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

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Abstract

Purpose: *This study compared 2 oral ketamine-diazepam regimens (8mg/kg and 10 mg/kg of ketamine in combination with 0.1 mg/kg diazepam) in preschool age children with respect to physiological, behavioral and amnestic parameters.*

Methods: *Twenty-five children completed the double-blind, crossover design. Physiologic, behavioral and amnestic effects were evaluated.*

Results: *ANOVA demonstrated significant changes in systolic blood pressures and heart rates in both the 8 mg/kg group and 10 mg/kg group ($P<0.05$), as well as significant changes in diastolic blood pressures in the 10 mg/kg group ($P<0.05$). However, these changes were not clinically significant. Success rates were 28% for the 8 mg/kg dosage and 44% for the 10 mg/kg dosage. There was a cumulative vomiting rate of 50% and a psychic phenomena rate of 10%. There were no statistically significant differences between the two dosages with regard to success rates, postoperative vomiting, or psychic phenomena using McNemar's test.*

Conclusions: *There is no advantage of 10mg/kg dose of ketamine over the 8 mg/kg dose. Ketamine did not demonstrate amnestic effects in this study. There were statistically but no clinically significant changes in physiological parameters in either group. This study does not support the use of either 8 mg/kg or 10 mg/kg oral ketamine for the sedation of uncooperative children. (Pediatr Dent 23:223-231, 2001)*

The safe and effective treatment of the uncooperative or combative preschool-age child with extensive dental needs is one of pediatric dentistry's ongoing challenges. Practitioners may not accept some traditional behavior management techniques, including intimidation, coercion or the even more aggressive hand-over-mouth technique.

It has been proposed that the use of these techniques may cause traumatic memories for the child, which may result in lifelong dental phobias. Parents find these aversive techniques even less acceptable.[1,2] Current public scrutiny of behavior management in pediatric dentistry makes non-traumatic, safe and acceptable treatment imperative. Pharmacological intervention, in the form of general anesthesia or conscious sedation, is one solution.

Conscious sedation is often preferred to general anesthesia because it is convenient to use in the office and does not have the increased risk and cost of general anesthesia.[3] Most pediatric dentists consider oral sedation the method of choice[4] due to the increased liability insurance costs associated with parenteral administration. The child is also usually familiar with taking drugs by mouth. No one agent or regimen is recognized as the standard for comparison. Rather, an array of sedative agents is available for pediatric dental procedures. Nationwide surveys of pediatric dentists have shown that the most widely used sedation regimen is chloral hydrate, with or without promethazine or hydroxyzine, followed by meperidine and promethazine.[5,6] The benzodiazepines diazepam and midazolam are also widely used.[7]

When consideration is given to the limitations of the most common sedative agents, lack of evidence to support one regimen over another, and less than desired success rates, it is apparent that these regimens may be inadequate for the preschool-age child. A dosage of any medication sufficient to sedate the truly resistive child may cause concomitant depression of the cardiorespiratory system or loss of protective reflexes. Viable alternatives to the current methods must be investigated through further research. Oral administration of ketamine offers one promising alternative.

Ketamine hydrochloride was initially discovered as a derivative of phencyclidine hydrochloride. It produces a characteristic effect best termed dissociative anesthesia,[8] which most closely resembles a state of trance-like catalepsy, rather than sedation or hypnosis. Corssen et al[9] described its mode of action as a functional and electrophysiological dissociation between the thalamoneocortical and limbic systems. Sensory impulses are thought to reach the cortical areas, but fail to be perceived. This failure of perception occurs because ketamine depresses the association centers of the cortex and thalamus, creating a sensory isolation. Ketamine produces well-documented anesthetic, analgesic and amnestic effects.[8-15] It has a wide safety margin; protective reflexes are usually maintained even at anesthetic doses.[16] Its side effects include mild cardiorespiratory elevations, increased secretions, nystagmus, random limb movements, vomiting, and emergence reactions.[11] Ketamine has mainly been utilized as an IV or IM agent, but recent studies have evaluated its use orally.

Three recent medical studies evaluated oral ketamine as a preinduction agent for general anesthesia at dosages ranging from 3 mg/kg to 6 mg/kg. Gutstein et al[17] evaluated 3 mg/kg compared to 6 mg/kg oral ketamine for patient acceptance of IV cannulation prior to mask induction. The authors reported a success rate of 13% in the 3 mg/kg group and 67% in the 6 mg/kg group. Warner et al[18] compared 6 mg/kg oral ketamine

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to 0.5 mg/kg oral midazolam and to a mixture of 4 mg/kg oral ketamine and 0.4 mg/kg oral midazolam. Success rates for mask induction were 65% for oral ketamine, 45% for oral midazolam, and 85% for oral midazolam and ketamine combined. Sekerci et al[19] compared 3 mg/kg and 6 mg/kg oral ketamine to a placebo control and evaluated behavior during separation from parents and acceptance of mask induction. Success rates were 80% in the 3 mg/kg group, 71% in the 6 mg/kg group, and 36% in the control group. Gutstein et al[17] reported vomiting at a rate of 13% for the 3mg/kg dosage and 20% for the 6mg/kg dosage, while Sekerci et al[19] reported 7% and 33%, respectively, for the same dosages.

