Modification of Behavior With 50% Nitrous Oxide/Oxygen Conscious Sedation Over Repeated Visits for Dental Treatment

A 3-Year Prospective Study

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Abstract: In various medical domains, inhalation of nitrous oxide (N_2O) in oxygen (O_2) is indicated to alleviate pain and anxiety during routine treatment. Repeat treatment may often be indicated. Little data are available, however, to evaluate the long-term efficacy and side effects of reiterated N_2O/O_2 sedation. The aim of this study was to compare behavior during dental treatment under a premix of 50% N_2O/O_2 between first experience and repeat experiences of sedation in a cohort of uncooperative patients. Five hundred forty-three patients (age range, 1–94 years; mean, 17 ± 16 years) experiencing conscious sedation for dental treatment for the first time were recruited at a special care unit during 3 years. A modified Venham scale was used to evaluate patient behavior at 5 steps during each session. Completion of planned treatment and occurrence of adverse side effects of sedation were additional criteria. Patients experienced sedation for the first time for 378 sessions, and the session was a repeat experience in 843 cases (number of visits: range, 1–16). Patient cooperation significantly improved during visits at first contact with the dentist and when applying the mask ($P < 0.0001$, between sessions 1 and 2). Between the first and the third sessions, the percentage of very uncooperative patients decreased from 23% to 3.7% at first contact with the dentist and from 22.3% to 8.5% on application of the mask. Experience of reiterated dental treatment under sedation with 50% N_2O/O_2 premix helps uncooperative patients to cope with dental treatment in the long term.

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Inhalation of nitrous oxide (N_2O) in oxygen (O_2) is widely used to induce both analgesia and sedation and to improve patient cooperation during treatment in various medical domains.[1–4] Conscious sedation with a N_2O/O_2 mixture has been studied extensively in dentistry, and the short-term, perioperative effects of the technique have been well documented for various concentrations of N_2O in O_2[5–8] and for the premix 50% N_2O/50% O_2.[2] Nitrous oxide sedation has been shown to reduce opposition, improve cooperation, and reduce the gag reflex associated with anxiety. The ability to overcome fear and receive treatment in the normal setting, with the help of inhalation sedation, has also been shown to be positive in the reduction of subsequent anxiety compared with behavior management alone.[5–9] Another study showed that postoperative anxiety was lower in 9- to 15-year-old children treated under nitrous oxide sedation than for those treated under general anesthesia.[10]

In some domains, for example, accident and emergency or minor surgery, the indications for N_2O/O_2 administration are one-off. In other disciplines, such as oncology or dentistry, the procedure may be repeated routinely with an individual receiving regular administrations for all or part of his life or treatment. Despite extensive literature on nitrous oxide sedation, the longitudinal effect on patient behavior of repeat sedation sessions has not been fully evaluated. There is no conclusive evidence to show whether this technique is sufficient to reduce anxiety and improve cooperation during subsequent care sessions in all patients. Moreover, in most previous studies, the criteria for failure and success did not take into account behavioral aspects[11,12] or combined both behavioral criteria and completion of the dental treatment in the same scale.[13] Thus, treatment completed with an uncooperative patient (eg, with physical restraint) might still be considered a success. Ethical considerations call for greater knowledge regarding the long-term impact of conscious sedation on patient behavior.

The aim of this study was to compare behavior during treatment under inhalation sedation with 50% N_2O/O_2 between the first experience and repeat experiences of sedation in a cohort of uncooperative dental patients.

MATERIALS AND METHODS

This prospective longitudinal study was designed in accordance with the process of good clinical practice.[14] It was conducted at the special care dental unit of the university hospital of Clermont-Ferrand. Approval was obtained from the local ethical committee (CCPPRB Auvergne, project AU 402). Informed written consent for participation in the trial was obtained from all patients and/or their legal guardians.

