Scientific Article

End-expired Nitrous Oxide Concentrations Compared to Flowmeter Settings During Operative Dental Treatment in Children

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Abstract: ***Purpose:*** *The purpose of this study was to analyze inspired and end-expired alveolar nitrous oxide (N_2O) concentrations during operative dental treatment in 6- to 9- year-old children and compare them to the concentrations dispensed by the dental N_2O delivery system's flowmeter.* ***Methods:*** *Twenty-three healthy 6- to 9-year-olds who received restorative dental care underwent placement of a sampling probe in the posterior nasopharynx. Via nasal mask, 100% oxygen was administered at a rate of 3L/minute for 2 minutes. N_2O was then introduced at a flowmeter reading of 50% for 5 minutes and thereafter reduced to 30% for the duration of treatment, followed by 100% oxygen for 5 minutes postoperatively. Respiratory rate, inspired and end-expired nitrous oxide and oxygen concentrations, and pressure of end-tidal carbon dioxide values were measured and recorded from the nasopharyngeal probe with an anesthesia gas monitor.* ***Results:*** *End-expired alveolar N_2O concentrations were, on average, 63% below flowmeter settings. After rapid induction with 50% N_2O, an end-expired N_2O saturation maximum of 11% was attained, on average, after 90 seconds. The time to flush out remaining N_2O after delivery of 100% oxygen varied between 30 and 195 seconds.* ***Conclusions:*** *End-expired alveolar nitrous oxide and oxygen concentrations and pressure of end-tidal carbon dioxide values were successfully recorded during operative dental treatment of 6- to 9-year-old awake and non-intubated children in the traditional dental setting.* *(Pediatr Dent 2011;33:56-62) Received July 30, 2009 / Last Revision November 8, 2009 Accepted November 9, 2009*

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Nitrous oxide (N_2O) is a popular anxiolytic and analgesic. In outpatient settings, it is used to help mild to moderately anxious children and adults cope with the stress and pain of minor medical and dental procedures. N_2O has nearly all the characteristics of an ideal analgesic agent: safety, noninvasive delivery, lack of serious side effects, simplicity of use, and a rapid onset and offset. Its desired effects, however, are not always fully predictable, and it is rarely given as the sole agent but rather in combination with local anesthetics or narcotic analgesics. In dentistry, generalists and specialists alike use N_2O to reduce fear and discomfort associated with the provision of local anesthesia and the surgical procedure itself. N_2O is ideally suited and widely used in pediatric dentistry to facilitate dental treatment in uncooperative and/or fearful children.[1,2]

Nitrous oxide's pediatric applications range from fracture reduction in the ED[3] to otologic minor procedures,[4] easing venipuncture,[5] and nasolacrimal duct probing.[6] Adult applications include: administration in laboring women[7]; prehospital analgesia[8]; and pain and anxiety reduction during transoesophageal echocardiography,[9] ultrasound guided biopsies,[10] or colonoscopies.[11]

In general anesthesia, N_2O is commonly administered together with other volatile anesthetic agents to achieve successful clinical anesthesia.[12] Its use, however, is not without controversy. Considerable efforts are under way to investigate the effects of N_2O on perioperative cardiac morbidity for major noncardiac surgery.[13] In a large, randomized, controlled trial, avoidance of N_2O and the concomitant increase in inspired oxygen (O_2) concentrations resulted in significantly lower rates of severe nausea and vomiting and postoperative major complications such as fever, wound infection or pneumonia.[14] Omission of N_2O from general anesthesia was thought to increase intraoperative awareness,[15] but light anesthesia was identified as the most common cause.[16]

Patients with metabolic disorders related to vitamin B_{12}-mediated processes are susceptible to reduced methionine synthase activity as a consequence of lengthy anesthetics with high N_2O concentrations.[17] As long as recommended contraindications are considered, however, the current level of evidence does not justify N_2O's exclusion from clinical practice.[18]

The purpose and mode of how N_2O is applied in general anesthesia is markedly different from the delivery method in the outpatient setting. Intubated patients receive the gas from the anesthesia machine through an endotracheal tube in combination with other volatile anesthetic agents that induce

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and maintain a state of general anesthesia. Generally, only minimal leakage occurs in such a semiclosed system and gas concentrations can be continuously monitored through a sampling line in the ET-tube.