Additional medical studies evaluated oral ketamine at a higher dosage of 10 mg/kg for sedating pediatric patients during noxious invasive procedures. Tobias et al[20] reported on the use of oral ketamine for invasive oncological procedures, including bone marrow aspiration, with a success rate of 87%. Qureshi et al[21] administered oral ketamine in the emergency room for lacerations requiring suturing in pediatric patients, with a success rate of 80%. Humphries et al[22] used oral ketamine for burn ward procedures, comparing it to a mixture of Tylenol® No. 3 codeine elixir at a dosage of 0.5 mg/kg plus diphenhydramine at a dosage of 2.5 mg/kg. The ketamine group was reported to be significantly more sedated and to have significantly less pain, but no exact success rate was reported. Vomiting was limited to only a few episodes in each study. These studies which utilized oral ketamine at a higher dosage are significant, because they demonstrated its effective use for noxious and invasive medical procedures which correspond more closely to dental procedures.

Recent dental studies have evaluated oral ketamine for sedation of children. Alfonzo-Echeverri et al[23] in 1993 compared oral ketamine, 6 mg/kg, to oral meperidine and promethazine, 2 mg/kg and 0.5 mg/kg, respectively. The authors reported a success rate of 65% for ketamine compared to 45% for meperidine and promethazine. A vomiting rate of 40% for ketamine and 5% for meperidine and promethazine was found.

Roelofse et al[24] compared oral ketamine, 12.5 mg/kg, to standard oral premedication, or SOP, a well-known pre-anesthetic regimen in South Africa. The SOP was a combination of trimeprazine, physeptone linctus and droperidol. The success rates were 90% for ketamine and 67% for SOP. This dosage of ketamine resulted in a vomiting rate of 7% and a hallucination rate of 17%, the highest rate recorded in the pediatric literature.

Reinemer et al[25] in 1996 conducted a double-blind, crossover study comparing 2 oral regimens of 4 mg/kg and 8 mg/kg ketamine, each with 0.1 mg/kg diazepam. They reported a success rate of 56% and 86% for the 4 mg/kg dosage and the 8 mg/kg dosage, respectively. Vomiting was limited to 2 episodes in 39 sedations: a 5.1% vomiting rate.

Although the small sample size of the Reinemer study yielded few statistically significant results, the initial findings were promising. Based on these results, the present investigation was undertaken. The purposes of this investigation were to observe, describe, and compare 2 oral ketamine-diazepam regimens (8 mg/kg and 10 mg/kg of ketamine, in combination with 0.1 mg/kg diazepam) in preschool age children with respect to 1) physiological parameters 2) behavioral parameters and 3) amnestic effects.

Methods

Thirty-two patients of record from the Department of Pediatric Dentistry at Baylor College of Dentistry, a member of the Texas A&M University System Health Science Center, were recruited to participate in this investigation. Approval was granted by the Institutional Review Board of Baylor College of Dentistry. The investigation was conducted by a team of three dentists. The principal investigator (DS) conducted a memory test with the patient, administered the prepared sedation medications, and performed the operative dentistry. The co-investigator (CW), who was calibrated and has rated behavior in multiple sedation studies, evaluated patient behavior. The dental anesthesiologist (MW) assessed the patient's physical status, prepared the sedation medications, and monitored physiological parameters from sedation onset until discharge.

A double-blind, crossover design was employed, resulting in the same sample experiencing both drug regimens. The selection process followed strict criteria which included:

1. Patient age between 30 and 66 mo of age.
2. Documentation of negative behavior, classified as either Frankl 1 or 2, in the Patient Clinical Record during a previous dental appointment at the College of Dentistry.
3. Documentation of an overall score of 4 or less using behavior rating criteria modified from Houpt et al[26] (Table 1) at the previous appointment.
4. Treatment plan which required a minimum of two restorative appointments requiring local anesthesia.
5. Physical status of ASA I or II.
6. Tonsillar assessment of +2 or less, obstructing less than 50% of the airway, as specified by Brodsky.[27]
7. No contraindications for the use of ketamine, diazepam, or lidocaine.
8. Informed consent forms for dental treatment, conscious sedation, and investigational procedure completed by the parent or legal guardian.
9. Accompaniment by a parent or legal guardian during the dental appointment.

After the child met inclusion criteria for the study, the parent and/or legal guardian of each child was informed of the dental treatment plan and the indications for sedating their child. Explanation of this study was presented, and the parents were asked to participate. After consenting to enroll in the study, the parent and/or legal guardian was presented with the consent forms, which were explained in detail by the principal investigator. An opportunity to ask questions and address concerns was provided and alternative forms of treatment were presented.

