Effectiveness and Safety of Elevated Dosages of Nitrous Oxide on Behavior Management in Pediatric Dentistry

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Objective: *To determine if administering a higher dosage of nitrous oxide (>50%), with a nasal hood in pediatric dental restorative procedures, can allow for a safe and more cooperative experience for the pediatric patient as measured by observable adverse reactions and the Frankl Behavior Rating Scale.* ***Study Design:*** *A retrospective chart review was completed of 200 patients total, 100 for each nitrous oxide (N_2O) dosage group (≤50% vs >50%). Adverse reactions and The Frankl Behavior Rating Scale during pediatric restorative procedures with N_2O were compared between the two dosage groups.* ***Results:*** *There were few adverse reactions for both nitrous oxide groups (≤50% vs >50%) and there was no statistical difference in the Frankl Behavior Rating Scale for each group.* ***Conclusions:*** *Patients given more than 50% of nitrous oxide were not found to have an increase in adverse events. Higher concentrations of nitrous oxide (>50%) were not found to be associated with a better behavior score when completing pediatric restorative procedures.*

Keywords: *Behavior, anxiolysis, nitrous oxide, children.*

INTRODUCTION

Since its discovery in 1772 by Joseph Priestly and its utilization by Horace Wells in 1844 for dental extractions, inhalational analgesia through the administration of nitrous oxide gas (N_2O) has become a common practice in dentistry[1]. Many young patients, including those with special needs, have limitations in managing their anxiety, presenting challenges that must be circumvented in order to provide necessary dental care. While dentists are adept at alleviating these difficulties, in many instances pharmacological intervention is required[2]. The use of N_2O along with behavioral guidance is an efficient method of assuaging dental phobias such as fear of needles and handpieces [3].

Nitrous oxide is a colorless, non-irritating gas with a mild, sweet odor. It is an inert inorganic compound, non-explosive, non-flammable, but facilitates the combustion of other substances [4]. There are varying theories on N_2O's precise mechanism of action. The leading theory suggests that inhalational agents bind to proteins inside neuronal membranes and thus modifies ion fluxes and then synaptic transmission [4]. The effect seems to be a result of the release of endogenous opioid peptides (enkephalins) that activate opioid receptors and descending gamma-aminobutyric acid (GABAA) receptors, as well as noradrenergic pathways that moderate processing at the spinal level[2,5]. The anxiolytic effect appears to be due to the direct or indirect activation of GABAA receptors through benzodiazepine binding sites[5]. Inhaled anesthetic gases such as nitrous oxide are absorbed and disseminated due to pressure gradients and level out when the tensions of inspired gas equal those in alveoli, blood, and tissues[4]. The lower the solubility of a gas in blood, the more rapidly the absorption and dissemination of the gas occurs. Nitrous oxide

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has a very low blood solubility, does not bind to hemoglobin, does not undergo biotransformation, and therefore has the fastest onset of action and elimination of inhaled anesthetic agents[4].

Nitrous oxide and oxygen inhalation is generally regarded as a safe and efficacious technique to reduce anxiety and produce analgesia.[2] The safety of the gas mixture is due to the low potency of the gas and the additional supplemental oxygen that is provided to the patient. The minimum alveolar concentration (MAC) of N_2O is 104. Nitrous oxide causes a slight decrease in cardiac output; however, it also slightly increases peripheral resistance, maintaining blood pressure[1,4].

Nitrous oxide is not without its drawbacks however. It is stated there are no *absolute* contraindications by some to the use of N_2O, but there are multiple *relative* contraindications. These include upper respiratory tract infections, pneumothorax, intraocular gas injections, bowel obstruction, recent otitis media, chronic obstructive pulmonary disease, the first trimester of pregnancy, treatment with bleomycin sulfate, methylenetetrahydrofolate reductase deficiency, cobalamin deficiency, and nasopharyngeal obstruction[1, 2, 7]. Some side effects can include nausea, vomiting, and diffusion hypoxia (which is more theoretical)[5, 8, 9, 10].

Studies on the ratio of nitrous oxide to oxygen administered in the medical and dental setting have mostly focused on dosages of 50% or less of N_2O and 50% or more of oxygen[9- 13]. Langa utilized a dosage of 70% N_2O to 30% O_2 for dental extractions, often without using local anesthetic.[10] After noting many instances of nausea, vomiting, and hallucinations in patients, Langa developed the technique most often used today: 50% N_2O and 50% O_2 [10].

