Abstract

Aim The need to manage children using safe, effective and inexpensive conscious sedation materials and techniques in paediatric dentistry is high. This study evaluated the safety and effectiveness of a combination of low dose ketamine (5 mg/kg) and diazepam (0.2 mg/kg) used for conscious sedation in healthy children undergoing paediatric dental procedures at a paediatric dental outpatient clinic over a 3-year period.

Materials and methods All children who were scheduled for conscious sedation between 2009 and 2012 were included in the study. All children received ketamine 5 mg/kg body weight in combination with diazepam 0.2 mg/kg body weight in a single oral dose for use as conscious sedation. Patients were considered sedated when the Ramsey Score was 2 or 3. Time of onset and duration of surgical procedures were recorded. Side effects during and after discharge were recorded.

Result Twenty five patients participated in the study. The effectiveness of the sedation was 84.0%. The mean time of onset of action was 10.5 ± 7.2 minutes. All cases that needed additional sedation needed this after 35–36 minutes. Three cases (12.0%) developed high temperature in the night of the day of the procedure. There was a case (4.0%) of hallucination.

Conclusion Ketamine and diazepam as medication for conscious sedation was considered effective. The duration of effectiveness appears to be 35 minutes. The combination is considered safe for use for conscious sedation in healthy paediatric dental outpatients undergoing minor oral surgical procedures.

Keywords Diazepam; Ketamine; Nigeria; Paediatrics; Sedation.

Introduction

Methods adopted by dentists to manage dental anxiety in children are primarily aimed at avoiding unpleasant and unproductive confrontations with the child. The intention is to create an environment that will facilitate development of the child’s confidence and allow the dentists to carry out procedures with minimal disruption. Ideally, behavioural management techniques should be used alone to achieve treatment goals and to guide the child to develop most appropriate behaviour. While behaviour management techniques have been found to be effective in some patients [Folayan et al., 2003], analysis show that the use of behavioural management techniques for children was effective for a few non-invasive procedures but not for invasive procedures such as dental extraction [Folayan et al., 2005].

While there have been lots of studies conducted to understand how to best employ behaviour management strategies so as to ensure paediatric dental patients’ cooperation, behaviour management strategies may not be appropriate for all patients: fearful patients who require invasive procedures still come to the clinic. Where fear and pain may result in uncoperative behaviour, sedation in some form may be required.

The ideal sedation drug for short potentially painful or fear inducing procedures should provide ease of administration, rapid onset, effective analgesia, adequate immobilisation, minimum cardiac and respiratory effects, stable airway maintainance, a broad margin of safety, and a rapid smooth recovery. Ketamine satisfies most of these criteria [Green et al., 1990; Folayan et al., 2002].

Green and Johnson [1990] extensively reviewed the use of ketamine as a sedative agent in paediatric patients. There are reports that have noted its safe and effective use for dental procedures [Sporel, 1970; Birkhan et al., 1971; Bamber et al., 1973; Kaplan et al., 1975; Cohenour et al., 1978]. It rapidly produces profound sedation and analgesia without cardiorespiratory depressions typically seen with narcotics and benzodiazepines [Young and Epker, 1971; Reich and Silvay, 1989; Folayan et al., 2002].

The extensive review of the safety and efficacy of
ketamine as a sedative agent by Green and Johnson [1990] shows that ketamine has an exceptional wide safety margin and its recovery time, ranging from 30−120 minutes, makes it safe for outpatient use. The most often feared complication of aspiration and laryngospasm are also extremely rare when ketamine is used with proper precautions such as precluding its use in patients with upper respiratory infection [Green and Johnson, 1990]. The literature further demonstrates that combining ketamine with diazepam further precludes this rare event. Although ketamine is not usually associated with laryngospasm, it produces secretions which can play a trigger by irritating the vocal cords. When used with diazepam that decreases upper airway reflexes, this risk is almost eliminated [Folayan et al., 2002; Gilbertson and Langton, 1993; Murphy et al., 1993].

Unfortunately, available studies on the management of paediatric dental patients in Nigeria have focused mainly on the effectiveness of behavioural management techniques [Folayan and Idehen, 2004a; Folayan and Idehen, 2004b]. Yet there is a need to understand about the use of pharmaceutical agents in the management of paediatric dental patients in this study environment since there would always be an indication for its use. The primary aim of this study was to evaluate the effectiveness and safety of a combination of low dose ketamine (5 mg/kg) and diazepam (0.2 mg/kg) used for conscious sedation for paediatric dental procedures in a paediatric dental practice in Nigeria over a 3 years period (2009 to 2012).

