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Preanesthetic Medication with Intranasal Midazolam for Brief Pediatric Surgical Procedures

Effect on Recovery and Hospital Discharge Times

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Background: The perfect preanesthesia medication and its ideal route of administration are still debated, but for pediatric surgical patients undergoing brief procedures, preanesthesia medication is frequently omitted because of the concern that it will prolong the child's recovery from anesthesia. The effects of nasally administered midazolam on anesthetic recovery and hospital discharge times were determined in 88 ASA physical status 1 and 2 ambulatory surgical patients undergoing a brief surgical procedure.

Methods: Using a randomized, double-blind, placebo-controlled design, 88 ambulatory surgical patients 10–36 months of age undergoing myringotomy and tube insertion were entered into the study. All patients were randomly assigned to one of three medication groups. One group received 0.2 mg/kg intranasal midazolam; a second group received 0.3 mg/kg intranasal midazolam; and the third group received intranasal saline drops. All patients were anesthetized with nitrous oxide, oxygen, and halothane administered *via* mask. The duration of anesthesia lasted between 9 and 10 min. After preanesthetic medication, the children were evaluated for ease of separation and induction of anesthesia. In addition, the time from when the anesthetic was discontinued until the child recovered from anesthesia and the time the child was discharged home were recorded by a nurse observer blinded to the patient grouping.

Results: Children receiving midazolam had smoother, calmer parent-child separation and anesthesia induction scores, and their anesthesia recovery times and hospital discharge times were the same as those receiving placebo.

Conclusions: For children undergoing brief surgical procedures, nasal midazolam provides satisfactory anxiolysis without delaying anesthesia recovery and hospital discharge. (Key words: Anesthesia, pediatric: preinduction. Anesthetic techniques: transmucosal drug administration. Hypnotics, benzodiazepines: midazolam.)

SURGERY and anesthesia can cause considerable distress and psychologic consequences for both parents and children. Although it is difficult to determine which components of a child's hospitalization experience result in psychologic problems, age, parental anxiety level, previous hospital experiences, and the type of surgery are factors that can influence a child's anxiety level and psychologic well-being.¹⁻³

In children, preanesthetic medications frequently are administered as pharmacologic adjuncts to help alleviate the stress and fear of surgery as well as to ease child-parent separation and promote a smooth induction of anesthesia. For ambulatory surgery patients, pharmacologic adjuncts also should avoid prolonging anesthesia recovery and delaying hospital discharge time. Oral, rectal, and intramuscular routes of preanesthetic medication administration have been used; however, each route has disadvantages.⁴⁻⁸ Although nasal preanesthetic medications can cause irritation to the nasal mucosa and patient crying, its rapid and reliable onset of action, avoidance of painful injections, and ease of administration have made it a convenient way to premedicate children. Midazolam has been reported to produce partial anterograde amnesia, provide tranquil sedation, reduce separation anxiety, and facilitate induction of anesthesia.⁹⁻¹¹ However, the effect of intranasal midazolam on recovery of ambulatory pediatric surgical patients has not been evaluated.

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Table 1. Ease of Separation and Ease of Induction Score System

| | |
|-------------|------------------------------------------------------|
| 1 Excellent | Patient unafraid, cooperative, or asleep |
| 2 Good | Slight fear and/or crying, quiet with reassurance |
| 3 Fair | Moderate fear and crying, not quiet with reassurance |
| 4 Poor | Crying, need for restraint |

Myringotomy and tube insertions are among the most frequently performed ambulatory surgical procedures in children. Because the procedure is brief, the use of preanesthesia medication might be expected to prolong anesthesia recovery and hospital discharge. This study evaluated the effects of intranasal midazolam on anesthesia recovery and hospital discharge times, parent/child separation, and smoothness of the anesthetic induction in children undergoing myringotomy and tube insertion.