Many studies in medicine utilize a full mask that covers both the nose and oral cavity, allowing for maximum inhalation of the agent[12,13]. There are fewer studies completed with the pediatric dental population with utilization of nitrous oxide. In dentistry, because access to the oral cavity is necessary, a nasal hood is utilized for the administration of the gas. Leakage of N_2O can occur from the poorly fitting nasal mask and due to breathing through the mouth. Dead space and the ventilatory status of the patient also affect how much N_2O is actually received by the patient into the lungs. Therefore, despite equipment readings indicating, for example, 70% nitrous oxide being delivered, the actual concentration delivered to alveoli is unlikely to exceed 30% to 50%[4,5].

There is a sparsity of research conducted on the use of high concentrations of nitrous oxide during dental procedures with a pediatric population. Despite the lack of evidence against high dose administration, current dental practice is to utilize concentrations 50% or less of nitrous oxide. The overall purpose of the study was to determine if administering a higher dosage of nitrous oxide (>50%), with a nasal hood, can allow for a safe and more cooperative experience for the pediatric patient as measured as a Frankl behavior rating.

MATERIALS AND METHOD

This retrospective study, IRB approved, examined the overall behavior and adverse reactions of patients during restorative pediatric dental procedures while being administered N_2O. Enrollment criteria included healthy children (American Society of Anesthesiologists patient status Class I or Class II) requiring restorative procedures including single surface and/or two surface fillings, stainless steel full coverage crowns, as well as minor surgical procedures including tooth extractions. This study consisted of randomly and retrospectively reviewing 5 years' worth of patient records from Bon Secours Pediatric Dental Associates from June 28, 2013 to June 28, 2018 where 100 procedural notes from each dosage group (≤50% vs. >50%), totaling 200, were collected. One patient was omitted from the N_2O ≤50% group due to inaccurate charting. The clinical notes were analyzed in order to review two specific criteria: Frankl Behavioral Rating Scale score recorded by the dental provider in order to assess the effectiveness of N_2O; and any observed adverse reactions that occurred during the procedure in order to assess the safety of N_2O.

The Frankl Behavioral Rating Scale is based on a rating of 1 to 4 (Table 1). Behaviors with a rating of 1 (—) are "definitely negative" and consist of refusal of treatment, forceful crying, fearfulness, or any other overt evidence of extreme negativism. Behaviors with a rating of 2 (-) are "negative" and consist of reluctance to accept treatment, uncooperative, some evidence of negative attitude but not pronounced (sullen, withdrawn). Behaviors with a rating of 3 (+) are "positive" and consist of acceptance of treatment, cautious behavior at times, willingness to comply with the dentist, at times with reservation, but patient follows the dentist's directions cooperatively. Behaviors with a rating of 4 (++) are "definitely positive" and consist of good rapport with the dentist, interest in the dental procedures, laughter and enjoyment[14]. All providers are trained in the Frankl Behavior Rating Scale prior to treating patients.

Data Analysis

The chi-square test of independence was used to compare the effects from the two nitrous oxide dosages (50% or less and greater than 50%) on patients' behavior (SPSS, version 24)[15]. This test was appropriate because the effects on patients were categorized into two independent dimensions. Using the Frankl Behavioral Rating

Table 1: Description of the Frankl Behavior Rating Scale

Frankl Behavior Rating	Description	Definition
1	—	Definitely negative. Refusal of treatment, forceful crying, fearfulness, or any other overt evidence of extreme negativism
2	-	Negative. Reluctance to accept treatment, uncooperative, some evidence of negative attitude but not pronounced (sullen, withdrawn)
3	+	Positive. Acceptance of treatment; cautious of behavior at times; 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, interest in dental procedures, laughter and enjoyment.

Scale the effects on patients were categorized within two independent dimensions: desirable or successful behavior effect (coded 1 for + and ++) or undesirable or failed behavioral effect (coded 0 for – and —)[16].

Adverse reactions were also observed and were divided into mild (headache, nausea, vomiting) and severe (hypoxia [O_2 <94%], unconsciousness, change in systolic blood pressure +/- 20 from baseline, and bradycardia [<60 BPM]). The ages of the patients and the duration of time the N_2O was administered were noted as well.

RESULTS

There were few adverse reactions for both the groups, children given more than 50% nitrous oxide versus less than 50% nitrous oxide (Table 2). For the group of children receiving more than 50% nitrous oxide, there was one mild adverse reaction and one severe adverse reaction. For the group of children receiving less than 50% nitrous oxide there were no children with mild adverse reactions and three with severe adverse reactions.

The count of undesirable versus desirable behaviors in children when given nitrous oxide at concentrations either above or below 50% are shown in Table 2. For the group given concentrations of nitrous oxide less than 50%, there were 11 (11.1%) patients with undesirable behaviors versus 88 (88.9%) patients with desirable behavior outcomes. For the group given concentrations of nitrous oxide more than 50%, there were 10 (10%) patients with undesirable behaviors versus 90 (90%) patients with desirable behavior outcomes.

