British Journal of Anaesthesia **91 (6)**: 850–6 (2003)
DOI: 10.1093/bja/aeg278

BJA

Randomized, controlled, cross-over clinical trial comparing intravenous midazolam sedation with nitrous oxide sedation in children undergoing dental extractions

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Background. The use of benzodiazepines for paediatric dental sedation has received limited attention with regard to research into clinical effectiveness. A study was therefore designed to investigate the use of midazolam, for i.v. sedation in paediatric dental patients.

Method. The aim of the study was to assess the effectiveness of i.v. midazolam in a randomized, controlled, cross-over trial. Children aged 12–16 yr (ASA I and II), requiring two appointments for equivalent but contralateral dental extractions for orthodontic purposes, were recruited. Conscious sedation with either i.v. midazolam titrated at 0.5 mg min^{-1}, to a maximum of 5 mg, or nitrous oxide/oxygen titrated to 30%/70% inhalation sedation was used at the first visit, the alternative being used at the second visit. Vital signs including blood pressure, arterial oxygen saturation and ventilatory frequency, as well as sedation levels and behavioural scores, were recorded every 2 min.

Results. Forty patients, mean age 13.2 yr (range 12–16 yr), participated in the trial. A mean dose of midazolam 2.8 mg was administered in the test group. The median time to the maximum level of sedation was 8 min for midazolam compared with 6 min for nitrous oxide ($P<0.001$). Vital signs for both treatments were comparable and within acceptable clinical limits and communication with the patient was maintained at all times. The median (range) lowest arterial oxygen saturation level recorded for midazolam was 97 (91–99)% compared with 97 (92–100)% for nitrous oxide. The mean (range) recovery time for midazolam was 51.6 (39–65) min and 23.3 (20–34) min for nitrous oxide ($P<0.0001$). Fifty-one per cent said they preferred i.v. midazolam, 38% preferred nitrous oxide, and 11% had no preference.

Conclusion. I.V. midazolam sedation (0.5 mg min^{-1} to a maximum of 5 mg) appears to be as effective as nitrous oxide sedation in 12–16-yr-old healthy paediatric dental patients.

Br J Anaesth 2003; **91**: 850–6

Keywords: anaesthesia, dental; anaesthetics gases, nitrous oxide; children; hypnotics i.v.; hypnotics benzodiazepine, midazolam; sedation, conscious

Accepted for publication: May 28, 2003

In medicine and dentistry there is wide variation in the techniques used for the management of children requiring sedation for diagnostic and therapeutic procedures. Following a systematic review of validated clinical evidence and wide consultation, a recent document published by the Scottish Intercollegiate Guidelines Network (SIGN)[1] sought to establish guidance on the requirements for safe paediatric sedation practice. Particular attention was paid to establishing which techniques are appropriate to achieve safe sedation of children and how these techniques perform in terms of efficacy, adverse effects and safety.

With regard to the use of i.v. sedation in children, the guidance suggests the use of i.v. sedation for children under the age of 16 yr should be limited to use in a specialist or hospital setting. However, the evidence relating to the use of i.v. sedation techniques in paediatric sedation for dental treatment is very limited and has been obtained mainly from studies undertaken outside the UK, where multiple drug

techniques or the use of propofol has been advocated.[2 3] To date, the only safe and established sedation technique employed in the UK for paediatric dental patients is inhalation sedation with nitrous oxide and oxygen.[4–7] However, this technique is not appropriate for all children and there are certain health and safety issues regarding the use of nitrous oxide, which have been well documented.[8–11]

I.V. sedation with midazolam forms the mainstay of conscious sedation for adult dental patients in the UK. Midazolam has a number of favourable properties including; a relatively short half-life allowing rapid onset and recovery production of satisfactory levels of anxiolysis and few side-effects.[12 13]

In children, i.v. midazolam is widely used in procedures such as endoscopy, oesophageal manometry, biopsy, bone marrow aspiration and lumbar puncture.[14 15] However little research is available regarding its use for paediatric dental sedation.

One of the key concerns regarding the use of midazolam for paediatric dental sedation is the potential risk of adverse effects such as respiratory depression and dis-inhibition. However, the safety profile of i.v. midazolam in patients up to the age of 17 yr is similar to that of adults.[14] Midazolam has been described as having a safety and tolerability profile in children comparable with or superior to that observed in adults.[15]

The following study aims to evaluate the effectiveness of i.v. midazolam sedation in paediatric dental patients when compared with nitrous oxide/oxygen inhalation sedation.