Pre-sedation instructions were provided to ensure both patient safety and standardization of the procedure. These instructions included fasting times of at least 6 h for solid foods and 3 h for clear liquids prior to the appointment. Parents were asked to notify the dental clinic if the patient had any illness in the week prior to the appointment. The patient was scheduled to arrive at least 1 h before treatment to assess the recent health of the child and compliance with presedation instructions. The dental anesthesiologist examined the patient to assess medical status. The dental anesthesiologist obtained baseline vital signs including blood pressure, heart rate, respiratory rate, temperature and oxygen saturation. Adequacy of the airway by

Table 1. Behavior Rating Criteria*

Sleep
1. Awake, alert
2. Drowsy, disoriented
3. Intermittently asleep
4. Sound asleep
Body movement
1. Violent, uninterrupted movement
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 completed
5. Good-some limited crying or movement
6. Excellent—no crying or movement

*Modified from Houpt M, Sheskin RB, Koenigsberg SR, Desjardins PJ, Shey Z. Assessing chloral hydrate dosage for young children. *ASDC J Dent for Child* 52:364-369, 1985.

tonsillar assessment was also determined by the dental anesthesiologist.

If the patient was acceptable for sedation, he or she then began the first of 2 tasks to test for amnesia resulting from the ketamine. For the first task the child sniffed a cotton ball soaked in aromatic oil (orange, cinnamon or rose) and was asked to identify and remember the smell. For the second task the child was shown the location of a hidden prize box, rewarded with a prize, and asked to remember the location of the prize box. Both of these tests were done prior to giving the child the sedative agent. The dental anesthesiologist prepared the sedation medication during this time while the principal investigator and the co-investigator remained blind to the dosage. The patient received either the low or high dosage regimen (8 mg/kg or 10 mg/kg ketamine [Ketalar,® Parke-Davis, Morris Plains, NJ] in combination with diazepam 0.1 mg/kg [Diazepam Oral Solution,® Roxanne Laboratories, Inc., Columbus, OH]), delivered in a flavored carrier (Syrpalta,® Humco Laboratory, Texarkana, TX). A computer generated random number list was used to determine which dosage the patient received at the first visit. The alternate dosage was given at the second appointment.

The patient sat with the parent in the operatory for 30 min following administration. The patient then sniffed a cotton ball soaked in a different aromatic oil, identified the smell, and was instructed to remember it. Monitoring devices were applied and included a pulse oximeter (N100-Nellcor,® Nell Corp, Hayward, CA), a noninvasive automated blood pressure cuff (Dinamap,® Critikon, Tampa, FL), an ECG (MRL Porta Pak®90, Medical Research Laboratories, Inc., Buffalo Grove, IL), a capnograph (Criticare Poet II,® CSI, Waukesha, WI) and a precordial stethoscope. The dental anesthesiologist continuously monitored all vital signs and recorded them every 10 min until discharge. Radiographs were obtained if they were not obtained at the initial examination due to poor behavior.

The principal investigator applied topical anesthetic and injected 2% lidocaine with 1:100,000 epinephrine for local anesthesia, which did not exceed 4 mg/kg. Effectiveness of anesthesia was tested prior to rubber dam placement. Restorative treatment was performed as quadrant dentistry with rubber dam isolation when possible. Treatment was aborted if the patient became unmanageable to the extent that behavior jeopardized safety or compromised the dental treatment. All three investigators agreed to abortion of treatment and explained their decision to the parents. The investigators examined and released the patient following completion of treatment when discharge criteria were fulfilled. The discharge criteria included demonstrating stable and acceptable vital signs, and being awake, alert, and responsive to verbal stimulation. The parents received postoperative instructions, including emergency telephone numbers.

The modified Houpt scale (Table 1) was used for evaluation of the behavioral parameters of body movement, crying, head and oral resistance, sleep and verbalization at specific events. These events were the assessment of preoperative vital signs, administration of sedation medication, onset of sedation, local anesthetic administration, rubber dam application, 5 min into operative treatment, then at 10 min intervals throughout treatment until discharge. This rating was performed by the co-investigator. The principal investigator and the co-investigator independently assigned overall behavior ratings at the end of the appointment for comparison at the completion of the study.

At the beginning of the second appointment, the principal investigator presented the patient with 3 cotton balls scented with aromatic oils of orange, cinnamon, and rose and asked the patient to identify the aromas remembered from the previous appointment. Both the principal investigator and the co-investigator recorded success or failure of recall on amnesia response records. They then asked the patient to remember the location of the hidden prize box and recorded these results. The appointment proceeded following the protocol of the first appointment.

The principal investigator followed all patient visits with a telephone call the day of the procedure to determine if the patient experienced any postoperative side effects. A telephone call was also made the next day to question the parents concerning any dreams or additional side effects the child may have related. The investigators presented any parent of a patient who dropped out of the study, or who finished the study with remaining treatment needs, with options for treatment completion using a different oral sedation regimen, IV sedation, or general anesthesia.