Materials and methods

Ketamine hydrochloride and diazepam sedation was considered for use at the paediatric dentistry outpatient department for any healthy child who required minor oral surgery procedures that were considered painful (biopsy, apicectomy or cyst enucleation) or who was not cooperating during planned procedure (extractions, pulp therapy) using behavioural techniques. Uncooperative behaviours were disruptive behaviors resulting in delay of treatment or rendering treatment impossible. Yet for the management of these cases, immobilisation was critical for procedural success. Patients who were excluded from the procedure included those with organ dysfunction such as pulmonary infection or diseases, cardiovascular anomalies, psychosis, history of allergies, meal or drinks four hours before procedures.

All patients were seen and reviewed before surgery in the paediatric dentistry outpatient clinic of the Obafemi Awolowo University Teaching Hospitals Complex. Inclusion included all paediatric dental patients who exhibited behavioural problems in the dental chair. Parents were instructed not to feed their patients before coming to the hospital for the procedure.

On arrival in the clinic for surgery, patients were received by the anaesthetist who ensured compliance with prior feeding instructions. Thereafter, patients were seated on the dental chair and screened away from surrounding. Ketamine 5 mg/kg body weight was combined with diazepam 0.2 mg/kg body weight in a single oral dose and administered to patient after taking baseline vital signs using a pulse oximeter. The dose for ketamine was based on the outcome of the study of Roelofse et al. [1998]. The dose for diazepam was based on Schaeppi et al. [1976] recommendation that the effective bolus dose for benzodiazepine is 0.1 to 0.2 mg/kg body weight.

Patients were then monitored continuously by the anaesthetist. An estimate was made of the duration from sedative deposit to onset of sedation. Onset of sedation was determined by sign of drowsiness. A repeated dose of ketamine 1 mg/kg body weight IV alone was given when sedation was insufficient after onset of procedure. Patient was judged sedated enough when the Ramsey Sedation Score [Ramsey et al, 1974] was 2 or 3.

An intravenous line was then commenced and 0.15 mg/kg body weight of atropine was administered. All patients were administered with appropriate doses of local anaesthesia independent of level of sedation. The child’s level of cooperation during the procedure was recorded.

Suction machine was available along with a cardiac monitor, a pulse oximeter, airway equipment, and paediatric resuscitator. A cardiac defibillator was at hand in case of any emergency as well as suxamethonium.

Patient was transferred to a recovery room once oral procedure was completed and haemostasis achieved. The recovery room was quiet, cool and with low lights so as to minimise audiovisual stimuli. Patient was closely monitored by the dentist, the dental nurse and the anaesthetist from the time of injection till recovery was well established. A child was determined to be well recovered only when he/she returned to pre-treatment level of verbalization or awareness. At least a parent of the child was present during the procedure and the recovery.

Respiratory, pulse rates and the saturated peripheral oxygen were measured at the time of inception of procedure, at multiple time intervals during the procedure, during recovery and at discharge.

Discharge advice was given, including parents being advised to support the child and keep him/her under observation over the next 24 hours. Careful parental observation and no independent ambulation for 2 hours was emphasised. Any unusual behaviour or reactions had to be reported to the emergency department immediately or during the next day visit. The child was to continue without fluid or solid meals 2 hours post procedure.

Patients were reviewed the next day for any possible
signs of complications and side effects. Side effects were noted.

A data form for each child was filled as procedure was ongoing. Information recorded included time of administration of sedative agent, doses administered, time of onset of sedation, vital signs taken at every 10-minute intervals, time of completion of procedure and time of transfer to recovery room. Side effects after discharge were also recorded.

All the variables in the data were coded and data was input into a computer and analysed using StataIC 10 (StataCorp, USA). The mean time from onset to sedation to discharge in patients with a single dose of sedation and repeated dose was calculated. Comparison of baseline and end of procedure vital signs was done using paired t-test. Non parametric tools were used to assess for associations and correlation between variables. The effectiveness of the sedation was calculated by the number of children in the study who achieved Ramsey 2 or 3 level of arousal for the duration of the procedure.

**Results**

Twenty six patients were actually scheduled for conscious sedation in the clinic throughout the study period. One child was sedated but there were electricity challenges just at the onset of sedation and so procedure could not be continued. The age range of the 25 patients who undertook conscious sedation at the study centre was 3-12 years with a mean of $6.6 \pm 2.7$ yrs. The mean weight of the children was $24.8 \pm 9.6$ kg. Table 1 shows the profile of the patients. The most frequent indication for sedation was pulp therapy.

Conscious sedation was not achieved in four of the 25 patients. The failure rate for sedation using ketamine and diazepam in this study population was therefore 16.0% (4/25 patients). The effectiveness of ketamine and diazepam as medication for conscious sedation was therefore 84.0% (Table 1).

