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REVIEW

Safety of oral midazolam sedation use in paediatric dentistry: a review

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Background. Little information is available as to the safety of midazolam when used as an oral sedative.

Aim. To evaluate the side effects and other adverse outcomes following use of oral midazolam for behaviour management in paediatric dentistry.

Design. A review of published literature relating to the safety and side effects of oral midazolam for use in paediatric dental procedures was conducted. Both randomised controlled trials and non-randomised studies were assessed. Reported side effects were recorded and classified as either significant or minor. The percentage prevalence of significant or minor side effects per episode of treatment was calculated.

Results. Sixteen papers of randomised controlled trials met the inclusion criteria. None of the side effects recorded were considered as significant. Minor side effects were reported (n = 68, 14%), with nausea and vomiting being the most frequently recorded (n = 30, 6%). Eleven papers of non-randomised studies were included. No significant side effects were recorded. Minor side effects were recorded (n = 157, 8%), with paradoxical reaction being the most common at 3.8%.

Conclusion. Significant side effects associated with oral midazolam usage for behaviour management in children and adolescents requiring dental treatment appear to be rare. Minor side effects are more common but determining precise figures is complicated by poor reporting.

Introduction

Dental caries and its management remains a significant problem in paediatric dentistry. Young children needing multiple procedures often cannot be managed using local anaesthesia alone. General anaesthesia (GA) is an alternative but is associated with significant morbidity and expense[1]. Guidelines for the use of GA in paediatric dentistry encourage discussion of alternative treatment options prior to referral for dental GA[2].

Sedation is a possible alternative to GA for behaviour management but evidence in support of its use is weak. In a recent systematic review[3], oral midazolam was identified as being one of the few agents available whose efficacy in dental procedures for children is supported by evidence. A recently published guideline from the National Institute for Health and Clinical Excellence suggests that midazolam could be used for children requiring dental procedures[4]. Midazolam is potentially an ideal sedative agent for paediatric dentistry because it can be administered orally, has anxiolytic and anterograde amnesic effects and is short acting.

As with any other drug, there are known side effects, ranging from commonly observed minor effects to rarer but more severe side effects. These may be related to dose, route of administration and the age of the patient. Common side effects include transient desaturations, hiccough, nausea and vomiting, headache, vertigo, enuresis, hypersalivation, hallucinations, dizziness, diplopia and behavioural disinhibition (or paradoxical reaction). Severe side effects include cardiac arrest, heart rate changes, anaphylaxis,

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thrombosis, laryngospasm, bronchospasm, respiratory depression and respiratory arrest[5].

Little information is available as to the safety of this drug when used as an oral sedative in children needing dental treatment. Therefore, the aim of this study was to evaluate the side effects and any other adverse outcomes following use of oral midazolam for behaviour management in paediatric dentistry.

Methods

This study was a review of all published material relating to the safety and side effects of oral midazolam for use in dental procedures. As previously described, a systematic review already exists looking at the efficacy of oral midazolam for children. Although this review and the NICE guidelines do incorporate some assessment of side effects, no formal review of oral midazolam's side effects in paediatric dental procedures has thus far been carried out. The aforementioned systematic reviews were restricted to randomised controlled clinical trials (RCTs)[6]. Analyses restricted to clinical trials may miss rare but significant outcomes (e.g. mortality); therefore, there is value in carrying out a separate review with a wider range of studies included (such as cohort or case–control studies).

To be eligible for inclusion in this review, studies had to meet the following criteria:

1) Types of study subject: Children and adolescents aged 0–18 years of age (including children with specific medical or behavioural problems) undergoing dental treatment, regardless of baseline anxiety.

2) Types of interventions: Oral midazolam administered by a dentist, anaesthetist, sedationist or dental auxiliary in an outpatient setting or dental office. Studies that reported induction of deep sedation were excluded. Studies where oral midazolam was used as a premedication were excluded. Studies where supplemental nitrous oxide was given were excluded.

3) Types of outcome measures: The primary outcome measure was the percentage prevalence of significant side effects per episode of treatment. The secondary outcome measure was the percentage prevalence of minor side effects per episode of treatment.

Side effects were recorded individually and then categorised as being 'significant' or 'minor'. A significant side effect was defined as a potentially life-threatening adverse reaction. Examples were mortality, inability to maintain an airway or desaturations not corrected by head movements. Minor side effects were defined as any reported adverse events that were non-life-threatening. Examples of minor side effects were more difficult to subcategorise, principally due to an inconsistent use of terminology in studies. All have been reported.

