

Comparison of sevoflurane and nitrous oxide mixture with nitrous oxide alone for inhalation conscious sedation in children having dental treatment: a randomised controlled trial

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Summary

We studied 411 children aged 3–10 years who were referred for dental treatment. They were randomly allocated to have inhalation conscious sedation with either sevoflurane/nitrous oxide mixture or nitrous oxide alone. Dental treatment was satisfactorily completed in 215/241 children who were given sevoflurane/nitrous oxide mixture (89%) compared with 89/170 who were given nitrous oxide alone (52%) (Chi square 70.3, $p < 0.0001$). All children remained conscious and responsive to verbal contact throughout the treatment and in the recovery room. No adverse side-effects were recorded in either group and there were no significant differences in oxygen saturation, heart rate, recovery profile, or time to discharge home between the groups. The study concluded that, for every 100 children treated with sevoflurane/nitrous oxide mixture, 37 children would be saved a general anaesthetic if given combined sevoflurane and nitrous oxide mixture rather than nitrous oxide alone. The use of sevoflurane in low concentrations 0.1–0.3% to supplement nitrous oxide and oxygen for inhalation conscious sedation is safe, practical, and significantly more effective than nitrous oxide alone in children having dental treatment.

Keywords Surgery: dental. Anaesthesia: dental. Anaesthetics, volatile: sevoflurane. Conscious sedation.

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We published a pilot study of 75 healthy children aged 3–15 years who required dental treatment [1] and were given inhalation conscious sedation with sevoflurane 0.1–0.3% in conjunction with 40% nitrous oxide in oxygen. In 69 children (92%), dental treatment was completed successfully and the experience was regarded as excellent by 88% of children and 91% of their parents. Most children (93%) were fit for discharge home within 10 min with no side-effects.

The next step was to establish the efficacy and safety of sevoflurane in nitrous oxide for inhalation conscious sedation by comparing it with nitrous oxide alone inhalation conscious sedation in a randomised controlled trial.

Methods

Ethical and licensing approvals were obtained from the North Tees local research ethics committee and from the Department of Health, Medicines Control Agency.

A total of 411 healthy children aged 3–10 years were recruited at the Queensway Anxiety Management Clinic, Billingham. We used the same protocol as in the previous study [1]. Children were pre-assessed a few days before their scheduled treatment. Each child's degree of anxiety and need for dental treatment was assessed. Table 1 shows the criteria for inclusion in the trial (about 55% of children referred). Children were excluded if there was a family history of malignant hyperthermia or known

Table 1 Criteria used to identify children as suitable for inhalation conscious sedation.

Anxious children aged 3–10 years
English speaking children without learning difficulties
Children who can sit in the dental chair, able to tolerate an examination and will accept a nasal hood
Children who have unobstructed nasal airways
Children who would not be better served with intravenous sedation

hypersensitivity to sevoflurane or local anaesthetics. Children with body weights outside the 10th and 90th centile for ideal body weight, those with a history of psychiatric illness, and mentally or physically handicapped children were also excluded. The standard pre-assessment document included a medical questionnaire, which was completed by the child's parents or guardian with the help of the dentist [2]. Full verbal and written information about the study was given to the parents and written informed consent was obtained. The dentist showed each child how to breathe through a nasal hood.

Sedation technique

On the day the children came for treatment, they were randomly allocated by means of sealed envelopes to have either sevoflurane based inhalation conscious sedation ($n = 241$) or nitrous oxide based inhalation conscious sedation ($n = 170$).

A mixture of lidocaine and prilocaine (EMLA[®]) cream was applied to the dorsum of both hands of each child by the parent 1 h before treatment in case venous access was required if the inhalation technique failed.

Parents were invited to be present with their child in the room throughout the dental treatment. Children were

placed supine in the dental chair. A pulse oximeter was attached and a baseline Eve's test carried out [3]. This is a simple test of spatial awareness in which the child, with eyes closed, touches the tip of his or her nose with a forefinger. In children allocated to have sevoflurane, the anaesthetist gave a titrated concentration in the range 0.1–0.3% of sevoflurane delivered by a Drager Vapour 2000 vaporiser, in a fixed ratio of 40% nitrous oxide in oxygen at a gas flow of $6 \text{ l} \cdot \text{min}^{-1}$. Children allocated to have nitrous oxide were given a fixed ratio of 40% nitrous oxide in oxygen at the same gas flow. The gases were delivered by continuous flow from a Drager Julian anaesthetic machine into the inspiratory limb of the nasal hood. From the nasal hood the expiratory limb, which incorporated a one-way non-return valve, was connected to an active scavenging system. The nasal hood was adapted to incorporate a probe to measure fractional inspired and end-tidal oxygen, nitrous oxide, and sevoflurane concentrations.

