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Clinical Report

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Baclofen Overdose Resulting in Respiratory Failure and Coma in a Patient with Intrathecal Baclofen Pump

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Abstract

Intrathecal baclofen dosed through an (ITB) is an effective option for management of severe spasticity in patients with multiple sclerosis (MS). However, serious complications may occur to patients with potentially life-threatening consequences. Acute baclofen overdose mimics other fatal conditions. It's diagnosis can be very challenging, and may require emergency airway and hemodynamic support.

We present the case of a 53-year-old Caucasian woman with MS who underwent ITB pump implantation (Medtronic Synchromed II) in 2008 to treat disabling spasticity in her lower extremities, with excellent therapeutic benefits and minimal side effects. Two days after a routine pump refill with no change in pump settings, she became lethargic and hypotensive. In the emergency department her mental status deteriorated and she required endotracheal intubation to support ventilation. A comprehensive work-up revealed that an excessive dose of baclofen was delivered over several of days likely due to a mechanical problem with the pump.

Keywords: *Multiple sclerosis; Intrathecal baclofen; Spasticity; Baclofen toxicity*

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Introduction

The Medtronic Synchromed II is an implanted programmable pump with a reservoir attached to an implanted intrathecal catheter which delivers medication directly into the intrathecal space. The use of intrathecal baclofen, delivered through this pump is a well-known treatment of severe spasticity secondary to multiple sclerosis (MS) or other spastic medical conditions [1-3].

Baclofen binds to gamma-aminobutyric acid B ($GABA_B$) receptors and inhibits the release of excitatory neurotransmitters and mono-synaptic and polysynaptic spinal reflexes [3]. ITB pump delivers the baclofen at doses ranging between 50 to over 1000 mcg depending on the diagnosis, severity of spasticity, and the clinical response of the patient. Therefore; despite its wide therapeutic range the drug overdose can be life-threatening, [4]. Baclofen toxicity can present with profound hypotension, hypotonia, paralysis, altered mental status, respiratory depression, and coma.

We report the case of a 53-year-old woman with MS maintained for nearly five years on intrathecal baclofen (ITB) therapy via implanted pump (Medtronic SynchroMed II™, Medtronic Inc., inneapolis, MN, USA) to control her severe spasticity. She did very well since the implant in 2008, attaining her ultimate goal of maintaining independent ambulation. In April of 2013, she returned to clinic for a routine pump refill without any change in dose or rate of delivery.

Unexpectedly, 36 hours after the refill she presented to the emergency department (ED) with hypotension and somnolence [5]. Her mental status rapidly deteriorated and endotracheal intubation was required in the ED to protect the airway. Comprehensive work-up was negative, but further investigation of the pump revealed that the device had delivered an excessive amount of baclofen, which resulted in her presenting symptoms.

Case Report

A 53-year-old Caucasian woman suffering from severe spasticity secondary to MS with an ITB pump was presented to ED with hypotension and somnolence. An ITB pump was implanted in 2008 to control severe spasticity with excellent results (a decrease in the average lower 57 extremity Ashworth scale score from 5 to 3) and her current baclofen dose was 270 mcg/day.

She had maintained a regular follow-up with our pain clinic. Two days prior to this admission she had a routine pump refill without any change in baclofen dose or other settings. On physical exam upon arrival to ED her vital signs were as follows: blood pressure 82/40, heart rate 56, respiratory rate 9, temperature 36.5° 61 C, and oxygen saturation of 90% on 2 L/min oxygen via a nasal cannula. Her initial neurological exam showed a somnolent patient responding to loud voice with diffuse flaccidity and deep tendon reflexes ¼. The cardiac and abdominal examination was unremarkable. She was admitted to ICU and monitored carefully. Although we had high suspicions 65 for baclofen being the cause (given the temporal association with the refill time), a complete work-up was done to rule out sepsis, electrolyte abnormalities, illicit drug overdose, intracranial hemorrhage, and hypoglycemia. She underwent a magnetic resonance imaging of her central nervous system which demonstrated only demyelinated plaques consistent with multiple sclerosis. Her mental status deteriorated rapidly and endotracheal intubation was required. Her ITB pump was interrogated and baclofen dose was decreased incrementally up to 65% of initial dose. Her mental status improved slightly and very gradually after these adjustments. Surprisingly she did not regain the baseline function or mental status and remained in the ICU. Finally, during the exchange of her pump solution significantly less than expected volume in the reservoir suggested unexplained over-delivery of the medication. Of note, the medication solution was sent off for analysis and was found to be within expected concentrations and expected composition.