Methods

Study design

This study was designed as a prospective, randomized, controlled, cross-over clinical trial and had the approval of the Newcastle and North Tyneside Ethics Committee. Forty-two patients, aged 12–16 yr, ASA I and II, referred for orthodontic extraction of at least four teeth (premolars or canines), were recruited. Each patient required bilateral, identical extractions (upper and or lower) on opposite sides of the mouth. Before recruiting subjects, a full verbal and written explanation of the study was given to the patient and the parent. It was deemed essential that the patient was happy to take part in the study and only then was parental consent for both treatment and inclusion in the study obtained. The model used for this study was similar to that of previous work conducted in our department.[16]

Using computerized random numbers, the patient was allocated to receive either i.v. midazolam sedation (even number) or nitrous oxide inhalation sedation (odd number) at their first appointment. The alternative technique was used at their second appointment. The allocation to treatment groups was made by a dental nurse independent of the investigator. As nitrous oxide sedation is the standard paediatric sedation technique in current use in the UK, this form of sedation was used as the control. Dental extractions were carried out on opposite sides of the mouth at consecutive appointments, the order (right or left) being allocated randomly.

An experienced operator/sedationist (a dentist trained in sedation techniques and holding the University of Newcastle Diploma in Conscious Sedation), working under the supervision of a consultant in dental sedation, was responsible for administering the sedation. Assisted by an appropriately trained dental sedation nurse, the operator/sedationist monitored the patient's clinical status throughout each session. All patients were instructed to starve for 2 h before their treatment appointment. The authors accept there is ongoing controversy and discussion regarding what is an acceptable period of fasting for dental sedation. However, it is important to emphasize that, in accordance with national guidelines,[17] dental sedation is defined as 'conscious sedation' and as such the patient must always be able to maintain their own vital reflexes.

Inhalation sedation

Nitrous oxide/oxygen sedation was administered using a Quantiflex MDM relative analgesia machine, which is subject to annual calibration and servicing. The nitrous oxide was titrated in 10% increments to a final concentration of nitrous oxide 30%, oxygen 70%, whilst the clinician provided reassurance and positive reinforcement. A maximum concentration of nitrous oxide 30% was chosen as studies have shown that nitrous oxide 20–30% provides adequate sedation, without the risk of over-sedation.[18–20] Once nitrous oxide 30% had been reached, it was continued throughout the subsequent dental treatment. When the treatment was complete, the nitrous oxide flow was switched off and oxygen 100% administered for 3 min.

Before midazolam sedation

The patient was given EMLA (eutectic mixture of local anaesthetic) cream to place on the dorsum of each hand 90 min before their appointment. At the treatment appointment, a suitable peripheral vein was identified and a 24 gauge venous cannula placed. Midazolam was titrated i.v. by the operator at a rate of 0.5 mg min^{-1} to a maximum of 5 mg. The end-point was judged as the point when the patient showed slurring and slowing of speech, relaxed demeanour, delayed response to commands, mild pupillary ptosis and a willingness to commence treatment. The level of sedation was such that communication was maintained with the patient at all times.

The patient's blood pressure, pulse rate, arterial oxygen saturation and ventilatory frequency were monitored throughout treatment and recovery, as well as colour and level of responsiveness.

For dental treatment

Benzocaine 20% topical anaesthetic gel was applied to the dried mucosa for 2 min and then lidocaine 2% with epinephrine 1:80 000 local analgesic was administered in a

Table 1 Houpt Behaviour Rating Scale—sections 1–4[21]

Behaviour	Score
Rating for sleep	
Fully awake, alert	1
Drowsy, disorientated	2
Asleep	3
Rating for movement	
Violent movement interrupting treatment	1
Continuous movement making treatment difficult	2
Controllable movement that does not interfere with treatment	3
No movement	4
Rating for crying	
Hysterical crying that demands attention	1
Continuous, persistent crying that makes treatment difficult	2
Intermittent, mild crying that does not interfere with treatment	3
No crying	4
Rating for overall behaviour	
Aborted—no treatment rendered	1
Poor—treatment interrupted, only partial treatment completed	2
Fair—treatment interrupted, but eventually all completed	3
Good—difficult, but all treatment performed	4
Very good—some limited crying or movement, e.g. during anaesthesia or mouth prop insertion	5
Excellent—no crying or movement	6

