Scientific Article

A comparison of two oral ketamine-diazepam regimens for sedating anxious pediatric dental patients

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Abstract

This double-blind, crossover study assessed physiology and behavior following administration of two oral ketamine-diazepam sedation regimens (4 mg/kg and 8 mg/kg ketamine in conjunction with 0.1 mg/kg diazepam). Clinical success was achieved in 50% of sedations with 4 mg/kg and 78% of sedations with 8 mg/kg with no significant differences between the two regimens (Fisher's exact test). Within the crossover group, clinical success was achieved in 56% of sedations with 4 mg/kg and 87% of sedations with 8 mg/kg with no significant differences between the two regimens (Fisher's exact). Although clinically insignificant, ANOVA revealed statistical elevations in blood pressures and heart rates and decreases in oxygen saturations ($P < 0.05$). The 4-mg/kg regimen resulted in more negative behavior and less sleep. The 8-mg/kg regimen resulted in less negative behavior and more sleep. (Pediatr Dent 18:294–300, 1996)

Most children are cooperative in the dental environment, but pediatric dentists are often challenged by young, fearful, and uncooperative patients.[1] Pharmacological agents are sometimes necessary to obtain a quiescent, cooperative patient to perform quality dentistry. Pharmacological techniques that induce cooperative, yet conscious states in otherwise uncooperative children are most commonly referred to as techniques of conscious sedation.[2]

A considerable body of literature describes the pharmacology and clinical use of ketamine, a nonbarbiturate anesthetic agent derived from phencyclidine.[3] Like most pharmacological agents, ketamine produces a number of systemic effects. Ketamine produces a state of "dissociative anesthesia," which has been described as a peculiar state of unconsciousness in which the patient is in a cataleptic state, "disconnected" from surroundings and able to undergo surgery in comfort and without recall,[4] or as a functional and electrophysiological dissociation between the thalamoneocortical and limbic systems that produces a state of catalepsy in which the eyes remain open with a slow nystagmic gaze while corneal and light reflexes remain intact. Varying degrees of hypertonus and occasional purposeful movements, unrelated to painful stimuli, are noted in the presence of adequate surgical anesthesia. Additional minor changes in the central nervous system may interfere with the ability to organize thoughts and understand one's environment.[5]

Only a few reports describe ketamine as an oral sedative. These investigations reported the effectiveness of oral ketamine (2–10 mg/kg) in mentally handicapped patients receiving gynecological examination and a variety of invasive dental treatments, and young burn patients presenting for painful dressing changes.[6–9] Oral ketamine (6 mg/kg) also has been compared to meperidine (2 mg/kg) and promethazine (0.5 mg/kg). The efficacy of the ketamine sedations was reportedly greater, with shorter onset and postoperative recovery times.[10]

This limited literature proposes an alternative sedative regimen with unknown potential. The purposes of this investigation were to: 1) assess physiological parameters following the administration of two oral sedation regimens (4 mg/kg and 8 mg/kg of ketamine in conjunction with 0.1 mg/kg diazepam) in preschool-aged children; 2) assess behavioral parameters following the administration of these oral sedation regimens; and 3) identify statistically significant differences between the oral drug regimens with regard to physiological and behavioral parameters.

Methods and materials

Pediatric dental patients at Baylor College of Dentistry, ranging in age from 29 to 65 months (mean 46.9 ± 11.4), with health classification of ASA I were selected to participate in this investigation.[11] Selected patients all needed restorative dental treatment requiring the administration of local anesthetic in at least two sextants. Behavior was evaluated by the principal investigators, and participation mandated documentation of

"negative" or "definitely negative" behavior according to the Frankl scale at a previous dental appointment.[12] The crossover design required a single population to serve as its own control.

Parents of acceptable candidates were informed of the dental treatment plan, the indications for sedation, and the nature of this investigation, and provided informed written consent. The presedation instructions included: 1) to not eat or drink for at least 5 hr prior to the scheduled appointment; 2) to notify the dental clinic if the patient experienced any illness during the week prior to sedation; 3) to wear loose, comfortable clothing to each appointment to allow placement of monitoring equipment.

