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Administration of Nitrous Oxide to Pediatric Patients Provides Analgesia for Venous Cannulation

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To determine whether administration of nitrous oxide, 50% and 70%, could provide analgesia and anxiolysis during venous cannulation in pediatric patients, 165 ASA Physical Status 1 patients scheduled for elective surgery were studied. Children, 3 weeks to 18 yr of age, were randomly assigned either to receive nitrous oxide, 50% or 70% in oxygen, or 100% oxygen *via* mask or to a group breathing room air, for 3 min prior to and during venous cannulation. A blinded observer using a behavioral scale for rating pain in children performed assessments of behavior and pain before and following venous cannulation. Children who received 50% or 70% nitrous oxide were more likely to be relaxed, 59% and 84%, respectively, and had little evidence of pain. Of those given 100% oxygen or no mask, only 30% and 21%, respectively, were considered relaxed, and 16% and 15% had little evidence of pain during venous cannulation. Side effects were seen in 28% of the group given 70% nitrous oxide and included excitement, dysphoria, nausea, restlessness, and opisthotonic movements. Both 50% and 70% nitrous oxide in oxygen administered to pediatric patients are effective at decreasing the pain and anxiety associated with venous cannulation, but use of the latter is associated with side effects. (Key words: Analgesics: nitrous oxide. Anesthesia: pediatric.)

VENOUS CANNULATION performed on awake pediatric patients can be painful and frightening for the recipient and disconcerting for the anesthesiologist. Techniques to reduce the pain of venipuncture, such as local anesthesia administered subcutaneously or topically, have been described.[1–3] Although these are effective in reducing pain at the puncture site, there are disadvantages associated with their use, particularly in the pediatric age group. To determine whether both analgesia and reduction in anxiety could be provided for pediatric patients nitrous oxide (N_2O) in oxygen (O_2) was administered by mask before and during venous cannulation.

Materials and Methods

Approval by the Hospital Research Committee and informed consent were obtained to study 165 patients 3 weeks to 18 yr of age (table 1) scheduled for elective surgery. All patients were ASA Physical Status 1 and received no preanesthetic medication. Patients were separated from their parents and brought to the operating room where they were randomly assigned to receive one of four treatments for 3 min prior to and during venous cannulation: 50% N_2O in O_2; 70% N_2O in O_2; 100% O_2; or no mask; *i.e.*, no gas. Monitors were applied and the gas was administered by either an anesthesia resident or a nurse, using a soft, clear anesthesia mask gently but firmly applied to the patient's face. An anesthesia machine used only for administration of N_2O and O_2 delivered the gas *via* a Bain circuit with gas flows of 300 ml/kg. Venous cannulation, using a 22-G catheter, was performed by the same anesthesiologist throughout the study.

An observer, blinded to the treatment (except the no mask group), recorded the following: history of previous surgery; attendance at the preoperative class (conducted by the operating room nurses to familiarize the children with their upcoming experience); history of behavior problems, *e.g.*, extreme fear of needles, hyperactivity, lack of cooperation during previous visits to surgeon's office; behavior during separation from parents, application of monitors, application of anesthesia mask, and venous cannulation; pain score[4] (table 2) during venous cannulation (score ≤ 6 indicates absence of pain behavior); heart rate, blood pressure (Dinamap™), and oxygen saturation (Nellcor™), measured at three points during the study period: after monitors were attached (baseline); 3 min later, *i.e.*, after administration of gas and just prior to venipuncture (for patients in the no mask group this measurement was taken 3 min after monitors were attached); and immediately following venous cannulation; and, complications and side effects.

Data are reported as incidence or mean ± SD. Data were analyzed using chi-square analysis with Yates correction and Bonferroni inequality where indicated or analysis of variance. Post hoc comparisons were made using the least significant difference method. Interrater reliability of the pain scores was determined using the κ statistic, comparing scores given by two separate observers for 26 patients randomly chosen from all groups. $P < 0.05$ was considered statistically significant.

