



# A Case Report of Baclofen Toxicity in a Pediatric Patient With Normal Kidney Function Successfully Treated With Hemodialysis

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## Abstract

**Rationale:** Baclofen is a commonly prescribed medication used to decrease spasticity in children with cerebral palsy. Despite its widespread use, this medication has not demonstrated to be consistently effective in clinical studies. Baclofen is also associated with systemic adverse effects due to potent neuronal depression. The management of baclofen toxicity is mainly supportive; however, some studies have shown that hemodialysis may alleviate the symptoms of an overdose and shorten the recovery time.

**Presenting concerns:** In this case report, a 6-year-old boy with mild cerebral palsy, neuromyelitis optica, and normal kidney function was found unresponsive at home, with altered mental status, after ingesting 1300 mg of baclofen unobserved. The patient was intubated and mechanically ventilated because of significant neurologic depression with subsequent respiratory failure.

**Diagnosis:** The patient was diagnosed with baclofen-induced encephalopathy. An elevated serum baclofen level of 4.00 µg/mL (therapeutic range of 0.08–0.40 µg/mL) was observed 10 hours after he was found unresponsive. The patient's respiratory status deteriorated; he had high ventilatory requirements and remained comatose.

**Intervention:** With the worsening of his clinical condition in the intensive care unit, hemodialysis, administered via a high-efficiency high-flux dialyzer, was initiated approximately 18 hours after he was found unresponsive. The patient underwent 2 hemodialysis runs spaced 9 hours apart, with blood flow rates approaching 250 mL/min.

**Outcomes:** Within 3 hours of the first hemodialysis treatment, the patient started to regain consciousness. He was extubated to room air 6 hours after the second hemodialysis treatment.

**Novel findings:** Supportive management is the primary treatment of baclofen toxicity in a pediatric patient with normal kidney function. Hemodialysis may be considered in severe cases of baclofen toxicity and worsening clinical status, but further studies are needed to confirm this finding.

## Abrégé

**Justification:** Le baclofène est un médicament couramment prescrit pour réduire la spasticité chez les enfants atteints de paralysie cérébrale. Malgré son usage répandu, l'efficacité du baclofène n'a pas été démontrée de façon constante dans les études cliniques. Ce médicament est également associé à des effets secondaires systémiques en raison d'une forte dépression neuronale. La gestion de la toxicité du baclofène consiste principalement en un traitement de soutien. Certaines études ont toutefois démontré que l'hémodialyse pourrait atténuer les symptômes d'une surdose et hâter la convalescence.

**Présentation du cas:** Nous présentons les cas d'un garçon de six ans atteint d'une légère paralysie cérébrale et d'une neuromyélie optique. L'enfant, dont la fonction rénale était normale, avait été retrouvé inconscient à son domicile, avec un état mental altéré, après avoir ingéré accidentellement 1300 mg de baclofène. L'importante dépression neurologique et l'insuffisance respiratoire subséquente ont nécessité l'intubation et la ventilation mécanique du patient.

**Diagnostic:** Une encéphalopathie induite par le baclofène a été diagnostiquée. Un taux très élevé de baclofène sérique, soit de 4,00 µg/mL (l'intervalle thérapeutique se situe entre 0,08 et 0,40 µg/mL), a été observé dix heures après que l'enfant ait été retrouvé inconscient. Le patient demeurait comateux, son état respiratoire s'était dégradé et ses besoins ventilatoires étaient très élevés.



**Interventions:** À l'unité des soins intensifs, la dégradation de l'état clinique a nécessité l'amorce d'un traitement d'hémodialyse environ 18 heures après que l'enfant ait été retrouvé inconscient. Le traitement a été administré à l'aide d'un filtre avec une membrane à haute efficacité et à haute perméabilité. Le patient a subi deux séances d'hémodialyse à neuf heures d'intervalle, avec un débit sanguin approchant les 250 mL/min.

**Résultats:** L'enfant a lentement repris conscience moins de trois heures après le début du premier traitement d'hémodialyse, et a été extubé six heures après le deuxième traitement d'hémodialyse.