Prior to sedation, a dental anesthesiologist assessed current medical status and recorded the patient's age in months, weight in kg, and baseline vital signs, including blood pressure, heart rate, temperature, oxygen saturation, and respiratory rate, depth, and quality.

TABLE 1. BEHAVIOR RATING CRITERIA

Sleep
1. Awake, alert
2. Drowsy, disoriented
3. Intermittently asleep
4. Sound asleep

Body Movement
1. Violent, interrupting treatment
2. Continuous, making treatment difficult
3. Controllable, does not interfere with treatment
4. No body movement present

Head/Oral Resistance
1. Turns head, refuses to open mouth
2. Mouth closing, must request to open
3. Choking, gagging, spitting
4. No head/oral resistance present

Crying
1. Hysterical, demands attention
2. Continuous, making treatment difficult
3. Intermittent, mild, does not interfere with treatment
4. No crying present

Verbal
1. Verbal abuse, threats
2. Verbal protest
3. Statement of discomfort
4. Occasional talking or silence

Overall
1. Aborted — no treatment performed
2. Very Poor — treatment interrupted, partial treatment completed
3. Poor — treatment interrupted, all treatment completed
4. Fair — difficult, all treatment performed
5. Good — some limited crying or movement
6. Excellent — no crying or movement

The patient was administered 4 mg/kg or 8 mg/kg oral ketamine (Ketalar®, Parke-Davis, Morris Plains, NJ) in conjunction with 0.1 mg/kg diazepam (Diazepam Oral Solution®, Roxane Laboratories, Inc, Columbus, OH) and 3–5 ml of a grape flavoring agent (Syrpalta®, Humco Laboratory, Texarkana, TX). The initial ketamine regimen was determined randomly. The sedative agents were prepared by the dental anesthesiologist and administered by the operator who was blind to the ketamine dosage administered. Dental treatment commenced approximately 20 min after drug administration.

The dental anesthesiologist monitored physiological status with a precordial stethoscope, pulse oximeter (N100-Nellcor®, Nell Corp, Hayward, CA), noninvasive blood pressure unit (Dinamap®, Critikon, Tampa, FL), and electrocardiograph (MRL Porta Pak 90®, Medical Research Laboratories, Inc, Buffalo Grove, IL). Physiological data were recorded upon entry into the operatory and every 10 min thereafter for the duration of treatment.

An additional investigator, also blind to the ketamine dosage administered, monitored the behavioral status of the child by rating the amount of crying, verbal responsiveness, sleep, head/oral resistance, and body movement (Table 1). This investigator was trained previously in the use of the selected behavior rating scale for participation in numerous sedation studies and standardized for intra-rater reliability. These data were recorded during administration of sedative agents, at the onset of sedation, at entry into the operatory, during administration of local anesthetic, during rubber dam placement, every 10 min of operative treatment for the duration of the treatment, and at exit from the operatory. Following treatment, overall behavior ratings were recorded independently by this investigator and the operator.

If at any time during treatment the child became so uncooperative that the dental procedures could not be accomplished, or the child seemed in a position where injury might occur, the remaining treatment was aborted. In such cases, the parent or legal guardian was given an opportunity to reappoint the child with the alternative sedation regimen, or withdraw the child from the investigation.

Upon completion of operative treatment, the patient was examined, and released when discharge criteria were fulfilled. Discharge criteria included a patient who was afebrile, awake, alert, had stable and acceptable vital signs, and was responsive to verbal stimulation. Abnormal postoperative vital signs and/or delays in discharge for any reason were considered complications of sedation. Telephone contact was made with the parent or legal guardian during the afternoon following the sedation appointment to assess the incidence of psychic phenomena, headache, nausea/vom-

TABLE 2. OVERALL BEHAVIOR RATINGS OF SEDATED PATIENTS

Rating	*4 mg/kg Ketamine*	*8 mg/kg Ketamine*
1. Aborted	7	1
2. Poor	0	1
3. Fair	3	2
4. Good	5	7
5. Very good	4	4
6. Excellent	1	3
Totals	20	18