Of the 21 patients that achieved conscious sedation, one continued to be uncooperative, and this behaviour prolonged the management time.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male (n=14)</th>
<th>Female (n=11)</th>
<th>p value</th>
<th>Total (N=25)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>6.7 yr + 2.9 yrs</td>
<td>6.4 yrs +2.7 yrs</td>
<td>0.82</td>
<td>6.6 yrs + 2.6 yrs</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>24.6 kg +10.7 kg</td>
<td>25.0 kg + 8.6 kg</td>
<td>0.91</td>
<td>24.8 kg + 9.6 kg</td>
<td></td>
</tr>
<tr>
<td>Dose of diazepam</td>
<td>4.9 mg +2.1 mg</td>
<td>5.0 mg +1.7 mg</td>
<td>0.90</td>
<td>4.9 mg + 1.9 mg</td>
<td></td>
</tr>
<tr>
<td>Total dose of ketamine</td>
<td>134.8 mg +60.7 mg</td>
<td>126.4 mg +43.4 mg</td>
<td>0.70</td>
<td>131.1 mg +52.7 mg</td>
<td>3 children needed top up of ketamine after 35 minutes – one female and 2 males</td>
</tr>
<tr>
<td>Onset of action of agent</td>
<td>9.4 min + 5.7 min</td>
<td>11.7 min +8.6 min</td>
<td>0.46</td>
<td>10.5 min + 7.2 min</td>
<td></td>
</tr>
<tr>
<td>Duration of surgery</td>
<td>38.9 min+21.5 min</td>
<td>48.5 min +26.2 min</td>
<td>0.36</td>
<td>43.7 min+23.9 min</td>
<td></td>
</tr>
<tr>
<td>Ramsey score</td>
<td>1.9 +0.6</td>
<td>2.5 +0.9</td>
<td>0.03*</td>
<td>2.2 + 0.7</td>
<td>Score 1- 3 children</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Score 2- 15 children</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Score 3 – 6 children</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Score 4 – 1 child</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Score 5 – 0 child</td>
</tr>
</tbody>
</table>

**Complications**

- Sedation not achieved: 3
- Rise in temperature: 1
- Hallucination: 1

**Pulse rate**

- Baseline: 106.8 +14.9, 97.8 +9.7 (0.09, 102.9 + 13.4)
- End of procedure: 127.2 + 26.0, 107.5 + 15.1 (0.04*, 118.5 +23.7)

**Oxygen saturation rate**

- Baseline: 98.9 +1.2, 105.1 +10.9 (0.04*, 101.6 +7.8)

*Statistically significant

**TAB. 1** Profile of patients undergoing conscious sedation with ketamine/diazepam.
The mean time of onset of action of sedation was 10.5 ± 7.2 minutes (range: 3 – 26 minutes). Clinical response to the sedation procedure varied between patients independent of age, sex or weight. There was no association between onset of sedation and sex (p=0.15), and age (p=0.61). There was however a moderate (0.59) and significant (p=0.004) correlation between weight and onset of sedation: onset was faster in those who were heavier.

At onset of sedation, patient became drowsy and suddenly disengaged from conversation. There were occasional random, purposeless movement of the arms or legs which the dental nurse and/or parent needed to stabilise due to the narrow frame of the dental chair. The gaze also wandered unfixed.

Full adequate sedation was produced in all cases. Procedures could also be performed and concluded for all the 21 cases that achieved conscious sedation. Repeat dose due to incomplete sedation was not needed. Three cases needed additional sedation after 35-36 minutes. The average Ramsey score differed between gender significantly: females had lower Ramsey scores (Table 1).

Patients demonstrated a small but significant decrease in oxygen saturation between baseline and by the end of the procedure (3.9%; 95% CI: 0.29 to 7.6; p=0.04). There was also significant elevation of the pulse rate by the end of the procedure (-17.5%; 95% CI: -26.2 to -8.9; p=0.0004). Significant gender differences were observed between the pulse rate at the end of the procedure and oxygen saturation at the beginning of the procedure (Table 1).

During the recovery period, motor activity generally increased as recovery progressed. The children also made incoherent sounds as they recover from sedation with many attempting to sit upright. None of the episodes were unpleasant to both parent or staff.

Of the patients that were sedated, three (3/25-12.0%) reported having elevated body temperature during the night following sedation. The temperature rise was controlled by tepid sponging prior to arrival at the clinic the next day. The parents of one patient lamented that the temperature rise gave them serious concerns. One of the patients commenced antimalaria therapy prior to reporting back at the paediatric dental outpatient clinic the day after the procedure. One patient (1/25 – 4.0%) had hallucinations.

