

ORIGINAL ARTICLE

Nitrous oxide inhalation is a safe and effective way to facilitate procedures in paediatric outpatient departments

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Aims: To evaluate the efficacy and safety of nitrous oxide treatment given to children presenting procedural problems in a paediatric outpatient department.

Methods: The study comprised 70 children 6–18 years old. Two different groups were studied. (1) Children presenting with problems in establishing venous cannulation (VC) (n=50). The patients were randomised to conventional treatment (CO); cutaneous application of EMLA or nitrous oxide treatment (NO); N₂O and EMLA. (2) Anxious children/children undergoing painful procedures who repeatedly come to the clinic (n=20). These children underwent two procedures with CO/NO, the order of priority being randomised. Altogether the study included 90 procedures. Main outcome measures were procedure time, number of attempts required to establish VC, pain, and evaluation.

Results: All procedures were performed with NO while four VC (8%) were not possible to perform with CO. The number of attempts required to establish VC was lower when using NO (median 2, range 2–9), compared with CO (median 4, range 2–9). The estimated pain was lower with NO. The total mean time required was similar for NO and CO when the time required for the NO procedure was included. One complication, tinnitus, was observed; it disappeared within 3 minutes.

Conclusion: The pretreatment with nitrous oxide is a time effective and safe method for use at paediatric outpatient departments to reduce pain, facilitate venous cannulation, and thereby reduce the number of costly cancellations of planned procedures.

Pain, anxiety, and difficulties related to venipunctures (VP), venous cannulations (VC), and other procedures are recurrent problems in paediatric outpatient departments, resulting in trauma for the children and sometimes delayed and cancelled procedures.^{1–2}

Although the use of anaesthetic creams such as EMLA has significantly reduced the problems associated with VP, VC, painful injections, and implants,³ the pain alleviation obtained with EMLA is sometimes insufficient and a conflict easily arises between the need for speed, efficiency, and adequate pain reduction.

In obese patients, VC/VP is regularly associated with technical problems. The number of severely obese children is increasing dramatically in the western world and the need for examinations and treatments will increase in order to prevent and treat potential obesity complications. In obese children, the veins are hidden deep in the subcutaneous adipose tissue, which makes it impossible to visualise the veins and also very difficult to feel them.

Consequently, there is a demand for more efficient methods for patients in whom technical difficulties in effectuating VC or VP can be expected, for children who are treated on a regular basis with painful injections and implants, and finally, for generally anxious children.

Treatment with nitrous oxide (NO) is a well established method for pain alleviation^{4–7} and has been used with good results, in particular in children who fear the dentist.^{8–9} According to an extensive retrospective French survey, the method works very well in minor surgery.⁵

NO has both pain reduction and sedation effects,^{10–11} which may be useful when the VP is performed; it may also simplify the VC in cases where it is technically difficult to establish.^{12–15}

NO inhalation in paediatric outpatient care has not yet been evaluated; the aim of this study was to evaluate the advantages, disadvantages, and safety of NO in a paediatric outpatient setting.

METHODS

Patients

The study was approved by the Ethical Committee at Huddinge University Hospital and the written informed consent of all parents and children was obtained.

The study comprised 70 children aged 6–18 years. The inclusion criteria included: ASA status 1, American Society for Anesthesia classification of health (<http://www.asahq.org>), a classification as a normal healthy child with no disturbance,¹⁶ ability to breathe by means of a mask, and the ability to interpret a visual analogue scale (VAS).

Age, diagnosis, and sex are presented in table 1.

Two different groups of children were studied:

- Children with well known difficulties in effectuating VC (DVC). All of these children had previously experienced difficulties in connection with VP/VC and it was necessary to make several attempts at different sites before being able to take a sample or establish intravenous access (n=50). The children came for a double VC as preparation for an intravenous glucose tolerance test. The patients were randomised to conventional treatment (CO) or nitrous oxide treatment (NO) by envelope technique. A specialist nurse in anaesthesia effectuated 30 of the VCs using a 22 G catheter (15 CO/15 NO) and a general nurse established 20 VCs using a 22 G catheter (10 CO/10 NO).
- Anxious children and children undergoing painful procedures (ACP) who come repeatedly to the clinic for these procedures (n=20). The children were subjected to two procedures, one with CO and one with NO. The order was randomised. All procedures were performed by the same nurse.