N_2O delivery for the awake patient is generally provided through a nasal mask with the intent of reducing pain and anxiety. Nasal masks are available in different sizes from several manufacturers. These masks are held in place mainly by the weight of the breathing circuit attached to it and do not produce an airtight seal. Therefore, some degree of air entrainment is unavoidable due to patient movement and variations in facial and nasal anatomy.

The N_2O sedation system's flowmeter mixes N_2O and O_2 and displays the actual concentration of the gas mixture that is delivered through the breathing circuit to the nasal mask. The tubing also contains a scavenging circuit that carries in separate ducts the exhaled gases from the mask to an outside vent. The action of this scavenging system located in the mask is another variable that affects the delivered gas concentrations. It is designed to collect the expired gases as well as those that spill out of the mask as a consequence of gas leakage due to a less than ideal fit. Poorly adjusted and/or calibrated scavenging systems, however, can remove too much of the gas. As a result of all these variables, gas concentrations in the mask are markedly lower than the delivery system indicates and dispenses.

Several researchers described this reduction of N_2O concentration from the flowmeter to the inhaled air in the mask and lungs. In a dental setting, N_2O concentrations in 25 adult subjects decreased from a 45% flowmeter setting to an average of 23% in the mask and 16% in the pharynx.[19] In an analog lung model, concentrations of 34% N_2O and 44% O_2 were measured at the subglottic level, and end-expired N_2O concentrations varied between approximately 7% and 34% when a 50% N_2O/O_2 mixture was applied.[20] A 31% reduction in inspired nasal mask N_2O concentrations vs. flowmeter settings was found in 15 adult subjects.[21] In the same study, end-expired N_2O concentrations were reported to be 51% lower than the flowmeter indicated.

Collectively, these studies confirm that flowmeter settings and end-expired N_2O concentrations vary significantly when an open delivery system such as a nasal mask is used. Air entrainment through inadvertent patient movement or an ill-fitting nasal mask as well as variations in scavenging power are factors that contribute to significantly less N_2O being available for the intended purpose of analgesia and anxiolysis than flowmeter settings suggest.

Despite this variability in measured end-expired N_2O concentrations, the literature describing the use of N_2O for its various outpatient applications is rife with recommendations and clinical conclusions based on flowmeter settings alone.[1,22-27] Therefore, it is questionable whether the reported clinical outcomes are solely the result of the delivered N_2O or partially attributable to a placebo effect.

Based on the aforementioned studies, there should be a significant difference in alveolar N_2O concentrations when 30% N_2O is delivered through an endotracheal tube by an anesthesia machine vs. 30% N_2O delivered from a flowmeter through a nasal mask. While a methodology to measure end-expired gas concentrations in the awake patient was developed in a previous pilot study,[21] it was not used under real-life conditions.

The purpose of this study was to continuously record inspired and end-expired alveolar nitrous oxide concentrations during operative dental treatment of 6- to 9-year-olds in a traditional dental setting and to compare them to the concentrations dispensed by the N_2O delivery system's flowmeter. This study's results also may help to promote an understanding of the considerable differences in N_2O concentrations provided by the different delivery systems used in the operating room and outpatient setting and to present a methodology for evaluating more objectively the effects of N_2O applications.

