

The use of nasal midazolam in reducing preoperative anxiety in children

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Abstract

Background: Surgery and anesthesia can cause a considerable distress with psychological consequences for children. This preoperative anxiety can lead to post operative emergence delirium, maladaptive behavioral changes such as night time crying, enuresis, feeding difficulties, apathy, and withdrawal.

Objectives: The aim of this study is to investigate the effect of nasal midazolam as a routine intervention to reduce pre-operative anxiety and inducing anxiolysis in children undergoing day case procedure.

Method: One hundred children were randomly allocated into two groups. The study group (N=50) were premedicated with nasal midazolam 0.2mg/kg and the control group (N=50) who received 0.04ml of normal saline. The children response to nasal administration was noticed and after 15 minutes children were taken to operating room. Anxiety at parental separation and at induction of anesthesia was measured using modified-Yale Preoperative Anxiety Scale.

Results: Children who received nasal midazolam had a significantly better parental separation and induction of anesthesia. 88% of children who received nasal midazolam scored below 30-indicating absence of anxiety- on modified-Yale Preoperative Anxiety Scale compared to 32% in the control group. More than half of patients in both groups found nasal route to be unpleasant and stressful.

Conclusion: For children undergoing elective brief surgical procedure, nasal midazolam is effective in reducing preoperative anxiety. Nasal midazolam was associated in more than half of patients with nasal irritation and crying, a route can not be recommended in children.

Key Words: Pediatric, day surgery, preoperative anxiety, Jordan.

Surgery and anesthesia can cause a considerable distress with psychological consequences for children¹⁻³. The reasons for this distress are the separation of children from their parents, the strange hospital environment which is culturally associated with fear from pain and needles, and most importantly children are not fully able to understand the necessity for their surgery, nor are they likely to be amenable to reasoned explanation⁴.

This extremely traumatic experience for children can result in a preoperative anxiety in 65% of them. This preoperative anxiety can lead to postoperative emergence delirium, maladaptive behavioral changes such as night time crying, enuresis, feeding difficulties, apathy, and withdrawal. It is also reported that this group of children will need more post

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operative pain control medication^{3,5-7}.

Currently, there are several types of pharmacological intervention with sedative premedication such as midazolam and behavioral modalities such as the presence of clowns and parental presence during induction of anesthesia to treat preoperative anxiety in children^{5,7}.

In our very busy pediatric day case surgery we evaluated the use of nasal midazolam in reducing preoperative anxiety in children undergoing surgery.

Method:

This is a prospective study conducted at Prince Rashid Ben Alhassan Hospital in Irbid in Jordan. The study population included 100 child admitted to day case surgery unit undergoing elective surgery under general anesthesia. Those children with history of chronic illness or previous surgical intervention were excluded. For each patient baseline demographic data together with the

diagnosis and operative treatment were recorded.

After informed parental consent was obtained, and the approval of the ethical committee at the Royal Medical Services, the children were randomly allocated to receive intra nasal drops either 0.2mg/kg of midazolam or 0.04ml/kg of normal saline using 2ml syringes without a needle in both groups. The premedication was administrated by one member of the study team with the child sitting on the parents lap in the preoperative holding area. After 15-20 minutes of receiving either medication the preoperative anxiety in children was assessed using modified- Yale Preoperative Anxiety Scale (m-YPAS) at separation from parents and at induction of anesthesia.

The induction technique was inhalational induction done using Sevoflurane at a concentration of 8% decreased gradually to proper MAC. This was performed by applying the mask with three liters of oxygen with nitrous oxide until the patient is sleepy followed by I.V. line insertion. All data were

analyzed using t-test. Statistical significance was considered for $p < 0.05$.

Results:

One hundred children enrolled in the study from September to December 2010. Fifty patients were randomized to the control group to receive intranasal saline, 50 patients to study group to receive intranasal midazolam. Both groups were similar in age, weight and gender distribution. The procedures performed were similar in both groups, mostly inguino-scrotal conditions such as inguinal herniotomy, curing hydrocele, and meatotomy. Recovery behavior was similar in both groups and there was no change in our routine discharge policy either from recovery room or from hospital in both groups.

The patients receiving midazolam had significantly better parental separation and induction of anesthesia than the patients who received normal saline. The modified- Yale Preoperative Anxiety Scale was below 30 in 88% of the study group at both parental separation and induction of anesthesia compared to 32% in the control group at both occasions (table1).

Table1. Demographic and clinical characteristics of the two groups.

	Control group	Study group
Average age of children in months (range of age)	52 (18-111)	50 (18-136)
Average weight of children (kg) (range of weight)	16.8 (8-43)	16.6 (9-40)
Child's sex (male: female %)	88:12	80:20
Procedures:		
Inguinal Herniotomy	32	12
Curing Hydrocele	6	6
Orchidopexy	2	10
Circumcision and meatotomy	7	12
Others	4	10
Percentage of children with absence of anxiety at separation.	32%	88%
Percentage of children with absence of anxiety at induction.	32%	88%
Delay in recovery	0	0
Delay in discharge	0	0

Fifty six percent of children in both group responded to intranasal administration either by irritation, sneezing and crying.