Data related to the effectiveness of the sedative were not collected.

4) Types of study: Allocation concealment, patient, operator or assessor blinding were not used as entry criteria for this review. Evidence was ranked according to its quality, and the ranking was as follows (highest first):

- **(a)** Randomised controlled clinical trials of effectiveness and randomised controlled clinical trials looking at adverse outcomes
- **(b)** Non-randomised studies. Prospective or retrospective observational studies (including case reports)
- **(c)** Reference books and databases describing adverse effects as listed in Chapter 14 of the Cochrane Review Handbook[6].

Search strategy

The search for RCTs was modelled on that used by Matharu and Ashley[7] in their effectiveness review in 2005. This version was used as the updated review excludes crossover trials. The search for any other non-randomised studies used a combination of controlled vocabulary and free text terms based on the search strategy as described in Chapter 14 of the Cochrane Handbook[6]. See Fig. 1 for Medline search, Fig. 2 for Embase search [MEDLINE (OVID), 1950 to November 2011 week 1; EMBASE (OVID) 1947–2011 November 8].

Database: Ovid MEDLINE(R) <1950 to September Week 1 2010>

Search Strategy:

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1 Toxicity

2 Side effect

3 Paradoxical

4 Morbidity

5 Malaise

6 Nausea

7 Respiratory arrest

8 Vomiting

9 Death

10 Mortality

11 Adverse outcome*

12 Oral and midazolam and sedation and dental and (children or adolescent)

13 or/1-11

14 12 and 13

Fig. 1. Medline search strategy.

Database: EMBASE Classic+EMBASE<1947 to 2010 September 21>free text

Search Strategy:

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1 Toxicity

2 Side effect

3 Paradoxical

4 Morbidity

5 Malaise

6 Nausea

7 Respiratory arrest

8 Vomiting

9 Death

10 Mortality

11 Adverse outcome

12 Oral and midazolam and sedation and dental and (children or adolescent)

13 or/1-11

14 12 and 13

Fig. 2. Embase search strategy.

This was then supplemented by a further free text search as recommended in Chapter 14 of the Cochrane Handbook[6]. In addition, reference books and regulatory authorities were also searched for reports on oral midazolam using the website search engine and the free text term 'midazolam' (full list in Fig. 3)[8–11].

Specialist drug information databases were not searched due to subscription costs and as their usefulness or additional yield have yet to be formally evaluated in the systematic review setting.

The following journals were identified as being important to be hand searched for this review: *International Journal of Paediatric Dentistry*, *Pediatric Dentistry*, *Journal of American Dental Association*, *Anesthesia Progress*. The journals were hand searched by the review authors for the period January 2000 to November 2011.

Standard reference books on adverse effects:

Meyler's Side Effects of Drugs (Aronson 2006)

The Side Effects of Drugs Annuals (SEDA) (Curran and Lally, 1999)

Martindale: The Complete Drug Reference (Sweetman 1999)

Davies Textbook of Adverse Drug Reactions (Rawlins 1991)

Regulatory authorities:

UK: Current Problems in Pharmacovigilance (www.mhra.gov.uk);

Australia: The Australian Adverse Drug Reactions Bulletin (www.tga.gov.au/hp/aadrb.htm);

European Union: European Public Assessment Reports from the European Medicines Evaluation Agency (www.ema.europa.eu);

US: Food and Drug Administration FDA Medwatch (www.fda.gov/medwatch).

Fig. 3. Other databases and reference books searched.

(1) Year study started, if not available, year it was published

(2) Country study was carried out in

(3) Number of children

(4) Use of supplemental N2O

(5) Use of restraints during the procedure

(6) Dental treatment

(7) Co-morbidities

(8) Fasting before the procedure

(9) Level of consciousness throughout the procedure

(10) Monitoring used

(11) Recovery time

(12) Location e.g. primary or secondary care

(13) Who was available e.g. anaesthetist vs doctor vs dentist

(14) Depth of sedation

(15) Withdrawals or dropouts as this could be a proxy for an adverse event

(16) Was there a plausible biological mechanism that could link the cause to the adverse event?

Fig. 4. Descriptive data recorded (where available).

The reference lists of all eligible trials were checked for additional studies. The search attempted to identify all relevant studies irrespective of language. Non-English papers were translated where possible.

Results from these searches were combined together using Reference Manager (Thomson Corp, Carlsbad, CA, USA). The recommended adverse effects search terms as described by Loke *et al.*[6] were not used as only a relatively small numbers of papers were returned.

