Nasal versus oral midazolam sedation in routine pediatric dental care

NCT02679781

Research protocol 31/01/2016

Background: **C**onscious sedation is a frequently used behavior management technique for providing comprehensive dental treatment to fearful, uncooperative young children. It is well documented in the literature that midazolam is safe and effective in reducing anxiety and improving behavior in children prior to medical and dental procedures[1-2]. Midazolam can be administered by either enteral or parenteral routes. The practice of administering midazolam by either the oral or nasal route is becoming rapidly incorporated in routine pediatric dental care. The literature regarding the advantages and limitations of using different administration routes for midazolam, especially with respect to the ease of administration and patient acceptance is controversial[1-8]. Although the oral route of administration is popular among pediatric dentists, confrontation and frustration often arise when children refuse to accept the sedative medication. Despite efforts to disguise the taste, children can spit or regurgitate the medication when administered orally[4]. Similar contradictions existed in the literature regarding patient acceptance of nasal midazolam. Some authors have reported that the nasal route required less patient cooperation and was a simple, convenient, noninvasive, painless and reliable alternative to oral drug administration[2,3]. In contrast, other authors reported nasal midazolam to be noxious, painful and poorly tolerated[3,7,9].

Rationale: Based on previous studies done in our department, the oral route and the nasal route are both accepted and used for midazolam administration. Both routes has disadvantages, children can spit or regurgitate the medication when administered orally because of the bitter taste, nasal midazolam as drops can be painful and poorly tolerated. We want to assess the acceptability of nasal spray, which diffuses better than drops in the nose. Most of the studies assessed advantages and limitations of using different administration routes for midazolam as premedication before general anesthesia. In dental treatment, however, the child needs to receive the premedication few times and the tolerance and compliance are crucial for the success of the treatment, and can affect the compliance on the next visits. By comparing the tolerance and acceptability of these routes of administration and related factors, the pediatric dentist will be able to better select the route of administration to his patient.

Study goals and objectives

The main objective is to compare children's acceptance of midazolam premedication orally as syrup and nasally with a spray and to measure parents' satisfaction with these two routes of administration. The secondary objective is to examine the effects of various variables on the acceptance of premedication, such as age, gender and behavior in dental treatment.

Study design

Randomized controlled study

Methodology

Intervention: Midazolam premedication prior to dental treatment by means of two routes: orally and by nasal spray. The oral midazolam (Midolam 5mg/1ml) dose is 0.5mg/kg up to a maximum of 10mg. Nasal midazolam is administered with MAD Nasal™ Intranasal Mucosal Atomization Device, at a dose of 0.2mg/kg up to a maximum of 5mg. During dental treatment, both groups receive 50% nitrous oxide/ 50% oxygen via a nasal hood.

Study group: The study inclusion criteria are: healthy children (American Society of Anesthesiologists 1), aged 2-6 years, uncooperative (Frankl[10] 1-2) in a dental examination, and in need of at least two similar dental treatments under conscious sedation with midazolam. Exclusion criteria are: enlarged tonsils (Brodsky's[11] grading scale +3 = 50–75% airway obstruction, and +4 = >75% airway obstruction), upper respiratory tract infection and nasal discharge.

Randomization: Children are assigned by a single trained disinterested investigator to one of the groups (oral or nasal midazolam) by simple randomization (flip of a coin). Randomization performed after meeting study inclusion criteria.

Observations and measurements:

1. Participants' age, gender and weight will be documented.
2. Acceptability of the medication: compliance in taking the medication will be assessed and recorded by the treating dentist as: willingly, coaxed, forced. Duration of crying, if any, after taking the medicament will be recorded by an observer blind to the route of administration.
3. Parent's satisfaction will also be recorded by the blind observer. Parents will be asked to rank their satisfaction with the premedication administering as high,

moderate or low. High satisfaction is ranked as 1 point and low is ranked as 3 points.

4. Behavior during dental treatment: Houpt[12] scale measures behavior by rating sleep, movement, crying and overall behavior. Children's overall behavior during dental treatment will be rated by observer blind to the route of administration.

Safety considerations

Midazolam dose do not exceed maximum dose.

Patients and parents can stop participating in the study at any time.

In cases of refusal to take the medication or a low cooperation in dental treatment, other treatment options will be discussed and offered to the patient.