Methods and Materials

This study was approved by the Children's Hospital of Pittsburgh Institutional Review Board, and informed, written consent from a parent was obtained. Eighty-eight children (ASA physical status 1 or 2) aged 10–36 months scheduled for myringotomy and tube insertions were studied. The children were randomized into one of three preanesthetic medication groups: group A received 0.2 mg/kg intranasal midazolam, group B received 0.3 mg/kg intranasal midazolam, and group C received 0.04 ml/kg of normal saline solution. All investigating observers, caregivers, and patients were blinded to the treatment administered. Each child was administered one of the preanesthetic medications by their admitting unit nurse. After the preanesthetic medication was administered, the children were transported with a parent to a play area adjacent to the operating room. As is the routine in our institution, children were separated from their parents in the playroom and taken to the operating room. Thus, no child's parents were present during the induction of anesthesia. At the time of parent-child separation, a four-point "separation score" was assigned and recorded for each child (table 1). In the operating room, after the appropriate monitors were placed (precordial stethoscope, electrocardiogram, pulse oximeter, blood pressure cuff), general anesthesia was induced and maintained with halothane and 60% N₂O in oxygen administered *via* mask. The inspired halothane con-

centration was adjusted to the patient's clinical needs. The quality of the anesthesia induction also was assessed using a four-point scale (table 1). For each patient, the induction and separation scores were assigned by the same person (blinded to premedication treatment) throughout the study. No other intravenous, intranasal, or intramuscular medication was administered. All myringotomy and tube insertions were performed by the same surgeon.

After surgery, the anesthetic agents were discontinued immediately, and the children were transported to the recovery room. Our institution has a two-stage recovery area. The first stage is in the postanesthesia care unit (PACU); the second stage occurs in the ambulatory surgical unit, which is located on a different floor of the hospital. The criterion for discharge from the PACU was a score of ≥ 8 on our institution's ten-point PACU score (table 2).

The criteria for hospital discharge included meeting the discharge requirement for the PACU and the ability of the child to drink fluids once in the ambulatory unit. The study nurse, blinded to the patient's treatment group, continuously observed each patient in the PACU and ambulatory unit. Times from discontinuation of the anesthetic agents until the patient was discharged from the PACU and hospital were recorded. For purposes of data analysis, satisfactory separation and induction scores were ratings of 1 and 2, whereas unsat-

Table 2. Post Anesthesia Care Unit Assessment and Recovery Score

| |
|-------------------------------------------------------------|
| Respiration |
| Apneic = 0 |
| Dyspnea or limited breathing = 1 |
| Able to breathe deeply and cough freely = 2 |
| Activity |
| Able to move no extremities voluntarily or on command = 0 |
| Able to move two extremities voluntarily or on command = 1 |
| Able to move four extremities voluntarily or on command = 2 |
| Consciousness |
| Nonresponsive = 0 |
| Responding to stimuli = 1 |
| Awake = 2 |
| Circulation, preoperative blood pressure (BP) |
| BP > 120% of preanesthetic level = 0 |
| BP > 111% < 120% of preanesthetic level = 1 |
| BP \leq 110% of preanesthetic level = 2 |
| Temperature |
| Axillary temperature < 35°C or > 35.5°C = 0 |
| Axillary temperature between 35°C and 35.5°C = 1 |
| Axillary temperature 35.6–37.5°C = 2 |

Table 3. Demographic Data

| | Age (mo) | Weight (kg) | Time Premed Administered to Parental Separation (min) | Duration of General Anesthesia (min) |
|----------------------------------------------|------------|-------------|-------------------------------------------------------|--------------------------------------|
| Normal saline 0.4 ml/kg (n = 26) | 19 ± 6.9 | 11.9 ± 1.8 | 26 ± 18.6 | 10 ± 4.1 |
| Midazolam (combined) 0.2 and 0.3 kg (n = 64) | 19.5 ± 6.5 | 11.7 ± 1.8 | 27 ± 17.1 | 9.5 ± 3.1 |

Values are mean ± SD.

isfactory separation and induction scores were ratings of 3 and 4. Chi-squared and unpaired Student's *t* tests were used to assess the data. Statistical significance was considered for $P < 0.05$.

Results

Eighty-eight children were enrolled in the study. Thirty-two patients were randomized to group A, 30 patients to group B, and 26 patients to group C. Both midazolam groups were similar in age (mean ± SD, 19.1 ± 6.9 months *vs.* 19.9 ± 7.9 months), weight (11.8 ± 1.8 kg *vs.* 11.6 ± 1.7 kg), duration from premedication to parental separation (26.8 ± 20.6 min *vs.* 27.4 ± 13.3 min), duration of anesthesia (9.2 ± 3.7 min *vs.* 10 ± 2.5 min), time in the PACU (12.4 ± 10.3 min *vs.* 13.7 ± 11 min), time until hospital discharge (30.6 ± 12.7 min *vs.* 31.7 ± 13 min), and percentage of satisfactory separation (91% *vs.* 90%) and induction scores (60% *vs.* 80%). Consequently, both of these groups were combined for further analysis.