Titles and abstracts were assessed by two review authors [Arathi Papineni (AP) and Paul Ashley (PA)] for inclusion in the review.

Data collection and analysis

Data extraction was carried out using a specially designed form independently by two of the review authors (AP and PA). Any disagreements were resolved by discussion. Review authors were not blinded to the journal of publication or the author's names on the papers. The descriptive data recorded is shown in Figure 4.

Assessment of studies

These were characterised under the following headings (see tables 13.2a and b in the Cochrane Handbook for more details[12]): whether there was an intervention; how groups were created; which parts of the study were prospective if any.

Risk of bias was assessed by ranking studies according to a hierarchy of evidence. Across studies, a summary assessment was rated as low risk of bias when most information was from studies at low risk of bias, unclear risk of bias when most information was from studies at low or unclear risk of bias, and high risk of bias when the proportion of information was from studies at high risk of bias sufficient to affect the interpretation of the results.

Data synthesis

Data from individual studies were presented; where possible, data from studies were to be pooled to allow some estimate of the number of adverse effects overall. Ideally, dichotomous or continuous outcome variables with means and standard deviations were to be recorded where available. To further evaluate side effects following use of oral midazolam for behaviour management in paediatric dentistry, the following subgroup analyses were also proposed if data were available: age; dose.

Results

Randomised controlled clinical trials of effectiveness and randomised controlled clinical trials looking at side effects

There were no RCTs found looking at side effects alone. After combining the results from Medline and Embase searches and removing papers that did not meet the criteria, 16 papers were included[13–28]. Data from these papers are summarised in Table 1. Only the numbers of subjects receiving oral midazolam are described. Summary data are at the bottom of the table; only simple summary measures could be calculated due to the limited data available from some studies.

Table 1. Summary of randomised controlled clinical trials[13–28].

Study ID	Number of subjects taking oral midazolam Mean age (SD) in years RCT design	Dose oral midazolam and drug compared with	Number of patients with significant adverse reaction (%)	Number of patients with minor adverse reaction (%)	Significant adverse effects reported (may be more than one per patient)	Minor adverse effects reported (may be more than one per patient)
Al-Zahrani *et al.*[13]	*n* = 30 4.6 (0.77) Crossover	0.6 mg/kg midazolam *vs* 0.6 mg/kg oral midazolam and N_2O	0	1 (3)	–	Sleeping (*n* = 1)
Aydintug *et al.*[14]	*n* = 25 5.36 (1.7) Parallel	0.5 mg/kg midazolam *vs* 0.35 mg/kg rectal midazolam	0	14 (56)	–	Hypoxaemia, or disinhibition (*n* = 6) Vomiting and nausea (*n* = 2) Vertigo, vomiting, speaking disability (*n* = 3) Euphoria, hypoxaemia, disinhibition and headache (*n* = 1) Vertigo, disinhibition and nausea, salivation, speaking disability (*n* = 2) Nb – hypoxaemia not defined, assumed to be minor
Gallardo *et al.*[15]	*n* = 16 (unclear) Age range = 4–10 years Parallel	7.5 mg midazolam *vs* Placebo	0	0	–	–
Haas *et al.*[16]	*n* = 23 6.8 Crossover	0.6 mg/kg midazolam *vs* 50 mg/kg oral chloral hydrate	0	3 (13)	–	Minor visual disturbances: one diplopia and a mild hallucination (*n* = 2) Ataxia (*n* = 1)
Johnson *et al.*[17]	*n* = 31 4.7 Crossover	0.5 mg/kg midazolam *vs* 0.3 mg/kg intranasal midazolam	0	7 (23)		Transient desaturation (*n* = 4) Vomiting (*n* = 1) Confrontational/defiant behaviour (*n* = 2)
Kapur *et al.*[18]	*n* = 20 Younger than 4 years old Parallel	0.5 mg/kg oral/transmucosal midazolam *vs* Placebo	0	0	–	–
Koirala *et al.*[19]	*n* = 20 No age given Parallel	0.5 mg/kg midazolam *vs* 5 mg/kg ketamine *vs* 0.4 mg/kg zolpidem *vs* 0.4 mg/kg midazolam + 3 mg/kg ketamine *vs* 0.5 mg/kg midazolam + 2 mg/kg tramadol *vs* 0.4 mg/kg zolpidem + 2 mg/kg tramadol (all oral)	0	0	–	–
Lima *et al.*[20]	*n* = 11 3.3 Crossover	1 mg/kg midazolam *vs* 0.75 mg/kg midazolam + 2 mg/kg hydroxyzine *vs* placebo	0	1 (9)	–	Dizziness (*n* = 1)