Methods

Following approval by the Colorado Multiple Institutional Review Board (#07-0131), 23 healthy 6- to 9-year-olds requiring routine operative dental treatment with N_2O were recruited from the continuous outpatient pool of The Children's Hospital Dental Center. A dental N_2O delivery system with a standard analog flowmeter (MDS Matrx, Midmark Corp, Orchard Park, NY) was recently calibrated by the manufacturer and utilized for all subjects. The gas mixture was delivered through standard nasal masks (Matrx, Midmark Corp) connected to the flowmeter via a scavenging circuit. The scavenging power was adjusted to -5 inches Hg and maintained at this level throughout the entire procedure.

Subjects underwent placement of a probe positioned 1.5- to 2.5-inches deep into the nasopharynx. The probe was modified from a 1.5-mm diameter replacement sample line (no. 625N, Criticare Systems Inc., Waukesha, WI) to a 2.5-mm wide and 7-mm long solid, blunt polyvinylchloride tip. This rigid and elevated ending prevented the probe from picking up secretions or being suctioned against the nasal mucosa. In cases of sensitivity during probe insertion, 1 to 2 puffs of a lidocaine 4% and oxymetazoline 0.05% mixture were sprayed into the nostril into which the probe was inserted.

Inspired and end-expired O_2 and N_2O, as well as related pressure of end-tidal carbon dioxide ($P_{ET}CO_2$), were measured during the course of the subjects' dental treatment with a Criticare Poet® IQ2 Model 8500 Agent Gas Monitor (Criticare Systems, Inc., Waukesha, WI). All data were recorded on a computer using HyperAccess® software (V 8.4; Hilgraeve Inc., Monroe, MI) and later converted to a spreadsheet file (Microsoft Excel 2007, Microsoft Inc., Redmond, WA).

At the beginning of the procedure, 100% O_2 was administered for 2 minutes at a rate of 3 L/minute to achieve baseline values. If necessary, the flow rate was adjusted to meet the subject's breathing volume. N_2O was then introduced at a concentration of 50% for 5 minutes and lowered to 30% for the duration of treatment. These noted concentrations refer to the setting of the dial on the N_2O delivery system.

End-inspired and expired alveolar N_2O and O_2 concentrations and $P_{ET}CO_2$ were analyzed continuously from the nasopharyngeal probe. At the termination of dental treatment and after cessation of N_2O administration, 100% O_2 was administered a flow rate of 5 L/minute to achieve a washout of the remaining N_2O.

Following placement of the nasal probe and apart from the continuously measured parameters, all planned restorative dental treatment was performed in the same fashion as it is customarily done. Each subject received local anesthesia as indicated for the type of procedure to be performed, and a non-latex rubber dam was placed for the duration of the operative treatment. For data analysis, the entire procedure was divided into 4 phases:

1. the period when nasal mask was placed and 100% O_2 was given until 50% N_2O was added (2 minutes counted back from start of phase 2);
2. from the time 50% N_2O was given until it was reduced to 30% (5 minutes);
3. the period N_2O was reduced to 30% until it was discontinued (variable duration);
4. the time 100% O_2 was given after N_2O was discontinued to wash out any remaining N_2O (an additional 5 minutes).

Measurements were obtained in 5-second increments for 6 variables from each subject: (1) inspired N_2O concentrations; (2) inspired O_2 concentrations; (3) respiratory rate; (4) end-expired O_2 concentrations; (5) end-expired N_2O concentrations; and (6) $P_{ET}CO_2$. Two of the 23 subjects with median end-expired CO_2 measurements outside the normal range ($P_{ET}CO_2$ 34±3 mmHg) for this altitude were excluded.

Phases 1, 2, and 4 were of equal length for each subject, whereas phase 3 varied by subject depending on the restorative treatment's duration. The number of data points per patient was: 24 for phase 1; 60 for phases 2 and 4; and 60 to 295 for phase 3.

