## It is illegated post this copyrighted PDF on any website Acute Withdrawal After Dialysis in a Patient With transpiration. When 3 core symptoms or 2 core and 4 additional

## **Chronic Stimulation of the GABAergic Receptors**

To the Editor: Baclofen is a muscle relaxant that works as an agonist of  $GABA_B$  (γ-aminobutyric acid) receptors. It is registered for the treatment of spasticity, and off label it is prescribed in the treatment of alcohol dependence.<sup>1</sup> Abrupt withdrawal is known to cause a life-threatening syndrome.<sup>2</sup> We present a patient who was treated with dialysis after a suicide attempt with several medications working on the GABAergic receptors. She had symptoms similar to neuroleptic malignant syndrome (NMS).

Case report. A 41-year-old white woman was taken to the emergency department after a suicide attempt with multiple drugs (18 capsules of oxazepam 10 mg, 30 capsules of baclofen 25 mg, and 2 bottles of wine). Her medical history included a borderline personality disorder and attention-deficit/hyperactivity disorder (DSM-5). Her medication prior to admission included methylphenidate (10 mg twice a day), sertraline (50 mg once a day), and baclofen (10 mg every other day). Alcohol intake varied from 3 glasses up to 2 bottles of wine per day. Before arrival of the emergency medical technicians, she had been unconscious for approximately 5 to 6 hours. At that time, the patient had respiratory depressions and an EMV (eve-motor-verbal) score of 3 (E1M1V1). Empty baclofen pill strips were found. On arrival at the hospital, blood laboratory values showed an increased creatine kinase (CK) of 551 U/L. Her blood pressure was high but stable around 170/95 mm Hg, and she had a pulse of 40-65 beats/min. The patient was intubated and admitted to the intensive care unit (ICU). Approximately 12 hours after admission, she developed convulsions. Due to the life-threatening probability of the baclofen intoxication,<sup>3</sup> hemodialysis was given for 3 continuous hours. After dialysis, convulsions were no longer observed.

On her second day in the ICU, approximately 12 hours after dialysis, she was detubated. However, her clinical presentation changed over time; the patient was agitated, which required mechanical restraints in the following hours. Upon neurologic evaluation, she did not open her eyes or speak, and she did not follow commands. During the following hours, she developed hyperthermia, elevated CK (up to 2,080 U/L), and decreased levels of consciousness, which led to the suspicion of NMS.<sup>4</sup> On the basis of these observations, lorazepam was intravenously administered (3 mg daily), resulting in a significant clinical improvement, ie, shortly after administration, she regained consciousness and the elevated CK decreased as well as the agitation. Lastly, the hyperthermia disappeared too. On the third day, she was discharged from the hospital. The patient was symptom-free during the follow-up 1 month after discharge.

With this case, we illustrate how acute withdrawal symptoms can occur after dialysis in a patient with multidrug intoxication acting on the GABAergic receptors. Although empty pill strips were found, the blood drug levels upon arrival at the hospital were not measured. In addition, it is noteworthy that the dosage of the chronic use of baclofen differed from pills taken with the overdose.

The core symptoms of NMS are hyperthermia (>38°C [>100°F]), muscle rigidity, and elevated levels of CK (>1,000 U/L). Additional symptoms include tachycardia, changing systolic blood pressure, tachypnea, altered consciousness, leukocytosis, and

symptoms are present, NMS can be diagnosed.<sup>2</sup>

Different presentations are possible after baclofen withdrawal (ie, hallucinations, agitation, disorientation,<sup>5</sup> tachycardia, fever, seizures, and rigidity<sup>6–8</sup>). In some cases, the muscle rigidity can be so severe that rhabdomyolysis results in a pattern that mimics NMS.<sup>9</sup> Risk factors for baclofen withdrawal include duration of exposure to medication, abruptness of discontinuation, higher dose, and oral administration.<sup>5</sup> We find that forced elimination in the form of dialysis is an important risk factor as well. Although dialysis is the quickest way to eliminate potentially life-threatening high levels of specific drugs, we think the danger of intoxication should be counterbalanced against the danger of acute withdrawal. In this case, both baclofen and alcohol were removed by dialysis. In our opinion, it is therefore important to interpret the risk category (low, intermediate, or high) of intoxication clinically rather than (only) theoretically.

To our knowledge, no data are available describing the minimum duration of exposure to baclofen to develop symptoms of withdrawal (in previous reports, a minimum duration of 1 to 5 months has been suggested<sup>10–12</sup>). After 1 year of exposure to baclofen and use of other GABAergic-acting drugs (eg, oxazepam, alcohol), it is plausible that up- and down-regulation of specific subunits of GABA receptors has occurred.<sup>13,14</sup> In case of forced elimination, disinhibiting the pathways leads to a shift in GABA receptor occupancy and release of norepinephrine and dopamine onto supersensitized receptors causing the symptoms mentioned above.<sup>10,15</sup> Thus, clinicians should be cautioned about withdrawal symptoms after forced elimination.

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## Letter to the Editor Departments of Psychiatry and <sup>P</sup>Hospital Pharmacy, Academic Medical Keegan DL, Richardson JS, Kirby AR. A possible neurochemical basis fo 15

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