**Nouveaux résultats:** Le principal traitement dans le cas d'une intoxication au baclofène chez un enfant avec une fonction rénale normale est la prise en charge symptomatique. L'hémodialyse pourrait être envisagée en cas d'intoxication grave avec dégradation de l'état clinique. D'autres études sont toutefois nécessaires pour confirmer ce résultat.

## Keywords

case report, baclofen toxicity, hemodialysis, baclofen-induced encephalopathy

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## Introduction

Baclofen is a gamma-aminobutyric acid type B receptor agonist that reduces the release of excitatory neurotransmitters and stimulates inhibitory neuronal signals.<sup>1</sup> Acute baclofen toxicity is characterized by coma, seizures, flaccid paralysis, and respiratory failure.<sup>2-5</sup> Few cases of baclofen overdose have been reported in pediatric patients, and the treatment is usually supportive.<sup>3-5</sup> In one study, baclofen overdose was treated with gastric lavage, vigorous hydration, and forced alkaline diuresis.<sup>3</sup> Elsewhere, hemodialysis therapy was administered to a pediatric patient with acute kidney injury.<sup>6</sup>

The current study describes a baclofen overdose in a 6-year-old boy with normal kidney function who was treated successfully with high-efficiency high-flux hemodialysis.

## Presenting Concerns

A 6-year-old boy weighing 22 kg, with a body surface area of 0.83 m<sup>2</sup>, presented at a community hospital emergency department with altered mental status after ingesting baclofen unobserved. On the day of admission, the patient had been in a reasonable state of health until the early afternoon when his mother found him unresponsive. In reviewing his medications, his mother noticed that a bottle that previously contained 130 tablets of baclofen (10 mg each) was empty, suggesting that he had mistakenly ingested 1300 mg (59 mg/kg) of baclofen.

## Clinical Findings

The patient's medical history was significant for cerebral palsy and spasticity secondary to intrauterine stroke and neuromyelitis optica. His medical treatment consisted of baclofen

(15 mg daily), gabapentin, oxcarbazepine, and sertraline. The baclofen dose of 15 mg daily to treat spasticity was in a range typical for his age (ie, 1540 mg/d). The mother reported that her son had normal cognition, mild language delay, moderate motor delay, and was able to move about with a walker. On presentation to hospital, his initial vital signs were a temperature of 36°C, a pulse of 94 beats/min, blood pressure of 81/44 mm Hg, respiration of 12 breaths/min, and oxygen saturation of 84% on room air. He was unresponsive and required emergency intubation. He experienced a brief generalized tonic-clonic seizure. The laboratory data showed a normal complete blood count and a negative urine and serum drug screen. He was transferred to our pediatric tertiary care facility.

## Diagnostic Focus and Assessment

Upon presentation to the pediatric intensive care unit (ICU), the patient had a Glasgow Coma Scale (GCS) score of 3T, was mechanically ventilated, hypotonic and unresponsive, with pupils of 3 mm in diameter. Computed tomography of the head without contrast demonstrated mild sinus disease, but the scan was otherwise normal. Kidney function panel testing showed blood urea nitrogen of 10 mg/dL (reference range of 7-20 mg/dL) and serum creatinine of 0.2 mg/dL (age-appropriate reference range of 0.3-0.7 mg/dL). Urine output remained  $\geq 2$  mL/kg/h during his stay in the ICU. Normal kidney function was assessed according to age-appropriate normal serum creatinine levels and maintenance of good urine output during admission. The serum baclofen level of 4.00  $\mu\text{g/mL}$ , obtained approximately 10 h after the patient was found unresponsive and prior to hemodialysis, was toxic (therapeutic range of 0.08-0.40  $\mu\text{g/mL}$ ).<sup>7</sup> There was no order placed for continuous infusion of sedatives. Within a few hours of ICU admission, his clinical status

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deteriorated; he remained comatose, with high ventilatory requirements (a GCS score of 2T). The patient was diagnosed with acute encephalopathy due to baclofen toxicity. Given his worsening clinical condition and the suggestion of the excessive dose taken, hemodialysis was initiated for baclofen clearance 18 hours after the patient was found unresponsive and 8 hours after admission to the ICU.