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Patients and Procedures

Patients who were to experience N_2O/O_2 inhalation for the first time were recruited between May 16, 2001, and April 20, 2004, to constitute a cohort of patients for whom each subsequent sedation session was observed. A "session" was defined as a patient visit in which dental treatment was undertaken under inhalation sedation. Informed consent was signed before the first session and was valid for all the sessions. The first session represents the first experience of inhalation sedation. Groups of sessions were considered according to the number of N_2O/O_2 premix administrations and were numbered from S1 to S*n*.

All patients were referred to the special care unit by a general dental practitioner, a physician, or member of the medical staff of a special institution. All had difficulty in cooperating with dental treatment. At all appointments, behavioral management techniques aimed at reducing anxiety (eg, clear explanation, demonstration, self-affirmation, transfer of control to patient, maintenance of physical and verbal contact, positive reinforcement, reassurance, positive suggestion, etc) were used in accordance with the age and communication skills of the patient. Patients were excluded if they had previously experienced N_2O/O_2 inhalation for dental care, if they had accepted dental treatment without sedation during the month before the appointment, if they accepted treatment without sedation spontaneously during the first appointment, or if they had a medical contraindication to the use of N_2O. Preschool children (<5 years old) needing extensive treatment or diagnosed with rampant early childhood caries were excluded and referred for treatment under general anesthesia.

The cohort included 543 patients (mean age, 17 ± 16 years; range, 1–94 years), of which 96 were precooperative children younger than 5 years (mean age, 3.1 ± 0.9 years), 163 were dentally anxious or phobic patients older than 5 years (mean age, 13.3 ± 12.9 years), and 284 were patients older than 5 years with intellectual disability (mean age, 23.1 ± 17 years). Patients were considered as having a disability if they had an appropriate medical diagnosis or if they attended a special school, home, or work placement.

A premix of 50% N_2O/50% O_2 at 170-bar pressure was used (Kalinox, Air Liquide Santé International, France). The N_2O/O_2 mixture was administered via a nasal or facial mask, chosen in relation to age, type of treatment, morphology, and type of spontaneous respiration of the patient (nose or mouth-breather). The gas was distributed via a valve and a closed Bain system (a modified Mappleson-D system, Intersurgical, Fontenay Sous Bois, 94, France). The evacuation tube for expired gas emptied outdoors. After each administration, the room was systematically ventilated by opening windows. Time was taken to accustom the patients to the use of the mask, and behavior management strategies were used continually during the care. Positive reinforcement was used after each session. An induction period of at least 3 minutes was systematically respected before beginning the dental care, and gas administration was prolonged until the end of treatment. When a facial mask was used, it was moved up and "pinched" over the nose for periods of 30 to 60 seconds to allow dental treatment while maintaining a sufficient level of sedation. Local anesthetic was used systematically if there was the least risk for pain, including for extraction of deciduous teeth and scaling. The patients' surveillance was essentially clinical. However, oxygen saturation was monitored if judged necessary by the practitioner.

Study Criteria

The first study criterion was related to the behavior of the patient during each treatment session. A modified Venham scale was used to rate behavior (Table 1). This scale offers a good description of behavior and anxiety in 1 score and could be repeated several times during 1 treatment session.[9] As it was originally developed for children, additional behavior descriptors were added to improve its use for adults. This French-language modified version was tested by a class of 31 final-year dental students who scored 13 different video sequences of dental care viewed at weekly intervals during 3 weeks. Intraexaminer and interexaminer reliability was verified, respectively, with the evaluation of the intraclass coefficient correlation α = 0.92 (95% confidence interval, 0.91–0.94) and with analysis of variance (P = 0.973). Four dentists participated in the current study. Interinvestigator variability for the French modified Venham scale was controlled and was not statistically significant (general linear models procedure). Patient behavior was scored by the dentist at 5 different periods during the session: (1) Ti: first contact with the dentist, whether in the waiting room or in the surgery, (2) T0: on placement of the mask over the face or nose, (3) T1: at least 3 minutes after the start of the sedation but before starting any treatment, (4) T2: during administration of local anesthesia, and (5) T3: during dental treatment.

The second study criterion was the success of the treatment session. The session was considered successful if the intended dental treatment could be completed under sedation. Failure was recorded either if the sedation could not be induced or maintained, or if the dental treatment could not be completed.

