



Two oral sedation regimens in pediatric dentistry: a randomized controlled trial

Awj Hammadyeh¹, Mohamed Altinawi² and Faten Rostom³

ABSTRACT

Objectives: Dental procedures are always associated with some degree of anxiety, and children are usually more prone to it. General anesthesia may have to be used in more complex procedures, but many dental procedures can successfully be undertaken with therapeutic sedation. The aim of this trial was to evaluate the effectiveness of oral sedation using dexmedetomidine in comparison with ketamine in the management of uncooperative pediatric patients during dental treatment.

Methodology: A randomized clinical trial was carried out on 40 ASA physical status-I children aged 2-6 y to investigate the effect of using dexmedetomidine and ketamine with atropine for sedation.

The children were equally and randomly divided into two groups: Group K: received oral ketamine 5 mg/kg with atropine 0.01 mg/kg, and Group D: received oral dexmedetomidine 3 µg/kg. Recovery time, vital signs, and side effects were all recorded. Behavior rating was also assessed using the Ohio State University Behavioral Rating Scale (OSUBRS).

Results: The children in Group D were more sedated than in Group K, but the difference was not statistically significant ($p = 0.22$). The median recovery time was significantly shorter in Group D than in Group K ($p = 0.003$). No adverse effects, episodes of respiratory or cardiovascular instability were noted in either groups.

Conclusions: Oral dexmedetomidine is equally effective to oral ketamine for sedation in children undergoing outpatient dental procedures, but has relatively a shorter recovery time.

Key words: Behavior; Dexmedetomidine; Ketamine; Sedation

Citation: Hammadyeh A, Altinawi M, Rostom F. Two oral sedation regimens in pediatric dentistry: a randomized controlled trial. *Anaesth pain & intensive care* 2019;23(4):377-381.

DOI: <https://doi.org/10.35975/apic.v23i4.1170>

¹ PhD Student, Department of Pediatric Dentistry, Faculty of Dental Medicine, Damascus University, Damascus, (Syria)

² Professor, Department of Pediatric Dentistry, Faculty of Dental Medicine, Damascus University, Al-Baramkeh, Damascus, (Syria)
E-mail: mohamedaltinawi@gmail.com

³ Associate Professor, Department of Anesthesia and Reanimation, Faculty of Medicine, Damascus University, Al-MazzeH Highway, Damascus, (Syria)

E-mail: fatenrostom@yahoo.fr
Correspondence: Awj Rasheed Hammadyeh
Al-Baramkeh, Damascus, (Syria)
E-mail: aoj.star@hotmail.com
Phone: +963932913839

Received: 20 June 2019,

Reviewed: 30 August, 3 October 2019,

Revised: 3 October, 23 November 2019,

Accepted: 26 November 2019

INTRODUCTION

The use of pharmacological regimens like conscious sedation come into help in some pediatric patients who are unable to tolerate dental treatment procedures despite the use of all psychological and behavioral management techniques.^{1,2}

Various pharmacological agents are used (through different routes) in conscious sedation. ketamine is a sedative drug with an analgesic effect without loss of consciousness when given in the adequate

doses.³ However, it may have different side effects,³ including hallucinations,⁴ nausea, vomiting, and excessive salivation, which may give rise to coughing and laryngospasm.⁵

Dexmedetomidine is a highly selective alpha-2 agonist which has sedative and analgesic effects.^{6,7} When dexmedetomidine is given within the appropriate doses provided by the clinical guidelines, it produces dose-dependent analgesia with no consequent respiratory depression.⁸

oral sedation in pediatric dentistry

The efficacy of oral ketamine has been proved time and again in various clinical studies,^{5,9-11} but very few trials have tested the use of dexmedetomidine in oral route.^{12,13}

Hence, the objectives of this randomized controlled study were to compare the safety and efficacy of oral dexmedetomidine to oral ketamine administered with atropine for uncooperative children undergoing dental procedures.

METHODOLOGY

The study was conducted on 40 normal, ASA-I children of both sexes aged 2–6 y, requiring dental treatment (pulpotomy) under conscious sedation because of their uncooperative behavior (negative and definitely negative behavior on Frankel's scale).¹⁴

All parents gave informed written consent, and ethical and licensing approvals were obtained from the Ethics Committee of Damascus University (No. 2088, date: 7/10/2017).

