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RESEARCH ARTICLE

# Effect of premedication on hemodynamics and bispectral index in pediatric dental rehabilitation

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ABSTRACT

**Objectives:** The aim of this study was to evaluate the effects of rectal midazolam premedication on hemodynamic parameters and Bispectral Index Scale (BIS) values in children undergoing general anesthesia (GA) for dental rehabilitation.

**Materials and Methods:** Records of 30 children aged 2 to 7 years were retrieved and divided into 2 groups. Group 1 received midazolam 0.3mg/kg body weight rectally and group 2 involved children who did not receive any presedative (control). Mean arterial blood pressure (MAP), heart rate (HR), oxygen saturation ($SpO_2$), and BIS were evaluated for six times; before laryngoscopy(1); 1 min(2); 5 min(3); 10 min after nasotracheal intubation(4); at the time of extubation (5) and at the time of recovery(6). Paired t-test was performed to analyze all data. $p<0.05$ was defined as statistically significant.

**Results:** MAP and HR did not differ significantly between both groups before laryngoscopy ($p>0.05$) but increased significantly in control group 1 min after intubation ($p<0.04$). $SpO_2$ was in the normal range in both groups, which was statistically insignificant ($p>0.05$). The BIS records of the midazolam group were slightly lower than the control group in general but this difference was insignificant ($p>0.05$).

**Conclusions:** Midazolam premedication prior to GA induction resulted with lower MAP and HR than the control group 1 minute after intubation whereas it did not alter BIS values remarkably at all time intervals. Therefore, the midazolam sedation did not produce a significant change in reducing GA awareness in children undergoing GA for dental rehabilitation.

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## INTRODUCTION

Young children might have extensive dental treatment needs that exceed their cooperation.[1] In general, the referral for general anesthesia (GA) has been accepted as the "last resort" for such children.[2] Premedication with a sedative agent is a commonly preferred approach in order to minimize emotional trauma in children undergoing surgery and facilitate a smoother induction of GA with minimal hemodynamic alterations.[3] The amnestic effect of such agents[4] appears to be an advantage in that it is beneficial for preventing the retention of unpleasant memories in this patient group.

Midazolam has been demonstrated as a useful premedication to decrease preoperative anxiety and enable separation from parents with fewer unwanted side effects.[5] Rectal route for the administration of midazolam is preferable in especially young children since it has a rapid onset and relatively short duration of action. Once the sedative has been absorbed, the first-pass metabolism in the liver is largely avoided.[6] The bioavailability of rectally administered midazolam has been shown to be 52%[7] with the sedative reaching the peak plasma concentration within 20 min.[8]

The electroencephalogram (EEG) is a noninvasive tool to monitor the level of unconsciousness, which is based on the principal that EEG waveforms change with the level of alertness.[9] In 1997, the bispectral index scale (BIS) monitor (Covidien Healthcare, formerly Aspect Medical Systems, Newton, Mass) emerged to clinical practice.[10] The main working principal of BIS is to gather the processed EEG parameters in an attempt to provide a numeric measure of the hypnotic effect of anesthetic or sedative drugs on brain activity. By this means, a single numeric value, scaled from 0 to 100 is produced.[11] According to the manufacturer, a BIS score of >90 indicates an awake patient; 71-90, mild to moderate sedation; 61-70, deep sedation; and 40-60, general anesthesia. The primary goals of BIS monitor are to prevent intraoperative awareness and recall during GA, to titrate anesthetic delivery to promote early recovery from GA, as well as to provide an objective, quantitative measurement of the level of hypnosis.[9,12,13]

Previous studies on BIS utilization in pediatric patients have indicated that BIS could possibly be used with children with the same benefit found in the adult patient population.[14,15] However, little information exists regarding the effect of rectal midazolam premedication on the BIS values of pediatric dental patients under GA. Therefore, the aim of this retrospective study was to evaluate the effects of rectal midazolam premedication on hemodynamic parameters and BIS values in children undergoing GA for dental rehabilitation.

## MATERIALS AND METHODS

Electronic database searches were conducted retrospectively for assessing GA records of healthy (ASA I) children aged 2 to 7 years within normal range of weight who underwent GA with nasotracheal intubation procedure for dental care in Yeditepe University, Faculty of Dentistry. Written informed consent forms were obtained from the parents of all children. Data of children with any mental retardation, physical disabilities or psychological disease were excluded. The anesthesia records were divided into 2 groups. The first group received midazolam 0.3mg/kg body weight (Dormicum, Roche) rectally and the second group involved children who did not receive any presedative (control). The same anesthesiologist performed all general anesthesia procedures. The anesthesiologist used 8% sevoflurane and oxygen or propofol induction 2mg/kg in

cases where intravenous (IV) access was established. After nasotracheal intubation, anesthesia was maintained with sevoflurane. The children were monitored with 3-lead electrocardiogram, noninvasive arterial blood pressure, pulse oximetry, and BIS. Mean arterial blood pressure (MAP), heart rate (HR), oxygen saturation ($SpO_2$), and BIS were evaluated before laryngoscopy(1); 1 min(2); 5 min(3); and 10 min after nasotracheal intubation(4); at the time of extubation(5); and at the time of recovery(6).