Statistical analysis

For each gas, the mean value across all patients was calculated at every 5-second time point and graphed with a 95% confidence interval (**CI**). Where 95% CI half-width values are reported in the text, the CI is the average across time for all CIs. Data in phase 3 after 16.5 minutes were excluded from analysis, because fewer than 5 patients had data available. Measured mean end-expired P_{ET} CO_2 was used to assess the data's validity, and patients with average and interquartile range (**IQR**) values outside of the expected range of 34±3 mm Hg were excluded from all analyses.

The respiratory rate is summarized across the study period with means and average CI half-widths. Patterns of inspired and expired end-tidal O_2 concentrations are described by phase as the IQR of differences in means over time.

In phase 2, the time at which the patient-specific and average maximum end-expired N_2O concentrations occurred was identified. The first occurrence of the maximum was identified as a leveling-off point and used to divide the observations in phase 2 for modeling purposes. A linear mixed effects model was fit to the data to quantify differences in the slope of end-expired N_2O concentrations over time before and after the leveling-off point. Time to complete end-expired N_2O concentration elimination in phase 4 is described with percentiles (minimum, median, maximum).

Results

Measured mean end-expired P_{ET} CO_2 was within the expected range of 34±3 mm Hg in 21 subjects. All data for the 2 subjects whose average end-tidal P_{ET} CO_2 were not within this range were excluded from analysis. Figure 1 displays the average respiratory rate for all remaining 21 subjects.

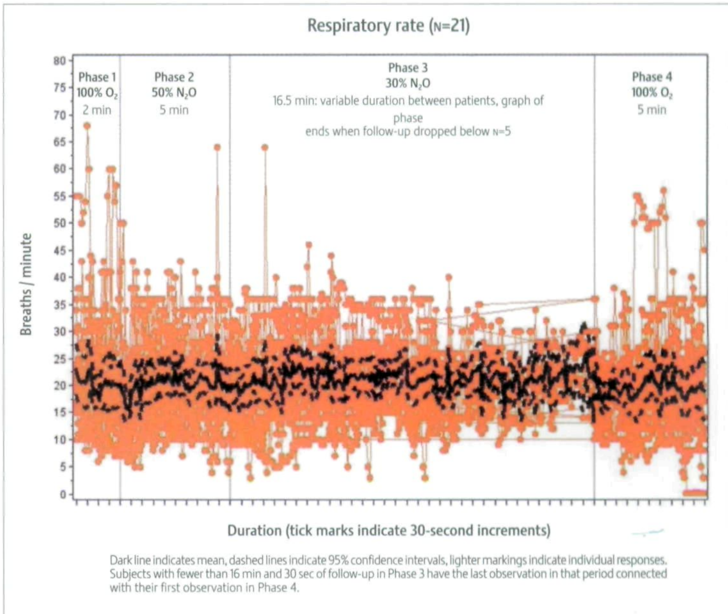

Figure 1. Average respiratory rate for all remaining 21 subjects.

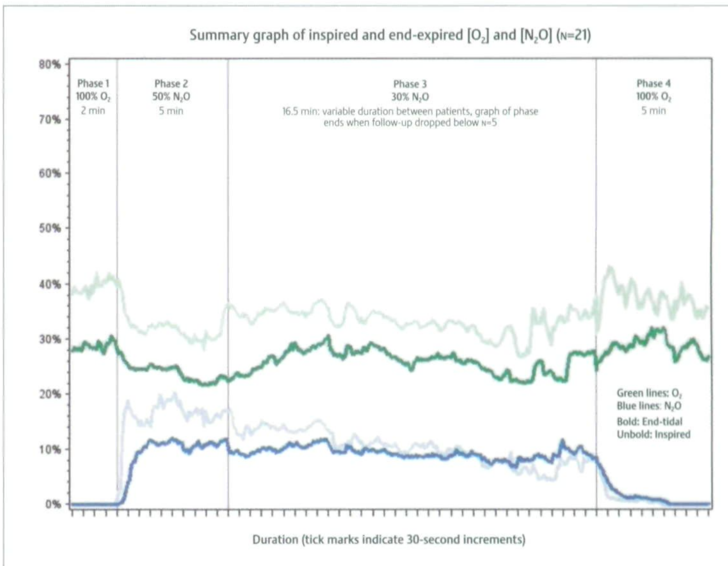

Figure 2. Mean inspired and expired end-tidal oxygen (O_2) and nitrous oxide (N_2O) concentrations.

