



An Extremely Low Dosage of Baclofen-induced Neurotoxicity in a Patient with End-stage Renal Disease and Parkinsonism

Dear Editor,

Baclofen is a gamma-aminobutyric acid derivative used for the treatment of muscle spasms or pain, intractable hiccups, and several movement disorders with predominant renal elimination. Many studies have emphasized the cautious use of baclofen in patients with chronic kidney disease (CKD),

especially end-stage renal disease (ESRD) as it could lead to intoxication based on its metabolic mechanism. Despite the raised awareness, 18 patients treated with baclofen showed neurotoxicity in the last 10 years. The symptoms generally include altered mental status, hypotonia, areflexia, and even coma after exposure to 10–400 mg baclofen.

Table 1: Clinical characteristics of baclofen-induced neurotoxicity in patients with renal failure in recent 10 years

Study	Age	Sex (male/ female)	Renal function	Baclofen indication	Dosage and frequency	Accumulative dosage (mg)	Duration	Presentation	Treatment modality	HD * sessions
El-Husseini <i>et al.</i> , 2011 ¹	75	Male	CKD stage IV	Intractable knee pain	10 mg TID	60	2 days	AMS, suspicious seizure	HD	2
Mousavi <i>et al.</i> , 2012 ²	48	Male	ESRD on HD	Low back pain	?	30	?	AMS, delirium	HD	?
	79	Male	ESRD on HD	Low back pain	?	20	?	AMS, delirium	HD	?
Lee <i>et al.</i> , 2013 ³	71	Male	ESRD	?	10 mg TID	90	3 days	AMS	HD	2
	35	Female	ESRD on PD	Rib fracture	10 mg BID	60	3 days	AMS	HD	3
Roberts <i>et al.</i> , 2015 ⁴	48	Male	ESRD	ETOH withdraw	10 mg TID	120	4 days	AMS, coma, respiratory failure	HD	5
	72	Female	ESRD on HD	Leg pain	5 mg TID	30	2 days	AMS	HD	2
	47	Female	ESRD on HD	Movement disorder	5 mg TID	about 400	27 days	AMS, seizure	CVVHDF	-
	65	Male	ESRD on HD	Neck pain	10 mg TID	20	1 day	AMS, somnolence	HD	2
	66	Male	ESRD on HD	Muscle spasm	5 mg BID	20	2 days	AMS, somnolence	HD	3
	57	Female	ESRD on HD	Muscle spasm	10 mg BID	140	7 days	AMS, hypotonia	HD	3
Ijaz <i>et al.</i> , 2015 ⁵	57	Female	ESRD on HD	Muscle spasm	10 mg BID	140	7 days	AMS, hypotonia	HD	3
Meillier <i>et al.</i> , 2015 ⁶	54	Male	ESRD on HD	Muscle spasm	10 mg BID	60	3 days	AMS	HD	2
Radhakrishnan, 2016 ⁷	58	Male	ESRD on HD	Intractable hiccups	10 mg BID	10	1 dose	AMS	HD	2
Porter <i>et al.</i> , 2017 ⁸	69	Female	ESRD on HD	Back pain	10 mg BID	160	7 days	AMS, somnolence, dystonia	HD	3
Wolf <i>et al.</i> , 2018 ⁹	58	Male	ESRD on HD	Muscle spasm	10 mg Q8H	210	7 days	AMS, visual hallucination	HD	1
Khazneh <i>et al.</i> , 2018 ¹⁰	47	Female	ESRD on HD	Low back pain	?	25	1 dose	AMS, somnolence, hyporeflexia	HD	5
Pathak <i>et al.</i> , 2019 ¹¹	58	Female	ESRD on HD	Intractable facial pain	10 mg BID	20	1 day	AMS, hyporeflexia, hypotonia	HD	2
Riaz <i>et al.</i> , 2020 ¹²	60	Male	ESRD on HD	?	?	30	3 doses	AMS, delirium	HD	2
Our case, 2020	58	Male	ESRD on HD	Intractable hiccups	5 mg Q12H	10	2 doses	AMS, hyporeflexia, dystonia	HD	3

