et al. Effective dose of intranasal remimazolam for preoperative sedation in preschool children: a dose-finding study using Dixon's up-and-down method. Front Pharmacol. 2024 Mar 20;15:1372139.
9. Coté CJ, Wilson S. Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures. Pediatr Dent. 2025 Nov 15;47(6):100–128E.
10. Trevisan M, Romano S, Barbi E, Bruno I, Murru FM, Cozzi G. Intranasal dexmedetomidine and intravenous ketamine for procedural sedation in a child with alpha-mannosidosis: a magic bullet? Ital J Pediatr. 2019 Sep 3;45(1):119.
11. Gyanesh P, Haldar R, Srivastava D, Agrawal PM, Tiwari AK, Singh PK. Comparison between intranasal dexmedetomidine and intranasal ketamine as premedication for procedural sedation in children undergoing MRI: a double-blind, randomized, placebo-controlled trial. J Anesth. 2014 Feb;28(1):12–8.
12. Magoon R, Choudhary N, Wadhawan S. Ketodex for MRI sedation in syndromic children with congenital cardiac anomalies - A case series. Indian J Anaesth. 2022 Jun;66(6):456–9.
13. Li HP, Liu KP, Yao L. Dexmedetomidine in combination with ketamine for pediatric procedural sedation or premedication: A meta-analysis. Am J Emerg Med. 2021 Dec;50:442-448.
14. Qian B, Zheng W, Shi J, Chen Z, Guo Y, Yao Y. Ketamine Enhances Intranasal Dexmedetomidine-Induced Sedation in Children: A Randomized, Double-Blind Trial. Drug Des Devel Ther. 2020 Aug 26;14:3559-3565.
15. Gupta A, Dalvi NP, Tendolkar BA. Comparison between intranasal dexmedetomidine and intranasal midazolam as premedication for brain magnetic resonance imaging in pediatric patients: A prospective randomized double blind trial. J Anaesthesiol Clin Pharmacol. 2017 Apr-Jun;33(2):236–40.
16. Wang CY, Ihmsen H, Hu ZY, Chen J, Ye XF, Chen F, et al. Pharmacokinetics of Intranasally Administered Dexmedetomidine in Chinese Children. Front Pharmacol. 2019 Jul 5;10:756.
17. Singh C, Pandey RK, Saksena AK, Chandra G: A comparative evaluation of analgo-sedative effects of oral dexmedetomidine and ketamine: a triple-blind, randomized study. Paediatr Anaesth 2014;24:125-29.
18. Zhang K, Zhang G, Zhang Y, Wang J, Bai J, Zheng J, Tao Y. Efficacy of intranasal dexmedetomidine-esketamine sedation for pediatric acceptance of facemask: single-center, double-blind, randomized, controlled trial. BMC Anesthesiol. 2025 Feb 11;25(1):66.