Effects of nitrous oxide on diazepam sedation of young children

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Abstract

This study was performed to test the hypothesis that nitrous oxide augments the effects of diazepam sedation of young children by reducing crying and movement and improving the overall quality of sedation. Twenty-four children (mean age of 32 months) were sedated on two occasions with two different treatment regimens. All subjects received a standard oral dose of 0.5 mg/kg of diazepam with and without nitrous oxide during each of two treatment visits. During one visit, the subjects received 50% nitrous oxide and 50% oxygen for the first 20 min followed by 100% oxygen for the balance of the procedure and, during the second visit, the reverse regimen was used. All subjects were restrained in a Papoose Board™ (Olympic Medical, Seattle, WA) with an auxiliary head restraint. Successful sedation, as evidenced by lack of crying or movement that interrupted treatment, occurred in 83% of administrations. Vital signs remained essentially unchanged throughout all treatment with the exception of transitory elevation of the pulse and respiratory rates, which usually occurred when the mouth prop was inserted, local anesthesia was administered, and the rubber dam was placed. When the evaluation of the overall sedation was compared with and without nitrous oxide, it was better with nitrous oxide 56% of the time, worse 13% of the time, and the same in the remaining 31% of the comparisons. It is concluded that nitrous oxide may slightly augment the effect of diazepam sedation of young children, but it does not do so uniformly for all children receiving sedation. (Pediatr Dent 18:236–41, 1996)

A variety of drug regimens are used when young children are sedated for dental treatment.[1] Benzodiazepine drugs have been advocated because they produce less sleep, have a wide margin of safety with few side effects, and may have anterograde amnesic effects.[2–8] These agents frequently are supplemented with 30–50% nitrous oxide and oxygen to increase the sedative effect. Despite widespread use of this technique, there has been relatively little clinical study of the influence of nitrous oxide on sedation. This study was performed to test the hypothesis that nitrous oxide would augment the effects of oral diazepam used to sedate young children for dental treatment.

Method

Subjects

Twenty-four children (19 male and five female), ranging in age from 25 to 44 months with a mean age of 31.8 months and a mean weight of 31 lbs (range 24–36 lbs), participated in the study. These children were selected consecutively as they presented for treatment. Requirements for participation were: 1) the child was in good health; 2) two separate restorative dentistry appointments were required; and 3) sedation was necessary to manage uncooperative behavior as determined during the detailed oral examination, which included necessary radiographs.

Medications

All subjects received an oral dose of 0.5 mg/kg of diazepam for both treatment visits. At the first appointment, subjects were randomly assigned to receive either regimen A or B for the first appointment, with the alternate regimen administered during the second appointment. Consequently, a crossover design was used with each subject serving as his own control and the 24 subjects participated in 48 treatment sessions. Treatment regimen A consisted of 50% nitrous oxide and 50% oxygen for the first 20 min of treatment, or 65 min after drug administration, followed by 100% oxygen for the remainder of the appointment, which was usually 40–60 min. Treatment regimen B consisted of 100% oxygen for the first 20 min followed by 50% nitrous oxide and 50% oxygen. The 20-min time period was selected for the time of gas change (nitrous oxide turned on or off) as it followed the more stressful procedures — mouth prop insertion, injection, and rubber dam application — thus providing the opportunity to examine the effect of nitrous oxide in more and less

stressful situations. A Brown™ scavenging hood (Porter Instrument Company, Hatfield, PA) was used during all procedures and all children were restrained in a Papoose Board™ (Olympic Medical, Seattle, WA) with auxiliary head restraint. Subjects were without food or fluids for at least 4 hr prior to treatment. After each subject arrived, vital signs and behavior were evaluated then oral diazepam was administered. On 15 occasions, the child was coaxed into drinking the diazepam solution, and for the remaining 33, the solution was administered orally with a syringe. The dosages of diazepam ranged from 6 to 8 mg with a mean of 7.3 mg. The child then remained with the parent for 45 min, during which the vital signs were monitored at 15-min intervals. After 45 min, the child was transferred to the operatory for the start of treatment.

