

# Administration of midazolam as sedative premedication for paediatric patients

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The paper aims to discuss effective presurgical modalities for reducing preanesthetic and preoperative anxiety in children. It reviews the existing research on psychological interventions and sedative premedication for presurgical anxiety management. Psychological and behavioural preoperative preparation of children, through presurgical preparation programs, combined with parental presence during induction of anaesthesia are regarded as alternatives to sedative premedication. A combination of these preparation strategies with midazolam premedication is presented as an effective way of helping children cope with preanesthetic and preoperative anxiety. It is highlighted that the use of low dose midazolam is sufficiently safe and beneficial if alternatives to sedative premedication prove ineffective, especially when dealing with increased feelings of anxiety immediately before anesthesia and the surgery.

**Key words:** preanesthetic and presurgery anxiety, presurgical preparation programs, parental presence, midazolam

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## INTRODUCTION

70% of children experience increased levels of stress and anxiety in the preoperative period (1, 2). Such psychological states most frequently stem from lack of detailed preanesthetic and presurgical information and a wide range of fears such as separation from primary caregivers, losing self-control, being alone in unfamiliar environment, and possible realization of health hazards associated with surgical intervention. It is sometimes difficult to

differentiate between fear, anxiety and pain. Pain and anxiety can also be inextricably linked, and this is identified as distress syndrome. High presurgery anxiety may lead to adverse postsurgery outcomes including emergence delirium and increased pain. 12–18% of children experience diverse psychic disturbances in the postoperative period (3). The most frequent changes in postoperative behaviour include but are not limited to continuing anxiety and fear, self-absorption, apathy, insomnia, screaming and crying at night, loss of appetite, temper tantrums, and experience of overwhelming helplessness. Recent studies have reported on the increase in steroid levels and subsequent increase of risk for postoperative infectious complications (4). Midazolam sedation is extremely important in paediatric

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odontology practice. Sedation is used in dental treatment of children who refuse to cooperate or who have the mental Parental rating of the child's discomfort after treatment was significantly higher in the midazolam group. Dental treatment under sedation becomes increasingly common (5). The present paper aims at exploring and analysing the latest developments in preanesthetic and preoperative anxiety management in children in relation to its effects on postoperative behaviour and outcomes.

## METHODS

Recent publications on the administration of midazolam as sedative premedication for paediatric patients have been analysed.

## RESULTS AND DISCUSSION

Up to date, three major modalities are used to relieve presurgical anxiety in children: psychological and behaviour interventions, parental presence during induction of anaesthesia, and sedative premedication. Psychological and behaviour preparation programs basically involve imparting information to the caregivers and the child about the course of events regarding the presurgical and postsurgical periods. Such programs, however, are ineffective as often as not. In some contexts, the involvement of a psychologist may maximize the intervention input. Administration of preparation programs, however, often fails to function as an alternative to midazolam premedication (6). Multicomponential behavioural preparation programs based on the whole family approach are gaining popularity. Both children and parents are given detailed information about the forthcoming anesthesia and surgery 1–2 days before the operation. To minimize anxiety levels, children and their parents can be given preparation books or can be familiarized with the operating room equipment either by being provided a hospital tour or given access to anesthesia and surgery related equipment in the play room. Preoperative anxiety and the need for pharmacological premedication can be also reduced by engaging children in giving mock anaesthesia and other age-appropriate preparation games involving mock presurgical component (6, 7).

Recent studies indicate that the effect of parental presence induction of anaesthesia can be very

significant but not sufficient in reducing preoperative anxiety (8). In this regard, parental presence on admission into treatment and patient-centred care undoubtedly lessen anxiety levels. It is also essential in this context that waiting and treatment areas for children be separate or screened from those used by adults. A combination of parental presence and favourable treatment settings can minimize the distress of children and help to avoid sedation. There are two prominent trends in attitudes to modes of intervention for preoperative anxiety in children: prioritisation and even overestimation of alternatives to sedation and prioritisation of sedation (9). Attitudes and practices vary among countries. In the USA, for example, parental presence has become a prevalent practice.

However, it is approached with caution, given differences in parents' coping styles and psychosocial behaviours. In other countries, like Italy, Japan, Kuwait and Thailand, parental presence is commonplace and is regarded as indisputably beneficial, let alone the basic right of parents. In Sweden parental involvement has been common practice for 20 years. Large differences in the use and prioritisation of preoperative anxiety management modalities for children lead to believe that homogenisation of the existing trends is hardly probable and highly disputable. It has become common knowledge, however, that preoperative stress can have a negative impact on postoperative behaviours and psycho-social development in children.