(Continued)

Table 1 (Continued)

Study ID	Number of subjects taking oral midazolam Mean age (SD) in years RCT design	Dose oral midazolam and drug compared with	Number of patients with significant adverse reaction (%)	Number of patients with minor adverse reaction (%)	Significant adverse effects reported (may be more than one per patient)	Minor adverse effects reported (may be more than one per patient)
Marshall *et al.*[21]	*n* = 37 Age range = 1.5–7 years Partial crossover	0.5 mg/kg midazolam *vs* 0.6 mg/kg midazolam *vs* 0.75 mg/kg midazolam (all oral)	0	1 (2.7)	–	Belligerent child (*n* = 1)
Mortazavi *et al.*[22]	*n* = 20 3.99 Parallel	0.25 mg/kg midazolam *vs* placebo	0	0	–	–
Silver *et al.*[23]	*n* = 31 9 Parallel	0.3 mg/kg midazolam *vs* 0.5 mg/kg midazolam	0	2 (13)	0	Transient desaturation (*n* = 2) 0.5 mg/kg midazolam
Singh *et al.*[24]	*n* = 30 Age range = 3–9 Parallel	0.5 mg/kg midazolam *vs* 70 mg/kg triclofos *vs* 1.2 mg/kg promethazine	0	0	–	–
Somri *et al.*[25]	*n* = 90 (30 per group) Age range = 3–10 Parallel	0.5 mg/kg midazolam *vs* 0.75 mg/kg midazolam *vs* 1 mg/kg midazolam (all oral)	0	36 (40)	–	Transient desaturation (*n* = 4) 0.75 mg/kg midazolam (*n* = 10) 1 mg/kg midazolam Nausea and drowsiness (*n* = 3) 0.5 mg/kg midazolam (*n* = 7) 0.75 mg/kg midazolam (*n* = 12) 1 mg/kg midazolam
Wan *et al.*[26]	*n* = 21 7.3 Parallel	0.5 mg/kg midazolam *vs* placebo	0	0	–	–
Wilson *et al.*[27]	*n* = 46 12.5 Crossover	0.5 mg/kg midazolam *vs* N_2O	0	1 (2)		Paradoxical reaction (*n* = 1)
Wilson *et al.*[28]	*n* = 35 7.4 Crossover	0.3 mg/kg midazolam *vs* N_2O	0	2 (5.7)		Paradoxical reaction (*n* = 2)
Summary	*n* = 486 Mean ages ranged from 3.3 to 12.5	Dose ranged from 0.25 to 1 mg/kg	0	68 (14)		

All of these studies had oral midazolam as an intervention and were prospective and subjects were assigned to groups randomly. More detailed assessment of the quality and risk of bias of these studies has been reported by Lourenço-Matharu *et al.*[3] In general, the quality of reporting was low and a significant proportion were crossover studies (7, 44%) with the attendant problem of the carryover effect.

No significant side effects were reported. Minor adverse events were more common (n = 68, 14% of cases); classifications are further summarised in Table 3, with nausea and vomiting being the most common side effect reported (n = 30, 6%).

Non-randomised studies

After combining the results from Medline and Embase searches, hand searching and removing papers that did not meet the criteria, nine papers were included. Two further papers were found after searching the reference lists of included papers to bring the total to eleven[29–39]. Data from these papers are summarised in Table 2. Only the numbers of subjects having oral midazolam are described. Summary data are at the bottom of the table; only simple summary measures could be calculated due to the limited data available from some studies.

Risk of bias was high for all of these studies, 4 (36%) were retrospective in nature, 6 (55%) prospective case series, and one was a non-randomised controlled clinical trial.

No significant adverse events were recorded. Minor adverse events were more common (n = 157, 8% of cases); classifications are further summarised in Table 3, with paradoxical reaction being the most commonly reported at 3.8%.

Reference books and databases

No data were found relating to adverse effects of midazolam when used in children as an oral sedative to facilitate dental treatment.

Due to the general poor quality of the data extracted, no further analysis was attempted.

Discussion

This review evaluated side effects following use of oral midazolam for behaviour management in paediatric dentistry. The results show that no significant side effects were reported. Minor side effects per episode of treatment were more common with 14% (n = 68) in the RCT group and 8% (n = 157) in the non-RCT group.

