

## The case series of baclofen intoxication

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### ABSTRACT

Baclofen, a gamma-amino butyric acid type B (GABA<sub>B</sub>) inhibitor, is commonly used in management of spasticity and other medical conditions, such as alcohol dependency. However, given its mechanism of action, increasing usage of baclofen raises concerns about possibility of intoxication. The authors present herein three cases of baclofen intoxication of patients in various age and general condition.

**KEYWORDS:** baclofen;intoxication

### INTRODUCTION

Baclofen is a Gamma-amino butyric acid type b (GABA<sub>B</sub>) receptor inhibitor used in the treatment of muscle spasticity in the course of various neurological conditions. Out of many indications to use baclofen the most prominent ones are cerebral palsy, traumatic spine injuries, multiple sclerosis, stroke or various neurodegenerative disorders. In some circumstances, especially in pediatric population, baclofen is applied in pumps in the course of intrathecal baclofen therapy [1,2]

Baclofen, as a lipophilic drug, is completely absorbed after oral ingestion. Up to 85% of its content in blood is quickly excreted (with half-life of 2-4 hours), whereas the rest is

metabolized in liver. When administered in toxic dose, Baclofen acts as a strong CNS depressant, which elicits muscular hypotonia, respiratory depression or seizures. Serious intoxication may lead to coma or arrhythmia [3].

Herein, we present 3 different cases of baclofen intoxication associated with intentional overdose. All of the patients were treated in the Toxicology Unit of Regional Hospital in Lublin.

## CASE REPORTS

### CASE REPORT I

Patient I, 22 years old female student, was admitted to the Toxicology Unit after she had been found unconscious in a toilet with an empty package of baclofen. Patient vomited after ingestion of the drug. She was treated with baclofen due to spasticity in the course of cerebral palsy. Notably, patient underwent two ablations in 2015 and 2016.

Emergency physician found the patient in deep areflexia, without reaction to pain (GCS=3). Due to bradypnea patient was intubated and received respiratory therapy prior to admission. Heart rate of patient was 50/minute and blood pressure was 108/75. No relevant findings in ECG were confirmed.

On admission, blood samples of patient were analyzed. Most of laboratory tests were normal. However, leukocytosis lead physicians to order RTG scan of lungs, which together with clinical symptoms resulted in the diagnosis of aspiration pneumonia. BAL was used to obtain bacteriological samples and cultures were grown, whereas patient was given empirical antibioticotherapy.

On the day 2, heart rate was 70/minute. No significant change in neurological state was observed. In the meantime, routine toxicological screening did not demonstrate neither any other drug nor alcohol in serum.

On the day 3 patient's neurological state changed dramatically and arterial blood gas tests improved. This resulted in weaning the patient off the mechanical ventilation. Besides, normalization of inflammatory markers occurred. Full psychiatric evaluation of patient was, however, impossible. Heart rate was 100/minute.

Next day patient experienced supraventricular tachycardia with heart rate of 150/minute. Consequently, metoprolol was administered and arrhythmia disappeared. The patient admitted she had taken baclofen but repeatedly changed her mind about the cause of this behavior. Impairment of memory concerning the circumstances of the drug ingestion was noted. Psychiatric examination did not reveal suicide intention or psychotic symptoms. However, patient remained reluctant towards psychologists and psychiatrists, which hampered proper diagnosis. The psychiatrists did not advise to refer patient to the Psychiatric Unit.

After discontinuation of antibiotic therapy patient was discharged home and referred to psychological treatment. The treatment with baclofen was sustained.

### CASE REPORT II

Patient II, 53 years old female, was found unconscious in her home with empty packages of baclofen and escitalopram, which suggested intake of up to 700 mg of baclofen and 260 mg of escitalopram. Patient was treated for mild depression and had a history of alcohol dependence. On admission, patient was unconscious and exhibited features of severe respirational insufficiency with low blood saturation and tachycardia (heart rate of 160/minute). This resulted in decision to intubate patient. Blood tests showed mild microcytic anemia (Hgb=11.2 g/dl)

On the next day, due to the fever of unknown origin with high CRP levels, empirical antibiotic therapy with ceftriaxone and clindamycin was started. No significant improvement in neurological state was observed.

On day 3, patient regained reactivity and was, therefore, extubated. Blood tests revealed severe anemia (Hgb = 6.9 g/dl), which suggested bleeding. As a result, upper gastrointestinal endoscopy was ordered, while patient received packed red cells. The later outcome of biopsy was histopathological diagnosis of Barret's esophagus.

On the next day patient experienced episodes of bradycardia, which resolved after administration of 0.5 mg intravenous atropine. Bacterial culture of patient's blood transpired to be negative

Meanwhile, patient underwent psychiatric and psychological evaluation. Such a conduct was continued during following days, showing only small improvement of cognitive function. Patient could not specify a reason of supposed suicide attempt. Moreover, she exhibited some features of mania, with euphoria, psychomotor agitation, hyposomnia and racing thoughts. In accordance with the statement of consulting psychiatrist, patient was subsequently referred to psychiatric treatment in closed psychiatric unit.

### CASE REPORT III

Patient III, 51 years old, was admitted to the Department from regional hospital on the base of the suspicion of drug poisoning. One day before the admission patient was found unconscious by the road with an empty package of baclofen. Patient had a history of alcohol dependence and hypertension. According to information provided by the physicians of regional hospital, he remained conscious, however unresponsive. Signs of either circulatory or respiratory insufficiency were not present in the time of initial examination. Patient was diagnosed there for one day and then referred to Toxicological Department in order to establish proper diagnosis and implement right treatment.