TABLE 3. SCHEFFE F-TEST: PHYSIOLOGICAL PARAMETERS; 4 MG/KG

Comparison	*Systolic*	*Diastolic*	*HR*	*O_2 Sat*
PreSed vs. Entry	Sig*	Sig*	Sig*	NS
PreSed vs. 10	Sig*	Sig*	Sig*	Sig*
PreSed vs. 20	Sig*	NS	Sig*	NS
Entry vs. 10	NS	NS	Sig*	NS
Entry vs. 20	NS	NS	Sig*	NS
10 vs. 20	NS	NS	NS	NS

PreSed = Prior to administration of medications; Entry = Beginning of treatment; 10 = 10 min from entry; 20 = 20 min from entry; NS = Nonsignificant statistical comparison; Sig* = $P < 0.05$.

iting, and/or skin rash, which were also considered complications of sedation.

Following collection of physiological and behavioral data, statistical analyses were performed to examine the physiological and behavioral parameters and the variation between drug regimens.

Results

The partial crossover design involved 22 patients who participated in 38 sedations. Fourteen patients were classified previously as "extremely negative" and eight patients as "negative" using the Frankl scale. Sixteen patients completed the crossover. Six patients were treated once with a single, randomly selected sedation regimen; four of these patients withdrew due to extremely poor behavior during the initial sedation, one patient withdrew for financial reasons, and one patient was completed during the initial appointment. Data from 20 patients sedated with 4 mg/kg ketamine and 18 patients sedated with the 8 mg/kg ketamine were available for statistical analyses.

Clinical success was defined as the ability to perform the planned operative treatment without significant opposition from the child. An overall behavior rating of 4 or better was considered a success. Clinical failure was defined as the inability to complete planned treatment, or when treatment time was greatly extended because of significant opposition from the child. An overall behavior rating of 3 or less was representative of failure.

Group A: 4 mg/kg ketamine sedation regimen

Twenty patients aged 29–65 months (mean 46.2 ± 10.4) were sedated with 4 mg/kg ketamine and 0.1 mg/kg diazepam. Ten sedations (50%) were rated as clinical successes and the remaining 10 sedations (50%) as failures (Table 2). One child would not remain in the dental chair without physical restraint. Consequently, dental treatment was aborted at entry. Two sedations were aborted during administration of local anesthesia, three during rubber dam application, and one during the initial minutes of operative treatment. A decreasing sample size beyond 20 min of operative treatment prohibited accurate statistical evaluation past this time period.

One patient exhibited drowsiness and disorientation at the onset of sedation, but returned to an awake and alert state upon entry into the dental operatory. All other patients remained awake and alert for the duration of dental treatment.

The incidence of body movement, head and oral resistance, and crying increased above entry values at all times thereafter and appeared to be most significant from the administration of local anesthesia through 20 min of operative treatment. Body movement tended to increase with time, especially during administration of local anesthesia.

The incidence of verbalization increased above entry values at all times thereafter and appeared to be most significant from entry through 20 min of operative treatment. Verbalization tended to increase with time, especially during entry and the administration of local anesthesia. Statements of discomfort tended to prevail in this time period.

ANOVA and Scheffe F-tests revealed statistically significant differences in systolic blood pressures, diastolic blood pressures, heart rates, and oxygen saturations ($P < 0.05$); (Table 3). Increases in systolic blood pressures were identified at entry, 10 min, and 20 min compared with presedation values. Increases in diastolic blood pressures were identified at entry and 10 min into treatment when compared with presedation values. Increases in heart rates were identified at entry when compared with the presedation values. Increases in heart rates also were identified 10 min and 20 min into treatment when compared with the presedation values and entry. Decreases in oxygen saturations were identified 10 min into treatment when compared with presedation values. However, oxygen saturation decreased below 97% only once and was transient. Statistical analysis of respirations was not possible because crying interfered with reliable data collection. No clinically significant changes in respiratory status were recorded. Although statistically significant variations existed, changes in systolic blood pressures, diastolic blood pressures, heart rates, and oxygen saturations were not clinically significant because no additional treatment was necessary. The elec-

trocardiographic data revealed no clinical deviations from normal.

