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Case Report

Intrathecal baclofen use in the management of tetanus related spasm: A case report

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Tetanus is an infectious disease of the central nervous system with high mortality rates characterized with respiratory distress and tonic muscle spasms. The most common cause of mortality is cardiovascular complications (40%) and respiratory distress (15%). Despite vaccination programs, tetanus remains to be a significant healthcare issue in developing nations. Prolonged sedation and administration of muscle relaxants prolongs the period on mechanical ventilation and duration of hospitalization in severe tetanus cases. However, intrathecal baclofen (ITB) therapy might shorten the duration of stay at intensive care units, improve patient outcomes, and constitute a treatment option alternative to paralytic agents and sedation. In this manuscript, we present a 12-years-old case diagnosed with tetanus and treated with ITB upon observation of spasms refractory to high dose sedation and muscle relaxants.

Key words: Clostridium tetani, intrathecal baclofen, tetanus, tetanus releated spasm, trismus,

Tetanus is a central nervous system (CNS) disorder with high mortality rates, caused by toxins of *Clostridium tetani* and characterized with persistent tonic spasms. Although the incidence rates have decreased with protective vaccination programs in developed nations, tetanus remains to be a significant healthcare issue in developing nations. The diagnosis is established mainly with medical history and physical examination. The disease results from the entry of *C. tetani* spores into the human body through trauma. From the alpha motor tips, the toxin responsible from spasms proceeds up to the CNS. The toxin then enters the synaptic space and accumulates at presynaptic nerve endings, and prevents the assumption of normal muscular tonus at the level of presynaptic inhibitory ganglion by inhibiting the release of gamma amino butiric acid (GABA) and glycin. Motor neuron stimulation and muscle spasms are therefore increased upon the removal of motor neuron inhibition.[1,2]

Patients with tetanus should be followed at intensive care units since severe muscle spasms might cause autonomic dysfunction, respiratory distress, and cardiovascular system involvement.[3] Although mechanical ventilation and deep sedation improves the prognosis, mortality remains high, particularly in developing nations due to prolonged hospitalization, development of severe complications and respiratory distress.[4]

Baclofen reveals its antispasmodic effects by releasing presynaptic acetylcholine via the agonist effect of binding to GABA-B receptors in the CNS, and inhibiting synaptic medullary reflexes. Baclofen infusion treatment was first tried in tetanus patients in 1986. In the following years, spasms associated with tetanus have been treated successfully with intrathecal baclofen (ITB).

We suggest that ITB therapy provides the advantage of avoiding prolonged sedation and shortening the duration of mechanical ventilation, as well as reducing the rates of associated complications and mortality. This treatment might provide an alternative treatment option to paralytic agents and

sedation by shortening hospitalization and improving patient outcomes.

Case Report

A twelve year-old female patient presented with spasms of the right foot and back, trismus and dysphagia. The patient was previously healthy, although her routine childhood vaccinations were missing, a nail had gotten stuck into her right foot 14 days earlier and tetanus vaccination was administered at an outpatient center at 48 hours of the incident. She was internalized at the Pediatric Intensive Care Unit upon development of increasing spasms of the right foot and back, tachycardia and hypertension. The patient was diagnosed with tetanus based on history and physical examination findings, and tetanus immunoglobulin and crystalized penicillin were administered. The patient was intubated upon increased spasms, emergence of opistotonus and respiratory distress. Diazepam, morphine, vecuronium, magnesium sulphate infusion therapies were initiated to treat muscle spasms, rigidity and autonomic dysfunction. However, rigidity and spasms persisted despite administration of sedatives and muscle relaxants at high dosages. ITB was administered at 75 mcg test dosage on day 9 of hospitalization since spasms could not be controlled with medical treatment. The patient had severe tonic tetanic spasms of the entire body, the degree of her spasticity was a Modified Ashworth Scale (MAS) score of 3(+). The MAS score after treatment significantly decreased compared with that before treatment. These findings suggested that the patient might benefit from intrathecal baclofen therapy.

Intrathecal baclofen pump was implanted on day 11 of admission to the intensive care unit and tip of intrathecal catheter was left at the level of D5 vertebra corpus. Intrathecal baclofen therapy was initiated at 50 mcg/day and gradually increased while vecuronium, magnesium sulphate, diazepam and morphine infusion dosages were tapered and discontinued at day 23 of hospitalization. Tracheostomy was opened due to prolonged mechanical ventilation.

ITB dosage was increased up to 110 mcg/day over 2 months of follow up. MAS was 0 on both upper extremities and 1 on both lower extremities, and tonic spasms were improved. The patient was weaned from mechanical ventilation 13 days after the implantation of ITB pump.

The patient was discharged after closure of tracheostomy at 5 weeks. Spasticity improved completely and the patient could walk at 4 months of ITB therapy; baclofen dose was therefore tapered and the pump was closed upon cease of baclofen. The patient was followed for 2 more weeks with the pump closed, and the pump was removed at the outpatient control visit. The patient received 6 months of physical therapy for mild joint contractures, and continues to attend follow up visits with no sequel.

Discussion

Clinical findings of tetanus result from the tetanospasmin released by spores of tetanus bacilli, and emerge upon the arrival of the neurotoxins at the CNS. The resulting effect is prevention of the release of inhibitory mediators including glycine and GABA in the CNS.[1,2] A short incubation period is associated with poor prognosis. Initial disease findings are characterized with rigidity and muscle spasms, and spasms progress to involve the entire body. Trismus, risus sardonicus, opistotonus and generalized spasms might be seen.[3,4] Respiratory distress might occur due to increased spasms as well as laryngeal spasm. Prophylaxis with vaccination and tetanus immunoglobulin are lifesaving in the treatment, since tetanus is a preventable disease.