Table 2. Overall Behavior, 8 mg/kg and 10 mg/kg Ketamine

Overall Behavior Rating	8 mg/kg	10 mg/kg	Cross 8 mg/mg	Cross 10 mg/mg
1=Aborted	12	11	9	9
2=Very poor	1	0	1	0
3=Poor	9	5	8	6
4=Fair	2	2	2	1
5=Good	1	5	1	6
6=Excellent	4	5	4	4
Total	29	28	25	25
% Aborted	41	39	36	36
% Failure	35	18	36	20
% Success	24	43	28	44

The child's overall behavior rating (Table 1) determined clinical success or failure of the sedation. Behavior that was fair or better, rated 4 or greater, defined success. Behavior that was poor or worse, rated 3 or less, defined failure.

Results were compiled and statistical analyses were performed. Physiological parameters were analyzed using ANOVA and Sheffe's F-test while controlling for within-patient variability. Comparison between the 2 dosages for physiological parameters was accomplished by paired t-test. Behavioral parameters were analyzed using the Wilcoxon Signed Ranks Test. McNemar's test for correlated proportions was used to analyze overall behavior and the side effects of vomiting and psychic phenomena. Significance level was established at $P<0.05$.

Results

A total of 32 patients participated in the study, resulting in 57 sedations for data collection. Twenty-four of the patients were recruited following new patient examinations and 8 were recruited from previous operative appointments. Twenty-five patients received both the 8 mg/kg and 10 mg/kg dosages and completed the crossover. Seven parents withdrew their children from the investigation following the first appointment. Three of the parents were disconcerted by the side effects of the medication, 2 of the parents felt that better results could be achieved with another method of sedation, and 1 parent withdrew his child when he was rescheduled because fasting instructions were not followed. The remaining child's restorative needs were completed in 1 appointment.

Group A: 8 mg/kg ketamine regimen

Twenty-nine patients ranging from 30 to 66 mo of age (mean 49 mo) received 8 mg/kg ketamine with 0.1 mg/kg diazepam. There were 18 males and 11 females. Seventeen of the 29 patients accepted the sedation medication, with minimal expressions of distaste. Twelve children resisted taking the medication and required parental restraint and needleless syringe administration to the posterior buccal vestibule. Of the 29 sedations, there were 7 successes, all in the crossover group. This resulted in an overall success rate of 24% and a success rate of 28% in the crossover group (Table 2). The restorative procedures consisted of amalgam and composite fillings, pulpotomies, stainless steel crowns, and extractions. Treatment times for successful sedations ranged from 5 to 45 min, with an average treatment time of 24 min, including administration of local anesthesia.

There were 22 failed sedations in the total group of 29, with 18 failures occurring in the crossover group. Of the failed sedations, 12 resulted in treatment being aborted. Three were aborted at onset, when the child was not sufficiently cooperative to allow the administration of local anesthesia. Four were aborted during local anesthesia administration, and 3 were aborted at rubber dam application. Two were aborted after 24 and 26 min of unsuccessful attempts to begin restorative treatment. Three patients from this group required restraint for extraction of symptomatic, abscessed teeth.

After onset, the patients demonstrated negative behavior more with time for the parameters of body movement, crying, head and oral resistance, and verbalization. Wilcoxon Signed Ranks Test demonstrated that the 8 mg/kg group showed a significant increase in body movement, crying, and head and oral resistance at administration of local anesthesia, rubber dam application, and 5 and 15 min of treatment when compared to ratings at presedation and onset. There were no significant differences in verbalizations compared to presedation ratings. Verbalizations increased significantly at local anesthesia administration and rubber dam application compared to onset. There was significantly more sleep at onset, local anesthesia administration, and 15 min of treatment compared to presedation ratings, but there were no significant differences in the sleep ratings after onset. Only 1 patient had a rating greater than drowsy or disoriented.

The patients demonstrated a stable physiological course during sedation (Table 3). ANOVA and Scheffe's F-test showed significant increases above presedation readings for systolic blood pressures at onset and 10 min later, but diastolic blood pressures showed no significant changes. Heart rates increased significantly above presedation readings at onset and 10 and 20 min later. Five patients showed a heart rate of >150 beats per min during instances of increased crying and body movement. Although statistical analysis revealed significant changes in systolic blood pressures and heart rates compared to presedation readings, no patient demonstrated clinically sig-

Table 3. Scheffe F-Test: Physiologic Parameters, 8 mg/kg

Comparison	Systolic	Diastolic	HR	02 Sat	C02
PreSed vs Onset	Sig*	NS	Sig*	NS	N/A
PreSed vs 10	Sig*	NS	Sig*	NS	N/A
PreSed vs 20	NS	NS	Sig*	NS	N/A
Onset vs 10	NS	NS	NS	NS	NS
Onset vs 20	NS	NS	NS	NS	NS
10 vs 20	NS	NS	NS	NS	NS

PreSed = Prior to administration of medication; Onset = 30 min after administration; 10 = 10 min after onset; 20 = 20 min after onset; NS = not significant statistically; N/A = not applicable, value not obtained; Sig* = $P<0.05$