With regard to working time, six of the seven patients with overall ratings of 1 had treatment aborted prior to actual operative procedures. Following administration of local anesthesia and application of the rubber dam, treatment times ranged from 10 to 50 min. Behavior did not tend to deteriorate significantly over time, but remained fairly stable throughout the operative procedures, regardless of ratings. For example, patients who whined at 10 min may still have been whining at 30 min but did not progress to uncontrollable crying.

All patients remained conscious throughout the operative treatments. Nystagmus was recorded in one sedation. One patient experienced emesis immediately after operative treatment. There were no delays in discharge nor reports of psychic phenomena, headaches, nausea/vomiting, and/or skin rashes postoperatively.

Group B: 8 mg/kg ketamine sedation regimen

Eighteen patients aged 29–64 months (mean 45.8 ± 11.6) were sedated with 8 mg/kg ketamine and 0.1 mg/kg diazepam. Fourteen sedations (78%) were rated as clinical successes and the remaining four (22%) were rated as clinical failures (Table 2).

The one aborted case was deemed unsuccessful during local anesthesia administration. A decreasing sample size beyond 20 min of operative treatment prohibited accurate statistical analysis past this time period.

The 8 mg/kg ketamine regimen occasionally caused various degrees of sleep in this age group. A majority of patients (78%) exhibited awake, alert behavior during the onset of sedation. However, the presence of drowsy, disoriented behavior and intermittent sleep was highest during this same time period. Patients then tended to become more awake and alert with time, and only one patient exhibited a sound sleep during treatment.

Violent body movement rarely occurred with this regimen. The incidence of continuous body movement increased above entry values at all times thereafter. The incidence of controllable body movement increased above administration values at all times thereafter. Body movement tended to increase with time, especially during administration of local anesthesia.

Head turning, refusal to open mouth, and continuous mouth closing tended to increase above entry values at all times thereafter. Choking, gagging and spitting rarely occurred with this regimen. Head/oral resistance tended to increase with time, especially during application of the rubber dam.

Hysterical crying was rare while continuous crying tended to increase above entry values at all times thereafter. Mild, intermittent crying tended to increase above onset values for all times thereafter. Crying tended to increase with time, especially during the administration of local anesthesia and during treatment.

Verbal abuse and threats did not occur with this regimen. Verbal protests tended to increase above onset values for all times thereafter. Statements of discomfort tended to increase above onset values at all times thereafter and occurred most often during administration of local anesthesia and rubber dam application. Absence of verbalization tended to decrease below entry values for times thereafter and was lowest during administration of local anesthesia, rubber dam application, and 20 min into treatment.

ANOVA and Scheffe F-tests revealed statistically significant differences in systolic blood pressures, diastolic blood pressures, heart rates, and oxygen saturations ($P < 0.05$); (Table 4). Compared to presedation values, significant increases in systolic blood pressures were identified at entry, 10 min into treatment, and 20 min into treatment. Significant increases in diastolic blood pressures were identified at entry and 10 min into treatment. Significant increases in heart rates were identified at entry and 10 min into treatment compared with presedation values. Significant decreases in oxygen saturations were identified 10 min into treatment when compared with presedation values. However, at no time did oxygen saturation decrease below 95%. Statistical analysis of respiration was not possible because crying interfered with data collection. No clinically significant changes in respiratory status were recorded. Although statistically significant variations existed, changes in systolic blood pressures, diastolic blood pressures, heart rates, and oxygen saturations were not clinically significant. The electrocardiographic data revealed no clinical deviations from normal.

TABLE 4. SCHEFFE F-TEST: PHYSIOLOGICAL PARAMETERS; 8 MG/KG

Comparison	*Systolic*	*Diastolic*	*HR*	*O_2 Sat*
PreSed vs. Entry	Sig*	Sig*	Sig*	NS
PreSed vs. 10	Sig*	Sig*	Sig*	Sig*
PreSed vs. 20	Sig*	NS	NS	NS
Entry vs. 10	NS	NS	NS	NS
Entry vs. 20	NS	NS	NS	NS
10 vs. 20	NS	NS	NS	NS

PreSed = Prior to administration of medications; Entry = Beginning of treatment; 10 = 10 min from entry; 20 = 20 min from entry; NS = Nonsignificant statistical comparison; * = $P < 0.05$.

