Preanesthetic medication using midazolam in children undergoing dental surgery: Comparing Rectal and Intranasal Administration

Abu Kamar Maisa, Ghazi Aldehayat, Al Madain Saba

Abstract

Objective: To compare the effectiveness of rectal and intranasal midazolam in sedation level of children undergoing dental surgical procedures under general anesthesia.

Methodology: 80 patients ranged in age from 1 to 8 years who were scheduled to receive dental treatment were randomly allocated into two groups to receive either 0.3 mg/kg of rectal midazolam or 0.2 mg/kg of intranasal midazolam.

The sedation level was evaluated at the following time points: immediately before the drug was administered, 20 and 30 minutes after drug administration. Pulse rate, respiratory rate, arterial blood pressure, oxygen saturation also were recorded.

Results: Rectal midazolam was found to be statistically more effective in providing a better sedation level than intranasal administration. 37(92.5%) and 38(95%) of the forty patients who received rectal midazolam were either drowsy or asleep at 20 minutes and 30 minutes after drug administration, respectively. For Patients who were received intranasal midazolam 27(67.5%) of the forty patients were drowsy or asleep and 13(32.5%) were fully awake (rated as agitated, alert and calm) at 20 minutes, However, the number of drowsy sedation patients decreased to 26(65%) and the number of awake patients increased to 14(35%) at 30 minutes. None of the patients from the intranasal group were rated as being asleep.

Conclusion: The study illustrates that rectal midazolam to be more effective in ensuring preoperative sedation in children than intranasal route.

Keywords: Per-rectal, midazolam, general anesthesia, intranasal midazolam

Introduction:

The preanesthetic management of children is difficult task to achieve. They are aware of separation from their parents and of the strange hospital environment, so the use of preoperative sedation in this age group may help to decrease anxiety and minimize psychological trauma to the child.

Benzodiazepines are used routinely for premedication in children. Midazolam, a water soluble, short acting benzodiazepine, which has been shown to have anxiolytic, sedative hypnotic and amnesic properties is used for preoperative sedation by intramuscular, rectal, and oral routes.

The results of few studies suggest that rectal and intranasal administration of midazolam may be worth using for effective premedication in children. 

The different routes of administration of midazolam (intranasal, oral, and rectal) as a sedative premedication have been previously studied. A study by C. Lejus et al has compared the intranasal and rectal routes of administration of midazolam. Patients received either 0.3 mg kg⁻¹ of rectal midazolam or 0.2 mg kg of nasal midazolam. The authors concluded that nasal midazolam induced sedation similar to that following rectal administration of midazolam with a shorter delay of onset. Another
study demonstrated that the rectal route of administration should be preferred route because of the high success rate and had the fastest onset of sedative action. 10

The purpose of this study was to compare the effectiveness of rectal and intranasal midazolam in sedation level in children before surgery.

Materials and Methods:
After approval of the protocol by local medical committee, eighty Children between 2 and 8 years of age presenting for dental extraction under general anesthesia at King Hussein Medical Centre in Amman-Jordan were included in this study between June 2011 and March 2012. Patient with cardiorespiratory or mental diseases were excluded.

The demographic data for children included in the study is shown in Table 1.

After informed consent had been obtained from the parents, patients were randomly allocated to receive either 0.3 mg/kg of rectal midazolam or 0.2 mg/kg of intranasal midazolam.

Doses of 0.2 mg/kg for intranasal and 0.3 mg/kg for rectal administration were chosen within the dose-exposure range found in preliminary studies, 10, 11, 12

Half of the 80 patients received rectal midazolam, whereas the other patients received intranasal midazolam. The mean dose was 6.5 mg (range: 3.6–9mg) for rectal route and 4.2mg (range: 2.5-6.5) for nasal route. For the rectal route the medication was administered by the anesthetist using a gel - lubricated 3.5 mm outside diameter pediatric feeding tube inserted 3 to 4cm into the rectum. For the intranasal route the medication was administered as drops from a needleless syringe into the nose.

Randomization was performed as the following: Envelopes with letters r and n written on equal size papers were drawn; if letter r was drawn the patient was allocated to group rectal midazolam and if letter n was drawn the patient allocated to group intranasal midazolam.

Following drug administration, the child remained with the parent away from the treatment room for 20 minutes. The patient was then separated from the parent and taken into the treatment room.

The investigators remained unaware of the premeditation type.

Five points sedation scale was devised prior to the study:
1. Agitated, i.e., clinging to parent and / or crying.
2. Alert, i.e., a wake but not clinging to parent.
3. Calm, i.e., sitting or lying comfortably with eyes spontaneously open.
4. Drowsy, i.e., sitting or lying, comfortably with eyes closed but responding to minor stimulation.
5. A sleep, i.e., eyes closed and not responding to minor stimulation.