The third study criterion was the incidence of adverse events during the sedation and recuperation periods. Adverse events were prelisted according to 5 categories: respiratory problems (hyperventilation or hypoventilation, desaturation), digestive problems (nausea, vomiting), neurological problems (convulsions, epileptic fit), behavioral events (euphoria, hyperactivity), and vasovagal effects (sweating, pallor, faint).

Statistical Analysis

The statistical analysis was designed to study any potential differences between the modified Venham scores at Ti, T0, T1, T2, and T3 between the sessions of first experience of sedation (group S1) and the reiterated sedation sessions (groups S2, S3, S*n*...). The minimum number of patients necessary for statistical analysis was calculated using data from a previous study.[2] The number of patients required in each group of reiterated sessions (S2, S3, S*n*...) was calculated to have 80% power to detect a probability of

TABLE 1. English Translation of the French Modified Version of the Venham Scale Used in this Study

0	Relaxed, smiling, willing, able to converse, best possible working conditions; displays the behavior desired by the dentist spontaneously, or immediately upon being asked
1	Uneasy, concerned; eye contact but tense facial expression; suspicious of environment; sits spontaneously back in the chair; hands remain down or partially raised to signal discomfort; during a stressful procedure may briefly and rapidly protest to demonstrate discomfort; the patient is willing and able to describe experience as requested; breathing is sometimes held; capable of cooperating well with treatment
2	Tense; tone of voice, questions and answers reflect anxiety; multiple requests for information; hands clench armrests or may be tense or raised without interfering with treatment; sits back spontaneously in chair but head and neck tense; accepts handholding; eye contact; during stressful procedure verbal protest, quiet crying; patient interprets situation with reasonable accuracy and continues to work to cope with his/her anxiety; protests more troublesome; patient still complies with request to cooperate; continuity is undisturbed
3	Reluctant; tends to reject the treatment situation, difficulty in assessing situational threat; frequent sighs; pronounced protest, crying; only sits back in chair after being asked several times, the head and neck remain tense; slight movements of avoidance; tense hands, avoids eye contact; accepts handholding; minor attempts to use hands to stop procedure; wriggling; protest out of proportion to threat or is expressed well before the threat; copes with situation with great reluctance; treatment proceeds with difficulty
4	Very disturbed by anxiety and unable to assess situation; physically very tense, wrinkled eyebrows, eye contact avoided or eyes shut; general crying not related to treatment; prominent avoiding movements, needing physical restraint on occasion; places hands over mouth or on dentist's arm to prevent treatment, but eventually allows care to progress; pinches lips together but ends up by opening mouth; regularly lifts head from chair; rejects physical contact but may still accept handholding; patient can be reached through oral communication and eventually with reluctance, and great effort begins to work to cope; dissociation is only partial; protest regularly disrupts procedure
5	Out of contact, fails to grasp the reality of the threat; inaccessible to oral and visual communication; rejects physical contact; clenches mouth and lips; closes mouth and clenches teeth whenever possible; violent head movements; screaming, shouting, swearing, fighting, aggressive; regardless of age, reverts to primitive flight responses; actively involved in escape behavior; physical restraint required

0.6 that a score between groups was reduced. A Wilcoxon (Mann-Whitney) rank sum test with a 2-sided significance level of 0.05 was used to test this (nQuery advisor 2.0, module MTT2, Statistical Solutions, Boston, MA). This calculation indicated that groups of reiterated sessions needed to include at least 131 patients to be considered for statistical analysis.

Comparison between the modified Venham scores at the different time intervals between groups of sessions was undertaken using the nonparametric Wilcoxon test. The success rate and the frequency of adverse events between subsequent sedation sessions were compared using Fisher exact test.

