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Case Report

Baclofen Neurotoxicity in a Pediatric Patient on Peritoneal Dialysis

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ABSTRACT

We describe a 2-year-old patient with End Stage Kidney Disease (ESKD) on Continuous Cycling Peritoneal Dialysis (CCPD), gastroesophageal reflux disease, gastric tube dependence who presented with hypotension, confusion and lethargy 1 day after initiating oral baclofen for chronic vomiting. Sepsis work up and baclofen level were sent, later showing baclofen level of 0.55 mcg/ml. The patient required norepinephrine and CCPD for 24 hours before returning to baseline. CCPD was continued for 33 hours and he was discharged home at baclofen level of 0.25 mcg/mL.

Keywords: Gastroesophageal; End Stage Kidney Disease (ESKD); Baclofen; Hyperparathyroidism; Metoclopramide

INTRODUCTION

There is limited information on oral baclofen toxicity in pediatric patients with End Stage Kidney Disease (ESKD). This medication is primarily excreted by the kidney and acts on the CNS [1]. There are no consensus guidelines on initial doses in patients using this medication in ESKD. There was one report and review which has guided dose adjustments to one third of the usual dose, in patients with severe chronic kidney disease [2]. The mechanism of action of baclofen is not fully known. It acts on the GABA-B receptor as an agonist; it is thought to inhibit both monosynaptic and polysynaptic reflexes in the spinal cord [1]. Baclofen is generally prescribed for symptoms related to severe muscle spasm. To achieve higher central nervous system concentrations, baclofen is often administered intrathecally, although oral administration is also common. Here we report the first case of a pediatric patient on chronic Continuous Cycling Peritoneal Dialysis (CCPD) who presented with baclofen neurotoxicity, the patient's treatment with CCPD, baclofen levels associated with symptoms and resolution of symptoms.

CASE REPORT

Here we describe a 2 year old Hispanic male, with history of ESKD secondary to posterior urethral valves, who was maintained on chronic CCPD since infancy (1 month). In addition, the patient developed seconday hyperparathyroidism, idiopathic central precocious puberty, gastroesophageal reflux disease, gastric tube dependence and chronic vomiting. He presented to the emergency department by ambulance for lethargy, low muscle tone and hypotension when disconnecting peritoneal dialysis. The day before presentation, he had been started on oral baclofen (0.25 mg/kg/day, divided three times daily) for chronic vomiting, previously failing to control vomiting with metaclopramide, famotidine and pantoprazole.

The patient presented to emergency services by ambulance for lethargy, low muscle tone, inability to keep eyes open and hypotension when disconnecting from CCPD and his initial blood pressures were 70 s/40 s mmHg with a heart rate fluctuating between 50-60 beats per minute. On exam he was arousable with noxious stimuli (nasal swab), but he was otherwise sleepy until norepinephrine and dopamine were initiated.

Diagnostic studies including a chest radiograph, computerized tomography scan of the brain, magnetic resonance imaging of the brain, blood culture and peritoneal fluid gram stain, cell count and culture, which were all negative. He received intravenous fluids (40 ml/kg of 0.9% normal saline) and empiric antimicrobial therapy (intravenous piperacillin-tazobactam and vancomycin).

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The patient was transferred to the pediatric intensive care unit, where his initial examination revealed truncal ataxia and mild hypotension, necessitating continuous infusion of norepinephrine. He was started on continuous peritoneal dialysis. Comprehensive urine drug testing via immunoassay and liquid chromatography/tandem mass spectrometry (Toxassure; ARUP laboratories) revealed only the presence of baclofen. An initial baclofen level was 0.55 mcg/mL (normal reference range 0.08-0.4 mcg/mL). Serial baclofen levels were obtained while patient continued CCPD and are depicted in Figure 1.

