Intranasal midazolam better at effecting amnesia after sedation than oral hydroxyzine: a pilot study

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Abstract

Providing amnesia about a surgery is a desired side effect of a medication. This study compares anterograde amnesic effects of midazolam with hydroxyzine in children undergoing dental treatment with those drugs plus nitrous oxide, using a recall test. Thirty ASAI children 24-28 months, were shown a Standard-Binet intelligence scale-memory for objects subtest before entering treatment room. Twenty-one randomly determined children received 3.7 mg/kg hydroxyzine 45 min before treatment or 0.2 mg/kg intranasal midazolam in two succeeding appointments, alternatively. Recall in the 30-subject treatment group was 90%. Recall in the 21-subject treatment group was 71% for hydroxyzine and 29% for midazolam. Midazolam was more effective in creating amnesia than hydroxyzine in this study. (Pediatr Dent 18:32-34, 1996)

Midazolam as a premedication and sedative in adult patients is well established as more potent, faster acting, and inducing amnesia of a procedure better than diazepam.1,2 Its use as a premedication for the conscious sedation of children during dental treatment is not as well described, particularly its amnesic effect, which is of specific interest to the pediatric dentist.3-10 Past studies employed a simple memory test to evaluate the drug’s amnesic effect including questionnaires, pictures, parents' and patients' recall of the visit, and willingness to return for future visits.2,11-13 Patients were shown a picture or a series of pictures before or during treatment and were requested to recall the picture after treatment.14-16 This technique may be reliable in adults or older children, however studies are lacking on whether this test is suitable for detecting amnesia in 2- to 4-year-olds.

The purpose of this pilot study was to investigate the degree of anterograde amnesia obtained with midazolam compared with hydroxyzine in children undergoing dental treatment under conscious sedation with nitrous oxide by using a recall test.

Methods and materials

Development of memory recall procedure

Thirty subjects between the ages of 24 and 48 months (mean age of 36.4 months) participated in this part of the study. All participants arrived at the dental clinic for a first-time appointment with no previous dental experience.

Each child was shown a picture from the Stanford-Binet Intelligence Scale - Memory for Objects subtest (Level I-K, Items 1 and 2s, pp 142-44, 150-52. Item book #3, Sattler JM, Hagen EP, Thorndike RL, 4th Ed, The Riverside Publishing Company, 1986) prior to entering the treatment room. The test consists of common objects (e.g., shoe, flower, telephone, etc.) presented one at a time by the examiner. The child then chooses the previously presented picture from a larger array of pictures. One randomly chosen picture from two sets of pictures was shown to the child. The child was asked to point to the picture and identify it three times. Children who were not familiar with the picture were asked to repeat the name of the picture following the examiner. Parents were present but asked to refrain from commenting or assisting the child. After examining the child in the treatment room and returning the child to the waiting area, the child was shown an arrangement of five pictures that included the previously shown picture. The child was requested to point to the picture previously shown. Children reluctant to cooperate were coaxed or persuaded to point to the picture with the promise of a reward. Children who did not understand the request, particularly those younger than 3 years, were asked to point to or touch any picture.

Assessment of memory in sedated children

Twenty-one subjects between the ages of 22 and 48 months (mean age of 34.0 months), participated in the experimental group. An initial screening examination and behavior assessment were performed by a senior pediatric dentist. All participants were in good health (ASA 1), had no previous dental experience, and re-
The patients required sedation for treatment because of a "definitely negative" or "negative" rating according to the Frankl behavior rating scale.17

Procedure

The subjects were assigned randomly to receive either 3.7 mg/kg oral hydroxyzine 45 min prior to treatment or 0.2 mg/kg intranasal midazolam 10 min prior to treatment with the alternative drug regimen administered at the next appointment. All drugs were administered by an independent clinician. Before entering the treatment room, subjects were shown a picture as described in part one of the study and were then carried into the treatment room. The sedation procedure, monitoring, and evaluation of success scales were similar to those used in previous studies and are described in detail elsewhere.17 Both the operator and the evaluator were unaware of the medication used. Ten minutes after termination of treatment and after transferring the child to the waiting room the child was shown an array of pictures as described above. The examiner also was unaware of the medication given to the child for the sedation procedure. During the alternative session a different set of pictures was randomly shown so that each subject was shown a set of pictures not previously seen.

Data analysis

Since the rating scales used the nominal scale of measurement with related samples, the nonparametric McNemar matched pairs analysis test was used at the 95% level of significance. The treatment group was designed so that each subject served as its own control in a cross-over design, with time of day and operator being constant between the two treatment visits. The independent variable was the type of drug administered and the dependent variable was its effect on the child's memory.

