

Intranasal Midazolam Spray-in Pediatric Dental Practice-A Review

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Abstract

Most of the preschool children suffer from anxiety and apprehension towards dental treatments and they are managed with behavioral management techniques. When such techniques fail, sedation becomes essential. Midazolam is one of the commonly used preanesthetic sedations in adults and now it is commonly employed in pediatric patients. It may be delivered by several routes. Every one of the routes of administration has its own advantages and disadvantages. This article reviews about the intranasal route of administration of midazolam.

Keywords Sedation, Midazolam, Mucosal Atomization Device

INTRODUCTION

Children with anxiety due to anticipation of pain, unfamiliar environment, parental separation or any previous unpleasant experience can be treated with intranasal midazolam sedation. Midazolam may be a commonly used preanesthetic medication in children. It has demonstrated to have a protective effect against these above stated behaviours. The main aim of administering preanesthetic sedation is to provide a peaceful and cooperative environment to the pediatric patient as well as for the dentist. (1)

Pharmacology Of Midazolam

Fryer and Walser synthesized midazolam in the year 1976. It is a short-acting, water soluble drug which belongs to a new class of benzodiazepine called imidazobenzodiazepine. It acts on Gamma Amino Butyric Acid (GABA) associated benzodiazepine receptors which is one among the most important inhibitory neurotransmitter of Central Nervous System (CNS). Midazolam has got properties like sedative,

hypnotic, anxiolytic, anticonvulsive, muscle-relaxant, and anterograde amnesia.(2,3). Midazolam can be prepared as a water soluble salt which may be given through IV and IM routes with minimal irritation.

After administration, midazolam becomes highly lipophilic. The high lipid soluble property of the drug provides rapid absorption and penetration into the CNS. The drug is oxidized by the liver more rapidly than other benzodiazepines. It also has a short duration of action. (2)

Midazolam is hydroxylated by cytochrome P450 3A4 to its primary metabolite, alpha-hydroxy-midazolam. It is conjugated by glucuronic acid to make a pharmacologically inactive end product which is eliminated through urine. (3)

Routes Of Administration

Midazolam can be given through various routes like oral, rectal, sublingual, parenteral. Each and every route of administration has its own advantages, disadvantages, indications and contraindications. Oral administration needs patient cooperation whereas rectal route is rather uncomfortable or has less systemic absorption. IV administration in children may cause anxiety, discomfort and pain. In order to overcome these disadvantages intranasal route of administration is demonstrated which is less invasive and less painful. (2,3)

Intranasal Route

Wilton in 1988 conducted the first study using intranasal midazolam in children. In this study a dose of 0.2mg/kg-0.3mg/kg in a 1 ml syringe was given.(2) Many studies have been conducted since then and administration through nasal route has become popular during the last decade in Pediatric dentistry. A study revealed that 0.2mg/kg dose is an effective premedication for producing effective sedation and anxiolysis in children without much side effects.(4) Intranasal midazolam offers rapid onset of action and relatively high plasma concentration which makes it more acceptable when compared to other routes. This administration is particularly useful in dental treatments, allowing the administration to occur just a little time prior to the treatment. It is relatively simple and a painless technique. Intranasal midazolam is absorbed from nasal mucosa which is a rich area of blood supply hence it avoids the passage of drug through portal circulation.(2,5) Intranasal administration can be administered by two methods, intranasal drops or intranasal spray.(6) Intranasal midazolam has been used by conventional and aerosolized methods.(5) A study revealed that midazolam of 0.2-0.3 mg/kg given as nasal drops(1) from a syringe provided adequate plasma concentrations and good effect but there was spillage and swallowing of the drug.(6) The recent availability is Nasal- Mucosal Atomization Device (MAD). The advantages of using this device includes less drug-penetration into oropharynx, better patient acceptability and improved sedative effect. Most of the studies on intranasal midazolam atomizer spray with a dose of 0.2, 0.3 and 0.5 mg have been used with apparent difference in the observations which includes safety, efficacy, acceptability, anxiolysis, degree of sedation and ease of administration.(5) Similarly in other studies, intranasal midazolam spray was used in the dose of 0.2mg/kg (7) while a mucosal atomizer device was used to administer midazolam intranasally in the dose of 0.4mg/kg.(8) The effective delivery of the drug through the atomizer helps in large dispersion of drug over the nasal mucosa and this results in better absorption(9,5). Atomized midazolam spray provides accurate drug delivery.(9) Midazolam has a high hepatic clearance and as the intranasal route avoids first pass metabolism, there is an increased systemic bioavailability of the drug.(5) Under optimal conditions, absorption of midazolam through the nasal mucosa is quick and virtually complete. Mean peak plasma concentrations of the drug are reached within 10–20 minutes.(10,6) Bioavailability ranges between 55% to 57% (10). In some studies bioavailability of 83% with complete absorption of the drug was present however there was a disadvantage of nasal stinging. (6)

Procedure

Initially proper Airway, Breathing, Circulation should be checked. 100% Oxygen is provided to the patient with the use of an oxygen mask. The proper volume of Midazolam for atomisation should be provided based on patients age and weight. The syringe is loaded with appropriate volume of Midazolam and it is attached to the Nasal Atomizer Device. Atomizer is placed inside the nostril and compressed briskly. Half the volume of drug is sprayed with the help of Atomizer Device. Similarly the procedure is repeated in the other nostril. (1,6,11)

Advantages

Midazolam has many advantages and because of these advantages it is commonly used in conscious sedation. The main advantage of intranasal administration is that there is no first pass metabolism. Intranasal midazolam has rapid onset of action when compared to other routes of administration. The nasal mucosa has high vascular supply and because of this rich blood supply the drug is completely absorbed by the systemic circulation within one to two hours. (4,5) Clinical advantages of midazolam includes water solubility, short-acting capacity, muscle relaxant and high marginal safety. (2)

Disadvantages

Midazolam cannot be used during upper respiratory tract infections since absorption is completely dependent on the nasal mucous membrane. (2) While administering the drug through intranasal route it could sometimes be swallowed which provides a bitter taste. (1) Irritation to nasal mucosa is also a disadvantage of this technique. (12)

Contraindications

Midazolam nasal spray cannot be used in myasthenia gravis patients. It should not be used in patients with CNS depression, shock, acute alcohol intoxication, coma, and uncontrolled pain. It is also contraindicated in patients who have allergic reactions to benzodiazepines. (9,12)

Adverse Effects Of Midazolam

Midazolam is mostly free of side effects. The most common adverse effect is respiratory depression. The major risk associated with high doses of midazolam is hypoventilation and hypoxemia. Other less common adverse effects are hypotension, paradoxical reactions, hiccough, seizures, nystagmus. (2,3)

CONCLUSION

Although many drugs are used in conscious sedation, midazolam is a new class of benzodiazepine which has a lot of advantages and a very few side effects. Even though Midazolam can be given through various other routes, intranasal administration with an atomizer device produces faster sedation and anxiolytic action. It is comparatively easier and less technique-sensitive, has faster rate of absorption, requires less patient cooperation and is relatively painless, thus making it an effective method of conscious sedation in paediatric dental patients.

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