Thus viewed, a crucial factor is predicting a child's reaction to separation from parents and deciding on the effectiveness of different interventional strategies (alternative and/or sedative) to reduce preoperative anxiety. While relieving of preoperative anxiety should become an indispensable part of surgical treatment, it is essential that decision for premedication be individualised (10). Studies report that sedative premedication is more important and effective than alternative preoperative anxiety management strategies. However, combined modalities yield best results (11, 12).

### Use of benzodiazepines in pre-surgical sedation

From the sedatives used in paediatric premedication such as thiopental, clonidine, and midazolam, the latter has become the most common one for the following reasons (10):

1. It is effective for reducing preoperative anxiety in children and parents. This is especially important in light of the fact that preoperative anxiety may influence the patient's outcome.

2. Midazolam premedication positively influences postoperative behaviours and psychological states.

3. There is a correlation between the use of midazolam and antegrade amnesia which is a beneficial phenomenon from the perspective of preoperative anxiety management.

4. Midazolam sedation yields high rates of patient and parent satisfaction with surgery (11).

Benzodiazepines can be administered via oral, sublingual, intravenous, intramuscular, intranasal, and suppository routes. Midazolam is a short acting benzodiazepine, highly lipophilic at physiological pH. This conditions a short latency of onset. The elimination half-life of intravenously suppository administered midazolam for 3–10 year-olds is 1–1.5 h. Midazolam is a strong sedative that requires titration to reach the desired effect. When used in intravenous or intramuscular sedation, the dosage should be titrated in small increments to provide optimal premedication according to the patient's age, clinical status, and psychological state. In pediatric premedication the dosage should be determined with extreme caution and individual level risk factors should be taken into consideration. The dosage of intramuscular sedation for children of 1–15 years of age is in the range 0.08–0.2 mg/kg body weight. Doses should be tailored to the individual patient. The onset of action is within 2 minutes, with the peak effect occurring within 5–10 minutes following injection administered at carefully titrated intervals. It has been reported that low dose midazolam, at 0.08–0.2 mg/kg body weight, given by oral route is safe and effective.

Suppositorial midazolam allows avoiding pain caused on injection, which in itself is a source of anxiety for children. The recommended doses of midazolam via the rectal route for children over 6 months are 0.3–0.5 mg/kg body weight to be administered 15–30 minutes before the induction of anaesthesia. Rectal forms of medication, however, can cause irritation, unpleasant sensations in the rectum, defecation or constipation. Children over 6 years of age may dislike rectal administration of midazolam, and this can evoke spontaneous bodily reaction, including psychoemotional stress (13).

The oral form is becoming increasingly popular. For paediatric premedication, the doses are 0.2–0.3 mg/kg. Variations in dosage are possible between 0.05 mg/kg and 0.1 mg/kg body weight. Doses should be carefully titrated to avoid adverse effects related to metabolism (14). It has to be taken into account that one of the disadvantages of oral midazolam is related to limited titration possibilities.

Oral midazolam premedication reduces preoperative anxiety for 80% of patients. The onset of action is 10–20 minutes at 0.25 mg/kg and produces its peak effect in about 30 minutes. The half-life is 2 hours and is related to a good amnesic effect (14). Such dosage of midazolam causes amnesia and is thus suitable for use in children for improving the postoperative behaviour and mood. It also reduces the incidence of nightmares, apathy, eating disorders, enuresis, stress, and other forms of adverse postoperative behaviours (15). Furthermore, oral midazolam at 0.3 mg/kg was found to decrease the activity of the respiratory muscle system. The assessment of ventilation homogeneity using the functional residual capacity (FLT) and a lung clearance index showed a slight decrease in FLT and ventilation homogeneity, together with an increase of respiratory resistance. In children with the normal pulmonary function, slight changes in the respiratory function can occur shortly after the start of premedication. However, extreme caution should be exercised about giving midazolam premedication to children that are at high risk of respiratory failure under anaesthesia as it can result in further decrease of the respiratory function (16). Midazolam can impair the explicit memory but preserve the implicit memory (10).

Premedication is used to focus on preparation and providing a uniform and smooth anaesthesia. This can be achieved by administration of morphine derivatives and anticholinergic agents. The present day practice underscores reducing presurgical stress, controlling autonomous reflexes, especially *n. vagus* reactions, and eliminating side effects of anaesthetics. At present, the prevailing view is that midazolam is an optimal choice for sedative premedication (10). The shift in focus in modern anaesthesiology is related to the fact that the use of new generation anaesthetics eliminates the need to control autonomous reflexes and side effects of anaesthetics. E. g. sevoflurane does not cause salivation, nor does it impact catecholamine or promote *n. vagus* activity. Vagal activity remains for infants

up to 12 months, but it is reduced after administration of atropine (10).