Evaluation

The degree of sleep, body movement, crying, pulse, respiration rate, and color were evaluated before, during, and after operative procedures. In the operatory these variables, together with the blood oxygen saturation level, were rated by an independent observer and recorded during mouth prop insertion, administration of local anesthesia, placement of rubber dam, and every 15 min thereafter using separate rating scales (Table 1). Each behavioral rating represented a summary of behavior exhibited since the previous rating. An overall rating was made using a separate scale for each of the two segments of treatment, that is, before and after the gas change (Table 1). Both the operator and the independent observer were kept blind as to whether the patient was receiving nitrous oxide or 100% oxygen by having a third person responsible for all settings to the nitrous oxide machine. Further, the flow meters were kept covered at all times. An average of 6 months later, a consensus rating was made by two investigators (MH and SK) from videotapes of the procedures to verify the reliability of the rating scales, which had been established previously.[9,10]

In the operatory, pulse and blood oxygen saturation level were continuously monitored with the Nelcor™ pulse oximeter; respiration was monitored with the Trimed™ apnea monitor (Trimed Inc, Bellevue, WA) connected to the nitrous oxide nasal hood. A precordial stethoscope also was used to monitor respiration.

Data analysis

This experiment was designed so that each subject served as his own control with the same time of day, the same operator, and similar types of procedures performed during both treatment sessions. The independent variable was the administration of nitrous oxide and the dependent variable was the effectiveness of sedation as measured by the degree of crying and movement that interfered with treatment. Since the rating scales used the ordinal scale of measurement with related samples, the nonparametric sign test was used to compare the groups for statistically significant differences at the 0.05 level of significance.

TABLE 1. RATING SCALES FOR SLEEP, MOVEMENT, CRYING AND OVERALL BEHAVIOR

Rating Scale for Sleep		*Score*
Fully awake, alert		1
Drowsy, disoriented		2
Asleep		3
Rating Scale for Movement		
Violent movement that interrupts treatment		1
Continuous movement that makes treatment difficult		2
Controllable movement that does not interfere with treatment		3
No movement		4
Rating Scale for Crying		
Hysterical crying that interrupts treatment		1
Continuous, persistent crying that makes treatment difficult		2
Intermittent, mild crying that does not interfere with treatment		3
No crying		4
Rating Scale for Overall Behavior		
Aborted	No treatment	1
Poor	Treatment interrupted, only partial treatment completed	2
Fair	Treatment interrupted but eventually all completed	3
Good	Difficult, but all treatment performed	4
Very Good	Some limited crying or movement, e.g. during anesthesia or mouth prop insertion	5
Excellent	No crying or movement	6

Results

The results of this study are presented in Figs 1, 2, and 3 and in Tables 2 and 3. Since each of the 24 sub-

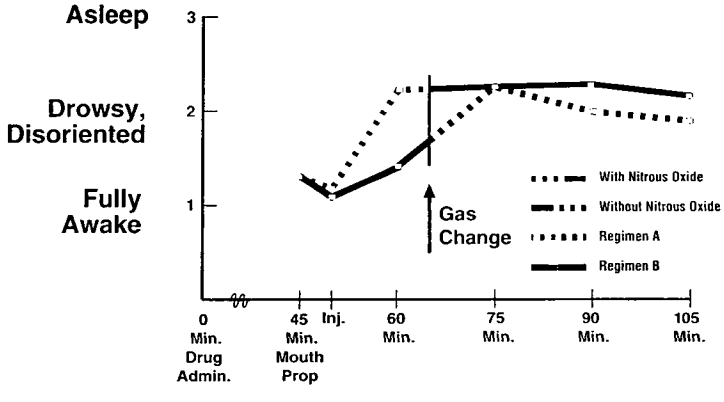

Fig 1. Evaluation of sleep.