Statistical differences between and within the groups and sessions of GA were determined with SPSS 10.0 program. Since standard deviations did not exceed 20% of the mean values, paired t-test was performed to analyze all data. *p* values lower than 0.05 were defined as statistically significant.

## RESULTS

A total of 30 children, who received general anesthesia for dental treatment, were enrolled in the study. The demographic data of the participants are shown in Table 1. Both groups were comparable with respect to age, gender and body weight. MAP did not differ significantly between both groups before laryngoscopy ($p>0.05$), but increased significantly in control group 1 min after intubation compared with midazolam group ($p<0.04$. There were no significant differences in MAP between groups at the following time intervals ($p>0.05$) (Table 2). HR significantly increased in control group 1 min after intubation ($p<0.05$) whereas no significant differences were found at the other time intervals ($p>0.05$) (Table 3). $SpO_2$ was in the normal range throughout the surgical procedure in both groups, which was statistically insignificant ($p>0.05$) (Table 4). The BIS records of the midazolam group were slightly lower than the control group in general, but this difference was not statistically significant ($p>0.05$) (Table 5).

**Table 1.** Demographic data of the children who received GA

| | Mean age (years±SD) | Gender |
|---|---|---|
| Midazolam group | 5.6±2 | 7 boys, 8 girls |
| Control group | 5.5±1 | 8 boys, 7 girls |

## DISCUSSION

Fear, anxiety, lack of cooperation or painful and unpleasant procedures such as establishing an IV access or applying an anesthesia facemask may produce stormy anesthetic inductions in unpremedicated children.[16] Thus, premedication has become fundamental in pediatric anesthetic practice. Midazolam is the most commonly used drug for this purpose. Sedative, anxiolytic and amnesic characteristics of midazolam are considered to create a calming effect, which reduces the anxiety of children during separation from their parents, establishment of IV access, mask placement and after emergence.[17] Ko et al.[18] have shown 0.2mg/kg oral midazolam to be effective in reducing emergence agitation and postoperative analgesic requirements.

Tolksdorf and Eick[19] compared rectal, oral and nasal routes of midazolam premedication in children aged 1 to 6 years and suggested that the fastest onset of sedation was found after rectal route of administration. They concluded that the main disadvantage of oral route was that its effect was less predictable leading to a significant delay in transport to the operating room. Moreover, they found the effect of nasal midazolam rather euphoric than sedative. The authors recommended

**Table 2.** Mean arterial blood pressure (MAP) of the children who received GA
(1) before laryngoscopy;
(2) 1 min;
(3) 5 min; and
(4) 10 min after nasotracheal intubation;
(5) at the time of extubation;
(6) at the time of recovery

| Mean arterial blood pressure | Mean±SD (mmHg) (n=15) | | p |
|---|---|---|---|
| | Midazolam group | Control group | |
| MAP1 | 88.20±2.44 | 89.29±2.95 | 0.66 |
| MAP2 | 95.45±9.44 | *115.82±19.37 | 0.04 |
| MAP3 | 80.45±11.33 | 78.64±13.11 | 0.52 |
| MAP4 | 78.54±10.16 | 74.58±9.45 | 0.55 |
| MAP5 | 93.74±14.06 | 90.94±11.74 | 0.66 |
| MAP6 | 93.48±17.14 | 90.58±10.08 | 0.71 |

*p<0.05

**Table 3.** Heart rate of the children who received GA

| Heart rate | Mean±SD (n=15) | | p |
|---|---|---|---|
| | Midazolam group | Control group | |
| HR1 | 118.42±12.98 | 112.64±12.03 | 0.80 |
| HR2 | 121.14±11.84 | *133.05±11.90 | 0.04 |
| HR3 | 115.94±17.04 | 99.82±17.81 | 0.60 |
| HR4 | 111.31±15.03 | 95.82±17.45 | 0.54 |
| HR5 | 129.05±17.82 | 121.82±16.61 | 0.55 |
| HR6 | 128.62±16.59 | 115.00±16.04 | 0.80 |

*p<0.05

rectal route of administration because of high success rate and few side effects in children. This finding was corroborated by Houi et al.[20] and Jensen and Matsson[1]. Therefore, rectal route was preferred for the midazolam premedication in the present study.