The average rate of 20.7 (C±3.4) breaths per minute was observed over the course of the entire treatment.

Mean inspired and expired end-tidal O_2 and N_2O concentrations obtained from all subjects in 5-second increments during the entire experimental period of the restorative procedure are summarized in Figure 2. CIs for all measurements widened toward the end of phase 3 as sample size decreases (data not shown).

Inspired gas measurement rose and fell more noticeably at the start of each phase when gas levels were adjusted and were more variable during each phase, whereas end-expired gas measurements varied more smoothly with time. Inspired O_2 concentrations were, on average, 8% higher (IQR of means over time=approximately 6-9%) than expired concentrations. In contrast to N_2O, both oxygen curves moved in a parallel fashion. When 100% O_2 was administered during phases 1 and 4, expired O_2 concentrations were similar (29%±5% CI and 29%±4% CI, respectively. We observed an average of 24%±3% CI O_2 concentrations during phase 2 when 50% O_2 was delivered and 26%±4% CI during phase 3 when 70% O_2 was in the gas mixture.

Phase 2 end-expired N_2O concentration trend and saturation point. The pattern of end-expired N_2O concentrations observed during phase 2 was that it began at zero, then, on average, increased with a quadratic shape. While individual patients reached their own maxima at points between 60 and 270 seconds, the trend across all patients leveled off at 90 seconds at 11%±2% CI (Figure 3).

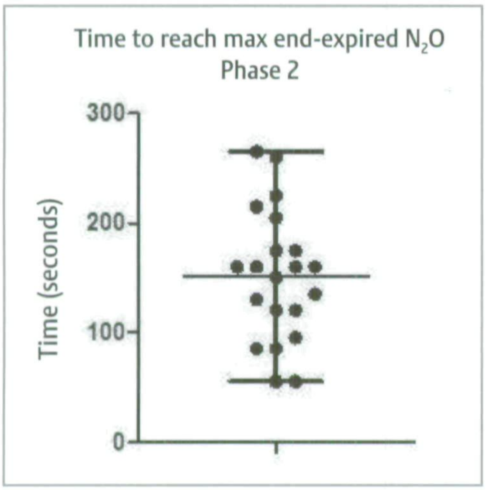

Figure 3. End-expired nitrous oxide concentrations trend and saturation point during phase 2.

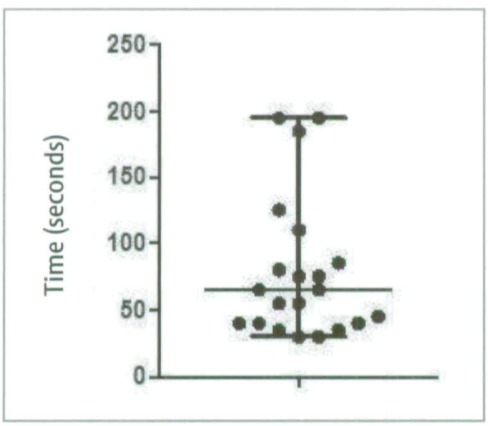

Figure 4. Time to complete nitrous oxide (N_2O) elimination in Phase 4.

Phase 3 end-expired N_2O concentration trend. The plot of end-expired N_2O concentrations in phase 3 was visually inspected for changes in trends during the phase. A linear mixed effects model was fit to the data to quantify the slope of end-expired N_2O concentrations. A pattern in end-expired N_2O concentrations during this phase was not clearly visible. From the mixed-effects model, the linear relationship between time and end-expired N_2O concentrations was negative, with 1 additional minute associated with a decrease of 0.18% end-expired N_2O concentrations, on average. During phase 3, end-expired N_2O concentration was found to be approximately 9%±3% CI, on average. The end-expired N_2O concentration after the saturation point 90 seconds into phase 2 and during the first 16.5 minutes of phase 3 was 9.5%±3% CI.