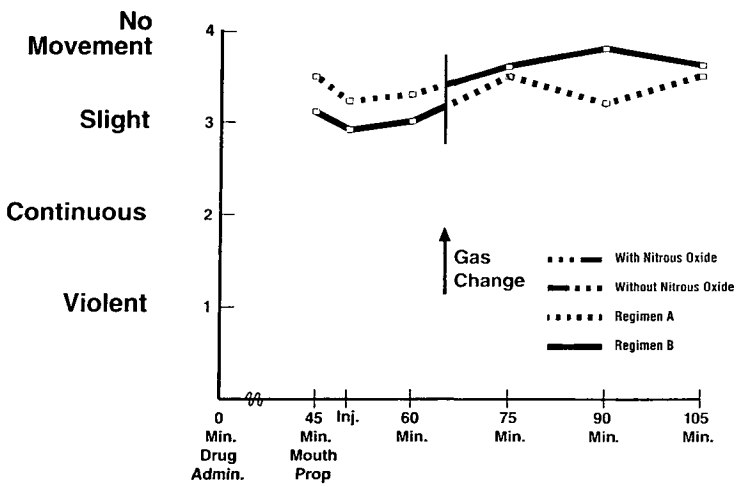

Fig 2. Evaluation of movement.

TABLE 2. DISTRIBUTION OF RATINGS (PERCENTAGE) FOR THE VARIOUS VARIABLES MEASURED

		Nitrous Oxide Administration	
Evaluation	*Score*	*With*	*Without*
Sleep			
Asleep	3	37	22
Drowsy	2	17	19
Awake	1	46	59
Movement			
No Movement	4	63	45
Slight	3	25	38
Continuous	2	12	11
Violent	1	0	6
Crying			
No crying	4	42	25
Intermittent	3	24	22
Continuous	2	23	38
Hysterical	1	11	16
Overall Evaluation			
Excellent	6	19	4
Very good	5	52	27
Good	4	19	46
Fair	3	8	15
Poor	2	2	8
Aborted	1	0	0

jects was treated twice, data were obtained from 48 sedations. In addition, each visit was divided into two segments representing procedures before and procedure after the gas change.

The data were analyzed by within-visit comparisons and between-visit comparisons. Figs 1, 2, and 3 illustrate between-visit comparisons of procedures with and without nitrous oxide regardless of which visit received regimen A (first or second appointment) and which received regimen B. Consequently, in Figs 1, 2, and 3, the data for the first segment of the appointment (mouthprop, injection and 60 min) represent average values for regimen A (nitrous oxide) compared with regimen B (100% oxygen); and the data for the second segment of the appointment (75, 90 and 105 minutes) represent average values for regimen B (nitrous oxide) compared with regimen A (100% oxygen).

Table 2 summarizes the data for all visits, regardless of which regimen was used; whereas, Table 3 reports findings when both within-appointment comparisons (nitrous oxide versus 100% oxygen) and between-appointment comparisons (by appointment or by regimen) were used.

Rater reliability

When the ratings made in the operatory were compared with the ratings made from videotapes, 647 ratings were identical, 155 differed by one scale point, and 38 differed by two scale points, producing 77% agreement between the two sets of ratings.

Evaluation of sleep

Of the 48 treatment sessions, on eight occasions patients fell asleep in the waiting area after an average of 29 min; in the remaining 40 treatment sessions, patients were awake when brought into the operatory. In 29% of the 288 occasions that sleep was evaluated during treatment, subjects were asleep. However, in 18% of the ratings, subjects were drowsy and disoriented, and in 52% of the ratings, subjects were fully awake. The means for ratings of sleep at various times of evaluation appear in Fig 1. For subjects receiving nitrous oxide, the mean ratings at the six periods of observation were 1.3, 1.2, 2.2, 2.3, 2.3, and 2.2, whereas, for subjects receiving only oxygen, the mean ratings were 1.3, 1.1, 1.4, 2.3, 2.0, and 1.9. These ratings indicate that subjects were more fully awake during the early than during