The combined midazolam and placebo groups were similar in age, weight, duration from premedication to parental separation, and duration of anesthesia (table 3). The patients receiving midazolam had significantly better separation and induction scores than the patients who received saline. Nevertheless, the times from when anesthetic agents were discontinued until the patients (1) received a recovery room score of 8 and (2) were ready to be discharged from the hospital were not significantly different between the two groups (table 4).

Discussion

This study was designed to evaluate the effects of intranasal midazolam on recovery and hospital discharge time in a group of children who frequently need sedation and who constitute a large percentage of the pediatric ambulatory population. Although midazolam has no approved indication for use in children, nevertheless it has been administered by a variety of routes for purposes of premedicating or sedating children for surgery and diagnostic procedures.⁴⁻¹² Numerous studies have demonstrated the effectiveness of intranasal midazolam for use as a preanesthesia medication; however, no studies have evaluated this drug with respect to anesthesia recovery and hospital discharge times in pediatric patients undergoing brief ambulatory surgical procedures.

This study demonstrates that intranasal midazolam effectively provides easier patient/parent separation and smoother anesthesia inductions than placebo and agrees with previously reported findings on the efficacy of nasal midazolam.^{9,10} However, after these brief procedures (actual surgical time, 4–7 min), recovery time from anesthesia and the time required for hospital discharge were unaffected. This assessment was unique in that a nurse-observer blinded to the treatment, and with no clinical responsibilities for patient care, observed these patients continuously. These patients were evaluated from the moment their anesthetic was discontinued until they met the requirements for discharge from the hospital. Consequently, because patient discharge was based on predefined criteria, patient

Table 4. Premedication Efficacy and Recovery Times

| | Patients with Satisfactory Separation Scores* (%) | Patients with Satisfactory Induction Scores* (%) | Time until PACU Discharge (min (mean ± SD)) | Time until Hospital Discharge (min) (mean ± SD) |
|-----------------------------|---------------------------------------------------|--------------------------------------------------|---------------------------------------------|-------------------------------------------------|
| Normal saline (n = 26) | 54 | 31 | 11 ± 5.8 | 29.9 ± 12.6 |
| Midazolam combined (n = 62) | 90† | 69† | 13 ± 10.1 | 31.5 ± 13 |

* Scores of 1 or 2.

† $P < 0.05$ versus normal saline.

discharge times or "street-readiness" were not based on the length of time the patients had been in the ambulatory unit.

Schreiner *et al.* have demonstrated that taking and retaining oral fluids unnecessarily delays hospital discharge.¹³ It could be argued, therefore, that our requirement of mandating patients to drink to be discharged could have masked differences in discharge times between the two groups. However, if oral fluids had not been a part of our hospital discharge criteria, then patients would have been discharged home based on the PACU discharge criterion. Because both hospital and PACU discharge times were similar between groups, it is unlikely that oral fluid administration influenced our results.

Although parental presence in the operating room, the type of anesthetic induction, and prehospital preparation of both child and parent can mitigate the need for preanesthetic medication,¹⁴ nonetheless, each patient's needs must be addressed individually. Thus, the relevance of our study must be viewed in the context of a specific institution's management of pediatric surgical patients. We do not routinely involve parents in the induction of anesthesia. The fact that intranasal midazolam is effective and does not delay anesthetic recovery or hospital discharge in patients undergoing brief surgical procedures has significantly altered our preanesthetic medication practice. Although we do not advocate such medicating by fiat, certain factors identify children who are at risk for a preoperative anxiety reaction.¹⁵ In our practice, when parents are not present for anesthetic induction, we have found preanesthetic medication to be an important adjunct for most children. Of note are the side effects (e.g., nasal burning, irritation, patient irritability) that may be associated with intranasal midazolam administration. Our study did not specifically address the issues of the drug's side effects or the patient's acceptance of the drug. However, in a study evaluating the intranasal and the sublingual routes of midazolam administration in children, Karl *et al.*¹⁶ noted that the intranasal and sublingual routes were associated with crying in 71% and 18% of the children, respectively. However, in both groups of children, the crying lasted on average less than 1 min.

In summary, although the perfect preanesthetic medication and its best route of administration are still debated, we have found intranasal midazolam to provide satisfactory anxiolysis and not to interfere with

children's anesthesia recovery and hospitalization course. Whether the burning, nasal irritation, and patient crying are significant enough deterrents for the use of intranasal midazolam is a decision each practitioner will have to make.

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