Table 2 Brietkopf and Buttner—Classification of Emotional Status[22 23]

Score	Description
1	Irritated: awake, restless, crying
2	Normal: awake, calm
3	Inactive: tired, hardly moving
4	Sleepy: drowsy, without reaction, but rousable

standard technique for each quadrant (e.g. upper premolar or canine: buccal infiltration and palatal infiltration via the buccal papilla; lower premolar or canine: buccal infiltration followed by lingual infiltration via the buccal papilla). Once analgesia had been achieved, the teeth were extracted.

At the completion of the dental treatment, the patient was transferred to recovery where monitoring continued; they were supervised by their parent and a sedation nurse. The patient remained in recovery for at least 20 min after the commencement of nitrous oxide inhalation sedation, and for at least 60 min after the last increment of i.v. midazolam. The criteria for discharge were; vital signs within normal limits, able to walk unaided, and full verbal communication. At the end of the recovery period the operator assessed the patient's fitness for discharge. Full written and verbal postoperative sedation and surgical instructions were provided.

In order to evaluate the i.v. sedation technique being used, the following parameters and outcome measures were used:

Physiological status. Baseline weight, blood pressure, pulse, ventilatory frequency, and oxygen saturation were recorded immediately before the administration of sedation. Once the sedative had been administered, the blood pressure, pulse rate, ventilatory frequency, and oxygen saturation were monitored continuously throughout treatment and the data recorded every 2 min up to 20 min, and at 5 min intervals thereafter. The treatment stage was also noted.

Behaviour during treatment. The first three categories of the Houpt Behaviour Rating Scale[21] for crying, movement, and sleep were used to grade the child's behaviour during treatment (Table 1).

Level of sedation and emotional status. The sedation level was recorded every 2 min up to 20 min and every 5 min thereafter using the Classification of Emotional Status designed by Brietkopf and Buttner (Table 2).[22 23] The criteria for over-sedation included loss of communication, respiratory depression and eventual loss of consciousness.

Overall behaviour. The Frankl Scale[24] was used to assess overall behaviour (Table 3).

Outcome of treatment. The fourth category of the Houpt Behaviour Rating Scale,[21] was used to indicate the outcome of the treatment session (Table 3).

Patient preference and recall of visit. At the end of each visit, the patient was given a questionnaire and asked to complete it at home the following day. The questionnaire asked the patient to grade how they found and how they felt about each type of sedation. After the second appointment, the preferred form of sedation and the reason for this was noted. In order to obtain information regarding amnesia of the visit, the patient was asked if they could remember certain stages of the treatment, namely cannulation, receiving the local anaesthetic, the dental extraction and being in recovery. The parent was also asked to record postoperative adverse effects and the patient was asked to describe what they liked best and least about the sedation.

Data were entered onto a PC database and analysed using Minitab v13 for Windows. Measurements of time and physiological status were analysed using paired *t*-test. However, where these data did not follow a normal distribution, the non-parametric Wilcoxon test was used. Emotion and behaviour scores were analysed using the χ^2-test. Qualitative data from the patient satisfaction questionnaire were transcribed for evaluation.

Results

Fifty-five patients were assessed for inclusion in the study. Forty-two patients (76%) were recruited, 13 (24%) being unwilling to take part. Two patients withdrew from the trial at their first visit, leaving 40 who completed all their treatment. The mean age of those who completed the study was 13.2 yr (range 12–16 yr); 10 were male and 30 female; 37 were classified as ASA I, and 3 as ASA II.

The mean dose of midazolam used to obtain satisfactory sedation was 2.8 mg (SD 0.94, range 1–5 mg). The mean dose used equates to ~0.055 mg kg^{-1}. Physiological variables can be seen in Table 4. For all stages of treatment they remained within normal limits. Using the Wilcoxon test, the difference in the values for the lowest oxygen saturation levels for the nitrous oxide treatment and the

Table 3 Frankl Behaviour Rating Score[24]

Score		Description
1	Definitely negative	Refusal of treatment, crying forcefully, fearful or any other overt evidence of extreme negativity
2	Negative	Reluctant to accept treatment, uncooperative, some evidence of negative attitude but not pronounced, i.e. sullen, withdrawn
3	Positive	Acceptance of treatment; at times cautious, willingness to comply with the dentist, at times with reservation but patient follows the dentist's directions cooperatively
4	Definitely positive	Good rapport with the dentist, interested in the dental procedure, laughing and enjoying the situation

midazolam treatment, for the sedation titration (100%, 98%) and dental treatment phases (100%, 98%), were statistically significant ($P<0.0001$ and $P<0.0001$, respectively). However, this difference was not of clinical significance.