Phase 4 time to complete N_2O elimination. The duration from the N_2O discontinuation to the moment of zero detectable end-expired N_2O is summarized for all 21 subjects in Figure 4. The minimum time necessary to achieve zero detectable end-expired N_2O concentration was 30 seconds; 50% of all patients had undetectable end-expired N_2O concentrations at 1 minute, and the maximum time was 195 seconds.

Discussion

While the absolute concentrations of N_2O may not matter for many clinicians as long as they obtain the intended results, this study could offer an answer for why N_2O application in some patients does not have the desired effect. Its results provide a basis for a better understanding between anesthesiologists and dentists as to their different perceptions of what delivery of a 50% N_2O/50% O_2 gas mixture means. In general anesthesia, where gases are delivered through an ET tube, only minimal air entrainment occurs. Significant reductions have been described, however, in situations where the N_2O/O_2 mixture was delivered via a nasal mask.[19-21] In an analog lung model, a 32% reduction of N_2O concentration was noted from mask to subglottic level[20] whereas in an vivo study with 25 adults, a 65% reduction of the delivered N_2O was found.[19] In contrast to the former study, the use of modern gas sampling and analyzing technology in 15 adult volunteers revealed a 31% reduction of N_2O concentration in the nasal mask, while end-expired N_2O concentrations were found to be 51% lower than the flowmeter indicated.[21]

The present study is different from the aforementioned others because the subjects were 6- to 9-year-olds, and it took place under normal clinical conditions. The gas concentrations were measured during the course of a typical restorative treatment session with a rubber dam in place. We used a rapid induction technique and administered 50% N_2O initially and reduced it after 5 minutes to 30%. During the entire N_2O administration that lasted a combined average of 21.5 minutes in phases 2 and 3, a steady N_2O concentration of 11%, on average, was recorded. This represented a 78% and 63% decrease, respectively, in N_2O concentrations that were dispensed by the dental N_2O delivery system. The fact that a rubber dam was routinely placed at the beginning of phase 3 after local anesthesia was applied may explain why the decrease in N_2O concentration was less than 2% during this phase, despite the reduction of delivered N_2O concentration from 50% to 30%.

Our results suggest that the rapid induction technique did not result in a high initial N_2O concentration and that a saturation point of 11% was reached after 90 seconds in most subjects. This end-expired N_2O concentration did not change outside of the 95% confidence range after N_2O delivery was reduced to 30% after 5 minutes. The average respiratory rate for all patients was 21±3 breaths per minute (**bpm**) and thus comparable to the 50% percentile standard resting respiratory rates of 19-21 bpm for 6- to 9-year-olds.[28] This recorded normal respiratory rate with a small variability indicates that the delivered N_2O levels were clinically effective and that the patients were comfortable despite the ongoing dental treatment.

Typical patient movements did not significantly affect the gas delivery. Although inspired gas measurement showed a higher amplitude, end-expired gas measurements were fairly steady since the gas distribution throughout a subject's body into tissues of the brain, muscle, and fat acted as a buffer. A similar stabilizing effect was observed in end-expired N_2O concentrations after inspired gas concentrations were reduced: expired gas concentrations were higher than inspired levels, while the opposite was true during the uptake phase.[21]

Analysis of the washout phase after N_2O was completely discontinued showed that the minimum time necessary to achieve zero detectable end-expired N_2O concentration was 30 seconds, while the maximum time was 195 seconds. Based on these results, the practice of delivering 100% oxygen for 5 minutes after N_2O appears safe and adequate.