RESULTS

Descriptive Results

Patient characteristics for the groups are given in Table 2. For the 543 patients who constituted the cohort, 1221 sedation sessions were performed. The patient experienced inhalation sedation for the first time for 378 sessions, and the session was a repeat experience in 843 cases. During the study period, the number of visits per patient ranged from 1 to 16. The groups S1, S2, and S3 reached the minimal size of 131 patients. Thus, statistical analysis was performed for the group of 164 patients who received at least 3 consecutive sedations. The average duration of the N_2O/O_2 inhalation was 27.7 ± 15.4 minutes.

Cooperation Level

The mean modified Venham score decreased progressively with repetition of the sedation sessions (Table 3), indicating that cooperation improved. In the group of 164 patients who received at least 3 consecutive sedations, intrasession comparison of the mean modified Venham scores at Ti, T0, T1, and T3 showed that cooperation improved significantly during the induction period, then worsened slightly during actual treatment for each sedation session (Wilcoxon test). However, cooperation was better during treatment than before starting sedation in each session. Intersession comparison showed that the mean modified Venham score measured at Ti, T0, and T1 decreased significantly during the reiterations. However, this difference was significant between S1 and S2 but not between S2 and S3 (Table 4) (Wilcoxon test).

The analysis of the evolution of behavior during the initial steps of the sedation session (Ti and T0) is representative of the patients' ability to cope with the stress of meeting the dentist and of application of the mask. At these steps, patients are fully conscious. At the first session, before any experience of sedation, patients were less cooperative (modified Venham score of $\geq$1) at Ti and T0 than for repeat sessions (Fig. 1). The percentage of patients who required a degree of restraint on induction (modified Venham score of 4 and 5) decreased, respectively, from 23% to 3.7% at Ti ($P = 10^{-7}$) and from 22.3% to 8.5% at T0 ($P = 0.001$) between the first and the third sedation sessions. In addition, the percentage of patients having a modified Venham score of 0 (relaxed) at Ti and T0 increased, respectively, from 13.7% to 28.7% ($P = 0.001$) and from 15.5% to 35.4% between S1 and S3 ($P = 10^{-4}$; Fisher exact tests).

The 50% N_2O/O_2 was shown to be effective from the end of the induction period (T1). At this step, the percentage of relaxed patients increased from 53% to 73% between S1 and S3 ($P = 10^{-4}$) (Fig. 1), and no patient required restraint (modified Venham score 4 or 5) during the third session. Nociceptive stimuli are induced during the injection of local anesthesia (T2) and during dental treatment (T3). The percentage of restrained patients (modified Venham

TABLE 2. Descriptive Results for the Control and Experimental Groups

Groups of Sedation Sessions	No. Sessions	Male/Female Patients	Age Mean (± SD)	Inhalation Duration Mean (± SD), min	No. Children <5 y	No. Patients With Intellectual Disabilities	No. Patients With Dental Anxiety
S1	543	274/269	16.7 (16.1)	24.2 (13.2)	96	284	163
S2	279	148/131	16.3 (14.3)	30.1 (16.7)	33	145	101
S3	164	76/88	17.7 (15.3)	29.3 (16.2)	14	87	63
S4	91	44/47	17.6 (14.4)	30.6 (15.7)	6	50	35
S5	54	27/27	17.1 (10.5)	31.7 (16.1)	3	31	20
S6	30	15/15	22.0 (10.8)	33.0 (16.0)	0	19	11
S7	19	9/10	23.5 (10.7)	31.4 (15.3)	0	11	8
S8	13	7/6	21.1 (11.7)	36.0 (13.6)	0	6	7
S9	9	4/5	18.7 (8.8)	43.6 (22.3)	0	3	6
S10	6	3/3	26.5 (13.3)	31.0 (13.5)	0	2	4
S11	4	2/2	30.3 (12.6)	34.8 (11.9)	0	2	2
S12	3	1/2	25.3 (5.1)	18.7 (5.1)	0	1	2
S13	2	0/2	26.0 (7.1)	56.5 (20.)5	0	1	1
S14	2	0/2	26.5 (6.4)	30 (7.1)	0	1	1
S15	1	0/1	22	15	0	1	0
S16	1	0/1	22	10	0	1	0

S1 indicates group of sessions where sedation was experienced for the first time; S2, group of sessions where sedation was experienced for the second time; S*n,* group of sessions where sedation was experienced *n* times.

score 4 or 5) varied from 3.7% to 3.5% during T2 (not significant), whereas it increased slightly from 2.6% to 8% during T3 ($P = 0.04$).