Abbreviations: ACP, anxious children and children undergoing painful procedures; CO, conventional treatment; DVC, difficulties in effectuating venous cannulation; NO, nitrous oxide; VAS, visual analogue scale; VC, venous cannulation; VP, venipuncture

Table 1 Clinical diagnosis and characteristics of the patients

	DVC Children with difficulties in effectuating venous cannulation (n = 50)	ACP Anxious children/children undergoing painful procedures (n = 20)
Age	13 (6–18)	11 (6–17)
Boys/girls	27/23	4/16
Diagnosis	49 OB/1 SS	8 OB/8 PP/2 SS/1 DI/1 AL
Procedure	50 VC	8 I/11 VP/1V

Results are presented as median (range).

Diagnosis: OB, obesity; PP, puberty praecox; SS, short stature; DI, diabetic AL, allergy.

Procedure: VP, venipuncture; VC, venous cannulation; V, vaccination; I, injection/implant: procren (n = 3), decapeptyl (n = 3), suprefact(n = 2).

The equipment included an anaesthetic block (Dräger RCD DS3) with separate rotameters for oxygen/nitrous oxide/air connected to a Bains circuit (partial rebreathing system), a regulator, a fail safe system which shuts off the N₂O if there is an oxygen pressure decrease, and a pulse oximeter (Date-Ohmeda TUFF SAT).

Children who fulfilled the inclusion criteria were consecutively asked if they wanted to participate in the study. Four children did not choose to participate (3 DVC/1 ACP).

These patients received conventional treatment (EMLA cream). In one case, the procedure was cancelled.

Procedures

All children had cutaneous application of anaesthetic EMLA cream one hour before the procedure. NO included N₂O and EMLA cream. The children in the DVC group were not given any solid food or liquid after midnight because of the glucose tolerance test. In order to diminish the risk of nausea/vomiting,^{17, 18} the children in the ACP group were not given any solid food within 4 hours and no liquid within 2 hours before the treatment.

A nurse specialised in paediatric anaesthesia performed all the nitrous oxide treatments. The nitrous oxide concentration was increased in gradual stages to facilitate the cooperation and participation of the child, starting with 2 l N₂O/6 l O₂ (8 l/min fresh gas flow) for 2 minutes, thereafter increasing to 3 l N₂O for 2 minutes, and 4 l N₂O for 1 minute; the procedure was then performed. Altogether the time required for introduction and emergency of N₂O was 8 minutes. The time required to achieve an adequate level of sedation/analgesia was 5 minutes; after the procedure there was an additional 3 minutes for nitrous oxide washout, with the child breathing 100% oxygen. The children held the mask themselves; if necessary, they were assisted by a parent.

Parameters

The following variables were assessed and recorded: *the number of attempts* that were required for double VC was measured as well as *the time required for the procedure* with and without the NO procedure. *Pain* was evaluated by means of a VAS ranging from 1 to 10,¹⁹ 5 minutes after performing the procedure or 5 minutes after accomplishing treatment with NO. *The children's and parents' evaluation of the procedure* were evaluated on a five point global rating scale: 1, poor; 2, fair; 3, good; 4, very good; 5, excellent.¹⁹ The children performed the evaluation before the parents and the parents were present when the children made their assessment; *the nurses' assessment of the treatment* was made using a three point scale: 1, procedure without complications; 2, the procedure was performed with difficulties since the child was protesting and found it difficult to remain lying down; 3, the procedure

could not be performed. The children in DVC were followed up 4 hours after NO treatment and children in ACP at the next visit to the clinic. The children who tested both CO and NO were asked which method they would prefer next time.

Heart rate and oxygen saturation were followed throughout the procedures by means of pulse oximetry. Side effects were recorded.

Statistics

All results are presented as median and range. In the first part the groups were compared by means of the Mann-Whitney test. For comparisons of paired data the Wilcoxon test was used in the second part of the study. All statistical analyses were performed using SPSS for Windows software.