Studies differed widely in the numbers of reported minor side effects; some reported none at all and others reported high proportions of patients (up to 50%) experiencing them. It is difficult to explain this solely in terms of dosage, patient age, or other factors; it may be that reporting itself was an issue. Terms and classifications for different types of side effects varied widely, particularly for so-called paradoxical reactions. In this group, we included adverse events described as a paradoxical reaction, confrontational or defiant behaviour, disinhibition, belligerent behaviour, crying and agitation. It is important to note that some of these reported side effects may instead have been a result of undersedation and failure of the procedure rather than a true paradoxical reaction. Furthermore, papoose boards will have been used in a proportion of the studies[3], which will have made assessment of paradoxical type reactions (where patients may struggle) difficult. Finally in some studies, side effects were not reported separately but were grouped together making it difficult to assess frequencies of individual events[14], or no figures were provided[32,34].

In general, side effects were less frequently reported in the non-RCT studies than in the RCT studies. In the hierarchy of evidence quality, the non-RCT studies would clearly be 'lower' than the RCT studies, and it would seem that one consequence of this is that side effects are less likely to be noted. This might be related to the fact that a significant proportion of these studies were retrospective in nature and presumably relied on good record keeping for the accuracy of the data.

Some conclusions can be made from this data however, with the most obvious being that significant or major side effects are

Table 2. Summary of non-randomised studies[29–39].

Study ID	Number of subjects taking oral midazolam Mean age (SD) in years Study type	Dose oral midazolam and drug compared with	Number of patients with significant adverse reaction (%)	Number of patients (or treatment episodes) with minor adverse reaction (% of total number patients or treatment episodes as appropriate)	Significant adverse effects reported (may be more than one per patient)	Minor adverse effects reported(may be more than one per patient)
Cagiran *et al.*[29]	*n* = 15 Age range = 3–9 Retrospective study	0.75 mg/kg midazolam *vs* 0.75 mg/kg midazolam + 5 mg/kg ketamine (both oral)	0	0	–	–
Day *et al.*[30]	*n* = 101 Mean age between 2.9 and 5 (SD 1.6, 1.0) Retrospective study	0.2–0.7 mg/kg midazolam	0	0	–	–
Erlandsson *et al.*[31]	250 treatment episodes (160 patients) 6.7 Prospective	0.2 mg/kg midazolam	0	4 (2)		Sleep (*n* = 3) Dizziness (*n* = 1)
Fraone *et al.*[32]	*n* = 61 Age range = 2–4.8 Non-randomised controlled trial comparing age range	0.5 mg/kg midazolam	0	No numbers given	–	Hiccups, loss of balance and paradoxical agitation. Supplemental oxygen given. No numbers given
Hulland *et al.*[33]	786 treatment episodes (579 patients) 5.4 Retrospective study	0.5 mg/kg midazolam *vs* N_2O	0	11 (1.4)	–	Hallucinations (*n* = 2) Vomiting (*n* = 9)
Jing *et al.*[34]	*n* = 109 Prospective study	0.5–0.75 mg/kg midazolam	0	19 (17)		Agitation Oversedation Mild 'inhalation problem' No numbers given
Kil *et al.*[35]	*n* = 24 3 years Prospective study	0.5 mg/kg oral midazolam	0	0	–	–

(Continued)

Table 2 (Continued)

Study ID	Number of subjects taking oral midazolam Mean age (SD) in years Study type	Dose oral midazolam and drug compared with	Number of patients with significant adverse reaction (%)	Number of patients (or treatment episodes) with minor adverse reaction (% of total number patients or treatment episodes as appropriate)	Significant adverse effects reported (may be more than one per patient)	Minor adverse effects reported(may be more than one per patient)
Krafft *et al.*[36]	91 treatment episodes (40 patients) Age range 1.3 and 9.3 Prospective study	0.7 mg/kg oral midazolam *vs* 0.6 mg/kg rectal midazolam	0	5 (5)	–	Paradoxical reactions (n = 3) Transient desaturation (n = 2) – group unclear, assumed oral
Lourenço-Matharu and Roberts[37]	n = 510 4.9 Prospective study	0.5 mg/kg midazolam	0	115 (22)		Hiccups (n = 18) Diplopia (n = 18) Crying/agitation (n = 74) Enuresis (n = 5)
Naqvi[38]	n = 45 2–4.9 Prospective study	7.5 mg midazolam	0	1 (2)	–	Vomiting (n = 1)
Nathan and Vargas[39]	n = 40 (20 per group) 2.5 (0.3) 0.7 mg/kg 1.7 (0.3) 1 mg/kg Retrospective study	0.7 mg/kg midazolam *vs* 1 mg/kg midazolam *vs* 0.7 mg/kg midazolam + 1.0 mg/kg meperidine *vs* 0.7 mg/kg midazolam + 1.5 mg/kg meperidine *vs* 1.0 mg/kg midazolam + 1.0 mg/kg meperidine *vs* 1.0 mg/kg midazolam + 1.5 mg/kg meperidine All oral	0	2 (5)	–	Transient desaturation (n = 2) 1 mg/kg midazolam
Summary	n = 2032* Mean ages ranged from 1.7 to 6.7	Dose ranged from 0.2 to 0.75 mg/kg	0	157 (8)		

