Case Report

Enteral Baclofen in the Management of Tetanus-Related Spasms: Case Report and Review of Literature

by Lokesh Guglani and Rakesh Lodha

Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India

Summary

We report here the successful use of baclofen administered by nasogastric route in a 3.5-year-old child with tetanus, whose spasms were not controlled even with high dose of midazolam infusion.

Introduction

Tetanus causes significant morbidity and mortality among neonates and children in the developing world, and despite advances in intensive care, secondary complications related to supportive care do occur. Several therapeutic strategies have been employed to control the spasticity, autonomic dysfunction and provide intensive care to cases with severe form of the disease. Tetanus produces clinical manifestations due to its two toxins, tetanospasmin and tetanolysin, which gain entry into the nervous system via the neuromuscular junction (NMJ) and travel in retrograde fashion to the neurons [1]. The effects of tetanospasmin are mediated at three levels [2] – (i) central motor effect, (ii) autonomic nervous system effect, and (iii) NMJ effect. Transport first occurs in motor and later in sensory and autonomic nerves.

The management of spasms in tetanus is challenging and may require several drugs with differing modes of action and supportive care till the patient recovers from the effects of these toxins [3]. Benzodiazepines have been used to reduce the frequency of spasms. Baclofen reduces the release of excitatory neurotransmitters and substance P by binding to the GABA_B receptors. Baclofen thus reduces spasticity by presynaptic inhibition of monosynaptic reflexes but does not affect the activity of the tetanus toxins. Baclofen has been administered via the intrathecal route for the control of spasticity in patients with tetanus [4] but it has several limitations (discussed below). We report a child with tetanus, whose spasms did not respond to the conventional treatment, and oral baclofen was used to reduce the spasticity, and also review the literature regarding its use in tetanus.

Case Report

A 3.5-year-old unimmunized boy presented with history of bilateral ear discharge off and on for 3 months and developed difficulty in opening the mouth and swallowing for 5 days prior to presentation and intermittent tonic posturing of limbs of 3 days’ duration. There was no history of trauma and there was no history of altered sensorium. There was no past history of any significant illness. At presentation, the child was hemodynamically stable but had intermittent tonic posturing with opisthotonus. There was no active ear discharge and he had normal sensorium, with increase tone in all four limbs and brisk reflexes. A diagnosis of otogenic tetanus was made and the child was started on intravenous (IV) antibiotics (Ceftriaxone and Metronidazole) and fluids, and was given a dose of Tetanus Immunoglobulin as well. In view of persistent spasms even with intermittent Diazepam and Chlorpromazine, IV midazolam infusion was started at 1 \( \mu \text{g kg}^{-1} \text{min}^{-1} \) and the child was subsequently transferred to the pediatric intensive care unit (PICU) for further monitoring and control of spasms on the day of admission. His spasms were persistent and were provoked by the slightest of stimuli and for this the infusion rate of midazolam had to be increased further up to 7.5 \( \mu \text{g kg}^{-1} \text{min}^{-1} \). The child had good spontaneous respiratory efforts and maintained saturations, except for occasional transient desaturations during spasms, which were short-lasting and did not require any intervention. Attempts were made to taper off midazolam infusion gradually, but spasms used to increase and so baclofen was added on day 13 of admission at a dose of 10 mg day\(^{-1}\) (in three divided doses, administered via the...
form of increased risk of infection with the infusion.

However, this may have several disadvantages in the port to allow regular infusion or bolus injections. The intrathecal route is preferred by the intrathecal route (either as an infusion or intermittent boluses) [6]. The intrathecal route is steroid by inhibiting spinal polysynaptic afferent pathways. It has been used in patients with cerebral palsy and spinal causes of rigidity and has shown good safety profile and efficacy in reducing spasticity. In cases of tetanus, it is usually administered by the intrathecal route (either as an infusion or as intermittent boluses) [6]. The intrathecal route is usually used in children weighing at least 15 kg, and requires the insertion of subcutaneous implantable port to allow regular infusion or bolus injections. However, this may have several disadvantages in the form of increased risk of infection with the infusion device, the cost of infusion device and the therapy itself and possible need for supportive care and mechanical ventilatory support [4, 6], and it also shows significant variability in pharmacokinetics following intrathecal injection in adults, with its elimination half life ranging from 0.9 to 5 h. There are several case reports of its use in cases of tetanus, the largest series being that of 10 patients (most of them were adults), where a continuous infusion was used (doses ranging from 500 to 2000 μg day⁻¹), given over varying time periods ranging from 4–54 days [6].

There is no published literature regarding use of enteral baclofen in the management of tetanus-related spasms and this is, to the best of our knowledge, the first report of its use in a child with severe tetanus-related spasms, which avoided the use of mechanical ventilation and also helped to wean him off IV midazolam infusion. The theory supporting baclofen use in tetanus is its action on GABA receptors to reduce excitability of the motor neurons, and reduce the muscular rigidity seen in tetanus [4].

In the reported case, the recovery of spasms started only after baclofen was administered; intermittent attempts to taper-off midazolam infusion prior to this had always led to an increase in the frequency and severity of spasms. The dose of baclofen was not increased further as the patient showed good response, allowing tapering off of the midazolam infusion.

Enteral baclofen avoids many of the adverse effects associated with intrathecal administration. Baclofen is rapidly absorbed after oral administration and it is partially metabolized by the liver but largely excreted unchanged by the kidneys. The doses recommended for children for other indications (other than tetanus) are as follows:

- Children ≥8 years: initially, 10–15 mg day⁻¹ PO in three divided doses, to be titrated slowly every 3 days in 5–15 mg increments to a maximum dose of 60 mg day⁻¹.
- Children 2–7 years: Initially, 10–15 mg day⁻¹ PO in three divided doses, to be titrated slowly every 3 days in 5–15 mg increments to a maximum dose of 40 mg day⁻¹.

Use in children ≤2 years of age and in patients with renal impairment (creatinine clearance <30 ml min⁻¹) is not recommended. Baclofen is usually administered with food or milk to minimize gastric irritation and can produce sedation that is dose-related and may be minimized by initiating treatment at a low dose. It may also cause impairments of cognitive functions such as confusion, memory and attention, and orthostatic hypotension, dizziness, weakness and ataxia. Acute discontinuation of oral and intrathecal baclofen may cause signs and symptoms of withdrawal, which may include spasticity with spasms, hallucinations, confusion, seizures and temperature elevation.
To conclude, enteral baclofen may be considered as a spasticity reducing measure in tetanus, especially in limited resource settings, but further studies are needed before its use can be recommended routinely in all cases of tetanus-related spasms.

References