In the group receiving i.v. midazolam, the mean (range) time from baseline to the cannula being in place was 2.6 (2–6) min. The median time to the maximum level of sedation for the i.v. midazolam treatment group was 8 (4–20) min, compared with 6 (2–18) min for the nitrous oxide group ($P<0.001$). There was a significant difference ($P<0.01$) for duration of dental treatment (i.e. from administration of local analgesic to completion of dental extractions between the two groups), with a median (range) of 8 (4–21) min for the midazolam group and 6 (4–19) min for the control group. The mean (SD; range) values for the time spent in the recovery room were 51.6 (6.61; 39–65) min and 23.3 (2.58; 20–34) min for the midazolam and nitrous oxide groups, respectively ($P<0.0001$). The total appointment time (time from entering surgery to discharge home) was 69.2 (4.7; 65–80) min and 34.8 (4.5; 25–50) min for the midazolam and nitrous oxide groups, respectively.

The maximum levels of sedation were collated for each stage of treatment and the scores according to the Brietkof and Buttner—Classification of Emotional Status[22 23] are presented for the two treatment groups in Figures 1 and 2. At baseline, the majority of patients scored '2' (awake and calm). Only one patient in the nitrous oxide group scored '1' (awake, but restless). During titration of the sedation, more patients in the midazolam group displayed greater levels of sedation than the nitrous oxide group. The difference between the two groups was not statistically significant. During the treatment, the sedation levels increased in both groups. For the recovery phase the sedation levels for the midazolam group remained higher than for the nitrous oxide group. However, when the patients were due to be discharged, the sedation levels in the midazolam group had reduced significantly.

The overall behaviour for the visit was recorded using the Frankl Behaviour Rating Scale.[24] No significant difference was demonstrated between the groups with the overall behaviour of 38 patients in the midazolam group being recorded as 'definitely positive' or 'positive' compared with 39 patients in the nitrous oxide group. Two patients in the midazolam group, compared with one in the nitrous oxide group, scored 'negative' for overall behaviour.

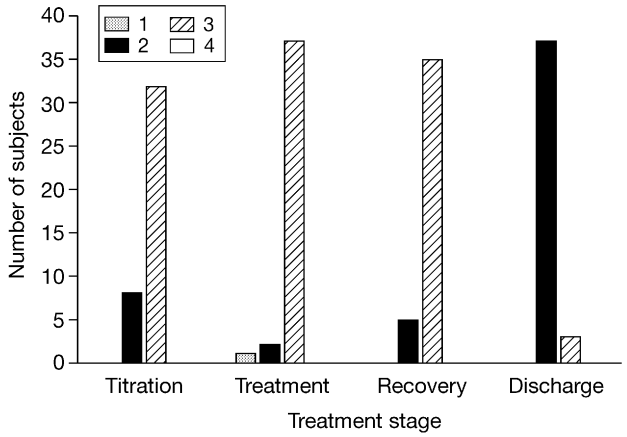

Fig 1 Maximum sedation levels for the midazolam group using the Brietkopf and Buttner—Classification of Emotional Status. The numbers of subjects scoring a maximum sedation score of: 1 (awake, restless), 2 (awake, calm), 3 (tired, hardly moving), or 4 (drowsy, but rousable) for each stage of the visit (i.e. sedation titration, dental treatment, recovery, and discharge) are shown.