Results

There was no difference between the treatment groups with respect to age, history of previous surgery or behavior

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TABLE 1. Age Distribution for Patients in Each Treatment Group

Age (yr)	50% N_2O	70% N_2O	100% O_2	No Mask
0–2	10	11	13	10
3–6	13	16	12	11
7–11	9	9	11	10
12–18	7	7	8	8
Total	39	43	44	39

problems, or attendance at the preoperative class (tables 1 and 3). There was also no difference in behavior during separation from parents, application of monitors, and acceptance of the mask. If a child was judged relaxed, the child was relaxed, drowsy, or asleep.

Children who received N_2O were more likely to be relaxed and have lower pain scores during venous cannulation (table 3). Interrater reliability of the pain scores was 93%. Heart rate increased significantly following insertion of the venous catheter in children who received 100% O_2 compared with those given 70% N_2O (table 4). There was no significant difference in systolic blood pressure. Oxygen saturation of patients in all groups did not decrease below 95% at any time during the study period.

TABLE 2. Behavioral Scale for Rating Pain in Children (CHEOPS)[4]

Item	Behavior	Score
Cry	No cry	1
	Moaning	2
	Crying	2
	Scream	3
Facial	Composed	1
	Grimace	2
	Smiling	0
Child verbal	None	1
	Other complaints	1
	Pain complaints	2
	Both complaints	2
	Positive	0
Torso	Neutral	1
	Shifting	2
	Tense	2
	Shivering	2
	Upright	2
	Restrained	2
Touch	Not touching	1
	Reach	2
	Touch	2
	Grab	2
	Restrained	2
Legs	Neutral	1
	Squirming/kicking	2
	Drawn up/tensed	2
	Standing	2
	Restrained	2

The maximum possible score is 13; a score of ≤6 indicates absence of pain behavior.

TABLE 3. Characteristics of Patients in Each Treatment Group

	50% N_2O	70% N_2O	100% O_2	No Mask
Previous surgery	46	35	34	38
Attended preoperative class	13	21	18	31
Behavioral problems	3	9	11	0
Relaxed during separation from parents	59	56	52	62
Relaxed during application of monitors	38	28	39	46
Accepted mask	74	63	70	n/a
Relaxed during venipuncture	59*	84*	30	21
Pain score ≤6	56*	77†	16	15
Side effects	0	28†	0	0

Data are reported as percentages.

* Different from both 100% O_2 and no mask by chi-square analysis ($P < 0.05$).

† Different from all groups by chi-square analysis with Yates correction ($P < 0.05$).

None of the children lost consciousness while breathing the N_2O, although side effects, such as excitement (eyes open but not responding to verbal stimuli) and restlessness, were seen in some patients who received 70% N_2O (table 5). These children did not require physical restraint. One 5-month-old infant exhibited opisthotonic movements, which involved stiffening of the whole body and arching of the back. The venous catheter was inserted quickly without difficulty and the N_2O was discontinued. The movements ceased and anesthesia was induced and surgery completed with no sequelae. None of the children who experienced side effects reacted to venous cannulation.

Discussion

The aim of anesthesiologists is to provide a safe, pleasant, and pain-free operative course for their patients. One of the first tasks is to alleviate discomfort associated with venipuncture. This discomfort may be exacerbated by

TABLE 4. Heart Rate and Systolic Blood Pressure Measured after Monitors Attached (baseline), 3 min after Administration of Gas Just Prior to Venipuncture, or 3 min after Monitors Attached in No Mask Group (prevenipuncture), and Immediately Following Venous Cannulation (postvenipuncture)

	50% N_2O	70% N_2O	100% O_2	No Mask
Heart rate (beats/min)				
Baseline	105 ± 29	117 ± 36	111 ± 31	110 ± 36
Prevenipuncture	99 ± 30	103 ± 31	105 ± 37	110 ± 36
Postvenipuncture	107 ± 36	105 ± 32	117 ± 37*	118 ± 41
Systolic blood pressure (mmHg)				
Baseline	117 ± 21	121 ± 14	124 ± 15	121 ± 19
Prevenipuncture	111 ± 21	110 ± 14	122 ± 17	118 ± 16
Postvenipuncture	113 ± 17	113 ± 16	125 ± 18	124 ± 16

Data are reported as mean ± SD.