During the procedure, the dentist chatted with the child using calming suggestions and imagery to reassure the child and to distract attention. Before the planned dental treatment, topical anaesthetic was applied to the gum, and 2 min later the dentist injected a local anaesthetic. At intervals of 5 min the dentist made an assessment of the degree of the child's co-operation using the six-point Venham scale (Table 2) [4]. Oxygen saturation, heart rate, fractional inspired and end-tidal sevoflurane were also measured and recorded every 5 min during the dental treatment.

During treatment the level of consciousness was observed continuously [5, 6]. Children were maintained ideally between level 3 and 4 (Table 3).

Table 2 The six-point Venham scale.

1. Relaxed:	Smiling, able to converse, best possible working conditions. Displays the behaviour desired by the dentist spontaneously, or immediately when asked.
2. Uneasy:	Concerned. During stressful procedure may protest briefly and quietly to indicate discomfort. Child willing and able to interpret experience as requested. Tense facial expression. Breath is sometimes held in. Capable of co-operating well with treatment.
3. Tense:	Tone of voice, questions and answers reflect anxiety. During stressful procedure, verbal protest, quiet crying, hands tense and raised, but not interfering much. Child interprets situation with reasonable accuracy and continues to cope with his or her anxiety. Protest more distracting and troublesome. Child still complies with request to co-operate. Continuity is undisturbed.
4. Reluctant:	Tends to reject the treatment, difficulty in assessing threat. Pronounced verbal protest, crying. Using hands to try to stop the procedure. Protest out of proportion to threat, or is expressed well before the threat. Copes with situation with great reluctance. Treatment proceeds with difficulty.
5. Anxious:	Anxiety interferes with ability to assess situation. General crying not related to the treatment. Prominent body movements, needing restraint on occasion. Child can be reached through oral communication, and eventually with reluctance and great effort begins to cope. Protest disrupts procedure.
6. Out of control:	Fails to grasp the reality of the threat, hard loud crying. Screaming, swearing. Unable to listen to oral communication. Regardless of age reverts to primitive flight responses. Actively involved in escape behaviour. Treatment impossible to complete.

Table 3 Scale used to monitor the level of consciousness during treatment.

1.	Awake and not anxious
2.	Awake and anxious
3.	Partial ptosis and/or slurred speech
4.	Eyes closed and responds to speech
5.	Eyes closed, responds to mild physical stimulation
6.	Unresponsive to mild stimulation

Recovery

When treatment had been completed, all gases were withdrawn and 100% oxygen was given through the nasal hood for 3 min. The child was monitored during recovery by a nurse who recorded the following information:

- 1 time of the child's arrival in the recovery room;
- 2 oxygen saturations;
- 3 heart rate;
- 4 level of anxiety and cooperation using the six-point Venham scale;
- 5 the child's performance of an Eve's test after 2 min and 5 min.

When the child had completed the Eve's test, he or she was asked to walk unaided in a straight line across the room under close supervision and this was recorded. Pain was recorded by means of a visual analogue scale on a 0–10 scale [7]. Finally, the parent's opinion of the overall management of the child and the time to discharge home (when the child was considered to have recovered fully) were recorded.

Statistical methods

The main outcome event was the success or failure of the sedation. The data were therefore analysed using Chi square test of the validity of the null hypothesis that the failure rate was equal in the two treatment groups. The absolute risk reduction, relative risk reduction, and the numbers needed to treat are presented with their associated 95% confidence intervals (CI). Continuous data such as age and weight are presented as mean (SD) values for each group. The Venham scores of the two groups, being ordinal data, were compared using the non-parametric Mann–Whitney test. The data were also subjected to a multivariate logistic regression analysis with success or failure as the dichotomous response variable and the other variables as independent variables. The only independent variable that was significant in this analysis was the treatment group and consequently we have presented the Chi square analysis of the outcome data rather than details of the logistic regression. All the data were analysed using the MINITAB statistical package version 12.0.