TABLE 3. EFFECTS OF 50% NITROUS OXIDE/50% OXYGEN VERSUS 100% OXYGEN

	Nitrous Oxide/Oxygen Is:			
	Better	*Same*	*Worse*	*Total*
By Appointment				
1st Appt.	11	8	5	
2nd Appt.	16	7	1	
By Regimen				
Regimen A	9	10	5	
Regimen B	18	5	1	
Combined	27 (56%)	15 (31%)	6 (13%)	48 (100%)

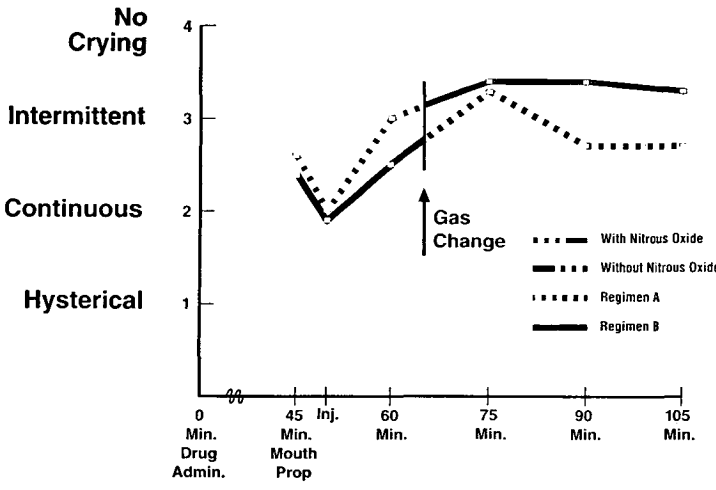

Fig 3. Evaluation of crying.

the later part of each appointment, regardless of which regimen was being used. Overall subjects were awake 46% of the time, drowsy 17% of the time, and asleep 37% of the time that they received nitrous oxide, compared with 59, 19, and 22% respectively when they received pure oxygen (Table 2). Differences in the scores between the two groups were slight and not statistically significant according to the sign test.

Evaluation of movement

When subjects received nitrous oxide, they exhibited no movement 63% of the time or slight movement 25% of the time, compared with 45 and 38% respectively when only oxygen was administered (Table 2). Continuous movement was evident 12% of the time with nitrous oxide compared with 11% continuous and 6% violent movement when nitrous oxide was not administered. Such violent movement occurred when the child struggled and, by squirming, was able to free a hand or leg. The means of ratings of movement for all subjects at the various times of evaluation are illustrated in Fig 2. For subjects receiving nitrous oxide, the mean ratings at the six periods of observation were 3.5, 3.2, 3.3, 3.6, 3.8, and 3.6, and the range of ratings at all periods was 1 to 4. For subjects receiving only oxygen, the mean ratings were 3.1, 2.9, 3.0, 3.5, 3.2 and 3.5, and the range similarly was 1 to 4. These ratings indicated that subjects moved slightly more during the early than during the later part of each appointment. Differences in ratings between the two groups were slight and not statistically significant according to the sign test.

Evaluation of crying

Fig 3 shows the means of ratings of crying for all subjects at the various evaluation times. For subjects receiving nitrous oxide, the mean ratings at the six periods of observation were 2.6, 2.0, 3.0, 3.4, 3.4, and 3.3 (range 1 to 4). For subjects receiving only oxygen, the mean ratings were 2.4, 1.9, 2.5, 3.3, 2.7, and 2.7 (range 1 to 4). When nitrous oxide was administered, subjects exhibited no crying 42% of the time or occasional mild crying 24% of the time, compared with 25 and 22% respectively when subjects did not receive nitrous oxide (Table 2). Continuous persistent crying was exhibited 23% of the time with nitrous oxide and 38% without, and hysterical crying occurred 11% of the time with nitrous oxide and 16% of the time with only oxygen. Crying was more evident during the early part of the treatment when the more stressful procedures of mouth prop insertion, injection, and rubber dam application were performed. However, differences in crying between groups were not statistically significant.