Following local anesthesia administration and rubber dam application, treatment times ranged from 10 to 50 min. Behavior did not tend to deteriorate significantly over time, but remained stable throughout the operative procedures, regardless of ratings.

All the patients remained conscious throughout operative treatment. There were few side effects noted with this regimen. Nystagmus was recorded in six sedations and watery eyes in four sedations. There were no delays in discharge. One patient experienced emesis 6–8 hr following operative treatment. There were no

reports of psychic phenomena, headaches, nausea/vomiting, and/or skin rashes postoperatively.

Comparison of group A with group B

Upon evaluation of all patients, clinical success was achieved in 10 of 20 (50%) sedations with 4 mg/kg ketamine and 14 of 18 (78%) sedations with 8 mg/kg ketamine. A one-sided Fisher's exact test revealed no statistically significant differences between success rates of the sedation regimens ($P = 0.07$).

Upon evaluation of crossover patients, clinical success was achieved in five of 16 (56%) sedations with 4 mg/kg ketamine and 14 of 16 (87%) sedations with 8 mg/kg ketamine. A one-sided Fisher's exact test revealed no statistically significant differences between success rates of the sedation regimens ($P = 0.06$).

Both high- and low-dose ketamine regimens showed statistically significant changes in physiological parameters. Systolic and diastolic blood pressures increased for both groups at similar time intervals. Heart rates increased for both groups as compared with presedation values through 10 min of treatment, but remained elevated for the 4 mg/kg group through 20 min of treatment. Oxygen saturations decreased for both groups 10 min into treatment when compared with the presedation values. However, changes in vital signs were not clinically significant. Therefore, physiological parameters were not different between groups.

Discussion

The dental literature is overwhelmed with investigations and case reports that introduce and/or support sedative agents and procedures for pediatric dental patients. Many sedative agents have been suggested, including ketamine, which has received considerable attention in medicine. The purpose of this study was to define and execute a well-controlled clinical investigation of the efficacy and safety of orally administered ketamine for outpatient pediatric dentistry.

A significant limitation of many previous conscious sedation studies has been the method by which behavior was evaluated. The Frankl Scale has been utilized for its simplicity.[12] Broad, nondescriptive behavior assessments such as very positive, positive, negative, or definitely negative do not provide enough detail about a child's specific reactions either to a stressful experience or when sedated. Several studies have attempted to describe behavior more thoroughly.[13-15] Their methods of evaluation were models for our behavior rating scale. The behavior rating scale developed for this investigation considered the presence or absence of sleep, body movement, crying, verbalization, and head/oral resistance. The addition of a verbalization category separated verbal abuse and threats, verbal protests, statements of discomfort, and/or occasional talking from various degrees of crying. The scale used did contain categories in which the ratings were not mutually exclusive in that the patient could exhibit behavior described by two different ratings simultaneously. For example, in evaluating head/oral resistance, the child could refuse to open his or her mouth (1) while attempting to spit at the operator (3). However, the investigators used the ratings in a heirarchical manner. Thus, the behavior considered to be the most disruptive to treatment (lowest rating) was used for each time period. These ratings give the practitioner a better idea of what kinds of behavior to expect. The overall assessment, rated independently by the operator and the other investigator, had 100% inter-rater reliability. Although the operator based his rating on his evaluation of how difficult and time-comsuming it was to complete treatment, it paralleled the other investigator's compilation of scores, which indicated disruptions in treatment.