Success Rate

The overall success rate for the 1221 sessions was 94.8%. For 42 patients, treatment failed at first experience. Among the 64 sessions that led to a failure, 6 sessions were a repeat attempt after a previous failure to treat. In the group undergoing at least 3 sedation sessions, the success rate remained unchanged during the repeated sessions.

Adverse Events

No severe adverse event was recorded during the study. Minor adverse events were recorded during 6.5% of all the sessions: nausea (n = 24), vomiting (n = 48), and other (n = 14) (agitation, euphoria, sudation, etc). The number of adverse events decreased during the reiterated sessions in the whole cohort (Table 3), but this variation was not significant in the group of 164 patients who had at least 3 sedation sessions (Table 4). Cardiac frequency and oxygen saturation were monitored during 66 inhalation sedation sessions for 56 patients (mean age, 18.2 ± 11.1 years). Oxygen saturation as measured by pulse oximetry ranged from 92.1 to 99.9, with a mean value of 98.1 ± 1.6 (Table 5).

DISCUSSION

This is the first behavioral study that investigates the long-term effect of a 50% N_2O/O_2 premix in uncooperative outpatients. The ability to cope with dental treatment was shown to improve progressively when sedation sessions were repeated. The most behavioral progress was made between the first and second experiences of treatment under sedation. Despite the fact that the numbers of patients in groups S4 to S16 were too small to allow extended statistical analysis, repetition of inhalation sedation was shown to improve cooperation for patients from different categories of age and cognitive profile.

In other studies, acute and chronic tolerance of the analgesic effects of N_2O/O_2 has been reported using an induced-pain model.[15,16] In the current study, neither an acute nor a chronic tolerance effect was observed. The aim of these previous experimental studies, however, was to analyze the analgesic effect of nitrous oxide in healthy subjects submitted to a pain stimulus. The aim of the current study was to analyze the decrease in anxiety and opposition in patients requiring treatment. In healthy human subjects, the use of an induced-pain model may activate the sensitization process in both experimental and placebo groups. The induced-pain model in itself may thus lead to a decrease in the pain threshold during repetition of nociceptive stimulation, independent of the analgesic effect of the drug to be tested. In clinical studies, conducted with patients needing treatment, both placebo and drug groups may reap direct benefit from the study,[17,18] and this may result in more cooperative behavior during care.

In the group of 164 patients who received at least 3 sedation sessions in this study, the behavior score worsened slightly during actual treatment (T3) compared with the end of the induction period (T1), despite pain control with local

