Baclofen intoxication in a patient with chronic renal failure: A Case Report

Eurasian Clinical and Analytical Medicine Case Report

Baclofen in renal failure

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Abstract

Introduction: Baclofen is a derivative of γ-aminobutyric acid (GABA), is used in the treatment of spasticity.

Case Presentation: Baclofen toxicity can cause muscle flaccidity, severe respiratory depression, seizure, coma, bradycardia/tachcardia, or hypotension/hypertension.

Conclusion: We report on a 60-year-old female patient with chronic renal failure who presented with stupor due to baclofen intoxication in spite of low dosage.

Keywords

baclofen intoxication, chronic renal failure, impaired consciousness

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Introduction

Baclofen, a β-(p-chlorophenyl) derivative of the neurotransmitter γ-aminobutyric acid (GABA), is currently used in the treatment of muscle spasticity, especially in patients with neurological diseases. Baclofen is eliminated predominantly by the kidneys, and patients with impaired renal function are at particular risk for baclofen accumulation.[1] Some authors have suggested that haemodialysis is effective in the removal of baclofen; however, the pharmacokinetics of baclofen elimination during haemodialysis remain unclear.[2] In this article, we report a case of baclofen intoxication in a patient with chronic renal failure that was successfully resolved by haemodialysis.

Case Presentation

A 60-year-old female patient presented to our hospital with nausea, vomiting, and impaired consciousness. Her family reported that the patient had mistakenly taken 5 baclofen tablets (50 mg) six hours earlier. Her husband had been using baclofen for the treatment of intractable hiccup. Her past medical history included hypertension, diabetes mellitus, coronary artery disease, chronic renal failure, and congestive heart failure. She had been receiving regular haemodialysis twice weekly for 18 months. The patient was taking furosemide, amlodipine, and carvedilol for antihypertensive therapy. On admission, her blood pressure was 150/85 mmHg, heart rate was 108 beats/min, and oxygen saturation was 96%. She was afebrile (36.4 °C) and had vomited three times during emergency monitoring. Laboratory data revealed hemoglobin of 11.1 g/dL, leukocyte count of 9700/mm^3 with a normal differential count, and platelets of 236,000/mm^3. Serum glucose was 299 mg/dL, urea 58 mmol/L, and creatinine 2.5 mg/dL. Sodium was 137 mmol/L, potassium 5.7 mmol/L, chloride 112 mmol/L, lactate dehydrogenase 428 U/L (125–220), and gamma-glutamyl transpeptidase 57 U/L (9–36). Other transaminases were within normal limits. Arterial blood gas analysis showed mild metabolic acidosis and hypoxia: pH 7.34, pO_2 74.3 mmHg, pCO_2 36 mmHg, HCO_2 19.8 mmol/L, sO_2 95.8%, and lactate 1.8 mmol/L. Electrocardiography revealed sinus tachycardia. Chest radiography showed no abnormalities. Neurological examination revealed no response to verbal stimuli, eye opening, or incomprehensible sounds; there was withdrawal motor response to pain. Pupils were bilaterally affected, with neither direct nor consensual light reflex. Bilateral Babinski signs were present, with no signs of meningeal irritation. Computed tomography (CT) of the brain was normal. During follow-up, the patient developed severe hypertension (220/110 mmHg) and tachycardia (140 beats/min). Intensive antihypertensive therapy with furosemide and continuous infusion of sodium nitroprusside was initiated, and she was transferred to the intensive care unit. Magnetic resonance imaging (MRI) showed no abnormalities. There was no change in neurological examination findings, and a repeat brain CT at 44 hours remained normal. At that time, her blood pressure was approximately 165/90 mmHg. Electroencephalography was normal. Over the following 47 hours, the patient underwent haemodialysis and was subsequently discharged with spontaneous eye opening and incomprehensible speech. She showed dramatic clinical improvement after the second haemodialysis session on the fourth day of admission, becoming awake, cooperative, and oriented, although she had retrograde amnesia for the previous two days.

Discussion

Baclofen is an inhibitory neurotransmitter (a GABA receptor agonist) and a centrally acting antispasmodic drug. An overdose of baclofen is considered above 80 mg/day, and the lethal dosage in adults is reported to be 1250–2500 mg/day. The classic clinical presentation of baclofen overdose usually occurs rapidly after ingestion. The effects of baclofen intoxication may include a wide range of clinical manifestations, such as impaired consciousness or coma, generalized muscular hypotonia with absent limb reflexes, respiratory depression, seizures, hemodynamic changes, and cardiac abnormalities including supraventricular tachycardia, bradycardia, premature atrial contractions, and first-degree heart block. Blood pressure abnormalities such as hypotension or hypertension, as well as either miosis or mydriasis, may also be observed.[3] Our patient presented with impaired consciousness, tachycardia, and mild hypertension six hours after ingestion. Chodorowski et al. reported that 12 out of 18 patients (66%) were admitted in deep coma, 10 out of 18 patients (55.5%) had acute respiratory failure, and cardiac abnormalities included bradycardia (44.4%), hypertension (33.0%), and hypotension (5.5%) in cases of intoxication.[1] Baclofen is excreted primarily by the kidney in unchanged form and there is relatively large intersubject variation in absorption and/or elimination. The patient had toxicity with lower dose despite of classical knowledge. We think that the patient's impaired renal function facilitated this event.

Baclofen toxicity is a clinical diagnosis; measuring plasma level is not possible and results can be misleading. We were unable to measure baclofen level at our institution as the techniques are generally available only in research laboratories. The half-life is 3,5 hours in therapeutic use but a serum half-life of up to 34 hours has been estimated after overdose.[4]

The appropriate serum level of baclofen in patients with severely impaired renal function remains unclear. Chen et al. have thought that patients with renal failure are more susceptible to baclofen toxicity.[2] Similarly our patient had toxicity with a low-dose (50 mg). On the other hand as most patients with severely-impaired renal function developed toxic symptoms soon after initiating a low-dose baclofen regimen, the accumulated dosage was small and severe complications were less common. We could not measure the baclofen level, but the patient had severe symptoms.

Chodorowski reported that there was no correlation between the dosage of baclofen and the clinical outcome.[5] This may explain why our patient had severe intoxication symptoms like alteration of consciousness, tachcardia, hypertension, even though she had ingested a low dose of baclofen.

Management of baclofen intoxication is primarily symptomatic. Our patient transferred to the intensive care unit and was treated for hypertension and tachycardia. Gastric lavage and activated charcoal were not used in the patient because they may not be effective if performed over 1 hour after ingestion.[6] The patient was treated with hemodialysis and showed dramatic clinical improvement. Wu et al. measured the changes of baclofen serum concentration during haemodialysis and found that the serum baclofen eliminated up to 79% during the 4 hours of the haemodialysis session.[7] The elimination half-life of baclofen before and during hemodialyses was 15,7 and 3,1 hours.

Conclusion

We report a case presenting with stupor associated with acute baclofen intoxication. It is important to be careful in clinical evaluation and to provide full supportive care in cases of baclofen toxicity. Otherwise, as demonstrated in our case, even low doses can lead to baclofen intoxication in patients with impaired renal function.

Declarations

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments.

Informed Consent
Informed consent for publication of this case was obtained from the patient.

Conflict of Interest
The authors declare no conflicts of interest.

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Scientific Responsibility Statement
The authors declare that they are responsible for the scientific content of the article, including the study design, data collection, analysis and interpretation, manuscript preparation, and approval of the final version of the manuscript.

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