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Case Report

Fatal multiorgan failure in baclofen overdose: An autopsy case report

Alagarasan Naveen[1], Manas R Sahu[1,*], Manoj K Mohanty[1], Rajanikanta Swain[1], Anupam Dey[2]

[1]*Dept. of Forensic Medicine & Toxicology, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India*
[2]*Dept. of General Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India*

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ABSTRACT

Baclofen is a synthetic derivative of GABA and is used as a muscle relaxant or antispasmodic agent. It is used in the management of various muscle spasticity resulting from conditions such as cerebral palsy, spinal cord injuries, and stroke. The reported potential adverse effects following overdose are marked impairment in consciousness, acute kidney injury, seizures, coma, and respiratory failure. Since there is no specific antidote available to treat baclofen toxicity, the mainstay of management remains supportive treatment. Herein we describe a case of baclofen overdose in a 62-years-old male who consumed 15 tablets of 25 mg tablets of baclofen (375 mg) and died due to multiorgan failure after 5 days of poisoning. Although many reports in the published medical literature describe the clinical manifestations and the management of baclofen toxicity, only a few reports presented the fatality in baclofen overdose. Furthermore, no report documented the death following lethal multiorgan failure resulting from baclofen overdose, and from India to the best of our knowledge.

1. Introduction

Baclofen or β-4-chlorophenyl gamma-aminobutyric acid is an agonist of γ-Aminobutyric acid (GABA), an inhibitory neurotransmitter.[1] Baclofen tablets are available in various concentrations (5 mg, 10 mg, and 20 mg) for oral use. It is commonly used as a muscle relaxant or antispasmodic agent in the treatment of spasticity arising from cerebral palsy in children and stroke or spinal cord lesions in adults. It is also used to treat hiccups and alcohol use disorders.[1,2]

It crosses the blood-brain barrier due to its moderate lipophilic nature and causes neurotoxicity and resulting in significant CNS depression.[3,4] It results in a wide range of side effects such as weakness, hypotonia, drowsiness, dizziness respiratory failure, altered consciousness (Encephalopathy), seizures, and coma.[2]

Although many reports in the published medical literature describe the clinical manifestations and the management of baclofen toxicity, only a few reports presented the fatality in baclofen overdose.[5–7] Furthermore, no report documented the death following lethal multiorgan failure resulting from baclofen overdose, and from India to the best of our knowledge.

2. Case History

A 62-years-old male, known hypertensive and post cerebrovascular accident was prescribed baclofen medication for right-sided hemiplegia for the last two years. He was referred to our tertiary care center in an unconscious state with an alleged history of self-ingestion of around 15 tablets of Baclofen (20 mg/tab) due to unknown reasons. He developed multiple episodes of vomiting and drowsiness

* *Corresponding author*.
E-mail address: fmt_manas@aiimsbhubaneswar.edu.in (M. R. Sahu).

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following the ingestion. On admission, he had a Glasgow Coma Scale (GCS) score of 10/15, blood pressure of 198/82 mm Hg, pulse rate of 65 beats/min, respiratory rate of 16 breaths/min, and SpO2 of 91% on room air. He was intubated on admission because of poor GCS and to protect the airways. His laboratory investigations were remarkable for elevated glucose, potassium, urea, and creatinine levels. The electrocardiograph was suggestive of right bundle branch block and the echocardiogram has revealed ischemic cardiomyopathy with a low ejection fraction (34%).

He was managed aggressively with diuretics, antibiotics, cardioprotective drugs, antacids, antiemetics, and other supportive measures in the intensive care unit. He was also treated for hyperkalemia with calcium gluconate, insulin, and salbutamol. However, his condition deteriorated clinically with continuous fall in blood pressure, and he succumbed to poisoning-related complications after five days while undergoing treatment. Clinically, the combined effect of refractory shock, acute kidney injury, and ischemic cardiomyopathy due to baclofen poisoning was opined as to the cause of death. Old cerebrovascular accident (CVA) was specified as the contributing cause of death.