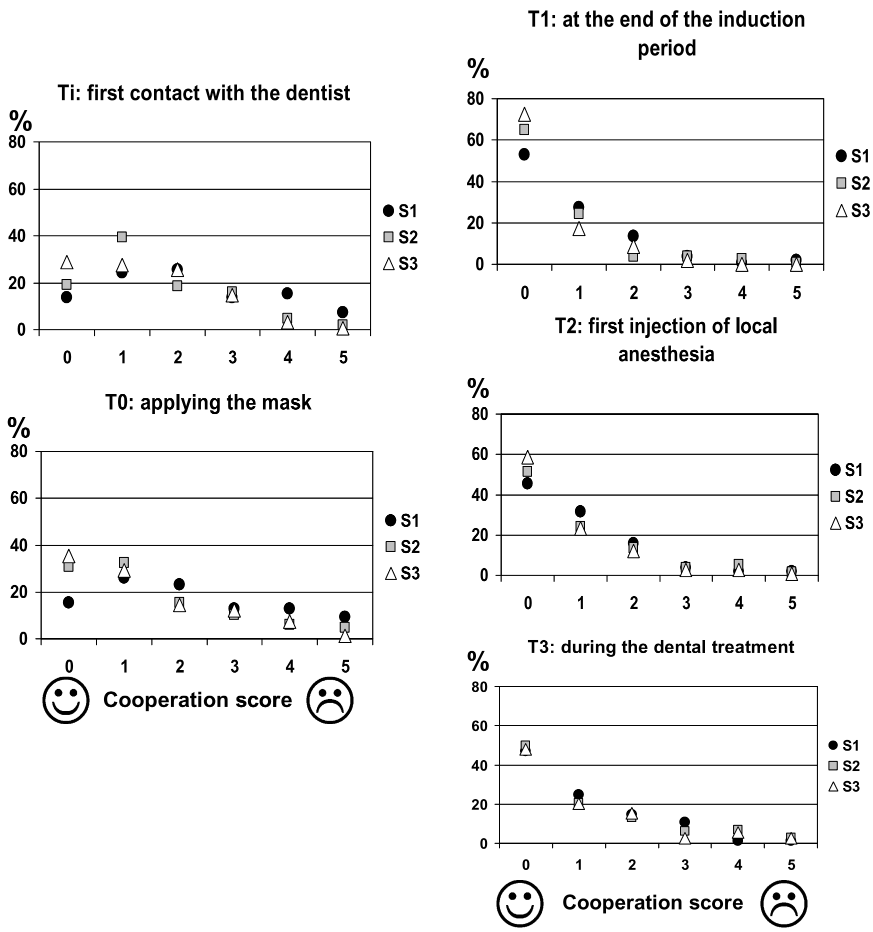

FIGURE 1. Distribution curves of the percentage of patients with each modified Venham score at Ti, T0, T1, T2, and T3 for the 164 patients receiving at least 3 consecutive sedation sessions for dental care (Venham score: 0 = relaxed; 1 = uneasy; 2 = tense; 3 = reluctant; 4 = very disturbed; and 5 = out of contact).

anesthesia when required. This was to be expected because stimulation during treatment tends to trigger specific fears in dental patients (eg, tastes, noises, vibration, smells, gag reflex, etc). Restorative treatment may be considered as particularly difficult for anxious patients because of the use of rotary instruments and the need for injection of local anesthetic.[19–21] This also explains why many patients had a relatively good behavior score at Ti and T0 (ie, before any treatment had been attempted), despite being referred to the unit specifically because of behavioral difficulties during dental treatment.

In addition, the percentage of patients who needed gentle restraint during treatment (T3) increased slightly between S2 and S3. However, despite increased opposition during actual treatment, the behavior score remained improved from baseline at Ti and T0 at subsequent sessions. The slight increase in behavioral difficulties during actual treatment at repeat sessions cannot be interpreted as a chronic tolerance effect, however, because it is unknown whether the different types of dental treatment performed induced the same level of stimulation. It is reasonable to assume that the most invasive care was only planned if the first experience of treatment under sedation was successful, thus increasing the risk for a higher modified Venham score during actual treatment at subsequent visits. This was confirmed in a preliminary analysis of the evolution of behavior during 2 years which showed that more complicated restorative treatment was performed during repeated sessions than during the first experiences of sedation.[22] To analyze these results further, a baseline score of difficulty would need to be established for each type of dental treatment, controlling for the use of local anesthesia which may present specific anxieties for certain patients.

Nitrous oxide enhances patient acceptance by reducing arousal and modifying anticipation of danger.[23] However, the state of conscious sedation can never be dissociated from the effect of the behavior management techniques used simultaneously. Patients can be expected to be more cooperative at subsequent appointments if a relationship of trust has been established with the practitioner and if they have not experienced pain during previous visits. This was illustrated here, as behavior at Ti (at the first contact with the dentist during a session) and T0 (when applying the mask) was also improved at subsequent visits, although the patient was not

TABLE 3. Evolution of the Mean Modified Venham Score, of the Percentage of Failure to Treat, and of Adverse Events for Each Subsequent Sedation Session at Each of the 5 Points in Time During the Session