It was important to assess the presence of confounding variables that may have obscured the results produced by ketamine. This investigation attempted to minimize the use of multiple pharmacological agents that exhibit additive sedative effects. The disadvantage of such combinations in research is the inability to distinguish the efficacy of one agent from another agent. Additionally, the efficacy of a particular agent is less obvious when high concentrations of nitrous oxide are administered during the treatment — a consideration in the one controlled oral ketamine investigation published recently.[10]

Despite this argument, diazepam was administered in an attempt to inhibit postoperative ketamine-induced psychic phenomena. However, the pharmacokinetics of diazepam and the dosage administered probably do not modify the sedative effects of ketamine. Peak antianxiety effects of diazepam occur approximately 60 min after administration.[16] Few patients participating in this study were subjected to operative treatment beyond 20 min. Moreover, no literature supports 0.1 mg/kg diazepam as an effective sedative agent in uncooperative and combative pediatric dental populations. Dosages of 0.3 mg/kg diazepam in conjunction with 50% nitrous oxide have been reported to be successful, but this represents a 300% increase in dosage and one of two sedative agents in use. With respect to the available literature, it appeared that diazepam would serve its primary role without augmenting the sedative effects of ketamine.

The second confounding variable present in previous investigations that this study eliminated was using physical restraint during operative treatment. The act of physically restraining a child prohibits an accurate assessment of how sedated the child is during treatment. The goal of conscious sedation is to modify previously anxious, uncooperative, and/or combative behavior. An effective sedation should produce a calm and cooperative patient willing to accept treatment. Without the ability to assess body movement and head/oral resistance, the efficacy of the sedative agent cannot be recorded accurately. Success rates of sedative agents tested with physical restraint are likely op-

timistic and should be reevaluated to determine their true ability to modify behavior. The lack of restraint in this study provided reliable information concerning the efficacy of ketamine to produce more cooperative behavior.

One of the most interesting aspects of oral ketamine sedation was its relatively short onset time. Alfonzo-Echeverri et al.[10] reported significantly shorter onset times for ketamine than for the commonly utilized meperidine and promethazine regimen. Our investigation supported the shorter onset time — in most cases within 20 min after administration. However, one child appeared to experience an unusual delayed onset 45 min following administration. These observations are in agreement with Grant, Nimmo, and Clements who reported mean peak plasma concentrations at 30 ± 5 min.[17] Short onset time is a distinct advantage for outpatient dental treatment.

A disadvantage to the reported short onset time may be an associated short working time. Alfonzo-Echeverri et al.[10] reported no significant difference in duration of treatment between the ketamine and meperidine/promethazine regimens, although working times were not provided. Most patients participating in our study appeared to perform well for at least 20 min of operative treatment. Several operative treatment times lasted 30–40 min.

Despite the relatively limited duration of sedative effects, the available working time was adequate in most instances to accomplish necessary dental treatment and to assess behavioral and physiological parameters. The working time allowed for completion of one to two sextants in most instances.

Although insignificant, the 8-mg/kg ketamine regimen produced more successful sedations, and virtually eliminated the most negative behaviors in all categories. However, this regimen did produce more sleep, which remains acceptable with appropriate monitoring. The 4-mg/kg regimen was associated with an increased incidence of extremely negative behavior within each category over time.

An encouraging result from this investigation was the fact that the behavior of 14 of 22 children selected for the study had been classified previously as "extremely negative." Four of these children were treated successfully with 4 mg/kg ketamine and eight children were treated successfully with 8 mg/kg ketamine. Much of the sedation research has focused on reluctant children who exhibited some evidence of negative behavior. However, the ketamine regimens were relatively successful in sedating children who exhibited a refusal to cooperate, forceful crying, fearful behavior, and other overt examples of extreme negativism. An oral sedation regimen capable of improving the anxious and uncooperative behavior of the most difficult children would be very exciting, because many patients might be successfully treated without resorting to the increased cost and risk of more aggressive techniques including traditional general anesthesia. Ketamine appears to have this potential but requires additional research.

Physiological parameters appeared to have been affected by ketamine also. Significant increases in systolic blood pressures, diastolic blood pressures, and heart rates at the start of treatment may indicate a ketamine-induced sympathomimetic effect.[5] It is difficult to distinguish ketamine-induced increases in blood pressure and heart rate within operative treatment from increases produced by the stress of operative treatment.