Each child was subjected to complete clinical evaluation, performed by a pediatric dentist. Fasting instructions were given to the parents preoperatively (6 h: solid foods and non-human milk, 4 h: human milk, and 2 h: water and clear liquids).¹⁵ Age, gender, body weight, baseline heart rate, oxygen saturation, and blood pressure were recorded before drug administration, at 10 min interval, and at the end of the procedure.¹⁵

Children were randomized into two equal groups (Group K and Group D) according to a computer-generated table of random numbers.

Children in Group K received oral ketamine hydrochloride 5 mg/kg with atropine 0.01 mg/kg.

In Group D, children received dexmedetomidine 3 µg/kg orally.

After preparing the drug appropriate to child's body weight, the drug was mixed with a cherry juice, to mask the taste and make it more palatable, and administered. When the desired level of sedation was achieved, the dental procedure was performed by an experienced pediatric dentist.

The behavior of each child was rated during treatment according to Ohio State University Behavioral Rating Scale (OSUBRS) (Table 1).

Sedation onset, and recovery times were recorded, and side effects were observed. The children were discharged when fully conscious, and all vital signs were within normal range.

Statistical analysis:

Data were analyzed using Mann–Whitney, U-test,

and Student's t-test. $p < 0.05$ was the criterion for statistical significance. The statistical package used for all data was SPSS® version 21 (IBM® SPSS, USA).

RESULTS

A total of 40 healthy children aged (2–6 years) were included in the study. They were homogenous with respect to age, weight, gender, preoperative behavior, and the type of procedure (Table 2).

The behavior scoring was based on OSUBRS. In Group K, the score was 1 (quiet behavior, no movement) in 4 (20%) children, 2 (crying, no struggling) in 9 (45%), 4 (Struggling movement without crying) in 4 (20%), and 4 (Struggling movement with crying) in 3 (15%) children. On the other hand, in Group D, 7 (35%) children had a score of 1, 7 (35%) had a score of 2, while it was 3 in 3 (15%), and 4 in 3 (15%) children.

Table 3 shows the mean OSUBRS scores in both groups. Children who received dexmedetomidine had achieved better behavior than Group K. However, there was no significant difference between the two groups in mean OSUBRS scores as noted by the external assessor during treatment, ($p = 0.22$, Mann–Whitney).

The median recovery time with dexmedetomidine was shorter than that for ketamine, 19.36 ± 1.9 min vs. 25.01 ± 1.8 min respectively. there were statistically significant differences according to Student's t-test, the p-value for this comparison is 0.003.

The oxygen saturation was $> 97\%$ in all children. No adverse effects, no episodes of respiratory or cardiovascular instability, and oxygen desaturation

Table 1: Ohio State University Behavior Rating Score (OSUBRS)

Score	Behavior
1	Quiet behavior, no movement
2	Crying, no struggling
3	Struggling movement without crying
4	Struggling movement with crying

Table 2: Demographic characteristics in two groups

Parameter	Group K (n=20)	Group D (n=20)
Age in Years (Mean ± SD)	3.9 ± 0.5	4.1 ± 1.1
Weight in Kg (Mean ± SD)	13.1 ± 5.1	14.3 ± 6.1
Male : Female	9:11	8:12

were recorded in both groups whether during the procedures or even throughout the recovery.

DISCUSSION

The greatest challenge faced by pediatric dentists in daily practice is an uncooperative patient. It can be a serious hindrance to provide the required dental care.^{17,18}

Most of the children can be managed effectively using the techniques involving basic behavior guidance and coaxing, but still a significant proportion of children require advanced behavior guidance techniques including conscious sedation with therapeutic agents.¹⁵

Dexmedetomidine is a sedative with analgesic properties, and has been proven to produce a desirable and safe sedation for children in daycare surgical settings. It exhibits minimal cardiovascular or respiratory effects.^{7,19,20} Despite these excellent attributes, data regarding the use of oral dexmedetomidine for outpatient dental treatment in pediatric dentistry are still limited.^{21,22}

This randomized clinical trial demonstrates that oral dexmedetomidine 3 mg/kg could provide effective and safe sedation for children undergoing outpatient dental procedures, comparable to that provided by ketamine.