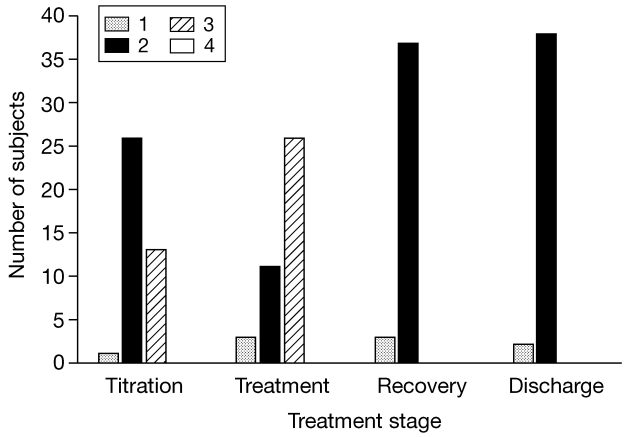

Fig 2 Maximum sedation levels for the nitrous oxide group using the Brietkopf and Buttner—Classification of Emotional Status. The numbers of subjects scoring a maximum sedation score of: 1 (awake, restless), 2 (awake, calm), 3 (tired, hardly moving), or 4 (drowsy, but rousable) for each stage of the visit (i.e. sedation titration, dental treatment, recovery, and discharge) are shown.

Outcome of treatment, as recorded by Section 4 of the Houpt Behaviour Rating Scale[21] indicated favourable results. All patients successfully completed treatment in both groups with 35 in the midazolam group and 36 in the

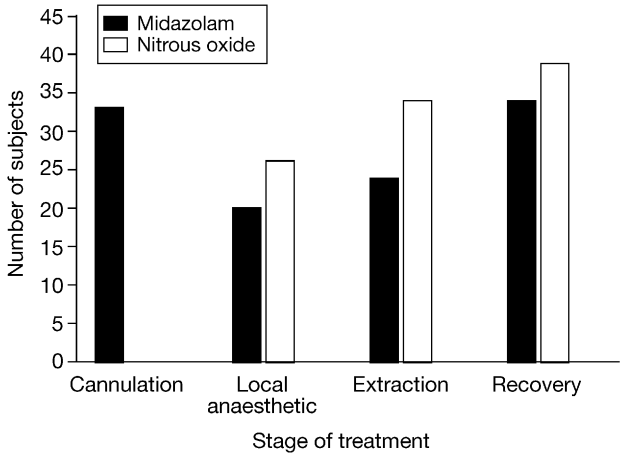

Fig 3 Positive recall of the appointment. The results are presented as the number of subjects who remembered having the cannula inserted, having the local anaesthetic, having teeth extracted, and being in recovery.

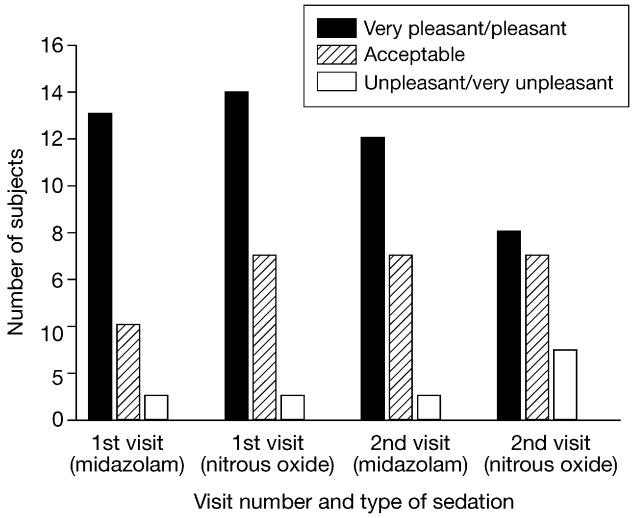

Fig 4 Patient's opinion of treatment. This was compared between those who had midazolam first and nitrous oxide second and those who had nitrous oxide first and midazolam second. The results are presented as the number of subjects who found the treatment: 'Very pleasant' or 'Pleasant'; 'Acceptable'; or 'Unpleasant' or 'Very unpleasant'.

nitrous oxide group scoring 'Excellent' or 'Very good'. Only two patients in each group scored 'Fair' or 'Poor'.

Recall of the visit was recorded for cannulation, local anaesthetic administration, dental extraction, and the recovery phase. The results are illustrated in Figure 3. It can be seen that there was greater recall in the nitrous oxide group than the midazolam group. However, χ^2-test analysis did not demonstrate any statistical significance.

How the patients found the treatment is illustrated in Figure 4. The majority found it 'Very pleasant' or 'Pleasant' in both groups. Relating these results to the type of sedation used at the first visit, it is evident that whether the patient had midazolam or nitrous oxide at the first visit, they were all less positive about the type of sedation at their second visit.

