Midazolam Nasal Spray

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ABSTRACT

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Midazolam is a short acting benzodiazepine available as Midazolam hydrochloride which is water soluble. It primarily acts as a CNS depressant enhancing the actions of inhibitory neurotransmitter GABA.

Midazolam nasal spray is a new special formulation which is specifically indicated for intranasal administration of Midazolam during emergency situations like acute management of ongoing seizures in the pre hospital and intrahospital settings. Intranasal Midazolam may be prescribed for a child with epilepsy or febrile seizures who often has seizures lasting longer than five minutes or has a pattern of seizures that recur close together. It is also being used as a sedative for short outpatient surgical procedures.

The clinical manifestations of Midazolam toxicity are mostly due to CNS depression and include somnolence, confusion, ataxia and coma.

Keywords: Midazolam, Short acting benzodiazepine, GABA, Nasal spray, Indications.

*See End Note for complete author details

Midazolam is a short acting benzodiazepine available as Midazolam hydrochloride which is water soluble. It primarily acts as a CNS depressant enhancing the actions of inhibitory neurotransmitter GABA. Midazolam hydrochloride has the molecular formula $C_{18}H_{13}ClFN_3.HCl$, and the following structural formula.

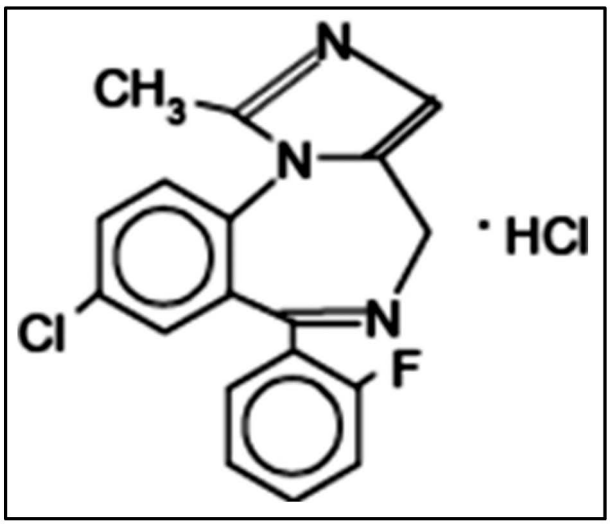

Figure 1. **Structural formula of Midazolam**

Indications

Midazolam nasal spray is a new special formulation which is specifically indicated for intranasal administration of Midazolam during emergency situations like acute management of ongoing seizures in the pre hospital and intrahospital settings. Intranasal Midazolam may be prescribed for a child with epilepsy or febrile seizures who often has seizures lasting longer than five minutes or has a pattern of seizures that recur close together. It is also being used as a sedative for short outpatient surgical procedures.

Intranasal drug delivery

The easily accessible vascular plexus of the nasal cavity permits topically administered drugs to rapidly achieve effective blood levels. This method of delivery may eliminate the need for intravenous catheters while still achieving rapid, effective blood levels of the medication administered. The relatively small surface area of the nasal mucosa is the major limiting factor for intranasal drug delivery. The absorption may be enhanced by distributing drug solutions as finer particles rather than as larger droplets which may aggregate and run off instead of being absorbed.

Sprayed or atomized medication delivery

Sprayed or atomized intranasal medication delivery is a recent technique to improve the usability as well as bioavailability. This delivery technique combines a method of measuring a unit dose of medication – either via a syringe or unit dose pump– with a spray tip that fragments the medication into finer particles as it is being sprayed into the nose. It appears that this method of delivery results in a broader distribution of the medication across the nasal mucosa and an

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increased bioavailability of the drug. As the medication is sprayed/atomized as a mist, it is less is likely to be blown back out the nose into the external environment.

ADVANTAGES

1. The rich vascular plexus of the nasal cavity provides a direct route into the blood stream for medications that easily cross mucous membranes.
2. The direct absorption into the blood stream avoids gastrointestinal destruction and hepatic first pass metabolism similar to intravenous administration. The rates of absorption and plasma concentrations after intranasal administration are better than subcutaneous or intramuscular routes.
3. Intranasal administration is essentially painless, and does not require sterile technique or invasive devices.
4. It is socially more acceptable than intrarectal administration.
5. There is no need for patient restraint.
6. As the nasal mucosa is very near to the brain, cerebrospinal fluid (CSF) drug concentrations may exceed plasma concentrations. Intranasal administration may rapidly achieve therapeutic brain and spinal cord (CNS) drug concentrations.

Dosage form

Sterile solution of Midazolam with a concentration of 5 mg/ ml. Each spray delivers 0.1ml solution containing 0.5 mg of Midazolam.

Recommended dosage

0.1-0.2 mg/kg/dose

Contraindications

Hypersensitivity to benzodiazepines

Pregnancy

Drug Interactions

Midazolam should be administered with caution along with other CNS depressant drugs like barbiturates, other benzodiazepines, opioids and alcohol.

Duration of action of Midazolam will be prolonged if the patient is using drugs that inhibit the hepatic cytochrome P450 system like valproate.

Adverse effects

Nasopharyngeal irritation, watering from eyes, and a bad taste were the common and usually clinically insignificant side effects of Midazolam nasal spray.

The clinical manifestations of Midazolam toxicity are mostly due to CNS depression and include somnolence, confusion, ataxia and coma. No other organ specific dysfunctions have been noted.

There is a potential for teratogenicity as in other benzodiazepines, even though data specific to Midazolam is scant.

END NOTE

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