The rectal dose used in the present study (0.3mg/kg) is reported to be sufficient to sedate 3-9 year-old children before GA.[1,8] In the previous reports, it was found that most children under 5 years of age had a good acceptance of rectal administration of midazolam.[21,22]

**Table 4.** Oxygen saturation of the children who received GA

| Oxygen saturation | Mean±SD (n=15) | | p |
|---|---|---|---|
| | Midazolam group | Control group | |
| $SpO_2$1 | 99.28±0.66 | 99.29±0.58 | 0.90 |
| $SpO_2$2 | 99.17±0.66 | 99.11±0.78 | 0.92 |
| $SpO_2$3 | 99.05±0.76 | 99.17±0.63 | 1.00 |
| $SpO_2$4 | 98.97±0.92 | 99.17±0.63 | 0.95 |
| $SpO_2$5 | 99.00±1.21 | 99.41±0.50 | 1.01 |
| $SpO_2$6 | 98.51±1.50 | 99.05±0.74 | 0.99 |

*p<0.05

**Table 5.** Bispectral index values of the children who received GA

| Bispectral index | Mean±SD (n=15) | | P |
|---|---|---|---|
| | Midazolam group | Control group | |
| BIS1 | 39.17±6.59 | 40.88±6.27 | 0.51 |
| BIS2 | 40.40±7.84 | 41.70±6.78 | 0.65 |
| BIS3 | 33.11±9.18 | 34.11±12.29 | 0.55 |
| BIS4 | 38.97±8.06 | 40.58±6.37 | 0.65 |
| BIS5 | 67.60±7.46 | 69.00±5.74 | 0.61 |
| BIS6 | 71.34±8.42 | 71.41±8.32 | 0.52 |

*p<0.05

The significant increase in MAP and HR 1 minute following nasotracheal intubation in control group as compared with the midazolam group was attributed to the effect rectal midazolam premedication regarding the depth of anesthesia. It might be assumed that rectal midazolam was able to better suppress cardiovascular responses to nasotracheal intubation unlike the control group. This was probably due to the beneficial effect of rectally administered midazolam premedication since the same anesthetic protocol was followed in both patient groups other than the midazolam administration. Similarly, Spear et al.[21] found that rectal midazolam as premedication did not alter MAP, HR and $SpO_2$ saturation over a wide dosage range (0.4-5.0mg/kg). In the present study, all hemodynamic parameters were in the normal range relevant with the age of the patient consistent with the above-mentioned findings.

BIS is a commonly used tool for intraoperative monitoring of anesthetic efficacy and cerebral ischemia. The use

of BIS as a guide for determining the intraoperative depth of anesthesia was extensively studied and it is mostly concluded that BIS is beneficial in reducing the time of extubation and duration of recovery in children.[23,24] Inadequate depth of anesthesia might precipitate laryngospasm and subsequent loss of airway patency during airway instrumentation and preparation.[15] Previous studies have shown that the incidence of intraoperative awareness is lower in patients receiving midazolam before the induction of general anesthesia than in those who did not receive it[25,26], suggesting that midazolam has a good amnesic effect and ability to prevent intraoperative awareness. In contrast, Barr et al.[27] reported a large variation of BIS during clinically adequate anesthesia with midazolam and fentanyl.

A BIS-assigned hypnosis level of 40 was shown to provide better conditions and lesser laryngeal reflexes compared with an assigned hypnosis level of 60.[28] Similarly, Messieha et al.[15] reported that mean BIS value of 34.7 provided adequate intubation conditions without significant complications. It is generally agreed that a BIS value higher than 40 may not provide the most ideal conditions for intubation and hence may increase the risk for intraoperative airway complications.[15] In line with these findings, mean BIS value was below 40 throughout the GA procedure in the midazolam group whereas there was the mean BIS value was increased to 41.7 in the control group 1 minute after intubation which was slightly above the above-mentioned BIS level.

In another study, Messieha et al.[23] suggested that children having oral rehabilitation under GA recover more quickly and are able to be discharged sooner if BIS is used to guide their anesthetic. It should be kept in mind that attempts to control depth of anesthesia based on cardiovascular and other physiological parameters would periodically require greater anesthetic doses thereby resulting in higher tissue anesthetic levels at the end of the surgical periods and prolonging the time for recovery.[23]

There are several limitations to the present study including the sample size, variety of the dental procedures performed and different lengths of the procedures, all of which could confound the results. Plasma concentrations of midazolam were not measured or the effect site concentrations of midazolam were not maintained at stable levels. Laryngoscopy and nasotracheal intubation are intense stimuli that might induce a remarkable sympathetic response following anesthesia induction.[29] However, BIS remained stable throughout the procedure with a statistically insignificant increase at the time of intubation in both groups.

BIS has gained popularity at the following years after it emerged to clinical practice. However, it could not gain importance, as it deserved over time. Still used by many anesthesiologists, BIS is a useful tool for assessing the intraoperative depth of anesthesia.[12,13] In the present study, BIS values were found between the normal ranges and showed no significant difference between groups as anticipated due to proper and adequate depth of anesthesia. On the other hand, this finding indicates that an effective and accurate depth of anesthesia was performed. Therefore, BIS values may not be the only means of assessing the efficiency of premedication prior to GA.

## CONCLUSION

Within the limitations of the present study, it is concluded that midazolam premedication prior to GA induction resulted with lower MAP and HR than the control group 1 minute after intubation, whereas it did not alter BIS values

remarkably at all-time intervals. Therefore, the midazolam sedation did not produce a significant change in reducing GA awareness in children undergoing GA for dental rehabilitation. Further studies are required to better observe the effects of midazolam premedication with different routes of administration in different age groups in children.

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