The use of a size 10 gauge oxygen catheter located in the nasopharynx for comfortable and successful oxygen administration to adult patients in the ICU and for gas sampling has been documented.[29,30] The methodology of measuring end-expired gas concentrations in the nasopharynx of awake and non-intubated patients has been validated for adults.[21,29] In these studies, the sampling probe was inserted either 5 to 8 cm beyond the nares or to a depth equaling the distance from the ala nasi to the tragus. Others inserted a PVC catheter close to the laryngeal inlet, for an average distance of 19 cm in males and 16 cm in females, and then withdrew it in 2 cm increments to 11 and 8 cm, respectively. They found that the position of the sampling catheter or whether a patient was breathing through the nose or mouth did not result in clinically relevant differences.[31] Our insertion depth of 1.5 to 2.5 inches in 6- to 9-year-olds appears appropriate in this context. The continuous recording of physiologic end-tidal carbon dioxide validates the adequacy of alveolar ventilation in all studies, including ours.

This study took place at an elevation of 5,390 feet, resulting in an overall lower average end-expired P_{ET} CO_2 (34 mm vs. 39 mm Hg). A comparable P_{ET} CO_2 of 33.6±2.8 mmHg was reported for residents living at an elevation of 6,340 feet.[32] Similarly, end-tidal N_2O concentrations were 63% lower at an elevation of 5,390 feet vs. a 50% reduction noted at 1,000 feet.[21] The pain threshold, as an indirect measure for the clinical effects of N_2O, increased by approximately 72% at sea level after administration of a 50% N_2O/50% O_2 gas mixture, but increased only 19% at 10,820 feet.[33]

Our sample size of 21 subjects was enhanced by repeated measurements every 5 seconds during treatment, providing a complete picture of the entire course of a patient-specific dental session when N_2O is utilized. The fact that this study was conducted at a higher altitude makes the results not directly comparable to lower elevations, where measured end-expired concentrations will be moderately higher.

This is the first known evidence-based study that objectively shows the average time needed to reach clinically relevant, maximum end-expired N_2O concentrations when using the rapid induction method in children. Its results help increase the understanding of N_2O applications with dental N_2O delivery systems using nasal masks and standard flowmeters. The results clearly demonstrate that gas concentrations dispensed by the flowmeter are significantly different from end-expired alveolar gas concentrations. We must realize, however, that only the latter are responsible for the clinical effects.

Future studies could employ this technique to compare the effectiveness of different nasal mask types to deliver high end-expired gas concentrations. Currently, only indirect conclusions can be made by comparing the leakage from scavenger mask systems.[34,35] In this context, the effect of the rubber dam should be further evaluated. Our study used the rapid induction technique. Since a clinician's desire is to increase efficiency, in a future trial it would be worthwhile to evaluate the difference in time needed to reach the saturation concentration when the titration technique is used. This method could be used in future studies to provide objective data to assess behavioral or other outcomes from N_2O application in outpatient settings.

Conclusions

Using a previously developed and described methodology, inspired and end-expired alveolar nitrous oxide and oxygen concentrations and pressure of end-tidal carbon dioxide values could be successfully recorded during complete operative dental treatment sessions of 6- to 9-year-old awake, non-intubated children in the traditional dental setting. Furthermore, based on this study's results, the following conclusions can be made:

1. At an altitude of 5,390 feet, delivery of a 30% N_2O/70% O_2 mixture resulted in an end-expired N_2O concentration of 11% to 12%. This represents a 63% decrease in the N_2O concentration that is dispensed by the flowmeter of a dental N_2O delivery system.
2. The average time to reach maximum N_2O saturation after rapid induction with a 50% N_2O/50% O_2 gas mixture was 90 seconds (range=60-270 seconds).

3. After cessation of N_2O delivery and delivery of 100% O_2 to flush out remaining N_2O from the alveoli, the times necessary to achieve zero detectable end-expired N_2O concentration were: 30 seconds (minimum); 60 seconds (median); and 195 seconds (maximum).

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