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Baclofen-Induced Neurotoxicity in Kidney Disease

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ABSTRACT

The widely used centrally acting GABA agonist baclofen is still a successful treatment for persistent hiccups and spasticity. The circulation concentrations are determined by renally dependent excretion, which also directs optimal dosing to reduce side effects. Baclofen should be used with caution to individuals who have impaired renal function. We describe a patient with end-stage renal disease who was receiving hemodialysis and had just taken baclofen. The patient had toxic encephalopathy, which was treated with further dialysis sessions.

Key words: Neurotoxicity, Baclofen, Dialysis

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INTRODUCTION

Gamma-aminobutyric acid (GABA) is a neurotransmitter, and baclofen (parachlorophenyl gamma-aminobutyric acid) is an agonist of GABA [1]. Spasticity and more recently chronic hiccups have both been treated using the centrally acting mechanism of action [2,3]. The optimal therapeutic amounts of 80–400 ng/mL of baclofen are best produced by the digestive system. The kidneys account for 70–80% of excretion, with the remaining portions being broken down in the liver or the gastrointestinal tract [4].

The desired effects are only produced by a small percentage, which cross blood–brain barrier. It takes about 6.8 hours for a half-life to occur [3]. Patients with impaired kidney function have longer half-life and increased blood-brain barrier bridging. The symptoms of the overall central nervous system (CNS) depression then become more severe, resulting in tiredness, loss of consciousness, hypotension, ataxia, psychological problems, and depression of the cardiovascular and respiratory systems [2,4].

With the initial dose of 5 mg t.i.d. within only a few days, previous reports showed severe adverse effects in patients with poor renal function [5]. Hemodialysis with excretion rates comparable to normal renal function has been proven to alleviate baclofen toxicity [6]. In this case report, we describe a dialysis patient who experienced baclofen-induced encephalopathy and recovered after receiving hemodialysis.

CASE REPORT

Our patient, a 54-year-old man with a history of Charcot joint, diabetes mellitus type 2, CKD stage 3 not on conservative management, hypertension, was seen for disturbed mental status. The patient had visited a local clinician due to fever and paraspinal muscle spasm and he was prescribed baclofen 10 mg twice-daily. On the day of admission, his son discovered the patient laying on the ground and mumbling something. Due to his altered mental state, he was taken to the hospital and admitted to the intensive care unit.

Temperature was 99.1°F, respiration rate was 28 breaths per minute, pulse was 54 beats per minute, blood pressure was 130/60 mm Hg, and pulse oxygenation was 92% on room air. The patient was unresponsive and arousable at the time of initial presentation. The results of the laboratory tests were as follows: blood urea nitrogen 40 mg/dL, sodium 141 mEq/L, potassium 5.2 mEq/L, chloride 101 mEq/L, bicarbonate 20 mEq/L, and creatinine 5.7mg/dL. Serum ammonia 30 µ/dL. Hemoglobin was 9.8 mg/dL, platelets were 2.4 Lakhs, and white blood cells were 12.4 mg/dL. Carbon dioxide levels of 44 mmHg and a pH of 7.41 were found in venous blood gas. Total bilirubin was 0.8 mg/dL, AST was 45 u/L, ALT was 26 u/L, alkaline phosphatase was 52 u/L, creatine kinase was 478 u/L, and ammonia was 52 u/L on a liver function panel. The results of a head computed tomography revealed age related atrophy and no obvious intracranial abnormalities. Hepatomegaly

with fatty infiltration was discovered by abdominal ultrasonography. A toxicological test on urine came up negative.

Three days before to admission, the patient's attender confirmed that the baclofen was given for para spinal spasm. The patient was dialyzed right away with a strong suspicion of baclofen-induced encephalopathy. He underwent hemodialysis for three sessions, and his mental state significantly improved. After being recovered, the patient stopped taking baclofen, and he has not experienced any similar incidents during the stay.

DISCUSSION

In the 1960s, baclofen was first discovered to be useful in the treatment of spasticity resulting from spinal cord lesions. A centrally acting presynaptic agonist of GABA is the mechanism of action to improve tone reduction and decrease stiffness [1]. It has been proven successful in treating chronic hiccups in recent research [3]. The principal route of excretion for baclofen is renal function [4]. In an excretion kinetic analysis, it was found that there was a strong link between renal clearance and creatinine clearance [7,8]. Since baclofen is a fairly lipophilic chemical, its ability to enter the blood brain barrier results in an enhanced response when it does [9]. These unfavourable effects include toxic encephalopathy, bradycardia, hypotension, and respiratory depression [5,9]. With the resolution of the neurologic consequence, baclofen serum concentrations were seen to have gradually declined over hemodialysis sessions [5].

In one instance, a patient took 200 mg of extended-release baclofen, which led to respiratory failure requiring a ventilator. After two sessions of heamodialysis, the side effects were successfully extubated, and further symptoms were also alleviated [9].

Baclofen's filtration rate was compared to that of healthy kidneys in a study on the effectiveness of hemodialysis [6]. Only 30% of the circulating concentration is bound to protein, which accounts for the great effectiveness of filtration [6]. According to case reports, there is a several-hour wait before symptoms improve, which is thought to be due to the need for dialysis and redistribution from the CNS to the intravascular system. It's interesting that patients with compromised renal function have been observed to experience side effects from the therapeutic range of baclofen 80-400 ng/mL [10].

CONCLUSION

Initial analyses into the cause of unconsciousness in baclofen overdose have utilised electroencephalography (EEG) which showed burst suppression pattern. Following treatment, these EEG abnormalities were reported to resolve. It has been advised against treating these modifications with antiepileptic drugs because they did not suggest a capability to cause epilepsy.

A 2011 research strongly encouraged label modifications with better dosing instructions. With a GFR of less than 30 mL/min/1.73 m2, it was suggested to forego this medication. A reduction in dose and titrating with a GFR > 30 to 60 mL/min/1.73 m2 provided more information on this. This continues to be a very suitable advice in light of the history of side effects and impaired renal function. Our case illustrates toxic encephalopathy caused by improper baclofen dosage, which was treated with hemodialysis. With this renally excreted medicine, special caution is needed, and more detailed instructions would probably further reduce the likelihood of side effects.

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