Overall evaluations

Overall evaluations were made of the periods before and after change of the gas from 100% oxygen to nitrous oxide or the reverse. A separate rating scale for overall behavior, which combined the scales for crying and movement, was used. In addition, the overall evaluations combined three individual assessments before the gas change (mouth prop, injection and 60 min) and three assessments after gas change (75, 90 and 105 min). The results are illustrated in Fig 4. Most subjects demonstrated good, very good, or excellent effects of the sedation; however, in 17% of the patients the overall evaluation was less than good and treatment had to be interrupted. With nitrous oxide, 71% of the overall ratings were very good or excellent, whereas

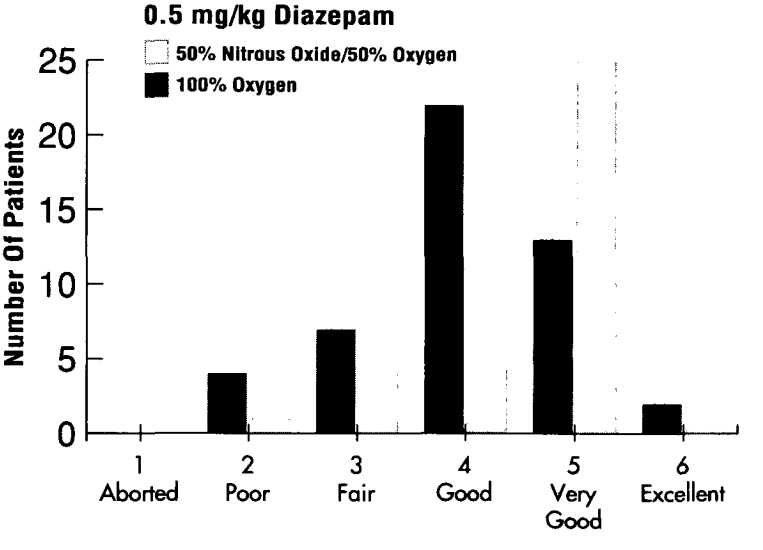

Fig 4. Overall evaluation of sedation.

without nitrous oxide only 31% of ratings were very good or excellent. Using the overall evaluations, the effect of the nitrous oxide was compared with the effect of 100% oxygen in Table 2. Overall, nitrous oxide augmented the sedation in 27 (56%) of 48 treatment sessions, it had no effect in 15 (31%) sessions, and it produced worse behavior in six (13%) sessions. Of the 27 sessions in which the nitrous oxide increased the effect of the diazepam, 11 (41%) occurred during first appointments, with the remainder during the second appointments. Eighteen (67%) occurred with regimen B when nitrous oxide was administered during the second part of the procedure compared with nine with regimen A. Although the nitrous oxide was beneficial for some patients some of the time, it was not uniformly beneficial for all patients all of the time.

All of these findings may be summarized as follows:

1. Behavior was better during the second segments of appointments.
2. With this combination of sedative agents, children were generally fully awake or drowsy and disoriented.
3. Subjects moved little during treatment, but cried continuously one-third of the time.
4. Few differences in sleep, crying and movement were statistically significant at specific points in time, however, half of the overall evaluations demonstrated a beneficial effect of nitrous oxide.

Vital signs

There were few changes in the vital signs throughout the procedures. Blood oxygen saturation level remained essentially unchanged and pulse rate exhibited transitory, although dramatic increases, for example spiking from 100 to 195, which were linked to specific occurrences when the child was stimulated.

The increase in pulse rate was transitory and quickly returned to normal when the stimulus ended. In regard to respiratory rate, similar transitory changes (for example, from 24 to 40) occurred at a time of particular stimulus.