Table 4. Scheffe F-Test: Physiologic Parameters, 10 mg/kg

Comparison	Systolic	Diastolic	HR	02 Sat	C02
PreSed vs Onset	Sig*	NS	Sig*	NS	N/A
PreSed vs 10	Sig*	NS	Sig*	NS	N/A
PreSed vs 20	NS	Sig*	Sig*	NS	N/A
Onset vs 10	NS	NS	Sig*	NS	NS
Onset vs 20	NS	NS	Sig*	NS	NS
10 vs 20	NS	NS	NS	NS	NS

PreSed = Prior to administration of medication; Onset = 30 min after administration; 10 = 10 min after onset; 20 = 20 min after onset; NS = not significant statistically; N/A = not applicable, value not obtained; Sig* = $P<0.05$

nificant changes in these physiologic parameters during their sedation. ECG monitoring showed normal sinus rhythms for all patients throughout the sedation. Neither oxygen saturation nor expired CO_2 changed significantly compared to presedation readings. One patient showed a transient decrease to 90% oxygen saturation, which was immediately corrected by repositioning of the head. All other patients maintained their oxygen saturation levels at 95% or greater. Respirations were recorded but were not analyzed statistically because the incidence of increased crying masked true respirations.

Major side effects are summarized in Fig 1. Three incidences interpreted as psychic phenomena occurred in patients receiving 8 mg/kg of ketamine. This interpretation was applied if behavior occurred that appeared to be bizarre, or if the patient appeared to be focusing on a fixed spot and responding to it in an inappropriate way. These incidents occurred at 7 min, 12 min, and 35 min after administration and lasted for 5 min, 7 min, and 15 min respectively before the symptoms disappeared. All 3 patients proceeded with their sedations and exhibited no further episodes. Psychic phenomena did not occur upon emergence from sedation. Two parents reported their children had unusual dreams the night of the sedations.

One patient had a delay in discharge because of prolonged drowsiness and was discharged 68 min after onset of sedation. All other patients were discharged within 10 min of treatment finish and within 1 h of onset of sedation. The patients in the 8 mg/kg group exhibited a vomiting rate of 45% overall; within the crossover group the rate was 40%. Vomiting occurred both in the dental clinic and at home post-operatively.

Nine of the 25 crossover patients received 8 mg/kg in their first sedation. When testing for amnesia of the patients, all but 2 of the patients remembered the location of the prize box. Four children remembered the smell introduced before administration of medications, and 5 could not remember it. Two children remembered the second smell, introduced after the onset of sedation, and 6 could not remember it. One patient refused to answer either way.

Group B: 10 mg/kg ketamine regimen

Twenty-eight patients ranging from 32 to 65 mo of age (mean 50 mo) received 10 mg/kg ketamine with 0.1 mg/kg diazepam. There were 15 males and 13 females. Twenty of the 28 patients accepted the medications, while 8 rejected the medications and required restraint with needleless syringe administration to the posterior buccal vestibule. Of the 28 sedations, there were12 total successes, with 11 occurring in the crossover group. This resulted in an overall success rate of 43% and a success rate of 44% in the crossover group (Table 2). The restorative procedures that were completed were the same as Group A. The successful sedations had treatment times that ranged from 7 to 55 min, with an average treatment time of 32 min, including administration of local anesthesia.

There were 16 failures overall, of which 11 resulted in abortion of the planned treatment. In the crossover group of 25 patients, there were 14 failures, of which 9 resulted in aborted treatment. Of the sedations which resulted in aborted treatment, 3 were aborted at onset, 3 were aborted at the administration of local anesthesia, 3 were aborted at the application of the rubber dam, and 2 were aborted during treatment. These 2 failures had to be restrained to extract symptomatic, abscessed teeth.

Patients demonstrated more negative behavior over time for all parameters, with the exception of verbalization, when compared to presedation ratings. Wilcoxon Signed Ranks Test demonstrated significantly increased body movement at local anesthesia administration and 5 and 15 min of treatment, compared to presedation ratings. Body movement was also significantly increased at local anesthesia administration, rubber dam application, and 5 and 15 min of treatment, compared to onset ratings. Crying increased significantly at 5 and 15 min of treatment compared to presedation ratings. Crying also significantly increased above onset ratings at local anesthesia administration, rubber dam application and 5 and 15 min of treatment.

Head and oral resistance increased significantly at rubber dam application and 5 and 15 min of treatment, compared to presedation ratings. Head and oral resistance also significantly increased above onset ratings at local anesthesia administration, rubber dam application, and 5 and 15 min of treatment. Verbalizations increased significantly above onset ratings at local anesthesia administration and rubber dam application. Sleep increased significantly at onset, local anesthesia administration, rubber dam application and 5 min of treatment compared to presedation ratings. Sleep also increased significantly at rubber dam application and 5 and 15 min of treatment compared to onset ratings. Only 1 patient demonstrated intermittent sleep, while none exhibited sound sleep.