Table 3 shows the observed and expected frequencies as well as statistics about the impact of the nitrous oxide dosage on the patients. As reflected on Table 3, at a 95% confidence level (alpha=.05), a chi-square test of these frequencies was not statistically significant. As a result, we found no difference in the Frankl score of pediatric patients between the greater than 50% and the 50% or less dosages.

Table 2: Count of Frankl Score and Adverse Reactions in Children When Given Nitrous Oxide

		Frankl Score		Adverse Reaction	
		Undesirable	Desirable	Mild	Severe
$N_20 \leq 50\%$	Count	11	88	1	1
	% within group	11.1%	88.9%	1%	1%
$N_20 > 50\%$	Count	10	90	0	3
	% within group	10%	90%	0%	3%
Total	Count	21	178	1	4

Table 3: Chi-square Analysis of Frankl Score

	Value	df	Asymptomatic Significance (2-sided)	Exact Sig (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.065[a]	1	.799		
Continuity Correction	.001	1	.981		
Likelihood Ratio	.065	1	.799		
Fisher's Exact Test				.822	.490
Liner-by-Linear Association	.065	1	.799		
N of Valid Cases	199				

0 cells (0.0%) have expected count less than 5. The minimum expected count is 10.45.

DISCUSSION

Nitrous oxide is a safe and effective adjuvant to behavior management for children in the dental setting in its anxiolytic attributes and in reducing the painful stimuli of anesthetic injections and restorative procedures such as fillings and crowns. Its utilization is beneficial in creating a less stressful atmosphere for receiving dental treatment, thereby protecting the developing psyche of pediatric patients. There are studies for the adult population in dentistry with administration of nitrous oxide and many studies in medicine, but studies in pediatric dentistry are lacking.

Additional studies have found similar results of no significance in adverse events from administering N_2O at a concentration greater than 50% compared to a concentration of 50% or less. Zier *et al* (2010) evaluated the level of sedation and adverse events in children receiving N_2O for procedural sedation in medicine through their children's hospital system[17]. The results of their retrospective chart review showed no difference in the level of sedation achieved or the number of adverse events resulting from administering N_2O at a concentration greater than 50% compared to a concentration of 50% or less[17]. The safe delivery of nitrous oxide at a concentration of 70% has also been studied in the emergency department where children undergo minor procedures.[18] It was found that N_2O, when administered with a full-coverage face mask, is a safe analgesic in children older than 12 months, and it may be safely used in concentrations of up to 70% after appropriate training of the practitioner[18].

While this study did not find a difference in behavior management, other studies have found higher levels of nitrous oxide to be beneficial for completion of dental procedures. De Veaux *et al* (2016) performed a study on patients 24 to 77 years old and the effects of different nitrous oxide/oxygen concentrations on the hypersensitive gag reflex, a protective reaction that can cause dental procedures to be much more challenging or even impossible[19]. They found that using a dosage of 70% nitrous oxide and 30% oxygen allowed all patients with this reflex to tolerate the placement and holding of a digital x-ray sensor long enough to take a periapical radiograph[19]. In medicine, Kanagasundaram *et al* (2001) found that administering 50-70% nitrous oxide to a level of consciousness where the patient can maintain verbal and tactile communication is effective in alleviating distress during painful procedures (such as lumbar punctures and bone marrow aspirates), with minimal side effects and short recovery time.[20]

Limitations in this study include not differentiating between the different dental procedures and use of local anesthesia, and if a higher concentration of nitrous oxide was more effective for particular procedure as in the Veaux *et al* (2016) study. Additionally, the level of sedation was not assessed in this study due to its retrospective nature and this

data not being collected. Future studies should assess the type of dental procedure performed, local anesthesia use, and the level of sedation obtained.

For future research, a prospective study focusing on the analgesic and anxiolytic effect of nitrous oxide and specific behaviors that might occur during the administration of local anesthetic is recommended. This could be analyzed by using the North Carolina Behavioral Rating Scale.[21] These studies should breakdown Frankl Behavioral scores into different key moments of the dental procedure including pre-operative, during local anesthetic administration, during treatment procedure, and post-operative recovery time. The type of dental procedure should also be collected and level of sedation. Additionally, it would be useful to look at the average nitrous percentages in each group studied, the exact percentage of nitrous administered, to see if there is a difference.

CONCLUSIONS

Based on this study's results the following conclusions can be made:

- Patients that are administered more than 50% nitrous oxide were not found to be at an increased risk for adverse events.
- Higher concentrations of nitrous oxide (>50%) were not found to be associated with a better behavior score.
- Prospective studies are needed to better understand the effects of nitrous oxide at higher concentrations in pediatric dentistry.

Acknowledgments

The authors wish to thank Benjamin Djeukeng PhD for his assistance in the data analysis.

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