## Therapeutic Focus and Assessment

Based on the low molecular weight of baclofen (213 daltons), a high-efficiency dialyzer having a larger membrane surface area (KoA urea > 800) was used to improve clearance in keeping with previously published literature.<sup>8</sup> The patient underwent 2 runs of high-efficiency high-flux hemodialysis on a 2008K Hemodialysis Machine (Fresenius) with the following settings: Opti Flux F160NR Dialyzer (Fresenius) (advanced polysulfone membrane, membrane wall thickness of 40 microns, inner diameter of 200 microns, surface area of 1.5 m<sup>2</sup>, KUF of 45 mL/h/mm Hg, and KoA urea of 1064), blood flow rate of between 200 mL/min and 250 mL/min, dialysate flow of 500 mL/min, potassium bath of 3 mEq/L, and calcium bath of 3 mEq/L. The first hemodialysis treatment lasted 240 minutes; the second hemodialysis run was initiated 9 hours after the first for 150 minutes. Blood pressure remained stable during hemodialysis without any additional pressor requirements. The patient required serum phosphorus monitoring every hour and multiple intravenous phosphorus replacement.

## Follow-up and Outcome

After the first hemodialysis treatment, the patient started to regain consciousness. The ventilator settings were decreased within the 3 hours of first treatment completion. Complete recovery of consciousness and extubation to room air occurred 6 hours after the second hemodialysis treatment. The patient was transferred to a medical ward, and his clinical status returned to normal neurologic baseline levels. Baclofen was restarted at 5 mg (a third of the standard prescribed dose) to be titrated to 15 mg after discharge.

## Discussion

Baclofen is a commonly prescribed medication used to decrease spasticity in children with cerebral palsy.<sup>9</sup> Despite its widespread use, it has several therapeutic limitations. Baclofen has not shown consistent efficacy in clinical studies in children, and it has systemic adverse effects, including somnolence, confusion, weakness, and orthostatic hypotension.<sup>1,9</sup>

It is completely and rapidly absorbed by the gastrointestinal tract and partially metabolized by the liver (15%), but it is primarily excreted, unchanged, by the kidneys (>70%).<sup>1,10,11</sup> Baclofen-induced encephalopathy is characterized by altered consciousness and is commonly seen in

patients with end-stage kidney disease (ESKD) or acute kidney failure.<sup>12,13</sup> In pediatric patients with cerebral palsy, baclofen has variable absorption in the gastrointestinal tract, with a reported time lag of  $0.59 \pm 0.28$  hours, an apparent volume of distribution of 1.16 L/kg, and an elimination half-life of 4.5 hours.<sup>10</sup> Baclofen is 30% protein-bound and the time taken to reach peak serum levels following oral administration ranges from 0.5 to 4.0 hours.<sup>11</sup> Baclofen is a small molecule with a molecular weight of 213 daltons, low-protein binding properties, and low volume of distribution, which allows for efficient removal with hemodialysis.<sup>8,14</sup>

Although the primary treatment of baclofen toxicity is supportive, hemodialysis is used as a treatment option in association with compromised kidney function. In adult patients with impaired kidney function, hemodialysis alleviates baclofen toxicity symptoms and shortens the recovery time.<sup>12</sup> The successful treatment of baclofen toxicity using hemodialysis was reported in a 16-year-old pediatric male patient with acute kidney injury.<sup>6</sup>