ANOVA and Scheffe's F-test demonstrated significant increases in systolic blood pressures at onset and at 10 min after onset compared to presedation readings (Table 4). Diastolic blood pressures increased significantly at 20 min after onset. Heart rates showed significant increases at onset, 10 min and 20 min after onset when compared to presedation readings. Heart rates were significantly increased at 10 min and 20 min after onset when compared to onset. Six patients exhibited heart rates >150 beats per min during instances of increased crying and body movement. ECG monitoring showed normal sinus rhythms for all patients throughout the sedation. There were no significant changes in oxygen saturation or expired CO_2 compared to presedation readings. There was 1 transient decrease in oxygen saturation to a level <85%, which was immediately corrected by head repositioning. All remaining patients maintained their oxygen saturation levels above 95%. Although there were statistical changes, these were not clinically significant.

Major side effects are summarized in Fig 1. Two patients exhibited behavior interpreted as psychic phenomena. Both occurred shortly after onset of sedation. One lasted for 5 min and the other lasted for 11 min. Neither incident delayed or influenced treatment. No incidences of psychic phenomena occurred upon emergence from sedation. One parent reported their child had an unusual dream the night of the sedation.

There was 1 reported incidence of skin rash, which resolved by evening. This incident occurred during the child's first appointment and did not appear during the second appointment. Two patients experienced delay in discharge, one due to delayed onset of sedation and one due to prolonged drowsiness. The patient who experienced delayed onset showed no signs of sedation until 53 min after administration. He was discharged 45 min later. The patient with prolonged drowsiness was discharged 90 min after onset. The vomiting rate for the 10 mg/kg group was 61% overall; within the crossover group the rate was 60%. Vomiting occurred both in the dental clinic and postoperatively at home.

Sixteen of the 25 crossover patients received the 10 mg/kg dose in their first appointment. When testing for amnesia, all but 1 patient remembered the location of the prize box. Eight patients remembered the smell introduced before administration of medications and 8 did not remember it. Seven patients remembered the second smell, introduced after onset of sedation, while 9 failed to remember it.

Comparison of 8 mg/kg ketamine to 10 mg/kg ketamine regimen

Both groups showed similar increases in systolic blood pressures and heart rates compared to presedation readings. Only the 10 mg/kg group showed increases in diastolic blood pressures. Neither group demonstrated significant changes in oxygen saturation.

Paired t-tests revealed that between the 8 mg/kg group and the 10 mg/kg group there was a significant difference in expired CO_2. The 8 mg/kg group had significantly lower CO_2 readings at onset compared to the 10 mg/kg group. There were no other physiologic significant differences between the two groups and none of the changes were clinically significant.

Paired t-tests showed that there were no significant differences between the 8 mg/kg group and the 10 mg/kg group in any behavioral category. There were no significant differences between the two regimens in regards to vomiting or memory recall, according to McNemar's test. The success rates for the two groups were not significantly different using McNemar's test.

Discussion

Adjunctive nitrous oxide and restraints have been commonly used in other studies. It was important to this investigation to forego the use of nitrous oxide and physical restraint so as not to confound the pure effect of the two sedation regimens. Nitrous oxide was not utilized because it can be a significant modifier of behavior even when used alone, hence its widespread use in clinical practice.[28] If physical restraint was required, the sedation was not considered successful, because restraint can be used to perform treatment on an uncooperative non-sedated child. Physical restraint was utilized 5 times during the course of the study, after the decision was made to abort treatment, but at the request of parents for the extraction of symptomatic, abscessed teeth. This valid emergency treatment was appropriate. However, use of restraint precludes an accurate evaluation of sedated behavior, as restraints may falsely decrease ratings for body movement and falsely elevate ratings for success.

The rating scale (Table 1) used for the evaluation of behavior was an important aspect of this study. A more accurate picture of the ketamine-sedated child emerged when specific parameters of behavior such as body movement, crying, head and oral resistance, sleep and verbalizations, as well as overall behavior, were observed. For example, we know the patients having failed sedations in the 8 mg/kg group were exhibiting more than just "negative behavior." Nine of the 18 failed sedations were so disruptive that treatment was aborted. Three of these were restrained for emergency treatment because they were showing violent, uninterrupted movement, crying hysterically, turning their heads, and refusing to open their mouths.

An equally descriptive picture developed for the successful patients. For example, in the 10 mg/kg group, 11 patients had successful sedations, 9 of which had behavior that was either good or excellent. Body movement was limited to occasional arm or leg movement, corrected by simply placing the limb back in its proper position. The patients were able to open their mouths on request, heads remained still, and crying was only intermittent and mild. One of the patients rated fair was able to tolerate 38 min of treatment for stainless steel crown restoration with minimal, controllable movement; intermittent, mild crying; and mild head and oral resistance towards the end of treatment. This was remarkably improved behavior for a child rated a Frankl 1 at a previous operative appointment without ketamine sedation.