Children in the dexmedetomidine group showed a quieter attitude at all times during the treatment procedure, when compared to those who received ketamine. Seven out of 20 children in the dexmedetomidine group scored $1 \pm$ quiet behavior (no movement), compared to four in the ketamine group. The difference in mean OSUBRS scores was not significant as can be seen in Table 3. The lack of significance may be attributed to the small sample size.

There is no study in the dental field comparing the use of oral dexmedetomidine to ketamine with atropine. This is the first comparative study of its kind, especially with the mentioned dosage. The study resembling our study compared dexmedetomidine to ketamine alone, conducted by Singh et al., who reported that the novel sedative dexmedetomidine (3/4/5 $\mu\text{g}/\text{kg}$) provides dose-dependent effective analgo-sedation, comparable to ketamine (8 mg/kg), with less adverse effects. This comes in complete agreement to the results reached by the present study.²³

Regarding the results of our study, the use of dexmedetomidine led to an earlier awakening and discharge than ketamine. Children who received dexmedetomidine were effectively sedated yet were easily arousable; a feature not observed with children of the ketamine group. It may be due to dexmedetomidine-induced sedation is characterized by a quick recovery, actually mimicking some aspects of natural sleep.^{6,24} Similar results were found in a study carried out by Singh et al., who noted that children in the dexmedetomidine group had earlier recovery than those in the ketamine group.²³

In this study, no patient experienced serious complications in either of the two groups, nor any patient required termination of the procedure or any pharmacologic intervention. This finding confirms the safety of dexmedetomidine,^{25,26} and this is consistent with several earlier studies that utilized dexmedetomidine.^{23,27,28}

It also enhances the benefit of the prophylactic co-administration of atropine (anticholinergic) as an adjunct in sedation with ketamine. It is in accordance with the findings of other studies which reported that it reduces the hypersalivation, excessive secretions of the respiratory tract, and nausea and vomiting,^{29,30} which are the most common complications with ketamine.^{5,31}

CONCLUSION

Within the limitations of this study it can be concluded that both dexmedetomidine and ketamine produce good and effective oral sedation, and they were satisfactory in managing children during outpatient dental procedures, although the oral dexmedetomidine led to earlier recovery than ketamine, and the addition of atropine as an adjunct for oral ketamine sedation in children helps in preventing complications and side effects.

Acknowledgment: The authors are grateful for the financial support provided by the Faculty of Dentistry, and the Department of Anesthesia and Reanimation, Faculty of Medicine, Damascus University, Damascus (Syria).

Conflict of interest: None declared by the authors.

Authors' contribution:

AH: Conduction of the study work, data collection, statistical analysis, manuscript editing.

MA: Concept, conduction of the study work, manuscript editing.

REFERENCES

- Done V, Kotha R, Vasa AAK, Sahana S, Jadadoddi RK, Bezawada S. A Comparison of the Effectiveness of Oral Midazolam–N2O Versus Oral Ketamine–N2O in Pediatric Patients–An in–Vivo Study. *J Clin Diagn Res.* 2016;10:ZC45-8 [PubMed] [Free Full Text] DOI: 10.7860/JCDR/2016/16760.7592.
- Lourenço Matharu L, Ashley PF, Furness S. Sedation of children undergoing dental treatment. *Cochrane Database Syst Rev.* 2018;12:CD003877 [PubMed] [Free Full Text] DOI: 10.1002/14651858.CD003877.pub5.
- Rai K, Hegde A, Goel K. Sedation in uncooperative children undergoing dental procedures: a comparative evaluation of midazolam, propofol and ketamine. *J Clin Pediatr Dent.* 2007;32:1-4 [PubMed] DOI:10.17796/jcpd.32.1.v74872j8n74qu81k.
- Horiuchi T, Kawaguchi M, Kurehara K, Kawaraguchi Y, Sasaoka N, Furuya H. Evaluation of relatively low dose of oral transmucosal ketamine premedication in children: a comparison with oral midazolam. *Paediatr Anaesth.* 2005;15:643-7 [PubMed] DOI: 10.1111/j.1460-9592.2004.01513.x.
- Bui T, Redden RJ, Murphy S. A comparison study between ketamine and ketamine-promethazine combination for oral sedation in pediatric dental patients. *Anesth Prog.* 2002;49:14-18 [PubMed] [Free Full Text]
- Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. *Anesth Analg.* 2000;90:699-705 [PubMed] DOI:10.1097/00000539-200003000-00035
- Yuen VM, Hui TW, Irwin MG, Yuen MK. A comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric anesthesia: a double-blinded randomized controlled trial. *Anesth Analg.* 2008;106:1715-21 [PubMed] DOI: 10.1213/ane.0b013e31816c8929.
- Khan Z, Ferguson C, Jones R. Alpha2 and imidazoline receptor agonists Their pharmacology and therapeutic role. *Anaesthesia.* 1999;54:146-65 [PubMed] DOI: 10.1046/j.1365-2044.1999.00659.x
- Turhanoğlu S, Kararmaz A, Özyilmaz M, Kaya S, Tok D. Effects of different doses of oral ketamine for premedication of children. *Eur J Anaesthesiol.* 2003;20:56-60 [PubMed] [Free Full Text] DOI: 10.1017/s0265021503000103
- Reinemer HC, Wilson C, Webb M. A comparison of two oral ketamine-diazepam regimens for sedating anxious pediatric dental patients. *Pediatr Dent.* 1996;18:294-300 [PubMed]
- Şekerci S, Dönmez A, Ateş Y, Ökten F. Oral ketamine premedication in children (placebo controlled double-blind study). *Eur J Anaesthesiol.* 1996;13:606-11 [PubMed] DOI: 10.1046/j.1365-2346.1996.00058.x
- Zub D, Berkenbosch JW, Tobias JD. Preliminary experience with oral dexmedetomidine for procedural and anesthetic premedication. *Paediatr Anaesth.* 2005;15:932-8 [PubMed] DOI: 10.1111/j.1460-9592.2005.01623.x
- Ray T, Tobias JD. Dexmedetomidine for sedation during electroencephalographic analysis in children with autism, pervasive developmental disorders, and seizure disorders. *J Clin Anesth.* 2008;20:364-8 [PubMed] DOI: 10.1016/j.jclinane.2008.03.004.
- Malamed SF. The Spectrum of Pain and Anxiety Control. In: Malamed SF, editor. *Sedation: a guide to patient management.* 5th ed. St Louis, United States: Elsevier - Health Sciences Division; 2010. p. 14-22.
- Coté CJ, Wilson S. Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures: update 2016. *Pediatr Dent.* 2016;38:13-39. [PubMed] DOI: 10.1542/peds.2016-1212.
- Hitt JM, Corcoran T, Michienzi K, Creighton P, Heard C. An evaluation of intranasal sufentanil and dexmedetomidine for pediatric dental sedation. *Pharmaceutics.* 2014;6:175-84 [PubMed] [Free Full Text] DOI:10.3390/pharmaceutics6010175.
- Carter AE, Carter G, Boschen M, AlShwaimi E, George R. Pathways of fear and anxiety in dentistry: A review. *World J Clin Cases.* 2014;2:642 [PubMed] [Free Full Text] DOI: 10.12998/wjcc.v2.i11.642.
- Forehand R, Long N. Strong-willed children: a challenge to parents and pediatric dentists. *Pediatr Dent.* 1999;21:463-8 [PubMed]
- Talke P, Lobo E, Brown R. Systemically administered α_2 -agonist-induced peripheral vasoconstriction in humans. *Anesthesiology.* 2003;99:65-70 [PubMed] DOI: 10.1097/00000542-200307000-00014
- Corcuera-Flores J-R, Silvestre-Rangil J, Cutando-Soriano A, López-Jiménez J. Current methods of sedation in dental patients-a systematic review of the literature. *Med Oral Patol Oral Cir Bucal.* 2016;21:e579 [PubMed] [Free Full Text] DOI: 10.4317/medoral.20981
- Mahmoud M, Mason K. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. *Br J Anaesth.* 2015;115:171-82 [PubMed] DOI: 10.1093/bja/aev226.
- Buck ML. Dexmedetomidine use in pediatric intensive care and procedural sedation. *J Pediatr Pharmacol Ther.* 2010;15:17-29 [PubMed] [Free Full Text]
- Singh C, Pandey RK, Saksena AK, Chandra G. A comparative evaluation

