Anaesthesia, 2007, **62**, pages 1262–1265 doi:10.1111/j.1365-2044.2007.05260.x

The use of intranasal midazolam in the treatment of paediatric dental patients*

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Summary

The aim of this study was to assess the use of intranasal midazolam in paediatric dental patients requiring extractions or simple surgical procedures who may otherwise have required a general anaesthetic. Twenty children aged between 2–9 years who required simple surgical procedures were given 0.25 $mg.kg^{-1}$ midazolam, administered using a MAD® (Mucosal Atomization Device; Wolfe Tory Medical Inc., Salt Lake City, UT, USA). Compliance with the full dose was achieved in 14 patients, 13 of whom completed the treatment. One of two patients who allowed only partial administration completed the treatment and three patients did not comply. The mean time to starting treatment was 13 min (range 6–25 min) and patients were discharged after a mean of 46 min (range 25–67 min). Physiological parameters remained stable throughout with no clinically significant episodes of desaturation. One patient vomited at home postoperatively. Midazolam in a dose of 0.25 $mg.kg^{-1}$ administered intranasally provided adequate anxiolysis for the majority of children, allowing them to complete their treatment.

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**Presented at BSDR, Dundee, 5 April 2006.*
Accepted: 25 July 2007

Dental caries is the single greatest reason for general anaesthesia admission to hospital in children aged < 14 years. Dental extractions remain the largest reason for children receiving general anaesthesia in hospital and in 2003–2004, approximately 1500 young children aged 3–5 years had teeth extracted under general anaesthesia [1]. This procedure is associated with significant post-operative morbidity [2, 3].

Inhalational sedation using nitrous oxide is the most common method of delivery of conscious sedation in paediatric dentistry. The technique has been shown to be effective in reducing anxiety over sequential visits [4]. However, it has been shown to be of less value in very young children [5].

Midazolam is conventionally administered via the intravenous route; however, this technique is less suitable for use in very young children. Transmucosal routes of drug administration have been used as premedicants in this age group [6, 7]. Intranasal midazolam has been found to be effective in doses ranging from 0.2 to 0.6 $mg.kg^{-1}$ when used for conscious sedation and as a premedicant [8–10].

This technique has advantages when compared with oral administration as the bioavailability of intranasally administered midazolam is approximately 55%, compared with 15% when administered orally [11, 12]. The rate of onset and recovery are more rapid and the patient is not required to actively swallow or hold the bitter preparation in their mouth [13].

The aim of this study was to assess the use of intranasal midazolam in paediatric dental patients requiring extractions or simple surgical procedures who may otherwise have required a general anaesthetic.

Methods

The study was approved by the Hospital Ethics Committee. Twenty patients were recruited from the Accident and Emergency clinic and Child Dental Health Department of Glasgow Dental Hospital and School.

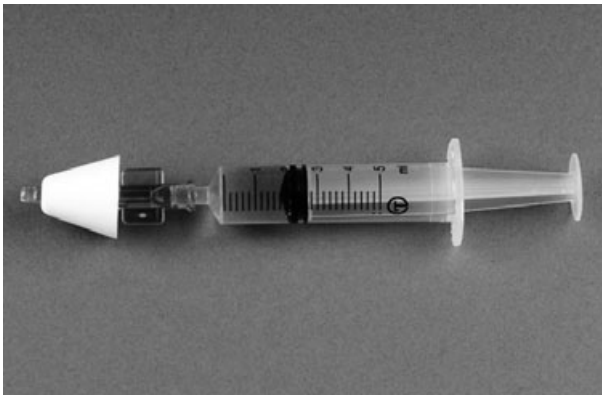

Figure 1 Mucosal Atomization Device attached to 5-ml syringe.

Parents were offered intranasal midazolam as a treatment option along with local anaesthesia alone or general anaesthesia.

Parents were given written and verbal information about the procedure at an assessment visit prior to their appointment, and written consent was gained for the sedation and the operative procedure.

The children were all ASA class I or II, they were weighed and had baseline readings of blood pressure and heart rate performed prior to administration of the drug. Pulse oximetry was monitored throughout and the lowest oxygen saturation recorded. Blood pressure was measured at 5-min intervals until discharge.

A 10-mg/2-ml solution of midazolam (Hypnovel®, Roche, Welwyn Garden City, UK) was used at a dose of 0.25 $mg.kg^{-1}$ and administered using a 5-ml syringe connected to a MAD® (Mucosal Atomization Device, Wolfe Tory Medical Inc., Salt Lake City, UT, USA). This is shown in Fig. 1. The midazolam was administered incrementally in alternate nostrils. Resistance to administration of the drug was recorded as follows: none, some verbal resistance but administration allowed, or verbal resistance with treatment discontinued. Side-effects of sneezing, coughing or vomiting were noted.