With normal kidney function, the treatment of baclofen toxicity is usually supportive.<sup>4</sup> In pediatric populations, most reported cases of baclofen-induced encephalopathy are the result of intentional or accidental overdose and are treated with supportive care measures.<sup>2-5</sup> In a case series of 14 adolescents who ingested between 60 mg and 600 mg of baclofen, the highest serum baclofen level obtained 2 hours post ingestion was 6.0 µg/mL; however, all subsequent serum levels at 14 hours post ingestion were <1 µg/mL. The patients were treated supportively and did not receive hemodialysis. Of those who required intubation, the duration of mechanical ventilation approached 61 hours.<sup>7</sup> A case report with literature review discussed that hemodialysis might not be beneficial to treat baclofen overdose if a patient had normal kidney function.<sup>4</sup> Elsewhere, hemodialysis was used to treat baclofen toxicity in 2 adult patients with normal kidney function.<sup>14,15</sup> The doses of baclofen ingested in these case reports were 200 mg and 420 mg. Both patients were intubated and required a ventilator; however, a rapid improvement in respiratory status and sensorium was reported following hemodialysis. The elimination of baclofen can significantly be prolonged in cases of baclofen overdose. The baclofen elimination half-life measured in a 55-year-old male patient who ingested 420 mg of baclofen was 15.7 hours prior to and 3.1 hours during dialysis.<sup>15</sup> Baclofen overdose in 2 patients caused prolonged coma, with the partial recovery of consciousness taking place after 5 and 7 days, respectively.<sup>16</sup> It was suspected that our patient had ingested 1300 mg of baclofen, which is one of the highest reported intakes in a pediatric patient. This high-dose consumption may also be the explanation of significantly high serum baclofen level of 4 µg/mL (therapeutic range of 0.08-0.4 µg/mL) persisting 10 h after the patient was found unresponsive. Given his worsening of clinical status, and the need for increased ventilatory requirements, hemodialysis was performed to treat the baclofen toxicity.

A high-efficiency dialyzer (KoA urea of >800) with a large membrane surface area is effective in clearing small molecules (molecular weight [MW] of <500 daltons) like baclofen. Similarly, compared with a normal flux dialyzer, a high-flux model (KUF of >20 mL/h/mm Hg) has greater efficacy removing middle molecules (i.e.,  $\beta$ 2-microglobulin, which has a MW of 11 800 daltons) owing to the larger pore size. The use of a high-flux dialyzer has been reported to successfully treat baclofen toxicity in impaired kidney function in a previous study. Baclofen clearance, calculated during a 4-hour hemodialysis session using a high-flux dialyzer in a 60-year-old patient with baclofen toxicity, was 2.14 mL/s or 128.4 mL/min.<sup>17</sup> High-efficiency and high-flux dialysis have also been used to treat baclofen toxicity in patients with ESKD.<sup>8</sup> Given our patient's critical status, a high-efficiency high-flux dialyzer (surface area of 1.5 m<sup>2</sup>, KUF of 45 mL/h/mm Hg, and KoA urea of 1064), along with high blood flow rate, was used during hemodialysis to increase baclofen clearance and removal.

Overall, the patient tolerated hemodialysis well, fully recovered consciousness, and his respiratory status improved. The endotracheal tube was removed soon after the completion of the hemodialysis treatments. Normal kidney function and baclofen clearance by the kidneys was observed in our patient, which contributed to his clinical improvement, along with hemodialysis. A pharmacokinetic baclofen clearance examination was not performed during hemodialysis, which was a limitation of this report. Further studies are needed to assess the benefits of hemodialysis in patients who present with baclofen-induced encephalopathy and respiratory failure. To the best of our knowledge, this is the first report on the use of hemodialysis to treat baclofen toxicity in a pediatric patient with normal kidney function.

## Conclusion

Baclofen overdose and toxicity are critical events, which lead to respiratory failure and encephalopathy in children. The primary treatment of baclofen toxicity in a pediatric patient with normal kidney function is supportive management. High-flux hemodialysis may be considered on a case-by-case basis where the critical presentation of baclofen toxicity is associated with exposure to an extreme dose that results in the deterioration of clinical status. Prompt treatment with high-flux dialysis in this scenario may help accelerate clinical recovery and decrease the length of stay in an ICU.

## Ethics Approval and Consent to Participate

We obtained ethical approval for this case report through the Institutional Review Board (IRB) at Louisville, KY, USA.

## Consent for Publication

We obtained consent from the family for the case report.

## Declaration of Conflicting Interests

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