- FR: Conducting of the study, work, data collection, manuscript editing
23. Conant of the study, work, data collection manuscript editing. *J Clin Pediatr Dent*. 2013;38:79-82 [PubMed] DOI: 10.17796/jcpd.38.1.w86t8k7r51k72617
24. Al Taher WM, Mansour EE, El Shafei MN. Comparative study between novel sedative drug (dexmedetomidine) versus midazolam-propofol for conscious sedation in pediatric patients undergoing oro-dental procedures. *Egypt J Anaesth*. 2010;26:299-304 [Free Full Text] DOI: 10.1016/j.ejja.2010.04.002
25. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. *Curr Opin Anaesthesiol*. 2005;18:412-8 [PubMed] DOI: 10.1097/01.aco.0000174958.05383.d5
26. Kim HS, Kim JW, Jang KT, Lee SH, Kim CC, Shin TJ. Initial experience with dexmedetomidine
27. Sheta SA, Al Sarheed MA, Abdelhalim AA. Intranasal dexmedetomidine vs midazolam for premedication in children undergoing complete dental rehabilitation: a double blinded randomized controlled trial. *Paediatr Anaesth*. 2014;24:181-9 [PubMed] DOI: 10.1111/pan.12287.
28. Malhotra PU, Thakur S, Singhal P, Chauhan D, Jayam C, Sood R, et al. Comparative evaluation of dexmedetomidine and midazolam-ketamine combination as sedative agents in pediatric dentistry: a double-blinded randomized controlled trial. *Contemp Clin Dent*. 2016;7:186 [PubMed] [Free Full Text] DOI: 10.4103/0976-237X.183058.
29. Bocskai T, Németh A, Bogár L, Pytel J. Sedation of children for auditory brainstem response using ketamine-midazolam-atropine combination—a retrospective analysis. *Springerplus*. 2013;2:178 [PubMed] [Free Full Text] DOI: 10.1186/2193-1801-2-178
30. Kye YC, Rhee JE, Kim K, Kim T, Jo YH, Jeong JH, et al. Clinical effects of adjunctive atropine during ketamine sedation in pediatric emergency patients. *Am J Emerg Med* 2012;30:1981-5 [PubMed] DOI: 10.1016/j.ajem.2012.04.030
31. Wood M, Manley M, Bezzina N, Hassan R. An audit of the use of intravenous ketamine for paediatric dental conscious sedation. *Br Dent J*. 2015;218:573 [PubMed] DOI: 10.1038/sj.bdj.2015.390.

MY MOST MEMORABLE PATIENT

A-Can't-Miss-it Critical Care Catastrophe

Muhammad Fuad Bangash, MD, FCCP

Chief, Pulmonary & Critical Care, Medical Director, ICU, Steward Norwood Hospital,
Norwood, MA 02062, (USA) E-mail: lifesavericu@icloud.com

Since Midwest in USA is very cold during winters, I see many cases of pneumonia. But this was a case of ‘missed pneumonia. A 49 year old African American male patient was not feeling well for two days and was admitted to the hospital with severe headache and high grade fever. Lumbar puncture was performed and the patient was put on inj ceftriaxone and inj vancomycin. Chest x-ray was performed on admission, was unremarkable and did not show any infiltrates. An infectious disease consultant was involved in the care of this patient and on his recommendation ceftriaxone and vancomycin were stopped after 24 h, as there was no evidence of meningitis.

Patient’s condition did not improve and he continued to have fever upto 104° F and severe headache. He developed respiratory distress, so was transferred to the ICU and placed on BiPAP. Chest x-ray now showed extensive bilateral

infiltrates. Patient was started on inj levofloxacin IV after cultures were obtained. His condition started to improve and he was weaned off BiPAP. Urine legionella antigen came back positive! This patient had legionella pneumonia. The initial ‘clear’ chest x-ray was likely due to dehydration, and the headache was related to the fever.

Legionella pneumonia is a can’t miss critical care catastrophe, which if missed can be fatal. I have seen another case of severe legionella pneumonia in a 22 year old college senior that led to ARDS.

Most guidelines for treating community acquired pneumonia recommend treatment covering ‘atypical’ pneumonia pathogens and this will cover legionella pneumonia. A clear chest x-ray on admission does not exclude pneumonia and if patient’s condition is not improving leading to high clinical suspicion, repeating a chest x-ray after hydration or obtaining a chest CT will be life-saving.