All patients were asked if they would be prepared to have the same form of sedation again and which method they preferred. Thirty-six responded to this question and 29 (80%) said they would have nitrous oxide inhalation sedation again compared with 29 (80%) who said they would have i.v. midazolam again. Thirty-seven patients responded to the question on which type of sedation they preferred. Nineteen (51%) preferred midazolam sedation, 14 (38%) preferred nitrous oxide inhalation sedation and 4 (11%) had no preference. The main reasons reported for preferring midazolam were: feeling more relaxed; the sedation worked faster; not having a mask. For nitrous oxide inhalation sedation the reasons for preference were: it wore off more quickly; feeling relaxed but being more aware.

The patients were also asked what they liked best and least about the treatment and the main comments for midazolam were: *Liked best*: 'the friendly staff', 'it was quicker', 'being more relaxed', 'when it was all over', 'not feeling the teeth coming out'. *Liked least*: 'injection in the hand', 'plastic tube being left in hand', 'time spent in recovery', 'having teeth taken out'.

The comments reported for nitrous oxide inhalation sedation included: *Liked best*: 'Coming round quickly', 'Having the gas', 'When it was over', 'Nothing, I found it very, very unpleasant'. *Liked least*: 'Needle in the gum', 'Waiting for the gas to work', 'Everything, it made me very, very anxious'.

Side-effects on returning home were reported by 14 patients in the midazolam group and 11 in the nitrous oxide group. Side-effects reported were: nausea, drowsiness, headache and sore mouth. The most commonly reported side-effect in the midazolam group was drowsiness (7 patients) with 3 reports of headache and 2 of nausea. In the nitrous oxide group there was 1 report of drowsiness, 1 of headache and 1 of nausea. None of the side-effects were considered to be serious and none required emergency attention.

Discussion

The i.v. route for midazolam administration has been shown to be very effective in adult dental patients.[12] However, its use in paediatric dental sedation has been discouraged because of a lack of clinical based evidence regarding the safety and effectiveness of the technique.[1 17] This study was therefore designed to establish such evidence.

The age range of the subjects (12–16 yr) was selected for several reasons. This is the age at which children may require orthodontic extractions, which allows use of the model of two visits for balanced extractions. It was believed that children of this age generally had the capacity to understand the proposed procedure and were therefore able to give informed consent. Older children were also more likely to be able to accept cannulation and to understand how they might feel when sedated.

Table 4 Physiological measurements. Data are presented as mean (range), except for oxygen saturation given as median (range)

Treatment stage	Blood pressure (mm Hg)	Pulse rate (beats min^{-1})	Ventilatory frequency (bpm)	Lowest oxygen saturation (%)
Baseline				
Midazolam	83.3 (65.6–102.3)	84.5 (55–117)	18.3 (14–24)	97 (91–99)
Nitrous oxide	84.9 (65.6–115.3)	82.2 (59–117)	19.2 (14–26)	97 (92–100)
Sedation titration				
Midazolam	79.2 (60.3–93.6)	83.3 (53–115)	18.6 (14–22)	98 (92–100)
Nitrous oxide	81.0 (67.1–95.3)	82.0 (56–119)	18.3 (14–24)	100 (97–100)
Dental treatment				
Midazolam	79.4 (67.9–90.2)	92.2 (72–122)	19.0 (14–22)	98 (91–100)
Nitrous oxide	78.2 (65.8–94.5)	87.6 (62–126)	19.3 (14–27)	100 (97–100)
Recovery				
Midazolam	79.4 (67.7–92.9)	83.0 (65–120)	18.6 (14–22)	99 (94–100)
Nitrous oxide	79.5 (65.6–93.2)	78.2 (60–99)	18.5 (14–24)	99 (94–100)
Discharge				
Midazolam	80.1 (62.0–99.6)	82.7 (62–120)	18.4 (14–22)	97 (92–100)
Nitrous oxide	78.4 (64.3–91.0)	77.4 (63–106)	18.2 (12–24)	97 (92–100)

However, one of the limitations of patient recruitment for this study was the fact that cannulation was involved. This may be borne out by the fact that, of the 55 patients approached to take part, 24% declined; the main reason being concern over the cannulation. Indeed the two recruits (~5% of patients) who withdrew from the study at the first treatment visit, were not happy to have i.v. sedation and requested inhalation sedation for each appointment. However, for those who took part in the study, the process of cannulation did not pose a problem. The use of preoperative EMLA cream and a small gauge needle (24 G) made the procedure relatively comfortable. The time to carry out the cannulation was acceptable with a median time of 2 (range 2–6) min; indeed in 35 patients the cannula was in place within 2 min.