Sessions	Ti Mean (SD)	T0 Mean (SD)	T1 Mean (SD)	T2 Mean (SD)	T3 Mean (SD)	No. Failures	No. Adverse Events	Mean Intersession Period (SD), d
S1	2.1 (1.5)	2.3 (1.6)	1.0 (1.3)	1.1 (1.3)	1.2 (1.4)	42	39	—
S2	1.6 (1.3)	1.5 (1.5)	0.6 (1.1)	1.0 (1.3)	1.2 (1.5)	10	22	139 (159)
S3	1.4 (1.2)	1.3 (1.3)	0.4 (0.7)	0.7 (1.0)	1.1 (1.4)	5	8	99 (96)
S4	1.2 (1.2)	1.1 (1.3)	0.4 (0.9)	0.9 (1.2)	1.3 (1.5)	4	3	108 (113)
S5	1.1 (1.1)	1.0 (1.4)	0.5 (1.1)	0.8 (1.4)	1.3 (1.5)	1	3	120 (121)
S6	1.1 (1.3)	0.8 (1.1)	0.4 (0.8)	0.9 (0.9)	0.8 (1.1)	0	1	126 (161)
S7	0.8 (0.5)	0.6 (0.8)	0.2 (0.4)	0.7 (1.1)	0.8 (1.2)	0	1	83 (99)
S8	0.8 (0.8)	0.5 (0.9)	0.2 (0.4)	0.4 (0.5)	1.0 (1.2)	1	0	103 (119)
S9	0.8 (0.7)	0.3 (0.5)	0.0 (0.0)	0.4 (0.8)	0.6 (0.9)	0	1	56 (76)
S10	1.0 (0.6)	0.5 (0.5)	0.0 (0.0)	0.5 (1.0)	0.7 (0.8)	0	0	98 (125)
S11	1.0 (0.8)	0.5 (0.6)	0.0 (0.0)	0.0 (0.0)	0.3 (0.5)	0	0	41 (39)
S12	0.7 (0.6)	0.3 (0.6)	0.7 (1.2)	1.5 (2.1)	0.5 (0.7)	1	1	114 (29)
S13	0.0 (0.0)	0.5 (0.7)	0.0 (0.0)	0.5 (0.7)	1.0 (0.0)	0	0	133 (153)

Ti, indicates at the beginning of the session during the first contact with the patient, either in the waiting room or in the surgery; T0, on application of the mask to the face; T1, at the end of the induction period, at least 3 minutes after the beginning of inhalation; T2, during the first injection of local anesthesia; T3, during dental treatment. Sessions above S13 were not considered because of their small sample size.

sedated at these points in time. The importance of traditional behavior management techniques cannot be underestimated and should be adapted to the cognitive profile of the patient. Systematic transfer of control to the patient is essential, combined with reassurance, positive reinforcement of desired behavior, and simple relaxation techniques. Although the "human factor" and the pharmacological effects of the gas cannot be distinguished in this study, both were essential to ensure the degree of success reported here.

The relatively short duration of the inhalation session was directly related to the time needed to complete the planned item(s) of dental care. Moreover, to limit nitrous oxide pollution in the surgery, the French license for use of the N_2O/O_2 premix suggests that the expected duration of the administration should not exceed 60 minutes.

For the whole cohort, failure at the first session was never followed by success at subsequent visits. Ability to perform planned dental care at first experience of inhalation sedation was thus a predictive indicator for subsequent sessions. However, there are no data in the literature to validate this hypothesis. Factors previously shown to have predictive power for behavioral problems in children include previous problems on seeing a dentist, dislike of the dentist, insufficient time to adjust to the situation, and fear of injection.[24] Nondental factors, such as problems with medical visits, parental dental fear, anxiety when meeting

TABLE 4. Comparison of the Modified Venham Scores for the 164 Patients Undergoing at Least 2 Reiterated Sessions (S2 and S3) After First Experience (S1)