Follow-up

Participants will be followed up for two dental visits.

For each visit they will be followed up in the dental clinic until full recovery from sedation.

Data management and statistical analysis

The information will be stored in a password-protected computer in a locked office, anonymously using a coding table.

Data is analyzed in SPSS software version 25. Descriptive statistics are produced using means, standard deviations (SD), ranges, frequencies and percentages. Differences according to route of premedication administration are assessed using the Mann-Whitney and Kruskal-Wallis tests for the continuous variables, and the Chi-square tests for the individual variables. A multivariate model for predicting forced drug administration is performed using logistic regression. Using Fisher's exact test, the correlation is analyzed between the categorical independent variables and the dichotomous dependent variable, namely, child's acceptance of the medication in the second session. The results considered significant for alpha less than 5%.

Expected outcomes of the study

By comparing the tolerance and acceptability of these routes of administration and related factors, the pediatric dentist will be able to better select the route of administration to his patient.

Duration of the project

Data collection will take one year. For each patient, participation duration is two dental visits.

Ethics

Patients of the Pediatric Dentistry Department that will meet inclusion criteria will be offered to participate. Detailed information in simple non-technical language will be provided in advance and parents/guardians of all the patients included in the study will be requested to sign an informed consent form. No compensation was provided for participation. Patients and parents can stop participating in the study at any time. In cases of refusal to take the medication or a low cooperation in dental treatment, other treatment options will be discussed and offered to the patient.

References:

1. Kupietzky, A. and Houpt, M.I.: Midazolam: a review of its use for conscious sedation of children. Pediatr Dent 15:237-241, July-August 1993.

2. Hartgraves, P.M and Primosch, R.E.: An evaluation of oral and nasal midazolam for pediatric dental sedation. J Dent Child,61:175-181, May-June 1994.

3. Fuks, A.B.; Kaufman, E.; Ram, D. *et al:* Assessment of two dosages of intranasal midazolam for sedation of young pediatric dental patients. Pediatr Dent, 16:301-305, July-August 1994.

4. Primosch RE, Bender F. Factors associated with administration route when using midazolam for pediatric conscious sedation. ASDC J Dent Child. 2001 68(4):233-8, 228.

5. Kogan A, Katz J, Efrat R, Eidelman LA. Premedication with midazolam in young children: a comparison of four routes of administration. Paediatr Anaesth. 2002 Oct;12(8):685-9.

6. Primosch RE, Guelmann M. Comparison of drops versus spray administration of intranasal midazolam in two- and three-year-old children for dental sedation.Pediatr Dent. 2005 Sep-Oct;27(5):401-8.

7. Verma RK, Paswan A, De A, Gupta S. Premedication with midazolam nasal spray: an alternative to oral midazolam in children. Anesth Pain Med. 2012 Spring;1(4):248-51. doi: 10.5812/aapm.4567. Epub 2012 Apr 1.

8. Fallahinejad Ghajari M, Ansari G, Soleymani AA, Shayeghi S, Fotuhi Ardakani F. Comparison of Oral and Intranasal Midazolam/Ketamine Sedation in 3-6-year-old Uncooperative Dental Patients. J Dent Res Dent Clin Dent Prospects. 2015 Spring;9(2):61-5. doi: 10.15171/joddd.2015.013. Epub 2015 Jun 10.

9. Baldwa NM, Padvi AV, Dave NM, Garasia MB. Atomised intranasal midazolam spray as premedication in pediatric patients: comparison between two doses of 0.2 and 0.3 mg/kg. J Anesth. 2012 Jun;26(3):346-50. doi: 10.1007/s00540-012-1341-6. Epub 2012 Mar 1.

10. Frankl SN, Shiere FR, Fogels HR. Should the parent remain with the child in the dental operatory? J Dent Child. 1962, 29: 150-163.

11. Brodsky L. Modern assessment of tonsils and adenoids.Pediatr Clin North Am. 1989 Dec;36(6):1551-69.

12. L. Lourenço-Matharu & G. J. Roberts**.** Effectiveness and acceptability of intravenous sedation in child and adolescent dental patients: report of a case series at King's College Hospital, London. *BDJ* 210, 567 - 572 (2011) Published online: 24 June 2011 doi:10.1038/sj.bdj.2011.482

13.

14.