

### Vignette

A 3 year-old male presents to the ED with his parents with a seizure. The patient has had 2 prior febrile seizures in the past. Parents note that he has been seizing for approximately 10 minutes. The triage nurse notes that the patient is actively seizing with generalized-tonic movements of all extremities, eyes rolled back, teeth clenched and unresponsive with peri-oral cyanosis. The patient is brought immediately back to a room.

His initial vital signs are: HR 144, BP 110/67, RR 14, SpO2 87% on RA. You provide oxygen for the patient with a 100% O2 by non-breather and optimize airway positioning. You order 0.1 mg/kg of IV lorazepam per the SLCH status epilepticus management guidelines.

2 nurses quickly attempt to place an IV and fail to obtain access x 3 attempts. You send someone to get the IO kit and ask for diastat (rectal diazepam). The nurse asks you how much Diastat you want to give and while you are trying to remember the age-based recommendations for dosing, you think about if there are any other options for delivery of a benzodiazepine without IV access. You remember that sometimes we give intranasal versed (midazolam) for sedation and wonder if that would work for seizures and be an acceptable alternative to Diastat.

You know that the effectiveness of anticonvulsants to terminate seizures decreases rapidly as the time between start of convulsions and drug administration lengthens, so you want to hasten your delivery of an anticonvulsant that works!

#### PICO Question

**Population:** Pediatric patients in status epilepticus

**Intervention:** Intranasal midazolam

**Comparison:** Rectal diazepam

**Outcome:** Resolution of seizure activity, return to normal mental status, ED length of stay

### Search Strategy

MEDLINE was searched via PubMed using the terms “(Seizures OR status epilepticus) AND intranasal AND rectal” ([tinyurl.com/puvvqx2](http://tinyurl.com/puvvqx2)). This resulted in 43 citations, from which the four most relevant articles were selected.

**Article 1:** [Fişgin T, Gurer Y, Teziç T, Senbil N, Zorlu P, Okuyaz C, Akgün D. Effects of intranasal midazolam and rectal diazepam on acute convulsions in children: prospective randomized study. J Child Neurol. 2002 Feb;17\(2\):123-6. Answer Key.](#)

**Article 2:** [Holsti M, Sill BL, Firth SD, Filloux FM, Joyce SM, Furnival RA. Prehospital intranasal midazolam for the treatment of pediatric seizures. \*Pediatr Emerg Care.\* 2007 Mar;23\(3\):148-53. \[Answer Key\]\(#\).](#)

**Article 3:** [Bhattacharyya M, Kalra V, Gulati S. Intranasal midazolam vs rectal diazepam in acute childhood seizures. \*Pediatr Neurol.\* 2006 May;34\(5\):355-9. \[Answer Key\]\(#\).](#)

**Article 4:** [Lahat E, Goldman M, Barr J, Bistrizter T, Berkovitch M. Comparison of intranasal midazolam with intravenous diazepam for treating febrile seizures in children: prospective randomised study. \*BMJ.\* 2000 Jul 8;321\(7253\):83-6. \[Answer Key\]\(#\).](#)

### Bottom Line

Rectal diazepam is commonly used in the management of pediatric seizures [at home](#) and by [EMS personnel](#). Given issues with administration and dosing, some EMS systems have moved to alternative routes of benzodiazepine administration, including intranasal administration of midazolam ([Holsti 2007](#)).

A handful of studies have directly compared rectal diazepam to intranasal midazolam for the treatment of pediatric seizures. One hospital-based study from Israel demonstrated a decrease in the time from hospital arrival to treatment and faster seizure control with intranasal midazolam compared to rectal diazepam in children with febrile seizures ([Lahat 2000](#)), with no adverse events in either group. In a similar study from India involving both febrile and afebrile seizure patients, there was a mean decrease of around 18 seconds in the time to prepare and administer intranasal midazolam compared with rectal diazepam, and greater than 60 second mean decrease in time between drug administration and cessation of seizure activity ([Bhattacharyya 2006](#)); seizure cessation was more likely to have occurred within 10 minutes of drug administration in the intranasal midazolam group (RR 1.1, 95% CO 1.0 to 1.2). Finally, a Turkish study demonstrated a similar decrease in the rate of seizure cessation within 10 minutes of drug administration with intranasal midazolam (RR 1.5, 95% CI 1.0-2.2), along with a decrease in overall seizure duration and a decrease in the need for additional drug administration ([Fisgin 2002](#)).

These three foreign studies were all limited by small sample sizes (n = 52, 188, and 55, respectively), poor randomization technique, [lack of blinding](#), lack of [sample size calculation](#), and lack of [primary outcome](#) identification. In addition, there were several patient characteristics (such as a large proportion of patients with a history of birth asphyxia in Bhattacharyya et al) making it difficult to generalize the results to children in the US ([external validity](#)).

A single US study was identified from Salt Lake City that compared intranasal midazolam with rectal diazepam in the prehospital setting ([Holsti 2007](#)). Patients enrolled after a change in EMS protocol that mandated seizure treatment with



intranasal midazolam were compared to historical controls. Patients receiving intranasal midazolam had a decrease in the duration of EMS-witness seizure activity (median 30 minutes vs. 11 minutes,  $p = 0.003$ ), and total seizure time (median 45 minutes vs. 25 minutes,  $p < 0.001$ ). Intranasal midazolam also led to lower overall hospital charges, decreased need for bag-valve mask ventilation, decreased need for intubation, and decreased need for hospital admission. This study was also limited by a small sample size ( $n = 57$ ), as well as by a [before-and-after study design](#), lack of randomization and blinding, and [missing outcome data](#) from the EMS records.

Overall, the evidence in support of the use of intranasal midazolam over rectal diazepam is limited and of poor quality, composed primarily of small, unblinded studies conducted in dissimilar populations with poor methodology. However, the evidence at least supports the premise that intranasal midazolam is safe and effective. It is reasonable, in light of this evidence, to use intranasal midazolam as an alternative to rectal diazepam in children with seizure activity, and may replace rectal diazepam for home treatment given its ease of administration.