In adult dental patients it is recommended that midazolam is titrated at a rate of 1 mg min^{-1} to an end-point that allows treatment to be carried out.[26] In order to ensure safe administration of midazolam in the age group studied this titration rate was halved to 0.5 mg min^{-1}. This would enable the child to be closely monitored and given the minimal effective dose for the procedure. Indeed, the mean dose used was 2.8 (range 1–5) mg, which equates to ~0.05 mg kg^{-1}. This is consistent with the work of Rosen and colleagues[14] who recommend 0.01–0.05 mg kg^{-1} i.v. midazolam. It is important to note that in our study the midazolam was not diluted and therefore the accuracy of titrating 0.5 mg min^{-1} (0.25 ml) may be in question. For future work, the authors advise that the midazolam be diluted to 10 mg in 10 ml.

The maximum level of sedation at any time for both groups was described as 'Inactive: tired, hardly moving'.[22 23] None of the patients in either group exhibited the highest score for sedation and verbal communication was maintained at all times.

In order to fully evaluate the effectiveness of the sedative technique being studied, it is important to consider the physiological variables. The main side-effect of benzodiazepines is respiratory depression and therefore recording of arterial oxygen saturation is essential for monitoring respiratory as well as cardiovascular function. Patients undergoing sedation should always have an oxygen saturation $\geqslant$90% and ideally well above this.[26] In our study, the median lowest arterial oxygen saturation recorded during the appointment in the midazolam group was 97% with a range of 91–99%. It is worth noting that arterial oxygen saturation readings of 91–93% were recorded for only 3 patients and for each patient at only 2 time intervals throughout the total visit. The mean values for ventilatory frequency, pulse rate, and blood pressure were all found to be within acceptable limits for this age group.

When using different sedation techniques it is important to consider the time factor for both the patient and the clinician. The time to reach the maximum level of sedation in the midazolam group was comparable with the nitrous oxide group (median of 8 and 6 min, respectively). The time to carry out the dental treatment was also within acceptable limits in both groups. The only stage of the visit that was more prolonged for those receiving midazolam was the recovery phase. It is common practice in patients who have received i.v. midazolam for dental treatment, to ensure they remain in recovery for at least 1 h after the last increment of sedation has been administered. However, even after this time, it is stressed that all discharge criteria must be fully met before the patient is allowed to leave the clinic.[26 27] In our study, the mean time spent in recovery following the dental treatment for those who had received midazolam, was 51.6 (range 39–65) min. This would appear to be consistent with recommended practice for this form of conscious sedation. By the very nature of the different sedation techniques being studied, it was expected that the total appointment time for the midazolam group would be significantly greater than the nitrous oxide group. This was indeed the case with a mean total appointment time of 69.2 min for midazolam, compared with 34.8 min for nitrous oxide.

One of the properties of midazolam is its amnesic effect.[28] The anterograde amnesia produced by midazolam may be beneficial when unpleasant procedures such as extractions are being carried out and indeed the study population exhibited greater amnesia of the treatment than the nitrous oxide group, which may be considered an advantage of the technique.

In conclusion, the results of the study presented indicate that the administration of i.v. midazolam sedation titrated at a rate of 0.5 mg min^{-1} appears to be as effective and acceptable as nitrous oxide sedation for healthy paediatric dental patients aged 12-16 yr. The technique produced no significant physiological changes, good anxiolysis, few side-effects, and was accepted by the majority of patients. It must be appreciated, however, that i.v. midazolam sedation is not a panacea for all paediatric dental patients and any one undertaking this technique must be appropriately trained in paediatric sedation and life support.

