ACTA SCIENTIFIC MEDICAL SCIENCES

Volume 2 Issue 8 November 2018

Case Report

Efficacy of A Second "Drug Holiday" in the Treatment of Intrathecal Baclofen Tolerance - A Case Study

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Received: September 26, 2018; **Published:** October 25, 2018

Abstract

Spasticity and muscle spasms are complications following a SCI (Spinal Cord Injury). Intrathecal Baclofen (ITB) is an effective treatment for severe spasticity of spinal cord origin.

Concerns over tolerance remain controversial. It is manifested by an escalation of dose required to produce a previously obtained effect or by a given dose of drug with continued administration.

To combat baclofen resistance, a "drug holiday" is an effective method, interrupting the trend of accelerated dosage by weaning off the baclofen for 4 - 6 weeks.

Keywords: Drug Holiday; Intrathecal Baclofen

Introduction

Spasticity is characterized by an increase in velocity - dependent muscle tone. Muscle spasms are spontaneous muscle contractions that are painful and can be elicited by stretch or cutaneous stimulation.

Spasticity and muscle spasms are common secondary complications following a spinal cord injury (SCI). These complications can interrupt an individual's ability to perform activities of daily living [1,2].

Baclofen (B-(aminomethyl)-4-chlorobenzenepropanoic acid), structurally related to gamma-aminobutyric acid (GABA), is able to inhibit spinal mono- and polysynaptic reflexes by acting on the GABAB receptors, located in the posterior horn of the spinal cord, causing membrane hyperpolarization and a blockade of calcium channels [3,4].

Continuous Intrathecal Baclofen Infusion (ITB) has been shown to be a safe and effective treatment for severe spasticity of spinal cord origin, resistant to oral treatment. However, concerns over the development of tolerance remain controversial [3].

Tolerance is manifested by an escalation of dose required to produce a previously obtained effect or by a given dose of drug with continued administration [4].

Development of tolerance has been described as rare. The numbers reported in some studies vary from 1 to 20%. Because there is no clear definition of tolerance in most studies, the numbers depend on the judgments of different investigators. Also, there are not determined predictive factors for the development of tolerance [1,6-8].

The mechanisms by which tolerance develops have not been fully elucidated. It could be due to changes in the GABAB receptors or intracellular changes. It appears that the number of receptors decreases after repeated drug infusion, causing the loss of efficacy of baclofen [4,5].

To combat baclofen resistance, there are three different treatment regimens: switch the infusion mode from simple to complex continuous, switch to pulsatile bolus infusion and conduct a "drug holiday". This is an effective method, interrupting the trend of ac-

celerated dosage by weaning an individual off the baclofen during 4 to 6 weeks and then restarting treatment [1].

Several authors have found this method to be successful, with some patients returning to a dose similar to their initial post-implantation dose. However, this method may cause 'baclofen withdrawal syndrome' with symptoms as hyperthermia, altered mental status and hypotension. Therefore, patients need to be hospitalized and treated with alternative muscle relaxants [1,9,10].

Case Description

We report a case of a 45-year-old patient who suffered a car accident on 1996 with SCI and vertebral fracture of C5 and C6. He has incomplete tetraplegia AIS B, motor level C5 and sensitive L1.

Due to severe uncontrolled spasticity (IV on Modified Ashworth Scale - MAS), he was implanted with an intrathecal baclofen pump on 2002. Since then, it remained controlled (MAS = II) with the daily dose of 310 µg.

On 2009, because of the resurgence of severe spasticity (MAS = V), resistant to a fast increase on daily dose until 360 µg/day, drug tolerance was suspected. We conducted a "drug holiday" over 4 weeks and gradually reintroduce baclofen. With a dose of 220 µg/day the patient showed a good control of spasticity (MAS = I).

During the year of 2017, he presented a new increase in spasticity (globally grade IV on MAS), combined with frequent clonus of lower limbs (he punctuated 2 on Spasm Frequency Scale - SFS). There was no response to the rise of the daily baclofen dose.

In this context, he was admitted to the Centro de Medicina de Reabilitação de Alcoitão on july/2017 for a second "drug holiday", to control spasticity. As the pump doesn't allow doses bellow 25 µg/day, it was only possible to reduce the dose to 25 ug/day and filled it with saline solution.

After 4 weeks without any baclofen, the pump was gradually refilled.

At a dose of 60 ug/day, a remarkable improvement on lower limbs spasticity, and subsequently the possibility to realize passive knee extension (Grade II on MAS), was achieved. The patient also noticed a decrease on muscle spasms frequency (SFS = 0). He was discharged with this dose, appreciably below the previous dose.

Figure 1: Before the second drug holiday.

Figure 2: Baclofen pump refill.

Figure 3: At discharge.

Conclusion

The use of intrathecal baclofen therapy on spasticity of medullar origin is increasing. We want to highlight the importance of being aware for cases of tolerance to this drug. In this case, both "drug holidays" were effective, as measured by MAS and SFS.

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