**Discussion**

Ketamine in combination with diazepam proved to be an effective sedation technique for managing and or preventing unpleasant reactions during paediatric dental procedures. It has a rapid onset, it is cheap with a smooth and relatively uneventful recovery. Most of the literature discusses the use of ketamine in combination with midazolam. Midazolam does have a number of properties that make it more suitable as a sedative agent when compared to diazepam. This includes production of a stable plasma concentration within hours of use, no tendency to cumulation, and rapid clearance following discontinuation [Lowry and Dundee, 1985]. However, in the absence of availability of midazolam, this study does show that diazepam still has a suitable role to play as a conscious sedation agent.

Diazepam is known to have a wide safety margin with relatively few side effects when used in combination with ketamine [Bamber et al., 1973], which adds an analgesic component to the sedation as well as counteracts the depressive side effects of diazepines (reduction of average blood oxygen level) on vital body function [Bamber et al., 1973].

Onset of action of sedation was faster in patients who were heavier. This association was not observed by Chiarette et al. [2011] who studied the efficacy of midazolam for procedural sedation in children. The reason for this observation could not be readily adduced since the dosage of the anaesthetic agent was based on weight. However, it is understandable that heavier children are also older and not so uncooperative as younger kids.

The study observed a significant decrease in oxygen saturation. This decrease is considered clinically mild since the oxygen saturation did not fall below 95. Decrease in oxygen saturation with the use of ketamine had earlier been observed [Tomlison, 1994]. This is however, not associated with any untoward effect. However, patients need to be observed closely, with some consideration to giving some oxygen during sedation [Tomlison, 1994].

Ketamine doses higher than 1 mg/kg body weight is also associated with an increase in pulse rate. The use of diazepam however ameliorates the potential for increased blood pressure and hallucination associated with the use of ketamine. The elevation in pulse rate observed in this study can be considered mild since this is less than the anticipated 20% often associated with the use of ketamine [Tomlison, 1994].

The recovery event in these patients were uneventful. Unlike reports by Green et al. [1990], no patient in this series reported post sedation vomiting. There were also no reports of laryngospasm nor were there reports of nightmares. While these complications may be a possibility, the small sample size for this study may be a reason why these possible complications were not picked up.

Twelve percent of the study participants reported elevated temperature within 24 hours post sedation which resulted in the parents resorting to tepid sponging to control temperature. This temperature was no longer observable when patients reported to the clinic for follow up visit 24 hours post procedure. The rise in temperature could be a result of the ketamine used in the drug mix as previous studies have reported increase in temperature associated with use of ketamine [López...
et al., 2002]. The rise in temperature may also be due to malaria which is endemic in the study environment. Faponle and Usang [2006] had earlier reported fever occurring at home within 24 hours of day case surgery and noted the potential for this to be an indication of malaria. Unfortunately, the patients were not followed up beyond the immediate 24 hours post-sedation and therefore this study could not conclude if the observed rise in temperature was malaria-induced. In view of the frequency of post surgery fever occurrence following sedation, it may be important to inform and counsel parents/guardians about this possible symptom in future sedation cases.

The study had taken needed precautions in the management of patients. Procedures were however performed in similar situations that could be simulated in any day to day paediatric dental practice. While conscious sedation using ketamine in combination with diazepam demonstrates a broad margin of safety, it is important that sedation should not be provided in settings were precautionary equipment and personnel do not exist. In this case series, anaesthesia was completely handled by trained anaesthetists. This study is however limited with respect to interpreting the outcome of the result which shows the combination of ketamine and diazepam as a conscious sedation agent to be effective. The study is simply descriptive with no control group for comparison. It is therefore difficult to make causal inferences regarding the efficacy of the conscious sedation agents being discussed. The study outcome remains relevant however, as access to midazolam is a challenge: midazolam has to be specially ordered from the pharmaceutical company whereas diazepam is readily available in hospital pharmacies. Evaluating for the effectiveness of ketamine and diazepam was therefore important as these were the chemical agents readily accessible.

Conclusion

Ketamine in combination with diazepam can be used effectively as a sedative agent for paediatric dental patients who require procedures that are not longer than 35 minutes in duration and who may not be able to benefit from behavioural management techniques. A rise in temperature within 24 hours of the procedure may be a possible complication and patients need to be warned about this and educated on its management.

References

› Faponle AF, Usang, UED. Post-operative symptoms at home in children following day case surgery. Southern African Journal of Anaesthesia and Analgesia. 2006; 101 - 104
› López KR, Gibbs PH, Reed DS. A comparison of body temperature changes due to the administration of ketamine-acpromazine and tiletamine-zolazepam anesthetics in cynomolgus macaques. Contemp Top Lab Anim Sci. 2002 Mar;41(2):47-50
› Lowry KG, Dundee JS. Pharmacokinetics of diazepam and midazolam when used for sedation following cardiopulmonary bypass. Br J of Anaesthesia. 1985; 57(9): 883-885