Despite a wide range of preoperative preparation programs, children tend to envision surgical treatment in terms of intimidating challenge and therefore experience high levels of distress prior to operation. It has been shown that administration of oral midazolam at 0.5 mg/kg, combined with parental presence, effectively reduces anxiety in children (17). Low-dose (from 0.3 mg/kg, with a maximum dose 10 mg) oral midazolam is a suitable pre-medical for children to reduce the distress syndrome before needle interventions not only for oncological patients but also for other paediatric patients (14). The same midazolam treatment modalities are used for neurosurgical paediatric patients from 6 months to 6 years. A study of 100 cases indicated that oral midazolam was the most effective at 0.75 mg/kg while a dose of 0.5 mg/kg was less effective. Increasing the dose to 1.0 mg/kg did not show any advantages if compared to 0.75 mg/kg (18).

63% of patients totally accepted dental treatment at 0.2 mg/kg while 30% demonstrated doubtful acceptance. 7% of patients totally refused treatment. No adverse effects of midazolam were registered. All of the treated children felt good enough to leave the clinic one hour after treatment and it indicates that conscious sedation with oral administration of midazolam is a safe form of premedication (5).

Midazolam can also be administered via the sublingual route with the dose of 0.2 mg/kg corresponding to that of 0.5 mg/kg oral midazolam. The use of sublingual midazolam sedation did not reveal higher incidence of side-effects or respiratory function impairment than oral treatment. Both forms were revealed to have the same effect on distress syndrome management (19). Study of the use of midazolam in children from 0 to 18 years of age indicates that 0.5 mg/kg of 20–30 min *per os* premedication is an acceptable, effective and safe method to reduce the presurgical distress syndrome (20).

#### Why is midazolam widely used?

The popularity of midazolam is a result of the short latency of onset. This benefit outweighs its potential side-effects that include, among others, post-anesthesia anxiety, diplopia, amnesia, hiccupping, anger, and sleep disorders. Serious midazolam induced side-effects are rare, and midazolam, when not combined with other sedative medications,

produces no significant respiratory effects (10). Midazolam can be used for treating both preoperative and postoperative anxiety. On the other hand, even successful midazolam premedicated anaesthesia is not a guarantee against preanesthesia and preoperative anxiety or adverse postoperative behaviours and psychological states. Children 2–3 years of age have the highest frequency of presurgical anxiety, hence the highest degree of sedative premedication care (10). Anxiety of separation from parents is considerably low in children under 8–12 months. In this age group midazolam premedication is rather uncommon; parents accompanying children to the operating room can be sufficiently beneficial. Sedative premedication is usually not necessary for infants under 3–6 months of age (10).

#### CONCLUSIONS

1. Low doses of orally administered midazolam are safe and effective for producing a rapid onset of paediatric sedation to reduce preanesthesia and the presurgical distress syndrome.

2. The use of midazolam can improve postoperative psychological and behaviour parameters especially in combination with alternative interventional strategies including patient and parents' preparation programmes.

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#### MIDAZOLAMO SKYRIMAS VAIKŲ SEDACINEI PREMEDIKACIJAI

##### *Santrauka*

Apie 70 % vaikų prieš chirurginę operaciją patiria stiprų stresą, nerimą, baimę. Priešoperacinis nerimas turi nemažą įtaką ne tik pooperaciniam elgesiui, bet ir klinikinėms komplikacijoms, todėl klinikinėje praktikoje ieškoma, kaip sumažinti šiuos negatyvius reiškinius. Straipsnyje aptariamos vaikų priešanestezinio ir priešoperacinio nerimo sumažinimo galimybės ir būdai, analizuojama sedacinės premedikacijos alternatyva: elgesio parengimo programa, šalia vaiko esančių tėvų galimybės sumažinti stresą, sedacinės premedikacijos midazolamu privalumai ir šių metodų derinimas. Mažų peroralinių midazolamo dozių naudojimas yra saugus ir ypač naudingas, kai alternatyvūs premedikacijos būdai nėra efektyvūs, taip pat esant stipriam, prieš pat anesteziją ir operaciją dar labiau sustiprėjusiam nerimui. Midazolamas kartu su alternatyviomis strategijomis – vaikų ir jų tėvų priešanestezinio ir priešoperacinio nerimo sumažinimo programomis – gali pagerinti vaikų psichologinę būklę ir jų elgseną.

**Raktažodžiai:** priešanestezinis ir priešoperacinis nerimas, elgesio parengimo programos, šalia vaiko esantys tėvai, midazolamas