References

1 Scottish Intercollegiate Guidelines Network. Safe sedation of children undergoing diagnostic and therapeutic procedures: a national clinical guideline. Scottish Intercollegiate Guidelines Network, 2002

2 Milnes AR, Maupome G, Cannon J. Intravenous sedation in pediatric dentistry using midazolam, nalbuphine and droperidol. *Pediatr Dent* 2000; **22**: 113–19

3 Veerkamp JS, Porcelijn T, Gruythuysen RJ. Intravenous sedation for outpatient treatment of child dental patients: an exploratory study. *ASDC J Dent Child* 1997; **64**: 48–54

4 Roberts GJ. Inhalation sedation (relative analgesia) with oxygen/nitrous oxide gas mixtures: I principles. *Dent Update* 1990; **17**: 139–146

5 Shaw AJ, Meechan JG, Kilpatrick NM, Welbury RR. The use of inhalation sedation and local anaesthesia instead of general anaesthesia for extraction and minor oral surgery in children: a prospective study. *Int J Paed Dent* 1996; **6**: 7–11

6 Blain KM, Hill FJ. The use of inhalation sedation and local analgesia as an alternative to general anaesthesia for dental extractions in children. *Br Dent J* 1998; **184**: 608–11

7 Shepherd AR, Hill FJ. Orthodontic extractions: a comparative study of inhalation sedation and general anaesthesia. *Br Dent J* 2000; **188**: 329–31

8 Donaldson D, Meechan JG. The hazards of chronic exposure to nitrous oxide: an update. *Br Dent J* 1995; **178**: 95–100

9 Yagiela JA. Health hazards and nitrous oxide: a time for reappraisal. *Anesth Prog* 1991; **38**: 1–11

10 Starch DJ. Nitrous oxide sedation: understanding the benefits and risks. *Am J Dent* 1995; **8**: 47–50

11 Girdler NM, Stirling PA. Investigation of nitrous oxide pollution arising from inhalational sedation for the extraction of teeth in child patients. *Int J Paed Dent* 1998; **8**: 93–102

12 Reeves IG, Fragen RJ, Vinik HR. Midazolam: pharmacology and uses. *Anaesthesia* 1985; **62**: 310–24

13 Payne K, Mattheyse FJ, Liebenberg D, Dawes T. The pharmacokinetics of midazolam in paediatric patients. *Eur J Clin Pharmacol* 1989; **37**: 267–72

14 Rosen DA, Rosen KR. Intravenous conscious sedation with midazolam in paediatric patients. *Int J Clin Pract* 1998; **52**: 46–50

15 Karl HW, Cote CJ, McCubbin MM, *et al.* Intravenous midazolam for sedation of children undergoing procedures: an analysis of age and procedure related factors. *Pediatr Emerg Care* 1999; **15**: 167–72

16 Wilson KE, Welbury RR, Girdler NM. A randomised, controlled, crossover trial of oral midazolam and nitrous oxide for paediatric dental sedation. *Anaesthesia* 2002; **57**: 860–7

17 General Dental Council. Maintaining standards: general anaesthesia and conscious sedation. London: General Dental Council, 2002

18 Cooper J, Jobling D, Edmunds DH. Sedation for minor oral surgery: inhalation sedation with 25 per cent nitrous oxide. *J Dent* 1978; **6**: 265–7

19 Roberts GJ. Relative Analgesia—an introduction. *Dent Update* 1979; **6**: 271–84

20 Holroyd I, Roberts GJ. Inhalation Sedation with nitrous oxide: a review. *Dent Update* 2000; **27**: 141–6

21 Houpt MI, Kupietzky A, Tofsky N, Koenigsberg S. Effects of nitrous oxide on diazepam sedation of young children. *Pediatr Dent* 1996; **18**: 236–41

22 Breitkopf L, Buttner W. Die Effekte fruherer Operationen auf Narkose und Operationsangste bei Kindern. *Anaesthesia* 1986; **35**: 30

23 Krafft TC, Kramer N, Kunzelmann R. Experience with midazolam sedative in the dental treatment of uncooperative children. *ASDC J Dent Child* 1993; **60**: 295–9

24 Frankl SN, Shiere F, Fogels H. Should the parent remain with the child in the dental operatory? *J Dent Child* 1962; **2nd quarter**: 151–63

25 General Dental Council. Maintaining standards: general anaesthesia and conscious sedation. London: General Dental Council, 2001

26 Girdler NM, Hill CM. Sedation in Dentistry. Reed Educational and Professional Publishing Limited, 1998

27 Meechan JG, Robb ND, Seymour RA. Pain and anxiety control for the conscious dental patient. Oxford: Oxford University Press, 1998

28 Thompson JM, Neave N, Moss MC, Scholey AB, Wesnes K, Girdler NM. Cognitive properties of sedation agents: comparison of the effects of nitrous oxide and midazolam on memory and mood. *Br Dent J* 2000; **188**: 354