Discussion:

Preoperative anxiety is manifested in 65% of children undergoing surgery. It can result in

adverse psychological reaction such as postoperative maladaptive behavior, as well as a negative children response to successive medical care^{2,5-7}. It also can result in adverse physiological reactions such as the need for more postoperative pain control medication

and the activation of human global peri-operative stress response. The later is characterized by a series of hormonal, immunological, and metabolic changes. These changes provoke a negative nitrogen balance, catabolism, and a delay in wound healing. Children are particularly vulnerable to this because of their limited physiological reserves^{5,6,8}.

There are several tools for assessment of preoperative anxiety, such as Visual Analog Scale (VAS), State-Trait Anxiety Inventory (STAI) and modified-Yale preoperative anxiety scale (m-YPAS). We used m-YPAS because it has good-to-excellent inter and intra observer reliability and good validity for measuring children's anxiety. It takes one minute to complete which is feasible in a busy unit and can be used for children as young as two years.^{2,3,7} The m-YPAS score ranges from 23 to 100. a score of 30 and above indicate the presence of anxiety².

Several researchers have shown the efficacy of several approaches to manage preoperative anxiety with non-pharmacological interventions such as preoperative preparation programs, parental presence at induction and/or the presence of clowns. This actually is widely practiced in United Kingdom and in 32% of United States hospitals^{3,5,7}. Our hospital is a very busy general district hospital with a common preoperative holding area for all patients with limited resources to gown parents, infrastructure issues, and lack of induction room. These issues limit the use of non-pharmacological interventions.

Different pharmacological modalities commonly midazolam followed by ketamine, fentanyl and meperidine are used to treat pre-operative anxiety. We opted to use nasal midazolam because of its rapid onset of action. It induces amnesia in the peri-operative process as early as 10 minutes and anxiolytic effects are apparent at 15 minutes of administration. This was seen in 88% of our patients who received it. The short timing of onset of action is very important in our busy hospital where the turnover of cases is very quick^{4,5,8}.

In our study we found that midazolam allowed easy child separation from parents and promoted a smooth mask induction of anesthesia. This is consistent with previous studies, which demonstrated the effectiveness of midazolam in pediatric sittings^{1,5,7}. On the other hand non-pharmacological interventions reduce anxiety at separation but could not maintain this low level of anxiety at induction⁷. In addition midazolam can be reversed by flumazenil^{4,5,8}.

Oral, rectal, nasal, and intramuscular routes of midazolam administration as a premedication have been used. Kogan et al, reported irrespective of route of administration, midazolam produces good level of sedation, anxiolysis, and mask acceptance was easy in the majority of children⁹. In the USA 80% of children are premeditated via oral route followed by nasal routes in 8% only. The disadvantages of these routes include painful injection via intramuscular route, slow onset and hiccups in 20% via oral and rectal routes and reported delayed recovery via oral route^{4,5,8}. Nasal administration of midazolam has the advantage of rapid absorption to the systemic circulation with a bioavailability of 55-83% as it has no first pass effect compared to a wide bioavailability of 18-44% when given via other routes. This could explain the peak sedative effect via nasal route at 20 minutes compared to 30 minutes in other routes^{1,5,9}.

We found in our study that 56% of children have found nasal route to be unpleasant and leads to sneezing, coughing, and crying. Kogan et al and Davis et al reported that more than 70% of children in their series cried^{8,9}. In addition some patient swallowed the nasal drops. To minimize this side effect Griffith et al, modified the nasal administration using spray device instead of drops, they found this method is effective as drops in inducing anxiolysis but it has equally poor acceptability and distress experienced by children as nasal drops. They recommended that nasal midazolam cannot be recommended as a method for routine premedication in children¹.

In adults midazolam has been given by nebulizer with good acceptability, a route of administration which should be explored in children. We found the dose of 0.2mg/kg of midazolam to be appropriate for premedication based on Niall et al study. They found a dose less than 0.2mg/kg to be ineffective. The doses of 0.2mg/kg and 0.3mg/kg produce similar degree of sedation but the higher the dose necessitated a larger volume, resulting in more cough, sneezing, and crying⁴.

Children in our study were observed from the moment general anesthesia was terminated until they were discharged from recovery room. There was no delay in recovery. The criteria for hospital discharge were not changed and there were no reports indicating hospital discharge delay. This is consistent with other studies^{4,5,8}.

Conclusion: Our conclusion is that midazolam is a good premedication agent in pediatric sittings. Despite the rapid onset of action nasal route is traumatic in the majority of children and cannot be recommended. The other routes are not without side effects. A future research should concentrate on developing new method of delivery system, for example, transdermal.

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