Results

Procedure development group

Twenty-seven of the 30 (90%) children examined remembered and positively identified the picture shown to them before their dental examination (Table). Two children failed to identify the picture and another refused to cooperate. No significant correlation was found between age and recall, however, all of the three children who failed or refused to recall the picture were 24 months old.

Treatment group

No significant differences were found between the procedure development and treatment groups with regard to age (see Table, t = 1.03, P > 0.05). However, the time interval between presenting the first picture and the subsequent showing of the array of pictures in the development control group was less than in the treatment groups (t = 6.68, P < 0.05).

All sedation procedures were completed successfully except on one subject who had received midazolam.

No significant differences were found between the two drug regimens with regard to treatment time (t = 0.89, P > 0.05). Three incidents (7.1%) of refusal to cooperate and identify any picture were recorded in two children. When subjects received midazolam, 66.7% were unable to successfully recall the picture previously shown to them. In contrast, when subjects received hydroxyzine, 28.6% were unable to successfully recall the picture previously shown to them. This change in the ability to recognize pictures previously shown was found to be statistically significant (McNemar's test value = 6.68, P < 0.05). No correlations were found between the ability to recall the picture and the first or second visit or on the age of the subjects. Also, the ability to recall was not dependent on the overall evaluation of the sedation or on the degree of crying during the sedation.

Discussion

This study used a simple memory test to evaluate the amnesic effects of medications in the very young dental patient. Previous studies employing this method failed to show whether a 2- to 4-year-old child is capable of recalling a picture when not being subjected to any treatment or medication.14, 15 Furthermore, the test used here was designed specifically for this age group. A 2-year-old child who does not understand the request to identify the picture previously shown will instinctively point to the last one because it is the most familiar. Failure to do so would be attributed to a degree of amnesia due to a medication. Indeed, 90% of the children in the development group, regardless of age, pointed to the picture shown to them. In contrast, less than 30% of the chil-

**Table. Characteristics and results of the groups**

<table>
<thead>
<tr>
<th></th>
<th>Development Group</th>
<th>Treatment Group</th>
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<tbody>
<tr>
<td>N</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>Age* (months)</td>
<td>36.4 ± 8.9</td>
<td>34 ± 7.9</td>
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<tr>
<td>Time interval* (min)</td>
<td>45 ± 4.6</td>
<td>52.9 ± 10.9</td>
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<tr>
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<td>56.2 ± 12.9</td>
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<tr>
<td>Subjects who refused to identify picture</td>
<td>3.3% (1)</td>
<td>9.5% (2)</td>
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<tr>
<td></td>
<td>4.8% (1)</td>
<td></td>
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<tr>
<td>Subjects who succeeded in identifying picture</td>
<td>90.0% (27)</td>
<td>71.4% (15)</td>
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<tr>
<td></td>
<td>28.6% (6)</td>
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<tr>
<td>Subjects who failed to identify picture</td>
<td>6.7% (2)</td>
<td>19.0% (4)</td>
</tr>
<tr>
<td></td>
<td>66.7% (14)</td>
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</table>

* Mean ± SD.
children in the treatment group, when under the influence of midazolam, were able to identify the picture. However, the children in the development group did not undergo intensive dental treatment and the time interval was slightly less than the study groups. The design of the study was corrected for this with the positive control group of children receiving hydroxyzine, a drug not known to possess amnesic qualities. Indeed, when the children received hydroxyzine, the percentage of children successfully recognizing the picture was significantly different from the midazolam group and similar to the development group.

The use of a common psychological test is more appropriate for this young group than are questionnaires or questions regarding the dental procedure itself. Memory is difficult to evaluate in young children because they frequently make inaccurate responses independent of memory function and because developmental influences vary with age. Increased anxiety or fatigue (due to dental treatment) may interfere with learning and the ability to recall. Recognition tasks are less difficult to perform and are less sensitive to developmental differences. The anterograde memory loss (the inability to recall from the period subsequent to drug administration) in children was, therefore, evaluated utilizing the memory task of recognition, a recommended mode of sampling memory phenomenon in children.

The pediatric dentist, when confronting the young fearful child must provide treatment that is both safe and effective. However, the parents' main concern is for their child to leave the dental office without any psychological or physical trauma. A drug that allows a certain degree of short-term amnesia is desirable. The child can undergo treatment with conscious sedation yet not fear returning for future treatment or check-ups. The limited results of this study suggest that midazolam facilitates this situation. Further research is needed to determine whether the degree of recall is related to the amount of crying and effectiveness of the sedation. Another issue to be investigated is the correlation between amnesia and a child's willingness to return for future dental visits.

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