The patient was taken to the operating room, where the pump was replaced. We also replaced 50 ml of her CSF with 50 ml of normal saline in 10 ml aliquots using the pump's side port. She tolerated the surgery without any problems and her trachea was extubated next morning. The patient's mental status improved rapidly and returned to baseline by the next morning. Oral baclofen was prescribed to avoid withdrawal symptoms but none occurred. The postoperative dose was within 20% of pre-event daily dose. The pump was sent to Manufacturer Company for further evaluation and we are waiting for final investigation report at this time.

Discussion

MS is a chronic autoimmune central nervous system disorder with a peak onset age between 20 to 40 years, more common in women [1,2]. Spasticity is a very common symptom among MS patients with significant impact on daily functionality and life quality. Oral baclofen does not cross the blood-brain barrier effectively; hence it's not suitable, if higher doses are required, to treat severe spasticity. [2,3].

The use of intrathecal baclofen through an ITB pump has been shown to be highly effective in treatment of spasticity of cerebral or spinal origin with a response rate of up to 97%, with increased bioavailability requiring one hundredth to one thousandth the corresponding oral dose [6,7]. The pump is usually implanted subcutaneously in the anterior abdominal wall and connected via a subcutaneous catheter whose tip is inserted in the subarachnoid space, usually in the lumbar region.

The pump and spinal catheter malfunction resulting in baclofen toxicity as was seen in this case or baclofen withdrawal, may occur in up to 40% of patients [8]. The most common causes of intrathecal catheter malfunction include punctures, breaks, kinks, disconnections, occlusions from fibrous scar tissue, and intraoperative nicks. [9] Programming errors may lead to either overdose or withdrawal as well. Actual mechanical malfunction of the SynchroMed pump is extremely rare [10]. Baclofen toxicity may present with nausea, drowsiness, dizziness, hypotonia, respiratory failure, hypothermia, seizure, and coma [11,12]. The clinical spectrum of baclofen toxicity must be recognized, as the diagnosis can be challenging and treatment is lifesaving. Management of ITB toxicity is to provide supportive care until the toxic dose level recedes, as there is no antidote available. The treatment involves maintaining a patent airway and supporting the patient's hemodynamics.

The pump reservoir should be emptied and aspirated volume should be recorded [12]. If an expert is not available immediately to stop the pump electronically, a Med tonic representative may need to be contacted emergently. The programming and filling status of the pump should be checked using the Medtronic Interrogator [8].

In cases of massive intrathecal delivery of baclofen, removal of 30 to 50 milliliters of cerebrospinal fluid has been shown to be beneficial in reducing central nervous system baclofen load [13]. Physostigmine may reverse central side effects of baclofen such as somnolence and respiratory depression. However, it is not recommended as first line treatment because it may worsen bradycardia, increases risk of seizures and increase respiratory secretions [10,12,14].

Patients may need to be admitted to ICU for mechanical ventilation and hemodynamic support [12]. It is usually difficult to identify the cause of pump malfunction.

Increasing popularity of ITB pumps for spasticity management mandates physicians practicing pain medicine, emergency medicine, and even primary care to be familiar with ITB pump complications and appropriate treatment of baclofen overdose or withdrawal. We report this case to highlight the importance of timely diagnosis and management of a life-threatening complication, which mimics other potentially fatal conditions. Our patient presented with baclofen toxicity most likely secondary to a pump malfunction. Even though we had a high suspicion for baclofen toxicity, we performed a comprehensive work-up to rule out other etiologies as well.

We recommend that even if baclofen toxicity is likely diagnosis, patients be monitored closely after discontinuation of baclofen for possible withdrawal syndromes and oral baclofen started immediately after patient returns to his/her baseline.

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