RESULTS

Table 2 summarises the results for children with previous difficulties with venous cannulation.

In the CO group, four VC procedures (8%) were not accomplished, three because of too many unsuccessfully attempts and in one case because only one attempt was allowed by the frightened adolescent. The procedures were interrupted when the child refused to cooperate. The time required for these four procedures was 21–85 minutes. Nine procedures (18%) were accomplished with difficulty. In 84% of the cases more than two attempts were required to establish double VC. The pain was rated as high. Children and parents considered the procedure trying. The time of the procedure varied considerably (range 7–95 minutes).

All procedures were accomplished in the NO group. The number of attempts required to establish double VC was significantly lower. In 40% of the cases, more than two attempts were required to effectuate double VC. The pain was rated as low in this group. Children and parents considered the treatment to be tolerable. There was no significant difference in time required for VC between CO and NO. If the time for induction and completion of NO was excluded, the time required was significantly lower. Whether a specialist nurse or general nurse performed the VC did not affect the results. No complications were detected during the treatment or at follow up after NO treatment.

Table 3 summarises the results of anxious children/children undergoing painful procedures.

With CO, one procedure (5%) could not be performed; on nine occasions (45%), it could only be performed with difficulty. The pain was estimated as high in each case according to VAS. The comments of children and parents indicated that they considered the procedure difficult. The time for the procedure varied (range 4–95 minutes).

All procedures with NO were performed without problems. The experience of pain was rated lower in all cases. The

Table 2 Children with difficulties in effectuating venous cannulation, DVC (n = 50) with CO (conventional treatment) or NO (nitrous oxide treatment)

	DVC/CO	DVC/NO	p†
No. of attempts	4 (2–9)	2 (2–6)	0.001
Pain, VAS	5 (2–10)	2 (1–4)	<0.001
Time required*, min	21 (7–95)	18 (5–57)	0.005
Satisfaction score, parents 1–5	3 (1–4)	5 (3–5)	<0.001
Satisfaction score, children 1–5	2 (1–4)	5 (4–5)	<0.001
Nurse's assessment 1–3	2 (1–3)	1 (1)	<0.001

Results are presented as median (range). In the satisfaction score, 5 is most satisfactory, in nurse's assessment, 1 is best (see Methods).

*In the time required for cannulation, the time for induction and completion of NO is not included (see Methods).

†Mann-Whitney test.

Table 3 Anxious children/children undergoing painful procedures, ACP(n = 20) with CO (conventional treatment), and NO (nitrous oxide treatment)

	ACP/CO	ACP/NO	Difference CO v NO	p†
Pain, VAS	5 (1–10)	1 (1–6)	3 (0 to 9)	<0.001
Time required*, min	9 (4–95)	5 (1–18)	4.5 (–1 to 88)	<0.01
Satisfaction score, parents 1–5	3 (1–4)	4 (3–5)	–1 (–4 to –1)	<0.001
Satisfaction score, child 1–5	2 (1–3)	5 (4–5)	–3 (–4 to –1)	<0.001
Nurse's assessment 1–3	1.5 (1–3)	1 (1)	0 (0 to 2)	<0.005

Data are presented as median (range). In the satisfaction score, 5 is most satisfactory, in nurse's assessment, 1 is best (see Material and Methods).

*In the time required for the procedure is the time for induction and completion of NO not included (see Material and Methods).

†Wilcoxon signed rank test.

comments of children and parents indicated that they considered the treatment to be tolerable. The time required for the procedure was significantly lower with NO if the time for induction and completion was excluded. Ten minutes after the procedure, all children were able to walk by themselves.

The number of side effects with NO was low. One complication was documented during the NO treatment, tinnitus, and it disappeared within 3 minutes after the completion of NO. There were no other side effects reported by the children when they came back for the next treatment.

Ninety per cent of the children who tried both treatments preferred NO. There was a weak correlation ($r = 0.21$) between age and the number of attempts for VC in the DVC (CO) group. No other correlations were found between pain, age, and time required.