On admission, patient was cardiovascularly and respiratorily stable and presented psychomotor agitation. Patient reacted to pain stimuli with localized movement and opened eyes spontaneously, nevertheless only the incomprehensible vocalization was observed (GCS=10). HR was 100/minute and BP reached 110/70.

Due to suspicion of acute drug intoxication, full toxicology screen was performed. It revealed the presence of benzodiazepines. Other abnormalities in blood tests included leukocytosis, hypernatremia and signs rhabdomyolysis. Empirical antibiotic therapy with ceftriaxone was implemented and electrolyte imbalances were normalized.

Despite such a treatment, patient experienced critical worsening of cardiovascular and respiratory state during next night, which resulted in implementation of ventilatory support on the day 2. Patient exhibited psychomotor agitation and there was no sign of hyporeflexia.

During next 2 days no change in neurological state nor cardiovascular state was present. Culture from patient's blood were sterile, thus antibiotic therapy was ended.

On day 5 patient regained spontaneous respiratory activity. After ceasing of respirator therapy, a short episode of bradycardia occurred. Shortly thereafter, it resolved spontaneously.

On day 6 patient underwent psychiatric examination. It revealed disorientation, disruption of circadian cycle and auditory as well as visual hallucinations. Neither positive nor negative symptoms of schizophrenia were, however, present.

Subsequently, on day 6, patient was transported to Psychiatric Unit in order to establish diagnosis and implement proper treatment.

## DISCUSSION

The baclofen's efficiency in the treatment of spasticity is comparable to that of benzodiazepines or tizanidine. Moreover, it seems to exhibit similar number of side effects as other myorelaxants [4]. Given growing prevalence of spasticity-related disorders, such as cerebral stroke or multiple sclerosis, there is a great potential for further growth of baclofen consumption.

Besides, some reports showed beneficial effects of baclofen in the treatment of alcohol-dependent patients, although there is still no consistent evidence to use this drug as a standard therapy [4–7]. In spite of conflicting results of clinical papers, some European countries, e.g. France, authorized use of high-dose baclofen in alcohol dependency treatment, whereas in other ones it is still being prescribed as an off-the-label medication.

As a result, the increasing consumption of baclofen may lead to many toxic exposures, not only unintentional, but also intentional ones. According to the study conducted in 2008-2013 timeframe, there were 294 reported toxic exposures to baclofen used solely in alcohol dependency, out of which nearly 75% were marked as suicide attempts [8]. Due to severe symptoms of overdose, baclofen should be considered as one of the most effective drugs in suicide attempts [9]. Moreover, baclofen’s mechanism of action enables its application as a recreational drug [10,11]. With that all taken into consideration, there is an enormous need for knowledge about baclofen intoxication symptoms among medical professionals.

All the three cases we have presented show clearly that symptoms of toxic exposure to baclofen are able to evolve rapidly and how crucial is the careful management of affected patients. Even in relatively benign cases, clinical manifestation may undergo a sea change, as was well pronounced in Cases II and III. Moreover, serious effects of overdose do not disappear after elimination of the drug, which should be associated with long-term changes in neurotransmission.

The symptoms of baclofen intoxication might be generally divided into acute and chronic ones. Table 1 summarizes these both groups and show the way they were present in shown cases. Clearly, most of the patients developed acute as well as chronic symptoms. In every single case presented patients exhibited psychiatric symptoms and were, therefore, referred to some form of psychiatric treatment.

Although most of the symptoms encountered in the presented cases might have been interpreted in the light of intoxication, there is still an uncertainty about its relation with baclofen withdrawal, which occasionally takes form of acute psychosis with manic symptoms. Apart from such a relatively rare manifestation, other possible symptoms include insomnia and apnea [12,13]. Both have been observed, especially in case III. Currently, many clinical reports highlight that the border between chronic intoxication and withdrawal symptoms might not be so obvious as it could be expected.

The underlying mechanism of baclofen withdrawal, although elusive, includes desensitization of GABA<sub>B</sub> receptor in central nervous system together with changes in serotonergic and noradrenergic neurotransmission. One of the suggested therapeutic strategies for baclofen withdrawal syndrome include administration of benzodiazepines that may alleviate most severe symptoms without any interference with GABA<sub>B</sub> receptors, as their mechanism of action involves GABA<sub>A</sub> ones [13].

As the presented cases are concerned, it might be just supposed that overingestion of baclofen could have been at least partially connected to suicide attempt. This suggests a necessity of psychiatric follow-up in baclofen-treated patients, especially in patients predisposed to depressive disorder.

<b>ACUTE INTOXICATION</b>				
Cases	Encefalopathy	Respiratory depression	Muscular hypotonia	Generalized hyporeflexia
I	+	+	+	-
II	+	+	+	+
III	+	+	-	-
<b>CHRONIC INTOXICATION</b>				
Cases	Hallucinosis	Impaired memory	Catatonía	Acute mania

I	-	+	-	-
II	-	+	-	+
III	+	+	-	+

**Table 1 The symptoms of acute and chronic baclofen intoxication in hospitalised patients.**

## CONCLUSIONS

Baclofen intoxication should be always taken into consideration when dealing with unconscious patient with respiratory insufficiency and neurological or psychiatric medical history. Lastly, proper treatment of baclofen intoxication should be administered in specialist units and include not only causative treatment but also support of vital functions.

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