Table 4 Characteristics of 411 children. Figures are mean (SD) or number (%).

	Nitrous oxide <i>n</i> = 170	Sevoflurane <i>n</i> = 241
Age in years	6.2 (1.9)	6.0 (1.7)
Weight in kg	23.7 (7.7)	22.9 (6.5)
Pulse rate	94.2 (10.3)	95.2 (9.3)
Sex: female	74 (44%)	110 (46%)
male	96 (56%)	131 (54%)
Duration of treatment in mins	17.8 (5.8)	19.7 (6.0)

Results

The characteristics of the children are shown in Table 4.

The technique was effective in 215 of the 241 children in the sevoflurane group, and in 89 of the 170 children in the nitrous oxide group. There is a highly significant difference in the failure rates (Chi square 70.3, $p < 0.0001$). There is therefore an absolute reduction in the risk of a child needing general anaesthesia of 36.9% (95% CI 28.4–45.4%) when using sevoflurane and nitrous oxide compared with nitrous oxide alone, a relative reduction in risk of 77%, and for every 2.7 children treated with sevoflurane, one patient will be saved a general anaesthetic. For every 100 children treated with sevoflurane and nitrous oxide rather than nitrous oxide alone, 37 will be saved a general anaesthetic (Table 5).

During treatment, the lowest observed arterial oxygen saturation was greater than 97% in 96% of children given nitrous oxide and 97% of children given sevoflurane. There were no significant differences in oxygen saturation between the groups during treatment or recovery (Table 6).

The remaining results refer to the 215/241 children successfully treated with sevoflurane, and the 89/170 successfully treated with nitrous oxide. During treatment, the dentist assessed the level of anxiety and co-operation in each child using the six point Venham scale [4]. The results showed that 144 of 215 children (67%) given sevoflurane had a score of 1 (relaxed and fully co-operative) compared with 28 of 89 children (32%) given nitrous oxide alone. Tables 7a and b, respectively, show

Table 5 Absolute and relative risk reduction with the use of sevoflurane inhalation conscious sedation.

	Estimate	95% confidence interval
Absolute risk reduction (%)	36.9	28.4–45.4
Relative risk reduction (%)	77.4	59.5–95.1
Number needed to treat	2.7	2.2–3.5

Table 6 Lowest observed oxygen saturation recordings of children during treatment and recovery.

% O ₂ saturation	94%	95%	96%	97%	98%	99%	100%	Total
Group N	0	2 (1.2%)	4 (2.4%)	15 (8.8%)	12 (7.1)	23 (13.5%)	114 (67.0%)	170 (100%)
Group S	1 (0.4%)	2 (0.8%)	5 (2.0%)	7 (2.9%)	18 (7.5%)	25 (10.4%)	183 (76.0%)	241 (100%)

Table 7a Worst Venham score during treatment. Data are percentage of subjects with score.

	Nitrous oxide <i>n</i> = 170	Sevoflurane <i>n</i> = 241
Relaxed	31.8	66.8
Uneasy	11.8	13.7
Tense	9.4	8.7
Reluctant	43.5	10.4
Anxious	1.7	0.0
Uncontrolled	1.8	0.4

Table 7b Venham score in recovery for successful treatment only. Data are percentage of subjects with score.

	Nitrous oxide <i>n</i> = 89	Sevoflurane <i>n</i> = 215
Relaxed	85.7	93
Uneasy	8.8	5.1
Tense	4.4	1.4
Reluctant	0.0	0.0
Anxious	0.0	0.5
Uncontrolled	1.1	0.0

the distribution of Venham scores during treatment and recovery. The scores during treatment are significantly different ($p < 0.0001$) as are those during recovery ($p = 0.04$, Mann–Whitney).

The mean (SD) sedation time in the sevoflurane group was 19.7 (6.0) min compared with 17.8 (5.8) min in the nitrous oxide group.

Parents of children who completed the treatment were satisfied; 74/89 (83%) parents in the nitrous oxide group and 188/215 (87%) in the sevoflurane group rated the treatment as excellent.

The median visual analogue score for pain in both groups was zero.

Table 8 shows what happened to the ‘failures’ in each group.