The body was referred for postmortem examination, which was conducted within 12 hours of death. The external examination was unremarkable. The brain was soft, congested, and edematous and weighed 1202 g. The gyri were flattened and the sulci were obliterated suggestive of cerebral edema. The lumen of the vertebral and basal arteries showed yellow atheromatous plaques in situ at places. Both lungs were congested and edematous. On the cut section, multiple consolidation patches were present in situ at places of both lungs suggestive of pneumonia. The heart and Pericardial sac were intact and weighed 416 g. Multiple epicardial petechial hemorrhages were present in situ at places over the posterior surface of the right and left ventricles. The root of the aorta and all coronary arteries showed atheromatous plaques of varying degrees at places. The left anterior descending artery showed about >75% luminal narrowing, the right coronary artery showed about 60% of luminal narrowing, and the left circumflex artery showed about 50% of luminal narrowing at places. The left ventricular wall thickened circumferentially measuring 1.8 cm and the right ventricular wall thickness was 0.7 cm.

The stomach contained about 100 ml of brown mucoid material with no specific odor. The mucosa of the stomach wall was congested and hemorrhagic in places. Both kidneys were remarkable for increased surface granularity and weighed 146 g on the right side and 170 g on the left side. On the cut section, the corticomedullary junction was indistinct and the medulla was congested in places. (Figure 1) Histopathological examination of kidneys was suggestive of acute tubular necrosis. (Figure 2) The rest of the viscera were remarkable for congestion and edema. The routine viscera were negative for any other common poisons and intoxicants. Considering the above history, clinical manifestations, and autopsy findings the cause of death was attributed to the Multiorgan failure as a result of Baclofen overdose.

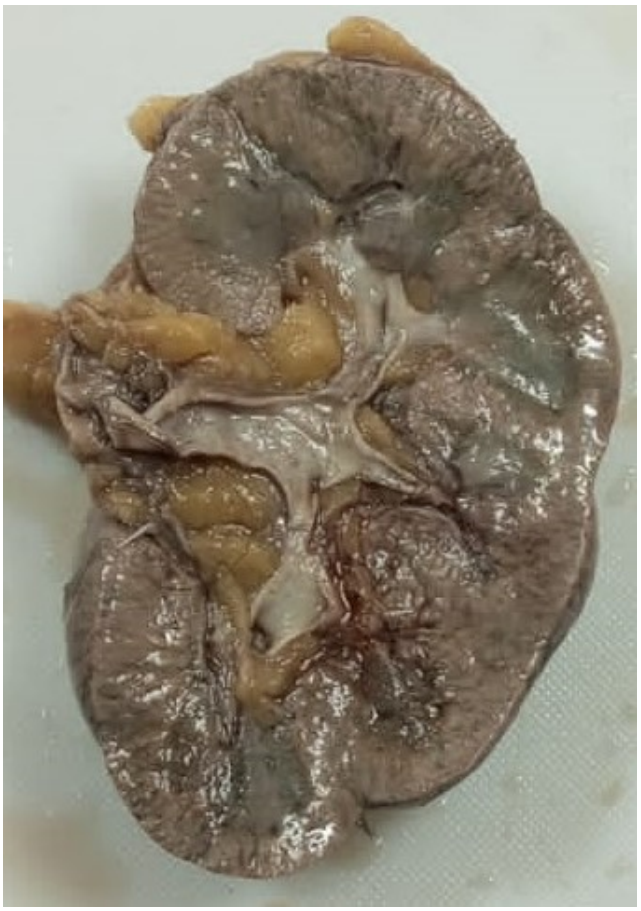

Fig. 1: Gross examination of the right kidney displays the congested medulla with indistinct corticomedullary differentiation

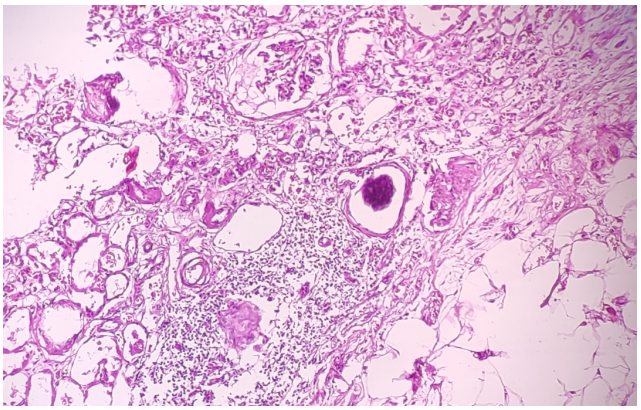

Fig. 2: Photomicrograph of the right kidney (H&E, 4X) shows patchy tubular necrosis with inflammatory cells infiltration along with clumping of bowman's capsule and hemorrhages at places.