Adverse effects

Two subjects coughed up small amounts of fluid during treatment and one spit up slightly at the end of treatment; otherwise vomiting or respiratory depression was not evident during this study. One child developed a hiccup that lasted through the procedure.

Discussion

This study produced expected and unexpected findings. It was expected that behavior during the first segment would not be as good as behavior during the second segment, since the first part of the appointment had the more noxious stimuli of mouth prop insertion, injection, and rubber dam application. In addition, by the time of the second segment, children who had cried from the beginning often became tired and, consequently, cried less.

Diazepam is an anxiolytic type drug rather than a hypnotic. Consequently, it was not unexpected, although it may be undesirable, to find that subjects were awake most of the time. Being awake could have produced more crying, however, this disadvantage might be ameliorated if amnesia is produced as has been suggested for diazepam. Future research should investigate the amnesic properties of the drug when it is used to sedate young children.

During this study, the Papoose Board™ with auxiliary head restraint was used, and this device, in addition to an auxiliary Velcro™ strap placed across the knees, tremendously restricted movement. Insofar as one of the measures of sedation success was lack of movement, the use of this device could explain the relatively good results of sedation on movement. It appears that there is a distinct advantage to using the special supplemental head holder attached to the Papoose Board™ in that not only does the head restraint prevent some undesirable movement, but it also facilitates the delivery of nitrous oxide by keeping the nasal hood directly over the nose. The auxiliary Velcro strap placed on the knees restricted squirming and usually prevented the legs from slipping out of the restraint.

In this study behavior was assessed in two different ways, sleep, crying, and movement were measured at six different points in time, and overall behavior was evaluated at the end of each of two segments of the sedation. It was surprising that these different methods did not produce similar findings, and this opens to question the validity of each method. The overall assessment might allow the forest to be seen in spite of the many trees and, consequently, it might be a more valid measure. Whereas there was generally no statistically significant effect of nitrous oxide as measured at distinct points in time, there was a measurable effect when the overall assessment was used. Using both methods demonstrates that nitrous oxide can have an effect on diazepam sedation, but when it does, the effect is small.

How success is defined will determine whether or not to include diazepam with nitrous oxide as successful agents to sedate children for dental treatment. Some practitioners reject the use of a restraint such as the Papoose Board suggesting that if external restraint was necessary, the sedation was a failure. Others suggest that, crying is an indication of failure of the sedation, and they are concerned about causing possible psychological trauma. However, there are those who expect some crying and/or movement and consider it a success if they are able to complete necessary treatment. In this study, when success of sedation was defined as lack of crying or movement that interrupted treatment, success occurred in 83% of administrations. These included sedations that received an overall rating of good (difficult, but all treatment performed). However, if the good group of sedations was considered to be unsuccessful — that is, although treatment was not inter-

rupted, there was too much crying or movement to be considered a successful sedation — then only 53% of administrations that were "very good" or "excellent" would be successful. If practitioners expected that diazepam supplemented with nitrous oxide produced a sedation with little or no crying, they would be disappointed to find that in almost half the cases, that criterion was not achieved. It is particularly important that criteria for success be defined carefully when clinicians compare the effects of different drug regimens and when researchers compare the results of different clinical studies. The results of this study indicate that diazepam and nitrous oxide sedation is successful at least half the time and as much as 83% of the time. The results suggest that practitioners should use nitrous oxide in an attempt to augment the effect of diazepam sedation. Although the beneficial effect would be small, there would likely be a positive effect with the addition of nitrous oxide and only a small chance of a negative effect.

Conclusion

From the results of this study, it may be concluded that nitrous oxide may slightly augment the effect of oral diazepam sedation in young children; however, it does not do so uniformly for all children receiving sedation.

This study was approved by the New Jersey Dental School Institutional Review Board. All benefits and risks were fully explained to the parents or guardians of the patients involved. The study was conducted in accordance with the American Academy of Pediatric Dentistry Guidelines for Conscious Sedation.

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