Within the 4-mg/kg sedations, the significant increase in heart rates at 10 and 20 min into operative treatment, when compared with treatment start was interesting, considering the fact that this phenomenon was not present in the 8 mg/kg sedations. This could have resulted from a decreased sedative effect, increased body movement, and increased stress associated with the lower dose. The decrease in oxygen saturations 10 min into operative treatment is likely associated with rubber dam application. This observation was clinically insignificant because at no time did oxygen saturation fall below 95%.

The incidence of systemic effects following ketamine administration was an important consideration. Subanesthetic dosages prevented significant systemic effects, although several notable effects were recorded in our population. There was a tendency for well-sedated patients in both groups to exhibit the "dissociated" appearance. With exception of one patient, the occasional nystagmic gaze and excessively watery eyes were limited to the 8 mg/kg ketamine regimen. Watery eyes always occurred in the presence of nystagmus, but the alternative was not true. Additionally, five of six patients with nystagmus and three of four patients with watery eyes were rated as clinical successes. Although sample size is limited within this subset, the presence of nystagmus may serve as a predictor of success. In addition to the aforementioned effects, several patients also appeared to be experiencing dizziness, diplopia, and/or other effects which would cause them to see multiple or distorted images of objects and people around them.

Respiratory compromise and/or loss of protective reflexes were not recorded during any sedation. An important consideration during sedation is the patient's ability to maintain spontaneous respiration and tolerate secretions and intraoral manipulations including water spray. All patients were treated in a reclined position and were subjected to water spray during tooth preparation. Although the rubber dam was utilized whenever possible, it was not always effective in maintaining a dry field or in preventing exposure of the intraoral cavity to excessive water. Despite these circumstances, all patients remained capable of clearing the airway and responding appropriately when necessary.

Initially, postoperative complications were a concern, because of the limited research with oral ketamine. Alfonzo-Echeverri et al.[10] reported a 40% incidence of emesis. Multiple unsuccessful flavoring agents were utilized in that investigation. Postoperative complications in this study were limited to two cases of emesis. The addition of grape Syrpalta® in this study apparently masked the poor taste of ketamine, was accepted very well by nearly all patients, and is recommended for future oral sedations.

One case of emesis occurred immediately after treatment and was likely induced by violent and uncontrollable behavior in addition to lack of compliance with NPO instructions despite parental declaration of compliance. The second case of emesis occurred following dinner 6 to 8 hr after treatment.

Additional postoperative findings include duration of postoperative sleep and the apparent amnesic property of these regimens. Upon returning home, most patients were reported to have slept from 2 to 5 hr, which may have been a result of diazepam or prolonged sedative effects of ketamine and might be considered a complication of treatment. Amnesia was observed but not quantified. Most patients experienced no recollection of the dental visit. This was remarkable for patients who had experienced poor sedation with anxious, fearful, and/or combative behavior.

Postoperative psychic phenomena were not reported in any patient. Since emergence phenomena are considered the significant drawback to ketamine administration, our data are encouraging.

The success rate of orally administered ketamine and diazepam is promising with consideration of these initial trials. Further studies should assess efficacy and safety with higher doses of ketamine. Additionally, the experimental design should incorporate the assessment and quantification of postoperative amnesia.

Conclusions

1. The regimen of 4 mg/kg ketamine in conjunction with 0.1 mg/kg diazepam was clinically successful in modifying behavior of nine of 16 (56%) crossover patients.
2. The regimen of 8 mg/kg ketamine in conjunction with 0.1 mg/kg diazepam was clinically successful in modifying behavior of 14 of 16 (87%) crossover patients.
3. There was no statistically significant difference between the clinical success rates for the alternative oral ketamine-diazepam sedation regimens within the crossover group.
4. Though clinically insignificant, blood pressures and heart rates increased, and oxygen saturations decreased from presedation values.
5. The 4 mg/kg ketamine regimen resulted in less sleep, more negative behavior, and more aborted treatments. The 8 mg/kg ketamine regimen resulted in more sleep, less negative behavior, and fewer aborted treatments.
6. Postoperative complications were limited to two cases of emesis.

This investigation was funded by Baylor College of Dentistry.

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