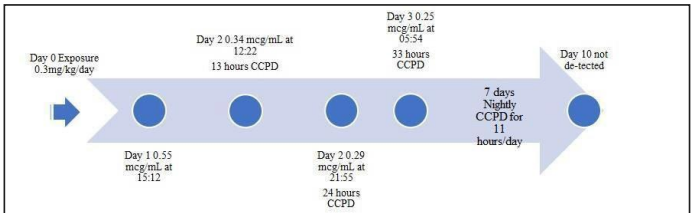

Figure 1: Serial baclofen levels were obtained while patient continued continuous peritoneal dialysis.

His motor function and mental status had recovered to approximately 90% baseline within 20 hours on continuous peritoneal dialysis. After 24 hours vasopressors and antimicrobials were discontinued. The patient remained on continuous peritoneal dialysis for 33 hours, at which time the patient had returned to a baseline normal mental status with normal vital signs. At the time of follow up 1 week after discharge, the baclofen level was undetectable.

DISCUSSION

We describe the first case report of a child with ESKD who presented with hypotension, bradycardia, hypotonia and lethargy found to have supratherapeutic baclofen levels and was successfully treated for baclofen toxicity with continuous peritoneal dialysis. While typical doses of baclofen for spasticity in children are 1 mg/kg/d (divided three times daily), this child was started on a reduced dose of 0.25 mg/kg/day (divided three times daily) owing to his kidney function. Despite this reduction, the patient still developed classic features of baclofen toxicity. Laboratory studies confirmed the elevated baclofen level and excluded other infectious or toxic etiologies of his symptoms.

Baclofen overdose commonly manifests with respiratory depression, hypotonia, hypertension, lack of tendon reflexes, coma, hypothermia, and bradycardia. As baclofen is a GABA-B agonist, seizures can occur with both overdose or withdrawal. In most cases, full recovery within 48-72 hours can occur with assisted ventilation and supportive treatment [2].

Baclofen is formulated intrathecally and orally as a tab or suspension. Baclofen is rapidly absorbed from the GI tract in a dose dependent manner with peak serum levels occurring after approximately 1 hour (wide range of 0.5 to 4 hours). Its volume of distribution is also highly variable in the pediatric patients, with about 44% interindividual variability. Baclofen is primarily excreted by the kidney as about 70% unchanged drug. Because baclofen is largely eliminated without significant metabolism, the elimination half-life is prolonged in kidney failure, resulting in accumulation of the drug, and resultant toxicity. At therapeutic dosing in patients with preserved kidney function, the serum half-life is nearly 5 hours in pediatric patients and a CSF half-life of 1.5 hours in intrathecal administration [1].

In the only case series in the literature of children with chronic kidney disease, a child who was previously Peritoneal Dialysis (PD) dependent was prescribed baclofen while taking pregabalin, and this patient experienced low respiratory drive, bradycardia and loss of consciousness. This child recovered after 12 hours of supportive care, but was not treated with PD. A 2nd pediatric patient who was also being treated with pregabalin, started baclofen for spasticity while treated with Continuous Veno-Venous Hemodialysis (CVVH) and required treatment for respiratory distress and hypertension. She recovered within 1 day as well, with CVVH [3]. In adult patients requiring continuous ambulatory peritoneal dialysis or hemodialysis, altered consciousness, abdominal pain and hypertension seem to be the most common symptoms of baclofen toxicity [4-6], but our patient presented differently with low blood pressure rather than high. Respiratory depression and hypotension, as we see in our case, have been rarer symptoms but are reported in some cases [2]. Our case is in agreement with previous cases, showing a recovery 1-3 days from exposure, with stopping baclofen, initiating dialysis and supportive care. Prospective studies are needed to study the pharmacokinetics of baclofen in ESKD.

CONCLUSION

This case report describes a child with a history of ESKD, on CCPD who developed moderate baclofen toxicity, despite a dose reduction. We do not recommend the use of baclofen for treatment of chronic vomiting in pediatric patients with ESKD and CCPD dependence for the risk of serious neurotoxicity, even with a significant dose reduction.

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