Information was obtained that further verified ketamine's safety with regard to physiologic parameters. There was no evidence of cardiorespiratory compromise with either dosage. Although there was evidence of sympathomimetic effects, seen as a rise in heart rates and systolic pressures in both groups, and an increase in diastolic pressures in the 10 mg/kg group, these effects were minimal and within clinical expectations of +/- 20% of normal. Decreased oxygen saturations occurred only twice in 57 sedations. Both occurred transiently and were immediately corrected by repositioning the head. Three patients showed a tendency to obstruct their airways, which was overcome by closely attending to proper jaw positioning. As an added precaution water spray was not used with these 3 patients. Secretions increased in most patients, but did not cause complications. Despite the overall safety of oral ketamine, practitioners using it should be aware of possible airway complications and be proficient in airway management.

The subject of monitoring deserves discussion for this investigation. For the purposes of this study, all patients experienced the placement of pulse oximeter electrode, ECG wrist clamps or electrodes, non-invasive blood pressure cuff, precordial stethoscope and CO_2 capnograph nasal cannula. As expected, many patients did not respond favorably to all of this stimulation. The placement of the nasal cannula for the CO_2 capnograph was especially noxious and irritating to many of the patients. Often its use was abandoned so that treatment could proceed. This is reflected in the decreased data collected for expired CO_2, which consisted of data from 19 patients in the 8 mg/kg group and 14 patients in the 10 mg/kg group. In

light of the adverse effect of the nasal cannula's stimulation, more work needs to be done to make this monitor less noxious and more acceptable if capnography is to be routinely used.

The side effects of oral ketamine demonstrated in this study were of interest. The occurrence of psychic phenomena was not expected, because there were no reported cases in the Reinemer study. A description of the patients experiencing these phenomena is important. A total of 5 patients (10%) experienced psychic phenomena in this investigation. Three occurred in the 8 mg/kg group. The symptoms presented 7-35 min after administration and consisted of patients appearing to see something that caused them to cry or try to escape from it. After 5-15 min all 3 patients had calmed down and demonstrated the typical trance-like appearance of ketamine.

In the 10 mg/kg group 2 patients also showed evidence of psychic phenomena. Both of these occurred during treatment. Both patients apparently saw things in the air and attempted to vocalize at these things. One boy began speaking, although his parent reported he rarely speaks. The second patient made sounds like a fire engine siren. Neither child seemed to be distressed and treatment progressed. Although clinically unremarkable, these experiences were disturbing to the parents who witnessed them. It is important for any clinician contemplating ketamine sedation to be prepared for the possible occurrence of these psychic phenomena and equally important that the parent of the sedated child be prepared.

A second significant side effect was that of vomiting, despite strict adherence to fasting times of at least 6 h for solid foods and 3 h for clear liquids. Parents were advised to give their children clear liquids and light meals postoperatively as a precautionary measure. Vomiting rates were not statistically different between the two groups, but the total number of vomiting episodes was clinically significant. The overall vomiting rate of 50% did not correspond to that in the original study by Reinemer et al,[25] which had a 5% vomiting rate. It is comparable, however, to studies by Gutstein,[17] Sekerci,[19] and Alfonzo-Echeverii,[23] which had 20-40% vomiting. Fifty percent of the patients vomited during treatment or immediately post-operatively in the dental clinic and 50% vomited at home. Four patients vomited both in the clinic and at home. Two children in the 8 mg/kg group and 5 children in the 10 mg/kg group had multiple vomiting episodes. The results of this study show that vomiting is indeed a regrettable side effect of oral ketamine administration.

Another interesting aspect of this study was the evaluation of ketamine's ability to cause anterograde amnesia. It is difficult, at best, to test for memory in very young children. Twersky et al[29] reported a higher number of false-positive responses in testing amnesia with children younger than 6 yr of age. There is also a wide variation in developmental influences during early childhood, which is reflected in children's varying abilities to perform standardized tests.[29] An additional confounding factor when testing children who have presented for medical or dental sedations, which require confirmed fasting status, is the incidence of decreased cognitive skills that has been correlated with fasting in children.[30]

Kupietsky et al[31] in 1996 used picture recall to compare amnesia produced by intranasal midazolam versus oral hydroxyzine. The authors demonstrated amnesia in 67% of children receiving midazolam and in 29% of those receiving hydroxyzine. The control group showed 10% amnesia. Flaitz et al[32] evaluated amnesia in children following rectal administration of diazepam by using a sample of toys with different textures and colors. The children receiving diazepam showed 58% amnesia, while the control group showed 8%. Other studies used dolls[33] or showed pictures[34-36] to children and had mixed results testing amnesia. No study has shown 100% of non-sedated children to recall either the picture or toy shown, nor has any study shown >71% of sedated patients to have amnesia. It has been speculated that the children remembered the item if they really liked it and otherwise forgot it regardless of whether it was shown before or after the child was sedated. In an attempt to eliminate this bias by the child we tested memory of smells.