DISCUSSION

In a considerable number of children treated at outpatient departments, as shown both in this study and in previous ones,^{2,20} anaesthetic cream does not induce sufficient analgesia. Among the 45 children in this study who underwent procedures with anaesthetic cream, 60% found it painful, defined as VAS >5.¹⁹ This might lead to a vicious circle of anxious children becoming even more afraid, and implants, injections, and venous cannulations becoming technically more difficult to perform. Scheduled procedures cannot be completed when the venous cannulation fails and has to be postponed, and this is often regarded as a failure by the children, their parents, and the nursing staff. Furthermore, it is uneconomical for both the parents, who are losing a day's income, and for the medical services when an examination is postponed.

Consequently, there is a demand for effective means of anxiety and pain reduction for a selected group of children at outpatient departments. The results show that treatment with nitrous oxide augments the quality of care by facilitating venipuncture/venous cannulation without prolonging the effective time and making it possible to complete all procedures and examinations. The number of attempts needed to establish venous cannulation was also significantly lower with nitrous oxide. It made no difference whether a specialist or general nurse performed the venous cannulation. Thus, our results indicate that the need for a better pain reduction and to facilitate procedures for this group of patients can not be fulfilled solely by improving the technical skills of the nurse.

With CO we found a weak correlation between the age of the child and the number of attempts at venous cannulation, which means the number of attempts does not decrease when the children get older. This also indicates that procedural problems exist in all age groups, and most probably also in adults.

The ideal procedural method for pain relief is non-invasive and effective, with a rapid onset, reversal, and brief duration and with minimal side effects. Midazolam is an alternative method^{20–24} or a complement to EMLA for anxious children, but it has no analgesic effect, a slow onset, and a long duration of action; it can also be difficult to administer orally or rectally. More efficient analgesic alternatives, like morphine or pethidine, require monitoring and personnel resources which are not available in paediatric outpatient clinics.

Administration of nitrous oxide is simple and painless, has a rapid onset and short duration, and its effects are analgesic, anxiolytic, and sedative with minimal side effects.^{17,18} It is well known that nitrous oxide has a weak emetic effect¹⁷ but no side effects like nausea/vomiting were documented in this study. This can be explained by the fact that obese children, who were performing glucose tolerance tests, were not given any solid food or liquid from midnight before the day of treatment and the other children were not given any food for four hours, and no liquid for two hours, before the treatment. However, there was no association between preprocedural fasting state and adverse events in a recent article; 50% of children having procedural sedation in the emergency department were not fasted.²⁵

The NO concentration was increased in gradual stages. We believe that this facilitated the cooperation and participation of the children who held the mask themselves; loss of response to verbal command were not seen in any case, which made over sedation with NO almost impossible. The children should be old enough to cooperate by holding the mask, which makes the lowest age limit around 5–6 years old. Avoiding the smaller children decreases dramatically the risk for unforeseen negative effects.¹⁸ In this study, only ASA I¹⁶ patients were included and only one minor complication was recorded, thereby confirming that nitrous oxide treatment is a safe method.^{10,11,18} Because of the good results, we see no reason why ASA 2¹⁶ patients could not be included when nitrous oxide is administered in this safe manner.

The treatment with nitrous oxide is easy to perform; the equipment required is an anaesthetic block, a suction unit, a scavenging system, and a pulse oximeter. The whole procedure, administration of NO and venous cannulation, when the maximum nitrous oxide concentration does not exceeded 50% and no other concomitant drugs are given apart from EMLA, can easily be performed by a single specially trained nurse if local regulations so permit. In the present study a registered specialised nurse in paediatric anaesthesia gave the sedation.

In conclusion, the described method, with nurse controlled self administered nitrous oxide has all the necessary properties to facilitate procedures and augment the quality of paediatric care for children, parents, and the nursing staff when needed.

What is already known on this topic

- Nitrous oxide is an anaesthetic gas commonly used in general anaesthesia
- In sub-anaesthetic concentrations, nitrous oxide has analgesic properties with rapid onset and offset of action that promotes its use in ambulatory setting

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What this study adds

- This study has shown that at a paediatric outpatient clinic, nitrous oxide inhalation is a time effective and safe method to facilitate venous cannulation, reduce pain, and thereby reduce the number of costly cancellations of planned procedures