According to the data released by the World Health Organization 1,254 and 2,172 tetanus cases have occurred in the USA and Turkey, respectively, between 1980-2004.[5,6] Worldwide, approximately 800,000-1,000,000 individuals die due to tetanus annually. The most common causes of mortality is cardiovascular complications (40%) and respiratory distress (15%).[7] Primary tetanus treatment consists of vaccination and tetanus immunoglobulin; however, support therapy at intensive care units are of paramount importance particularly in severe cases with respiratory distress, cardiovascular complications and severe spasms. The overall management of tetanus should encompass prevention of complications and autonomic dysfunction secondary to prolonged intensive care unit stay, spasm control with

sedatives and neuromuscular agents, cleaning of the primary focus, antibiotherapy and mechanical ventilation.[8,9]

Benzodiazepines, muscle relaxants and morphine might be used to alleviate the spasms, but intrathecal baclofen stands out as a good treatment option in severe and refractory cases. Baclofen shows its antispasmodic effect by inhibiting presynaptic acetylcholine release and synaptic medullary reflexes via agonist effect of binding to GABA-B receptors in the CNS.[2] ITB therapy provides the advantage of avoiding prolonged sedation and shortening the duration of mechanical ventilation, as well as reducing the rates of associated complications and mortality. Intrathecal baclofen starts to show its effects at 1-2 hours and maintains its efficacy for 12-48 hours.

Treatment with baclofen infusion was first tried in tetanus patients with severe spasticity in 1986. In the following years, spasms associated with tetanus have been treated successfully with intrathecal baclofen. The retrospective study of Santos et al.[10] performed in 2004 has demonstrated that patients with severe tetanus responded to treatment, and duration of mechanical ventilation was significantly shortened, need for sedation and muscle relaxants was significantly reduced. In 1999, Engrand et al.[11] successfully treated muscle rigidity and spasms of patients with severe tetanus using intrathecal baclofen. Also, patients receiving intrathecal baclofen were compared with patients who did not receive the treatment in the same study, and intubation rate was reported as 45.5% and mortality rate as 81.8%, and every patient required deep sedation in the non-baclofen treated group. Meanwhile the intubation rate was 14% (2/14) and mortality rate was 35% (5/14) in baclofen group, and ITB was shown to decrease the need for intubation and deep sedation as well as reduce mortality.

In 2000, Boots et al.[12] administered intrathecal baclofen to adult patients with tetanus and reported that spasms and spasticity had regressed, and the need for sedation and paralysis had decreased with treatment. However, the authors also emphasized that hypotension and CNS infection might be seen with ITB.

ITB therapy was administered to 57 patients with refractory spasticity by Philips et al.[13] between 2006-2012, and minor complications including nausea, headache, and urinary retention were reported, while spasticity was decreased markedly in 17 patients. Berman et al.[14] evaluated ITB treatment in 30 pediatric patients with severe spasticity refractory to prolonged medical treatment and concluded that the treatment was effective in 28 patients and early administration of ITB therapy was a good treatment option in pediatric patients with severe spasticity.

When the literature is examined it has been shown that the use of intrathecal baclofen improves the outcomes in many cases of spasticity other than tetanus (severe brain injury, spinal injury, etc.).[15]

The clinical efficacy of intrathecal baclofen is dosage dependent, onset dosage varies between patients and dose adjustments should be made upon extubation, and improvements in rigidity and spasticity. Prevention of prolonged sedation and mechanical ventilation, and shortening of the duration of hospitalization and intensive care unit stay should be the goal of treatment. Studies have demonstrated that 1-2 mg/day dosage should be administered to obtain treatment response in adults.[10] However, there are no exact data in pediatric patients. The most common side effects include hypotonia (34.7%), somnolence (20.9%), headache (10.7%), convulsion (10.0%), dizziness (8.0%), urinary retention (8.0%), nausea (7.3%), and paresthesia (6.7%). Furthermore, coma and death might result in high dosages.[16,17] The clinical spectrum of spasms and spasticity could not be controlled with high dose diazepam, morphine, vecuronium, and magnesium sulphate therapies in our case. The efficacy of intrathecal baclofen was assessed at two hours of test dose and intrathecal baclofen pump was implanted upon observation of significant improvement in spasms and rigidity. Treatment was initiated at 50 mcg/day and dose increases were made at every 2 days. Spasms decreased with increased dosages. Dosages of vecuronium, diazepam and morphine were reduced with observation of clinical improvement. Spasms were entirely controlled at 110 mcg/day dosage and all sedative and analgesic treatments were ceased at day 12 of ITB treatment. The patient was weaned from mechanical ventilation at day

24 of hospitalization.

Consequently, tetanus remains to be a significant healthcare issue in our country despite vaccination programs. Severe tetanus cases should be followed at intensive care units, and added that the prolonged hospitalization due to high dose sedation and use of muscle relaxants, mortality and morbidity rates are high. ITB therapy allows us to avoid prolonged sedation, shortens durations of intensive care unit stay and mechanical ventilation, and decreases the rates of complications and mortality. Therefore, intrathecal baclofen therapy might be an alternative treatment option to paralytic agent and sedative use with better patient outcomes.

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