?=Information not mentioned in the study or insignificant, *HD sessions required for recovery. ESRD=End-stage renal disease; HD=Hemodialysis; PD=Peritoneal dialysis; BID=Twice daily; TID=Three times daily; Q8H=Every 8 h; Q12H=Every 12 h; AMS=Altered mental status; CVVHDF=Continuous venovenous hemodiafiltration

These patients required 1–5 hemodialysis (HD) sessions to recover [Table 1].¹⁻¹² Here, we present a patient with ESRD and Parkinsonism suffering from extremely low dosage baclofen-induced neurotoxicity with distinct manifestations of dystonia.

A 58-year-old male with an intact mentality, Parkinsonism, and ESRD under maintenance HD presented at the emergency department (ED) due to agitation followed by poor response to external stimulations for a few hours. The physical examination showed a Glasgow coma score of seven, rigidity, and dystonia in all limbs, and diminishing light and deep-tendon reflexes (DTRs). Based on medical records, the patient visited the ED the day before for shortness of breath with possible acute pulmonary edema. He improved after emergency HD treatment. The discharge medications included newly prescribed baclofen (5 mg twice daily with 12 h intervals) for persistent hiccups noted during his last ED course. According to the family, the symptoms emerged 2 h after the second dosage of baclofen. Initial laboratory and radiologic examinations, including computed tomography of his brain, demonstrated unremarkable findings. Based on the clinical symptoms and medication history, baclofen-induced neurotoxicity was highly probable. Physicians discontinued the treatment with baclofen and arranged emergent intermittent HD sessions and admission. Magnetic resonance imaging and electroencephalography showed no significant results. We documented regained bilateral light reflexes, improved dystonia after the second HD session. Recovery of consciousness and normal reflexes were noted without obvious neurological sequelae after the third HD session.

The case demonstrates an adverse result in a patient with ESRD on maintenance HD having oral baclofen at a therapeutic dosage in the normal population. The daily therapeutic dosage of baclofen ranges between 5 and 60 mg.⁵ In general, baclofen intoxication is rarely seen in the normal population unless excessive dosage. In the other hand, the increased half-life of baclofen and the possibility of accumulation may easily induce toxicity in ESRD patients.¹³ However, there has been no standard dosage adjustment guideline of baclofen for this specific population until recently. El-Husseini *et al.* reported that the range of dosage of baclofen inducing toxicity among CKD patients was from 5 to 60 mg per day with a mean daily dosage of 20 mg.¹ A recent large cohort study demonstrated that a daily dosage of baclofen exceeding 20 mg may increase the risk of hospitalization and encephalopathy incidence in the older CKD population.¹⁴ Despite these results, our patient presented baclofen-induced toxicity even with the low dosage of 10 mg total.

For patients with Parkinsonism, which may sometimes present non-motor symptoms, including intractable hiccups,

the use of baclofen must be cautious, especially for patients with ESRD comorbidity. Nevertheless, we found that patients with baclofen-induced toxicity distinctly presented dystonia instead of classic hypotonia. Intermittent HD is the preferred modality for patients with severe baclofen poisoning. The required number of sessions remains; however, inconclusive.¹⁵

In summary, physicians should always use baclofen with caution, even in an extremely low dosage, for patients with impaired renal function, especially ESRD. The distinct presentation of dystonia in patients with baclofen-induced toxicity should also be assessed in combination with Parkinsonism.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Received: January 28, 2021; Revised: February 05, 2021; Accepted: February 09, 2021; Published: May 24, 2021;

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How to cite this article: Kuo CL, Liang CS, Sung YF, Tsai CK. An extremely low dosage of baclofen-induced neurotoxicity in a patient with end-stage renal disease and Parkinsonism. *J Med Sci* 2022;42:296-8.