	Proceed to sevoflurane sedation	Proceed to intravenous sedation	Proceed to general anaesthesia	Terminate	Total
Nitrous oxide	35 (43)	10 (12)	33 (41)	3 (4)	81 (100)
Sevoflurane	0	11 (42)	15 (58)	0	26 (100)

Table 8 The anxiety management technique used to complete treatment. Figures are number (%).

During treatment, the heart rate was within 20% of the baseline reading in both groups. No adverse incidents or side-effects were encountered in any child.

During recovery, 201/215 (93%) given sevoflurane and 81/89 (91%) given nitrous oxide alone completed Eve’s test satisfactorily and succeeded in walking unaided within 2 min; the rest took 5 min to complete the test.

The median time to recovery in both groups was 4 min (range 3–15 min in the nitrous oxide group and 2–9 min in the sevoflurane group). Using the Mann–Whitney test, the p -value for this comparison is 0.22 (non-significant).

Discussion

Queensway Anxiety Management Clinic is supported by Tees Health Authority, its aim being to substitute high quality conscious inhalation and intravenous sedation techniques for general anaesthesia in dentistry [2]. This is consistent with the consensus among policy makers and professionals that the use of general anaesthesia in dentistry should be minimised [8–15]. A recent review of general anaesthesia and conscious sedation recommended that general anaesthesia in dentistry should be restricted to hospitals from January 2002 [12]. Our options for preventing anxiety in children who need dental treatment will therefore be limited to local anaesthesia combined with either nitrous oxide inhalation sedation or intravenous conscious sedation. Nitrous oxide inhalation sedation is safe and well established. However, when it fails, children need either intravenous conscious sedation or general anaesthesia.

An acceptable alternative to intravenous conscious sedation is desirable for children with needle phobia, or when the risks of intravenous conscious sedation are considered unacceptable. Intravenous conscious sedation carries risks, particularly in young children. This risk is often associated with the use of more than one drug, even

when the drugs being given are within acceptable dose limits [16].

In a search for a new conscious sedation technique that may further reduce the need for general anaesthesia, particularly in children when nitrous oxide conscious sedation has failed and the use of intravenous conscious sedation is considered unsuitable or carries an unacceptable risk, we decided to investigate the addition of sevoflurane to nitrous oxide. After a successful pilot study [1], we designed a large randomised controlled clinical trial to compare this mixture with nitrous oxide alone inhalation sedation.

Initially, 1000 sealed envelopes containing 500 randomly allocated assignments to each group were made. After completion of 411 operations, it became apparent that there was a highly significant difference in the failure rate between the two groups (Chi square 70.3, $p < 0.0001$), and the trial was therefore stopped.

All children in both groups remained conscious and responsive to verbal contact throughout the treatment and during recovery. The use of low concentrations (0.1%–0.3%) of sevoflurane in conjunction with 40% nitrous oxide in oxygen showed that the margin of safety was wide enough to render loss of consciousness unlikely. Sevoflurane/nitrous oxide conscious sedation therefore meets the definition laid down by the General Dental Council [9]. Because this technique involves 60% inspired oxygen concentration the likelihood of desaturation below 95% is negligible.

Further applications of sevoflurane inhalation conscious sedation outside the field of dentistry are indicated and have been tried by the authors in patients having minor surgical procedures in outpatients and day surgery, Accident and Emergency Departments, in trauma and orthopaedics patients, particularly while performing regional anaesthesia or nerve blocks or during the insertion of invasive lines on conscious patients. Others have also tried the technique on children requiring neuro-radiological investigations and it has been considered for use during endoscopic procedures. Future use of sevoflurane inhalation conscious sedation for pain relief during labour is currently under investigation by the authors.

The technique is useful as an alternative to intravenous conscious sedation, particularly in patients with needle phobia, or when the use of intravenous conscious sedation is considered unsuitable or carries an unacceptable risk.

In conclusion, Sevoflurane inhalation conscious sedation is a promising new development and has the advantages of being well accepted and tolerated by children and adults alike. The technique is safe and more effective than nitrous oxide alone. It is also a simple and practical technique to use by trained anaesthetists, cost

effective and has wide clinical applications. We are working on the design of a practical and safe prototype delivery system, which in future will enable the use of sevoflurane inhalation conscious sedation by certified sedationists particularly in the field of dentistry

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