

Baclofen-Induced Coma Reversible by Dialysis in a Patient Affected by Acute Kidney Injury

Case Report

Oliver Malle¹, Tadeja Urbanic Purkart², Karin Amrein¹

Abstract

Baclofen is commonly used to treat muscular spasticity and other conditions such as pain, alcohol withdrawal, and myoclonus. It is contraindicated in chronic kidney disease. As it is eliminated predominantly by the kidneys, acute kidney injury can lead to acute baclofen overdose with central nervous system affection due to drug accumulation. Currently, there is no consensus about the treatment of baclofen intoxication.

A 67-year-old woman was admitted with altered mental status and vomiting. Initially, she was unresponsive/lethargic and kept the intermittent ability of nonverbal communication gradually sliding into a comatose state with apneas. Initial neurologic and radiologic examinations ruled out a structural lesion of the central nervous system. Laboratory data showed acute kidney injury and suspected urinary tract infection with extremely high inflammation parameters. The patient had a history of multiple sclerosis and received daily oral baclofen. Baclofen-induced coma secondary to baclofen overdose caused by renal insufficiency was suspected and renal dialysis started within 24 hours. Cystoscopy and implantation of a ureteric stent were necessary because of obstructive nephropathy. During hemodialysis, the patient's mental status steadily improved. The patient woke up and was oriented and cooperative. Both clinical and laboratory data were widely normalized within days.

Diagnosis of baclofen overdose can be challenging, but adequate supportive therapy, including hemodialysis, should be considered to reduce the length of comatose state and the risk of aspiration pneumonia.

Keywords: Baclofen; Overdose; Renal Insufficiency; Renal Dialysis
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- ¹ Medical University of Graz, Department of Internal Medicine, Division of Endocrinology and Diabetology, Graz, Austria
² Medical University of Graz, Department of Neurology, Graz, Austria

INTRODUCTION

Baclofen is an effective spasmolytic agent [1]. It is administered orally or via an intrathecal pump. The range between minimal therapeutic dose and minimal toxic dose is small and this drug is contraindicated in chronic kidney disease [2]. Its primary site of action is in the spinal cord, where it binds to the inhibitory GABA_B receptor [3]. After rapid absorption from the gastrointestinal tract, baclofen has 70-80% bioavailability [2]. Baclofen is predominantly excreted unchanged by passive glomerular

filtration, with only a small portion being metabolized by the liver. Its serum half-life of 2-6 hours [1] can be prolonged in re-

Why Do we Describe This Case

The diagnosis of baclofen-induced coma may be challenging, especially when approved doses were taken and an underlying renal insufficiency was not previously present. After a thorough diagnostic work-out, we suggest to promptly eliminate baclofen overdose by renal dialysis

Corresponding author
Oliver Malle
o.malle@gmx.at

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nal insufficiency and when overdosed [4]. Continuous absorption from the intestinal tract and redistribution from fatty tissue may further increase its half-life in renal insufficiency [5]. Baclofen overdose can lead to central nervous system toxicity with excitatory and inhibitory neurotransmitters changes. Baclofen does not readily cross the blood-brain barrier. Hence, a relatively high oral dose (60-100 mg/day) or direct intrathecal application is needed to achieve therapeutic effects [6]. When overdosed, patients may present with lethargy, respiratory and cardiac depression, muscular hypotonia as well as generalized hyporeflexia varying with the degree of intoxication [7]. No threshold dose has been established for the consistent onset of neurologic adverse effects. However, severe neurologic adverse effects have been observed even at very low dose in young patients with normal renal function [8]. A specific antagonist does not exist, but flumazenil has been reported to counteract the inhibitory effects of baclofen [9]. Several reports showed that renal dialysis could effectively and rapidly remove

baclofen in overdosed patients with renal failure, alleviating overdose symptoms and accelerating recovery time [7]. Nevertheless, no consensus exists on its true benefit [7,10].

Here, we report on a 67-year-old patient with no history of renal impairment who was admitted for coma of unknown origin.

