Comparison of Midazolam Nasal Spray to Nasal Drops for the Sedation of Children

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Objective: In pediatric nuclear medicine efforts to reduce the distress of the child is essential. Sedation is indicated when other means are not sufficient. The choice of sedative and the route of administration are important issues. Midazolam administered intranasally has proven to be safe and efficient. In this study we have compared midazolam given as nasal drops with midazolam given as nasal spray.
Methods: Of 376 children (age 0.5–15 yr), 233 received midazolam as nasal drops (0.3 mg/kg body weight) and 143 as nasal spray (0.2 mg/kg body weight) prior to venipuncture or during gamma camera examinations. The conditions for the procedures were judged on a four-level arbitrary scale.
Results: Mean time to adequate sedation was 7 min in both groups. Conditions during procedures were significantly better after spray administration. Good or acceptable cooperation was recorded in 77.3% for nasal drops compared to 86.7% for nasal spray. Nasal discomfort was frequent, 28% and 39%, respectively, for drops and spray. Other side effects were rare and not significantly different between the two groups.
Conclusion: This study shows that nasal administration of midazolam is an excellent alternative for sedation in pediatric nuclear medicine and that nasal spray is favorable to nasal drops.
Key Words: pediatric sedation; intranasal midazolam

J Nucl Med Technol 1996; 24:32–34

In pediatric nuclear medicine, repeated examinations are common and require special care and effort to reduce the distress of the child. In addition, the technical quality of the examination will be impaired if the child is unable to cooperate (*1*). Despite experienced and devoted staff, child-adapted equipment and environment, children of all age groups may, for various reasons, be incapable of dealing with the examination procedure. Fear of venipuncture is very common in spite of the fact that EMLA® (ASTRA Pain Control, Södertälje, Sweden), a local anesthetic cream, is used to diminish the pain.

A small child or a child with a psychiatric disorder may not be able to lie still even for a very short time. Frequently, acquisition time in gamma camera examinations is prolonged in small children due to the need to reduce radiation exposure. Sedation is indicated when other means are not sufficient.

In a diagnostic unit, conscious sedation is often preferred, and the choice of sedatives becomes especially important. A safe and efficient sedative drug for children should provide rapid onset, short recovery time and be without hazards. In our experience, midazolam fulfills these criteria.

The route of administration is another important issue. For children who do not have intravenous access, nasal administration has been found useful, in regard to the actual procedure of administration, the onset time and the sedative effect. When we started to validate the effects of intranasal midazolam only nasal drops were used. Due to the local irritating effect of the acid intravenous solution, the idea of giving midazolam as a nasal spray evolved. Spraying more effectively distributes the drug on the nasal mucosa and improves absorption conditions (*2*). We hypothesized that, by using a spray device, a dose reduction could be accomplished with maintenance of the sedative effect. A smaller volume might also reduce the irritation of the nasal mucosa.

MATERIALS AND METHODS

Sedation with intranasal midazolam was recorded in 376 children between the ages of 6 mo and 15 yr. The children were either judged by the staff to be uncooperative or had previously failed to participate during examinations. Midazolam (Dormicum/Versed®, F. Hoffman-La Roche Ltd, Basel, Switzerland) 5 mg/ml for injection was administered intranasally. It was given as nasal drops to 233 children consecutively and to the following 143 children as nasal spray. The dosage for nasal drops was 0.3 mg/kg body weight (BW) and for nasal spray 0.2 mg/kg BW. The maximal initial dose was set to 5 mg/kg BW in both groups. If judged necessary, a second dose, 50% of initial dose, was given after 15 min. As drops, the calculated dose was

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TABLE 1
Scale of Cooperability and Procedure Conditions

1	Good cooperation, easy procedure
2	Acceptable cooperation, procedure performed with minor disturbances
3	Cooperation difficulties, acceptable procedure conditions
4	Poor cooperation, unfavorable procedure conditions

drawn in a 1-ml syringe and given in portions into both nostrils. As spray, the drug was given with a graded pump device providing 0.5 mg per puff (Apoteksbolaget, Stockholm, Sweden). The time of onset, side effects during and after administration, and the conditions during the planned procedure were judged and recorded by the technologist responsible for the monitoring of the child. The conditions were judged on a four-level, arbitrary scale (Table 1). All children were observed for at least one hr.

The statistical analysis was performed using StatView 4.5 software (Abacus Concepts Inc., Berkley, CA). Unpaired t-test or chi-square test were used for comparison between groups. P values of <0.05 were considered significant.

RESULTS

Age, weight, dosage, additional dosage and time of onset data are given in Table 2. Mean weight and age were lower in the group receiving drops compared to the group receiving spray. There were no differences regarding additional dosage and time of onset. The conditions during the procedures and observed side effects are given in Table 3. The spray group demonstrated significantly better procedure conditions than the drops group. Nasal discomfort during administration was common in both groups and there was no significant difference regarding side effects.

DISCUSSION

Conscious sedation in pediatric nuclear medicine is indicated when other means to overcome a child's fear are not sufficient. Midazolam has proven to be a safe and efficient sedative to both adults and children. It is a benzodiazepin and

TABLE 2
Patient and Dose Characteristics

	Drops	Spray
Age (yr)	2.6 ± 2.1	3.4 ± 3.1*
Weight (kg)	13.2 ± 6.5	19.4 ± 13.2
Dose (mg/kg)	0.3 ± 0.03	0.18 ± 0.06*
Number of extra doses given	13	10
Time of onset (min)	7.3 ± 3.6	7.2 ± 4.0

Intranasal midazolam administered as drops (n = 233), or spray (n = 143). All values are mean ± s.d..

* = $p < 0.05$, unpaired t-test between groups.

TABLE 3
Conditions During Procedures and Observed Side Effects

	Number of patients	
	Drops	Spray
Conditions score		
1	75 (32.2%)	61 (42.7%)*
2	105 (45.1%)	63 (44.0%)*
3	42 (18.0%)	11 (7.7%)*
4	11 (4.7%)	8 (5.6%)*
Side effects		
None	160 (68.7%)	80 (55.9%)
Nasal discomfort	66 (28.3%)	56 (39.2%)
Nausea	2 (0.9%)	2 (1.4%)
Split vision	5 (2.1%)	5 (3.5%)

Intranasal midazolam administered as drops (n = 233) or spray (n = 143). Contingency tables of observed frequencies. Values in parentheses are percent of total observations in each group.

* = $p < 0.05$ Chi square test between groups.

available as a water-soluble intravenous solution. Once in the blood stream it changes to a highly lipid-soluble substance which readily passes the blood-brain barrier. Its water soluble properties makes it a drug that can be administered orally, nasally, rectally, intramuscullary or intravenously. Midazolam has a short time of onset (*3*), a reasonably rapid redistribution phase and a short plasma half-life, about 2 hr in all age groups except neonates (*4,5*). These pharmacokinetic properties and a very wide therapeutic window makes it a drug well-suited for use in children. Like most sedatives, when combined with other sedatives or opioids, side effects like respiratory depression are more likely to occur (*6,7*). Otherwise respiratory and circulatory depression is unlikely when used as a single drug.

In the present study, midazolam was used as the only drug to produce conscious sedation. The nasal route was chosen as the children had no vascular access at the time of study. Oral or rectal administration could be an alternative, but they both provide longer time of onset and somewhat less predictable effects due to variations in absorption (*8*).

Procedure conditions were significantly better with spray administration, thus supporting our main hypothesis. When given as spray, the child can sit in the lap of the parent, which is favorable for the child.

No serious side effects were noted in the present study. Nasal discomfort was frequent and may even be underestimated as many children were not old enough to express themselves. It was generally judged as mild by the staff and parents. Rescusitation equipment, a suction device and a pulse oximeter were available but never used. Clinical signs of respiratory depression or desaturation were not observed in any child.

Over the years we have tried various sedatives to provide conscious sedation to children in our department. So far, midazolam has proven to be the best choice. The present study shows that nasal administration of midazolam is an excellent alternative for sedation in pediatric nuclear medicine and that nasal spray is favorable to nasal drops.

REFERENCES

1. Weiss S. Sedation of pediatric patients for nuclear medicine procedures. *Sem Nucl Med* 1993;23:190–198.
2. Chien YW, Su KSE, Chang S. *Nasal systemic drug delivery*. New York: Marcel Dekker; 1989.
3. Walbergh EJ, Wills RJ, Eckhert J. Plasma concentrations of midazolam in children following intranasal administration. *Anesthesiology* 1991;74:233–235.
4. Rey E, Delaunay L, Pons G, et al. Pharmacokinetics of midazolam in children: comparative study of intranasal and intravenous administration. *Eur J Clin Pharmacol* 1991;41:355–357.
5. Jacqz-Aigrain E, Wood C, Robieux I. Pharmacokinetics of midazolam in critically ill neonates. *Eur J Clin Pharmacol* 1990;39:191–192.
6. Bailey PL, Pace NL, Ashburn MA, et al. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesiology* 1990;73:826–830.
7. Yaster M, Nichols DG, Deshpande JK, et al. Midazolam-fentanyl intravenous sedation in children: case report of respiratory arrest. *Pediatrics* 1990;86:463–467.
8. Payne K, Mattheyse FJ, Liebenberg D, et al. The pharmacokinetics of midazolam in paediatric patients. *Eur J Clin Pharmacol* 1989;37:267–272.

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J. Nucl. Med. Technol. 1996;24:32-34.

Journal of Nuclear Medicine Technology is published quarterly.
SNMMI | Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive, Reston, VA 20190.
(Print ISSN: 0091-4916, Online ISSN: 1535-5675)