The dose given was recorded along with the time of drug administration, the procedure start and finish time and discharge time.

All patients received topical anaesthesia prior to injection of local anaesthesia (2% lidocaine, 1 : 80 000 epinephrine).

Results

Six male and 14 female patients were recruited ranging in age between 2 and 9 years (median 4 years) and in weight from 12.9 to 27.7 kg (median 19 kg).

Compliance with the full dose was achieved in 14 patients, 13 of whom completed the treatment. Two patients allowed the administration of one increment and of these, one completed treatment. Three patients would not allow any midazolam to be administered.

Of the 14 patients who accepted the full dose, nine demonstrated no resistance. The remaining five showed some verbal resistance but with persuasion allowed the dose to be administered. During administration two patients sneezed, three coughed, one coughed and sneezed and 11 had no side-effects. All patients were awake and alert throughout and verbal contact was maintained.

Extraction of deciduous teeth was performed in 12 patients, of which eight were upper anterior teeth that had become non-vital as a consequence of dental trauma. Eight patients required only a single extraction. One patient had a mucocoele excised and one patient had surgical exposure of two upper central incisors. The mean time from administering the initial increment of midazolam to placing topical anaesthesia was 13 min (range 6–25 min). Treatment duration ranged from 5 to 20 min (mean 17 min). Patients were discharged home after a mean of 46 min (range 25–67 min).

Oxygen saturation levels ranged between 96 and 100% (mean 99%) pre-operatively and from 96 to 100% (mean 99%) postoperatively. During treatment the lowest oxygen saturation recorded ranged between 94% and 99% (mean 97%).

Physiological parameters remained stable throughout with no clinically significant episodes of desaturation, defined as a drop of $>4\%$ or to $<90\%$. One patient vomited postoperatively at home.

Discussion

Fourteen patients completed treatment. Only one of these did not have the full dose of midazolam. Patients were selected by parental preference and therefore a range of anxiety levels were encountered, although this was not formally measured.

The majority of teeth extracted were upper anterior teeth that required extraction due to dental trauma. The age of this sample reflects this, with the peak incidence of dental trauma occurring between 2 and 4 years in the deciduous dentition [14].

Midazolam produces profound anterograde amnesia and whereas this may not be of benefit in the anxious patient requiring routine treatment, it can be beneficial in those undergoing unpleasant procedures. The age of the majority of patients was <4 years of age and in most instances this was the child's first experience of active dental treatment and therefore a degree of amnesia was

desirable. This type of sedation is useful in those patients who require a higher level of anxiolysis than inhalational sedation with nitrous oxide can provide.

Eleven patients suffered no side-effects on delivery. The incidence of coughing and sneezing has been shown to be less when midazolam is administered using an atomiser when compared with drops [15].

The placement of the blood pressure cuff did appear to distress some of the children and although pre-operative measurement of blood pressure is recommended for all forms of conscious sedation, it could be argued that monitoring should be delayed until after anxiolysis is achieved. It is common practice in paediatric anaesthesia to place monitoring devices following induction of general anaesthesia.

Previous studies have reported that patients have complained of a burning sensation on administration of midazolam but this did not occur in this study [16]. The main complaints were restricted to the bitter taste when some of the solution escaped down the back of their throat. It may be possible to reduce this effect by using a more concentrated form of midazolam. This has been shown to increase bioavailability as more absorption occurs transmucosally and less by the orogastric route, and therefore lower doses might be used [17].

Currently, a metered dose system of intranasal midazolam is being developed for use in emergency drug boxes for treatment of status epilepticus (Special Products Ltd, Woking, UK). The initial product will contain 5 ml of 10 $mg.ml^{-1}$ midazolam maleate in a clear Usafe bottle with a 0.25 ml/spray nozzle and nasal adapter, this product may have a role in intranasal sedation.

No significant episodes of desaturation were found, which is in agreement with other studies [18–20]. All patients remained safely within the UK definition of conscious sedation [21].

The patient who vomited at home had been feeling slightly unwell at her appointment and it remains unclear as to whether the vomiting was a result of systemic illness or whether the midazolam was responsible.

A recent case report discussed an allergic reaction following administration of intranasal midazolam [22], which highlights the need for patients undergoing such treatment to be monitored by personnel with adequate training.

In conclusion, midazolam 0.25 $mg.kg^{-1}$ administered using a 5-ml syringe connected to a Mucosal Atomization Device provided adequate anxiolysis for the majority of children to complete their treatment whilst maintaining stable oxygen saturation and verbal contact.

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