CASE REPORT

A 67-year-old woman was admitted to the Neurological Emergency Unit of the Medical University of Graz with altered mental status and vomiting, progressing to a comatose state (Glasgow Coma Scale—GCS = 5). Her relatives reported normal communication and the absence of any symptoms the day before admission, with progressive unresponsiveness and dizziness within twelve hours. Upon arrival, the patient showed body temperature = 35.9°C, blood pressure = 110/60 mmHg, tachycardia (105 beats per minute), and eupnea. Though unconscious, the patient did initially non-verbally react to commands, but within min-

Table 1. Laboratory results at first presentation.

ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; CK = creatine kinase; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate (CKD-EPI-formula); γ GT = γ -glutamyl transferase; Hb = hemoglobin; HCT = hematocrit; INR = international normalized ratio; LDH = lactate dehydrogenase; RBC = red blood cell count; WBC = white blood cell count

Parameter	Detected level	Normal range
WBC (10 ⁹ /L)	25.14	4.4-11.3
RBC (10 ¹² /L)	5.64	4.1-5.1
Hb (g/dL)	16.8	12.0-15.3
HCT (%)	49.4	35.0-45.0
Thrombocytes (10 ⁹ /L)	216	140-440
CRP (mg/L)	369.4	0-5.0
Procalcitonin (ng/mL)	4.14	0-0.5
Glucose (mg/dL)	145	70-100
Sodium (mmol/L)	139	135-145
Potassium (mmol/L)	5.3	3.5-5.0
Chloride (mmol/L)	97	95-110
Calcium total (mmol/L)	2.59	2.2-2.65
Creatinine (mg/dL)	3.05	0-1.0
Urea (mg/dL)	106	10-45
eGFR (mL/min/1.73 m ²)	15.17	90-120
LDH (U/L)	300	120-240
AST (U/L)	32	0-30
ALT (U/L)	15	0-35
γ GT(U/L)	51	0-38
CK (U/L)	177	0-145
INR	0.95	
aPTT (s)	37.3	26.0-36.0

utes she reacted only to deep pain stimuli (GCS = 5). Flumazenil and naloxone did not have any effect. A rapid urine drug screen test was negative. Her medical history comprised longstanding multiple sclerosis with impaired mobility (wheelchair-bound), breast cancer, and osteoporosis. The patient had been on high-dose oral baclofen therapy for years (75 mg/day). Laboratory data (Table I) revealed leukocytosis (white blood cell count = $25 \times 10^9/L$, of which 86% neutrophils), acute kidney injury (creatinine = 3.0 mg/dL, while three weeks before it was = 1.0 mg/dl), and increased levels of C-reactive protein and procalcitonin. An initial arterial blood gas analysis showed no relevant pathology.

Electrocardiography showed sinus tachycardia. Neurologic examination revealed mydriatic pupils with direct and consensual pupillary light reflexes, muscular hypotension with no spontaneous movement and absent plantar reflexes, but no meningeal signs. Urinary analysis suggested a urinary tract infection. Brain computed tomography scan (Figure 1) excluded bleeding and infarct demarcation.

The synopsis of clinical findings and laboratory data initially suggested urosepsis with acute on chronic renal insufficiency. Empiric antibiotic treatment with piperacillin/tazobactam and intravenous fluids were administered. A toxic encephalopathy secondary to baclofen overdose due to renal failure was suspected regarding oral baclofen therapy with a relatively high daily dose. After consultation with the poison center, renal dialysis was considered as a therapeutic option, as baclofen may be easily removed by dialysis and there are other case reports in the literature showing recovery of consciousness in patients with baclofen overdose due to renal failure [7,11]. Renal dialysis started but had to be interrupted after 30 minutes for cystoscopy and implantation of ureteral stents during the night due to obstructive nephropathy. During this painful intervention, her neurologic status remained deeply comatose (GCS = 5), and the patient did not need any analgesic or sedative medication. A second renal dialysis treatment over 5 hours was performed subsequently. During this second renal dialysis, the patient's mental status steadily improved. The patient woke up and was completely orientated and cooperative. An obstructing ureteric calculus was assumed to be the cause for renal obstruction, but could not be objectified