*Where both patient numbers and number treatment episodes were given, treatment episodes were used in the calculation of the overall sum.

Table 3. Minor adverse effects.

Minor effect	Frequency in RCT (% of all RCT cases)	Frequency in non-RCT (% of all non-RCT cases)
Nausea and vomiting	30 (6.2)	10 (<1)
Transient desaturation	27 (5.6)	4 (<1)
Paradoxical reaction/ agitation	15 (3.1)	77 (3.8)
Hiccough	0	18 (<1)
Cough	0	0
Enuresis	0	5 (<1)
Headache	0	0
Hallucinations	1 (<1)	2 (<1)
Diplopia	1 (<1)	18 (<1)
Dizziness	1 (<1)	1 (<1)
Drowsiness	1 (<1)	3 (<1)
Ataxia	1 (<1)	0

uncommon. None were reported in any of the reference texts or the RCT and non-RCT groups (of a possible 486 + 2032 patients/ sedation episodes). There were significant side effects reported in two studies that were excluded from the review data due to supplemental use of nitrous oxide[40,41]. These side effects were persistent desaturation and bronchospasm and occurred at doses of 1 mg/kg and 0.7 mg/kg, respectively. Some readers may argue that these high doses of oral midazolam are candidates for deep sedation which, although not reported in the studies, may have been measurable if equipments such as bispectral index monitors were to be used to verify the depth of sedation.

Minor side effects were much more common and seen in 14% of all RCT studies with nausea/vomiting, transient desaturations and paradoxical reactions being the chief complaints. Further analysis of the relationship between oral midazolam dosage and prevalence of symptoms was felt to be unwise due to the generally poor quality of the data. The frequency of transient desaturations emphasises the importance of adequate monitoring during sedation. Of the six studies reporting a transient desaturation, two did not provide a figure for the lowest oxygen saturation level reached[14,39], whereas the remaining four studies reported that oxygen saturation reached low levels ranging from 78% to 94%[17,23,25,36]. The importance of safety in sedation is paramount and the authors advise the use of pulse oximetry and the availability of emergency equipment as standard.

What constitutes a significant side effect? An arbitrary description was made for this review which some readers may disagree with; however, given the data available, we felt it was the best compromise. Clearly, an inability to maintain an airway or persistent desaturation should be considered as significant but what about transient desaturations? We felt that if these were easily correctable through head repositioning, then they should be considered as minor, and this sort of transient desaturation could be due to a range of reasons including breath holding or crying.

It is important to recognise that all the side effects recorded here were very 'clinician-centred', that is, they could be considered as anything that might interfere with provision of the treatment. It might be interesting as part of any future work to look at patient-centred measures and perhaps get patients' views as to what events they would consider to be significant. In general, it would be helpful if more generally agreed descriptions of side effects existed that could be used in future studies, thus facilitating greater comparison between studies and between different methods of sedation.

In conclusion, significant or major side effects associated with oral midazolam usage for behaviour management in children and adolescents requiring dental treatment appear to be rare. Minor events are more common but determining precise figures was complicated by poor reporting.

Why this paper is important to paediatric dentists?

- There is currently little information available as to the safety of midazolam when used as an oral sedative in children needing dental treatment.
- This study revealed that significant side effects are uncommon. Minor side effects are more common, with paradoxical reactions and nausea and vomiting being the chief complaints. The frequency of transient desaturations emphasises the importance of adequate monitoring during sedation.
- The study highlights the need for more consistent reporting of adverse effects.

Conflict of interest

The authors declare no conflict of interest.

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