	S1	S2	S3	*P*, S1/S2	*P*, S2/S3
No. patients	164	164	164	—	—
No. successes	158	160	159	—	—
No. failures	6	4	5	NS	NS
Adverse events	7	8	8	NS	NS
Mean Venham score (SD) at Ti	2.16 (1.49)	1.54 (1.22)	1.38 (1.17)	<0.0001	NS
Mean Venham score (SD) at T0	2.10 (1.54)	1.44 (1.43)	1.30 (1.33)	<0.0001	NS
Mean Venham score (SD) at T1	0.78 (1.06)	0.56 (0.98)	0.40 (0.72)	0.02	NS
Mean Venham score (SD) at T2	0.91 (1.11)	0.92 (1.24)	0.70 (1.05)	NS	NS
Mean Venham score (SD) at T3	0.98 (1.17)	1.09 (1.42)	1.11 (1.37)	NS	NS

Ti, indicates at the beginning of the session during the first contact with the patient, either in the waiting room or in the surgery; T0, on application of the mask to the face; T1, at the end of the induction period, at least 3 minutes after the beginning of inhalation; T2, during the first injection of local anesthesia; T3, during dental treatment; NS, nonsignificant difference.

TABLE 5. Mean Cardiac Frequency and Mean Oxygen Saturation in 56 Patients During 66 Inhalation Sedation Sessions

Patient Groups	No. Patients	Age ± SD, y	Cardiac Frequency ± SD (Range)	O_2 Saturation ± SD (Range)
Patients with intellectual disability	36	24.5 ± 9.2	86.6 ± 15.3 (63–145)	97.9 ± 1.7 (92.1–99.7)
Precooperative children	3	3.3 ± 0.6	109.9 ± 20.6 (88–129)	98.2 ± 0.7 (97.5–99.3)
Patients with dental phobia	27	11.1 ± 7.8	82.3 ± 14.3 (56–109)	98.4 ± 1.7 (93–99.9)
Global	66	18.2 ± 11.1	92.4 ± 24.1 (56–145)	98.1 ± 1.6 (92.1–99.9)

unfamiliar persons, and sitting alone in the chair, are also good predictors for preschool children.[25] However, no factor has yet been shown to have a predictive power of need for either sedation or general anesthesia.

This study showed an incidence of adverse events similar to that in the literature for nitrous oxide sedation, whether administered at a fixed 50% proportion or whether titrated.[26] The level of adverse events was thus not increased by the use of a 50% premix, but the use of a fixed dose reduced variables for the study of efficacy and tolerance of the drug. The main side effects reported here were nausea and vomiting, which were recorded for approximately 5% of the sessions. Other studies have reported a greater frequency of vomiting (approximately 8%), when the gas was used in the context of oral surgery procedures,[27] the management of procedural diagnostic pain,[28] or in association with other drugs.[29] Behavioural responses to stimuli that induce fear involve action of the sympathetic nervous system that functions when the conscious or unconscious mind feels a need for defense.[30,31] This system is subject to complex regulation.[32] Some authors have shown that stimuli that alter autonomic nervous system activity systematically alter gastric myoelectrical activity.[33] However, the role of the autonomic nervous system in nausea is debated, and other authors have suggested that associated sympathetic symptoms could be a defensive reaction against nauseous sensation.[34] Moreover, in the context of dental care under inhalation sedation, barometric changes in the middle ear could contribute to the incidence of nausea and vomiting induced by nitrous oxide.[35,36] Although dental stress is unlikely to be the sole cause of nausea and vomiting in this study, it is recognized that anxiety, expectation, anticipation, and adaptation are psychological factors that participate in the complex control mechanism of nausea.[37] It has been shown that behavioral training can help certain patients with chronic gastric motility disorders associated with adrenergic dysfunction.[38] Thus, it could be hypothesized that the decrease in the rate of adverse events with reiteration could be related to the anxiolytic effect of the repetition of sedation, although this hypothesis cannot be confirmed statistically in the present study.

In conclusion, conscious sedation using a 50% premix of N_2O/O_2 may be used repeatedly if necessary and may gradually help to reduce anxiety and improve cooperation in the long term. Further research is needed to explore if this improvement could have a positive social and developmental impact on dentally anxious patients, independent of the care procedures and the cognitive profile of the patients.

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