It could be argued that the findings of this investigation indicate both retrograde and anterograde amnesia, based on the percentage of children who could not identify the smells. Retrograde amnesia, memory loss prior to the administration of the ketamine, was not proven in either dosage. The introduction of the first smell was no more than 5 min prior to the receipt of the prize from the box. However, the children remembered very well the location of the hidden prize box, which was important to them.

Ketamine apparently also failed to reliably produce anterograde amnesia, memory loss after the medication was given, in many of the children. A third of the children tested remembered the second smell administered. Also significant were some of the detailed stories related by the children concerning their memories of the previous dental visit. Several children stated forthrightly, "You pulled (fixed) my tooth." One child gave a vivid description of "flying through the air" (he was carried to another operatory to take a radiograph) and of being "kissed and kissed" during the procedure (the child received much praise, and several kisses on the head, for his excellent behavior). Another child played with her doll at home after the sedation appointment, placing bracelets (the euphemism used to describe the ECG wrist clips) on the doll's arms and placing a pencil in the doll's mouth. Both of these behaviors reflected procedures she only experienced while sedated. It is probable that children do not experience total anterograde amnesia while under the influence of ketamine, but they remember events or things that are important to them.

This investigation had numerous differences from the Reinemer study. Although the results from the Reinemer study were promising, they were not replicated by the 8 mg/kg dosage or improved by the 10 mg/kg dosage in the present investigation. Most important were the much lower success rates. Also of note was the incidence of psychic phenomena, which were not seen in the Reinemer study with either dosage, and the high incidence of vomiting. The patients in this study did not have the eye watering and pronounced nystagmus, which was seen in the Reinemer study. These results were so different from the original study that the drug manufacturer was telephoned to question for any changes in formulation since the original study. They stated that the formulation for ketamine is unchanged. Both the co-investigator and the dental anesthesiologist participated in the previous study, providing consistency between the 2 studies. The principal investigators in both studies were second year pediatric dental residents with comparable training and skills. The reasons for the differences in success between the 2 studies remain inexplicable. It may

be that the answer lies in the sample sizes of the 2 studies, as this investigation had a 50% increase in patients compared to the Reinemer study. It may also represent a normal variation in the populations.

Although this study was undertaken in the hope of finding a more successful sedation regimen than has been previously reported, this result was not achieved. This study indicated that oral ketamine produced low success rates, did not demonstrate reliable amnesia and had a high rate of complications that included vomiting and the need for airway support. A comparison between this investigation and other sedation studies shows that many other reported regimens have produced higher success rates, even in children who demonstrated previous negative behavior. Chloral hydrate produces unpredictable results, however, there are reports of high success rates ranging from 60% to 100% using it alone and in combination with other medications.[37,38] Other studies using different sedation regimens have reported similarly high success rates.[39,40] It is significant that while these studies had high success rates, most also used either nitrous oxide or physical restraint, or both. It is possible that without these aids, their success rates would have been lower. It is more likely, however, that even without the nitrous oxide and restraint, other sedation regimens have a higher rate of success than oral ketamine. Based on the 44% or less success rates of this study, oral ketamine does not appear to be as good a medication for the sedation of preschool age children as other commonly used medications. It is possible that the disorientation caused by the dissociative effects of ketamine may be so disturbing to the child that they are incapable of cooperating. This disorientation may be somewhat stimulating and thus a primary cause of the children's poor behavior. Other medications, which act as CNS depressants, may be more appropriate for the preschool age child.

Conclusions

1. There was no statistically significant difference in success between the 8mg/kg ketamine group and the 10 mg/kg ketamine group.
2. There were statistically significant increases in heart rates as well as blood pressures in both groups above pre-sedation levels. However, these were clinically insignificant.
3. There was no statistically significant difference between the 2 groups for psychic phenomena or vomiting.
4. The ability of ketamine to produce amnesia was not proven by this study.
5. Results of this study do not support the use of 8 mg/kg or 10 mg/kg oral ketamine for the sedation of uncooperative children.

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Abstract of the Scientific Literature

The Tunnel Restoration Results After 3.5 Years

This retrospective study evaluated the success rate for tunnel restorations in a low caries activity population. The data was for 242 tunnel restorations in permanent premolars and molars of 142 adults (mean = 18.8 years). The mean follow-up was 25 months. The material used was Ketac-Silver and a glass ionomer cement, (DeTrey). Most of the preparations were located about 1mm from the marginal ridge. The most frequent cause of failure was radiographically and clinical observed caries adjacent to the restoration. Failures occurred 5 times as often in molars than premolars. Marginal ridge fractures was 26% of the failures. The cumulative successful restorations was 82% after 2 years and 64% after 3.5 years.

Comments: The tunnel restoration has obvious drawbacks. No comparison was made with a CL II composite or amalgam. **LHS**

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Tunnel restorations in general practice. Influence of some clinical variables on the success rate. Pyk, M., and Mejare, I. Acta Odontol Scand 57(4):195-200, 1999.

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