3. Discussion

Oral ingestion results in rapid, complete absorption and is predominantly (> 70%) excreted via kidneys.[3,4] The daily therapeutic dose is predicted to be between five and sixty mg[1] with the therapeutic range ~ 80 to 400 ng/ml.[4] In the present case, he consumed 15 tablets, which lead to a concentration of 375 mg, more than six times above the maximum allowed therapeutic dose. An Australian study found that a dose of > 200 mg was found to associate with more significant adverse effects than < 200 mg.[8] However, a case with profound symptoms of baclofen toxicity following a single dose in the setting of ESRD was also reported in the literature.[1]

Baclofen induces encephalopathy which is commonly suspected when a patient presents with significantly altered consciousness, especially in patients with renal impairment.[3,9] At times, the patients with baclofen overdose may present with absent brainstem reflexes that mimic brain stem death.[10,11] Henceforth, it is medicolegally relevant to discuss here that the drug overdose should be excluded before certifying the brain death as per American Academy of Neurology Guidelines which recommend a period of five half-lives is necessary for such purpose.[12,13] The biological half-life of baclofen ranges from 2.5 to 4 h.[14] In the present case, the renal parameters were elevated (Creatinine: 4.4) on the admission day indicating acute kidney injury. Further, the pronounced loss of consciousness on admission in the backdrop of AKI is consistent with Wu et al.[4]

A high index of suspicion is needed to diagnose the toxicity of baclofen since the rapid screening tests cannot detect baclofen.[15] Hence Liquid or gas chromatography, liquid chromatography-tandem mass spectrometry, capillary electrophoresis, and recently high-resolution mass spectrometry (HRMS) based on liquid chromatography–hybrid quadrupole time-of-flight-mass spectrometry (LC-QTOF-MS) are validated to be the preferred methods for analyzing the biological fluids (e.g., femoral blood, urine) for baclofen concentration. The autopsy surgeons may also resort to these advanced techniques if feasible in their healthcare setup.[14] Elevated renal parameters (urea and creatinine) in the renal function tests may also suggest the possibility of baclofen toxicity clinically. In the present case, the son of the deceased probed him on noting multiple episodes of vomiting at home before shifting him to the emergency. Hence, he confessed to the son that he consumed fifteen tablets and showed him the empty strips which made the diagnosis less challenging.

Baclofen overdose warrants management in the intensive care unit with ventilatory support for respiratory failure.[8] There is no specific antidote available to treat baclofen toxicity.[10] Since the baclofen has a low molecular weight, low protein binding, and low volume of distribution, hemodialysis may be preferred in case of severe impairment in the renal function resulting from baclofen toxicity. It may also help to reverse the consciousness.[3,4] However, the treatment of baclofen toxicity with normal kidney function is mainly supportive.[16] The role of hemodialysis in patients with normal kidney function tests is still unclear. While some authors advocate the use of hemodialysis[16] while some are against its use.[17,18] Besides, hemodialysis was deferred considering the minimal derangement of renal parameters and old age with falling blood pressure.

The autopsy in the majority of poisoning cases is often non-specific except for congestion of visceral organs. However, in the present case, the postmortem examination revealed various systemic pathologies including cerebral edema, pneumonia of both lungs, and coronary artery disease. Both lung pneumonia in our case could be attributed to ventilator-associated pneumonia (VAP) which in turn likely aggravated the septicemia, multiorgan failure, and resultant fatality.

4. Conclusions

The relatively rare case of baclofen overdose resulting fatal multiorgan failure is described in the report. Although beneficial in the treatment of muscle spasticity, the patient and the relatives should be warned of its potential adverse effects. An effort should be made by the clinicians to counsel the relatives adequately and encourage the supervised administration of baclofen in presence of any of the family members. As in many other poisoning cases, the findings are non-specific in baclofen toxicity. However, the autopsy surgeons are expected to corroborate the renal pathology in severe toxicity, both gross and histopathological examination, before concluding baclofen toxicity.

5. Source of Funding

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6. Conflict of Interest

None.

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Author biography

Alagarasan Naveen, Senior Resident

Manas R Sahu, Additional Professor https://orcid.org/0000-0003-0514-8939

Manoj K Mohanty, Professor and Head

Rajanikanta Swain, Assistant Professor

Anupam Dey, Additional Professor

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