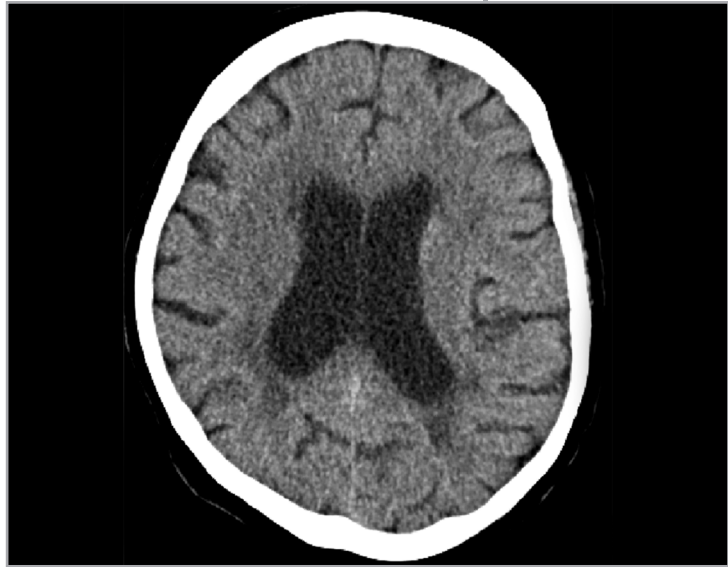


Figure 1. Brain computed tomography.

by CT that was performed during sepsis work-up. The fast recovery of consciousness is in line with other case reports, that described the rapid effect of renal dialysis in patients with baclofen overdose and renal failure [7,11,12]. Results of a blood culture revealed *Pseudomonas aeruginosa* infection. Subsequently, clinical and laboratory data, including renal function, were widely normalized, and communication was possible without any restriction.

DISCUSSION

This report demonstrates rapid and full neurological recovery in a patient with previously normal kidney function presenting with relative baclofen overdose using a high but approved daily dose of 75 mg caused by acute kidney injury associated with obstructive nephropathy and urosepsis.

First, we would like to prompt clinicians to consider baclofen as an important and reversible cause of unexplained coma in patients with acute deterioration of renal function. This is currently rarely considered, especially when baclofen is applied via an intrathecal pump.

Second, we suggest empiric use of renal dialysis in similar situations, although currently there is no consensus about renal dialysis in patients with baclofen intoxication. We postulate that in our case delayed elimination of baclofen due to acute renal insufficiency was the main reason for the comatose state of the patient. Because no specific therapy for baclofen overdose exists,

supportive therapy is usually recommended to prevent central nervous system complications, muscle spasticity, and blood pressure fluctuations. Baclofen possesses molecular features that make it ideal for removal by renal dialysis. In fact, it has low protein binding and small molecular weight, allowing for effective drug elimination and shortened half-life. In animal models, the half-life is reduced from 5 to 1.5 hours in the first two hours of renal dialysis [12]. In our case, the comatose state already improved within the first hours of renal dialysis, which is in line with similar reports in literature [7,10,13].

Neurotoxicity of baclofen can occur at approved oral doses when renal elimination is decreased. The use of baclofen is increasing especially in children and young adults [14]. To date, there is no approved antidote for this substance. However, physostigmine has been shown to reduce central nervous symptoms and respiratory depression [15].

We would like to point out that diagnosis of baclofen overdose can be challenging, but adequate supportive therapy as well as renal dialysis can lead to excellent prognosis, reduce time of comatose state and the relevant risks such as aspiration pneumonia. In aging patients, especially in those with impaired renal function, we suggest evaluating the risk-benefit ratio of baclofen treatment and observe them closely for toxicity.

CONCLUSION

Baclofen can cause nervous system depression due to accumulation following renal failure, thus resulting in deep comatose state. Renal dialysis may be an efficient and rapid method in treating patients with baclofen overdose.

Key points

- *Baclofen overdose may cause coma.*
- *Even approved dosages may result in a comatose state in case of impaired renal function, due to the delayed elimination of the drug.*
- *There are no approved antidotes.*
- *In the absence of a consensus about the management of baclofen-induced coma, renal dialysis is suggested by some reports.*
- *In this case, renal dialysis resulted in a rapid neurological improvement.*

Consent to publication

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Conflicts of interests

The authors declare they have no competing financial interests concerning the topics of this article.

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