Sedation scale, heart rate, respiratory rate measurements were recorded immediately before the the drug administration and at 20 and 30 min after drug administration.

The 20 min measurements were made immediately after the child was separated from his / her parents and so represents the response to separation.

A further set of measurements were made 30 minutes during the induction of anesthesia.

The induction technique was standardized to an inhaled induction using oxygen, Nitrous oxide and Halothane.

Mann-Whitney U test at the 95% significance level was used to compare the effectiveness of

<table>
<thead>
<tr>
<th>Table 1: Demographical data</th>
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<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>Age year mean(+SD)</td>
</tr>
<tr>
<td>Sex ( M/F)</td>
</tr>
<tr>
<td>Weight kg mean( +SD)</td>
</tr>
<tr>
<td>Duration of anesthesia minutes mean</td>
</tr>
</tbody>
</table>
the two routes of midazolam administration. (P values < 0.05 were considered significant)

The independent variable in the study was drug administration route (rectal or intranasal). The dependent variables in assessment of the effectiveness of each route were the sedation level.

**Results:**

The groups were broadly comparable with respect to age and weight using a t test (P values < 0.05 were considered significant). The two groups of patients did not differ significantly with respect to age and weight.

The behavior of children during the study period is shown in Table 2 and 3.

The Mann-Whitney U test indicated a statistical difference in sedation level at the time of parental separation, z = −3.613 (P= 0.00), and at the time of induction, z = −3.975 (P= 0.00).

Patients who were received rectal midazolam were more deeply sedated at the time of parental separation and at the time of induction of anesthesia than those receiving intranasal midazolam.

37(92.5%) and 38(95%) of the forty patients who received rectal midazolam were drowsy or asleep at 20 minutes and 30 minutes after drug administration respectively. None of the patients from the rectal group were rated as being agitated.

For patients who were received intranasal midazolam 27(67.5%) of the forty patients were drowsy or asleep and 13(32.5%) were fully awake (rated as agitated, alert and calm) at 20 minutes, however, the number of drowsy sedation patients decreased to 26(65%) and the number of awake participants increased to 14(35%) at 30 minutes. None of the patients from the intranasal group were rated as being asleep.

Heart rate and respiratory rate did not change during the study period in any of the groups.

Percent oxygen saturation remained stable throughout the study period.

There was no difference in duration of anesthesia or preoperative or post operative narcotic administration between the groups.

The time which was required to spontaneous eye opening post operatively was 10-15 minutes, and time for discharge from recovery room was 28-50 minutes which was similar in both groups.

**Discussion:**

Several studies have suggested that midazolam is an effective premeditation for children when administered intramuscularly, rectally, intranasal, or orally.

Like study by Chhibber AK and study by Tolksdorf W this study found that rectal midazolam to be a more effective as premedication than if given via the intranasal route. When assessing the level of sedation, the difference in sedation level between the 2 routes of administration was significant at the time of parenteral separation and at the time of anesthesia, also there was a deterioration of sedation over time for patients receiving intranasal midazolam, unlike rectal administration, where a better level of sedation level was obtained over time as shown in Chart I and II. This could be due to less drug absorption into the nasal mucosa in addition to loss of the medication into the oral cavity and, therefore, a lower blood level of the drug.

One study by Malinovsky JM in 1995 found that intranasal midazolam is an excellent method for premedication compared to the Oral and rectal routes. A more recent study by the same author found that the nasal midazolam induced Seda-

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**Table 2: Shows changes in sedation level following rectal and intranasal midazolam at 20 minutes after premedication administration**

<table>
<thead>
<tr>
<th>Group</th>
<th>Agitated</th>
<th>Alert</th>
<th>Calm</th>
<th>Drowsy</th>
<th>Asleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Midazolam (N=40)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>30</td>
<td>7</td>
</tr>
<tr>
<td>Intranasal Midazolam (N=40)</td>
<td>2</td>
<td>5</td>
<td>6</td>
<td>27</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 3: Shows change at 30 minutes**

<table>
<thead>
<tr>
<th>Group</th>
<th>Agitated</th>
<th>Alert</th>
<th>Calm</th>
<th>Drowsy</th>
<th>Asleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Midazolam (N=40)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>30</td>
<td>8</td>
</tr>
<tr>
<td>Intranasal Midazolam (N=40)</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>26</td>
<td>0</td>
</tr>
</tbody>
</table>
tion similar to that following rectal administration with a shorter delay of onset.\textsuperscript{11}

**Conclusion:**

This study demonstrates that rectal administration of midazolam in children undergoing surgical procedures under general anesthesia, compared to nasal routes, is more effective at alleviating preoperative uncooperativeness and anxiety.

**References:**