* Different from 70% N_2O by repeated measures analysis of variance and least significant difference ($P < 0.05$).

TABLE 5. Side Effects Following Administration of 70% N_2O

Side Effect	N	Age
Excitement	7	5–7 yr
Dysphoria	2	2 and 13 yr
Nausea	1	13 yr
Restlessness	1	1 yr
Opisthotonic movements	1	5 mo

anxiety surrounding anticipation of the event. Although inhalation induction of anesthesia avoids this problem, the presence of secure iv access before the patient loses consciousness increases the margin of safety, particularly in situations in which patients may have a full stomach, cardiovascular instability, or when patients requiring general anesthesia have a family history of malignant hyperthermia.

A eutectic mixture of lidocaine and prilocaine (EMLA) has been used to reduce the pain of venous cannulation in children.[1–3] When applied as a cream over the potential venipuncture site, it was found to be effective in reducing pain compared with placebo but not more effective than lidocaine 1% injected subcutaneously. Disadvantages to the use of EMLA include the following: 1) a 60-min delay to full efficacy following application; 2) failure to improve patient cooperation even when the venipuncture site was made analgesic with EMLA[3]; 3) need to reapply EMLA at a second site with a subsequent delay if venous cannulation fails at the first site; and 4) a possible risk of methemoglobinemia secondary to absorption of the prilocaine component of the EMLA.[5]

Local anesthetic administered subcutaneously is effective at reducing pain of venipuncture, but it necessitates an injection. Its use is also associated with some of the same disadvantages as EMLA, such as predetermination of the venipuncture site and the risk of inducing undue anxiety in an unsedated child because of anticipation of pain from an injection.

Nitrous oxide provides both anxiolysis and analgesia when administered prior to venous cannulation. More than one attempt at venipuncture in different locations may be made without the need to "reapply" the analgesic.

Disadvantages associated with the administration of N_2O include the presence of a mask, which can be frightening for a child. Only those children who attended the preoperative class were familiarized with the mask before coming to the operating room. Children receiving N_2O who were initially reluctant to have a mask applied to their face usually calmed after a few breaths of the N_2O. During present clinical use if the child is particularly afraid, the mask is removed from the circuit and the N_2O is blown over the airway. The child usually relaxes after a few breaths and then tolerates gentle application of the mask. Older children are able to hold the mask themselves, but for younger patients an assistant is required to perform this task while the anesthesiologist inserts the venous cannula. Oversedation may result if N_2O is used on patients who have received preanesthetic medication. Another disadvantage is the incidence of side effects following the administration of 70% N_2O. They occurred most commonly in the older age group; 75% were 5 yr or more. The inability of the patients experiencing excitement to respond to verbal stimuli implies the presence of an altered state of consciousness and, although not demonstrated in this study, the possible loss of protective airway reflexes. The same likely applies for the patient who exhibited opisthotonic movements, which may have been a form of excitement. Therefore, 70% N_2O for prevenipuncture analgesia is not recommended for use in patients at risk for vomiting and aspiration.

The safety and versatility of N_2O has been demonstrated by its role in the treatment of labor pain and as a prehospital analgesic for emergency patients.[6] Although easily administered by relatively untrained personnel, caution should be urged in the use of N_2O without proper instruction and supervision, particularly for patients who may be concomitantly receiving medications, such as opioids, in which the risk of oversedation and respiratory depression is increased.

We conclude that the administration of 50% or 70% N_2O in O_2 to pediatric patients is an effective method of decreasing the pain and anxiety associated with venous cannulation in the operating room. The use of 70% N_2O may lead to an altered state of consciousness and should not be used when this is contraindicated.

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