Baclofen-induced encephalopathy in patient with end stage renal disease: Two case reports

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ABSTRACT

We report two end stage renal disease (ESRD) patients, who rapidly developed neurotoxicity after taking baclofen, a centrally acting gamma-aminobutyric acid agonist. They presented to our hospital in a state of confusion. On physical examination, there were no focal neurological deficits and the remainder of the examination was also not diagnostic. Laboratory data were unremarkable. The consciousness improved with supportive treatment and intensive hemodialysis over 3-4 days. In conclusion, physicians should be aware of the possibility of baclofen-induced neurotoxicity in patients with renal disease, especially in ESRD patients and it is necessary to avoid or reduce baclofen dosage in these patients.

Key words: Baclofen, end stage renal disease, neurotoxicity

Introduction

Baclofen [4-amino-3-(-4-chlorophenyl)-butanoic acid] is a centrally acting gamma-aminobutyric acid (GABA) agonist. It is currently used for alleviation of signs and symptoms of skeletal muscle spasticity and spasm, particularly in patients with multiple sclerosis or in patients with spinal or cerebral disorders. Although the precise mechanism of action of baclofen is not fully known, it is capable of inhibiting polysynaptic and monosynaptic reflexes at the spinal level by hyperpolarization of afferent terminals.[1-3]

Ingested baclofen is rapidly and extensively absorbed; the rate of absorption may be reduced with increasing doses. There is relatively large variation in absorption and/or elimination. In addition, the drug is moderately lipophilic, approximately 30% of baclofen bound to protein and it can cross the blood-brain barrier.[4,5]

In a healthy person, most of the ingested baclofen (69–85%) is eliminated by the kidneys without changes in urine and 15% is metabolized by the liver to an inactive form. In the patients with the impaired renal function and especially in the patients with end stage renal disease (ESRD), half-life of the drug is prolonged; it is between 4.5 and 6.8 h in healthy people, but increases in patients with ESRD. Exposure to as little as 5 mg baclofen may cause severe toxicity soon after ingestion.[6,7]

Case Reports

Two ESRD patients, a 48-year-old diabetic man (case 1) and a 79-year-old non diabetic man (case 2) presented with a profound central nervous system depression due to baclofen toxicity. The causes of ESRD were diabetic nephropathy and unknown; also they were on maintenance hemodialysis (4 h, three times a week) for 1 and 2 years. They both had used this drug for their lower back pain.

After receiving low dose of baclofen, the patients became disoriented, in a state of confusion and were referred to our hospital for evaluation (cumulative dose of 30 mg in case 1 and 20 mg in case 2). On presentation, they were in a confused state (Glasgow coma scale E4V3M6 in case 1 and E3V3M5 in case 2) and therefore, they were

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admitted in the intensive care unit (ICU). The vital sign revealed mild hypertension (150/80 and 140/90 mm Hg in case 1, 2 respectively) and their respiratory rate and pulse rate were in the normal range, and they had no fever. In physical exam, there were no focal neurological deficits and the remainder of the examination was also not diagnostic.

Laboratory data including serum sodium, potassium, glucose, calcium, phosphorus, and magnesium, liver transaminases and thyroid function test were unremarkable except for azotemia and mild anemia as would normally be expected (in case 1 hemoglobin 9.8 g/dL, urea 87 mg/dL, creatinine 7.6 mg/dL and in case 2 hemoglobin 10.8 g/dL, urea 76 mg/dL, creatinine 6.8 mg/dL). Computed tomography (CT) of the brain was normal in case 1 and showed cortical atrophy in case 2.

According to the differential diagnosis of baclofen-induced encephalopathy and after exclusion of other identifiable causes, baclofen was stopped and they received intensive hemodialysis. With adequate supportive care including mechanical ventilation and intensive hemodialysis, their neurologic symptoms gradually disappeared without any neurologic sequelae over 3 and 4 days respectively.

Discussion

Although, nervous system side effects including transient drowsiness, sedation, dizziness, weakness, fatigue, coma and respiratory depression are known side effect of baclofen in patients with normal renal function, however, they usually do not occur after use of low dose of the drug, and, in addition, most of the severe nervous system side effects were reported following intrathecal injection. On the other hand, in the patients with the impaired renal function and especially in the patients with ESRD, the half-life of baclofen is significantly increased and the recommended dose or even low doses of baclofen as little as 5 mg daily or a cumulative dose of 15 mg could cause a rapid baclofen accumulation and severe baclofen intoxication. In addition, as we reported in the present case reports profound central nervous system side effects, including coma and respiratory depression could also develop soon after the initiation of therapy.[6,7]

There are few report of baclofen intoxication in the patients with chronic kidney disease who also demonstrated the importance of considering level of renal function when prescribing baclofen for each cause. Chu-Lin *et al*. reported two patients with chronic renal failure not requiring dialysis and baclofen-induced encephalopathy; a 68-year-old male with urea of 45 mg/dL and creatinine of 3.4 mg/dL and a 73-year-old woman with urea of 55 mg/dL and creatinine of 4.8 mg/dL, who were admitted with altered consciousness that rapidly developed after use a low dose of baclofen for intractable hiccups. With supportive treatment, cessation of baclofen and one course HD in second patient, neurologic symptoms recovered completely without any neurologic sequelae.[8]

Wu *et al*.[9] also reported a 70-year-old woman with ESRD who became disoriented and confused after receiving a cumulative dose of oral baclofen 45 mg in 3 days for leg muscle soreness. She received a single 4-h session of emergency HD, and the patient was discharged from the hospital 3 days later with complete recovery of consciousness.

Although, mechanism of baclofen elimination during hemodialysis is not well understood up to 79% of the serum baclofen eliminate during one hemodialysis session.[9]

Therefore, although, more data are needed for a routine recommendation, however, according to previous reports and our cases, it seems that HD may be an option for baclofen overdose in the patients with chronic renal failure and especially in the patients with ESRD.

Conclusion

The half-life of baclofen in patients with CRF and ESRD is significantly increased baclofen could cause rapid and severe intoxication. Therefore, physicians should be aware of this possibility and it is necessary to avoid use or reduce baclofen dosage in patients with the impaired renal function and in finally HD may be an option for baclofen toxicity in these patients and especially in the patients with ESRD.

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