Low-Dose Baclofen-Induced Encephalopathy in a Patient with End-Stage Renal Disease: A Case Report

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INTRODUCTION

Baclofen (β-4-chlorophenyl-γ-aminobutyric acid) is a gamma-aminobutyric acid (GABA)-B receptor agonist, which induces pre- and post-synaptic motor neuron inhibition, leading to a central antispastic response [1]. It is currently utilized to relieve muscle spasticity and spasm resulting from cerebral and spinal cord pathology, as well as to treat musculoskeletal pain and chronic hiccups [2]. Symptoms of baclofen toxicity include nausea/vomiting, somnolence, respiratory depression, confusion, seizure, and coma [3]. Severe toxicity is uncommon, but patients with impaired renal function may be at increased risk due to its predominant renal elimination [4]. Although the exact mechanism of baclofen-induced encephalopathy remains unclear, it is thought that toxic levels of baclofen crossing the blood-brain barrier may lead to prominent central nervous system depression [1]. Baclofen toxicity is generally associated with high dosages (approximately 80 mg daily), with severe symptoms manifesting at dosages exceeding 200 mg per day [5]. However, in patients with renal impairment, particularly those with end-stage renal disease (ESRD), encephalopathy has been reported even at very low doses (mean range, 5–60 mg/day). Here, we present a case of a patient with ESRD who exhibited acute confused mentality and myoclonus following the administration of a low dose of baclofen.

CASE REPORT

A 66-year-old woman visited Soonchunhyang University Bucheon Hospital presenting with acute confused mentality. She had been diagnosed with ESRD for 12 years. She underwent hemodialysis regularly, 3 times a week, with the last session performed 2 days before admission. Her medications included aspirin, carvedilol, olmesartan, nifedipine, esomeprazole, and pyridoxine. One day before admission, the patient visited the Department of Physical Medicine and Rehabilitation due to torticollis accompanied by cervical pain and began taking baclofen 10 mg in the morning. Twelve hours after taking it, she gradually became confused and developed involuntary jerky movement in her trunk and upper extremities. The patient had no history of drug abuse and no previous exposure to baclofen. On initial examination, her blood pressure was elevated at 190/100 mm Hg, while other vital signs were within the normal range. Routine laboratory tests revealed slightly low sodium (133 mmol/L; normal range, 136–145 mmol/L), elevated levels of blood urea nitrogen (52.4 mg/dL; normal range,
8–20 mg/dL), and creatinine (6.4 mg/dL; normal range, 0.5–1.2 mg/dL). Other parameters, such as glucose (85 mg/dL; normal range, 60–99 mg/dL), lactate (0.6 mmol/L; normal range, 0.5–2.0 mmol/L), ammonia (20 µmol/L; normal range, 12–66 µmol/L), phosphorus (4.4 mg/dL; normal range, 2.5–4.5 mg/dL), calcium (9.6 mg/dL; normal range, 8.8–10.6 mg/dL), and humoral infection parameters, urinary drug screening, and ethanol were all within the normal range. On neurological examination, the patient was confused and exhibited repetitive meaningless speech. Brain computed tomography revealed no specific findings, and brain diffusion-weighted imaging also showed no abnormalities (Fig. 1). Electroencephalogram (EEG) showed generalized periodic discharges with superimposed rhythmic sharp morphology (Fig. 2). Based on clinical course, persistent altered mental status, and EEG findings, we diagnosed the patient with non-convulsive status epilepticus. The patient was administered 300 mg of intravenous lacosamide, followed by a maintenance dose of 150 mg twice a day. The patient was initiated on continuous renal replacement therapy (CRRT) in the context of elevated serum urea nitrogen and creatinine with persistent mental status changes. Three days after starting CRRT, the patient’s mental status began to improve and her generalized myoclonus resolved completely. The follow-up EEG showed slow posterior dominant rhythm, as well as intermittent generalized theta slow waves (Fig. 3). She was discharged without any residual neurologic deficits.

The patient’s caregiver provided written informed consent for the publication of clinical details and images.

**DISCUSSION**

Baclofen, a natural derivative agonist of the GABA-B receptor, has been used to treat muscle spasticity, rigidity, and pain. Of the ingested baclofen, 65%–80% is primarily excreted unchanged in the urine, while the rest, 10%–15%, is metabolized in the liver. The usual therapeutic dose ranges from 15 to 80 mg daily, with an elimination half-life of 2–6 hours after oral administration in healthy patients [1]. However, for patients with impaired renal function, the half-life could be prolonged up to 14 hours, heightening the risk of baclofen accumulation [4]. Therefore, even a relatively low-dose of baclofen could precipitate severe intoxication such as respiratory depression, encephalopathy, and seizure in patients with impaired renal function. There have been only a few
reported cases of low-dose baclofen-induced encephalopathy in patients with ESRD, occurring within 24 hours of receiving a low dose ranging from 5 to 25 mg [6,7]. Interestingly, in our case, the patient developed confused mental state and exhibited generalized myoclonus after ingesting a single low dose (10 mg) of baclofen.

Although there is no standard renal dosage adjustment guideline for baclofen, recent study suggests that dosage reduction should be considered based on the estimated creatinine clearance (CrCl) when treating patients with renal impairment. The multicenter study on baclofen pharmacokinetics provides following recommendations: CrCl > 80 mL/min: 5 mg every 8 hours; CrCl 50–80 mL/min: 5 mg every 12 hours; CrCl 30–50 mL/min: 2.5 mg every 8 hours; and CrCl < 30 mL/min: 2.5 mg every 12 hours [8]. Recently, several studies suggest that use of baclofen should be
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avoided in patients with ESRD who require hemodialysis [1].

The diagnosis of baclofen-induced encephalopathy is based on clinical presentation. Neurological symptoms appear within 2–3 days after initiating baclofen. While brain imaging and laboratory tests do not show specific findings associated with baclofen-induced encephalopathy, they are essential for excluding other potential etiologies of encephalopathy. An increased serum baclofen concentration beyond therapeutic levels (0.08–0.40 µg/mL) could be helpful in the diagnosis of baclofen-induced encephalopathy [9]. Periodic sharp wave patterns such as triphasic waves and generalized periodic epileptiform discharges are often accompanied by baclofen-induced encephalopathy [10]. In our case, we suspected the baclofen-induced encephalopathy with non-convulsive status epilepticus rather than uremic encephalopathy, based on the following features: (1) no significant difference in concentrations of uremic toxins compared to the previous blood test and (2) temporal relationship between the timing of baclofen administration and symptom onset.

Currently, there are no standardized treatment guidelines for baclofen-induced encephalopathy. The most commonly employed approach involves supportive and symptomatic care, addressing associated complications, such as seizure, respiratory failure, and autonomic instability. Additionally, intensive hemodialysis is regarded as one of the most effective treatment options for baclofen-induced encephalopathy [1].

In conclusion, baclofen presents a heightened risk of adverse neurological effects in patients with ESRD. Therefore, clinicians should be aware of the need for careful monitoring and potentially adjusting dosages when prescribing the baclofen to patients, taking into account their reduced kidney function and the increased likelihood of drug accumulation and toxicity. Also, in cases where baclofen-induced encephalopathy is suspected, prompt management, including the initiation of hemodialysis should be instituted.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES