# "Don't underestimate the power of a common drug!"- An interesting case of Baclofen encephalopathy in a patient with acute on chronic renal impairment.

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**Search terms:**

| Name of the Author | Contribution to the manuscript |
|---|---|
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| Dr. Abhinav | Conceived, designed, and drafted the manuscript and critically reviewed the manuscript. |
| Dr. Vasundhara Aggarwal | Drafted the manuscript and critically reviewed the manuscript. |
| Dr. Divyani Garg | Drafted the manuscript and critically reviewed the manuscript. |
| Dr. (Lt. General) Ashok Kumar Hooda | Drafted the manuscript and critically reviewed the manuscript. |

***Abstract*- People with deranged renal functions are prone for baclofen encephalopathy. Baclofen is a centrally acting GABA receptor agonist and helps in reducing the muscle spasticity in upper motor neuron lesions like traumatic brain injury, spinal cord injuries, central demyelination and other off label indications like intractable hiccups, alcoholic liver disease, and trigeminal neuralgia. The most common neurological side effects of the drug include sedation, confusion, neuropsychiatric manifestations, tremors, insomnia, seizures etc. Baclofen has a renal mode of excretion and therefore, the side effects of the drug in usual therapeutic doses can get manifested in exaggerated manner early in patients with suboptimal renal functions. We present an interesting case of baclofen encephalopathy in our patient with renal dysfunction**

**to highlight early recognition and rapid management of this drug toxicity. He improved remarkably after two sessions of hemodialysis.**

***Keywords*: Baclofen, drug toxicity, renal impairment, hemodialysis**

## INTRODUCTION

Baclofen (Para-chloro-phenyl gamma-aminobutyric acid) is an agonist for the neurotransmitter gamma-aminobutyric acid (GABA). It is a centrally acting drug which is used to ameliorate skeletal muscle spasticity caused due to upper motor lesions of the central nervous system and spinal cord along with some off-label indications like intractable hiccups, alcoholic liver disease and trigeminal neuralgia. It is a slightly water-soluble compound and has a molecular mass of 213.66g/mol. It has good gastrointestinal absorption and is primarily excreted through the kidneys (80%). The half-life of baclofen is 4.5-6.5 hours which is prolonged in patients with renal dysfunction. As it can easily cross the blood-brain barrier and therefore, it has neurological side effects like pronounced fatigue, syncope, hypotension, ataxia, altered sensorium and respiratory depression. **Figure.1** shows various clinical and laboratory features of baclofen toxicity [1,2,3,4,5,6,7,8,9,10,11]. In clinical practice, blood baclofen levels are rarely measured. The toxic level ranges from 1.1 to 3.5 mg/l and in coma or fatal intoxication, the toxic level ranges from 6 to 9.6 mg/l [12].Patients with suboptimal renal functions can develop baclofen-induced encephalopathy at low doses of the drug which should be promptly recognized. These patients respond dramatically to hemodialysis. Thus hemodialysis is the treatment of choice for these patients.

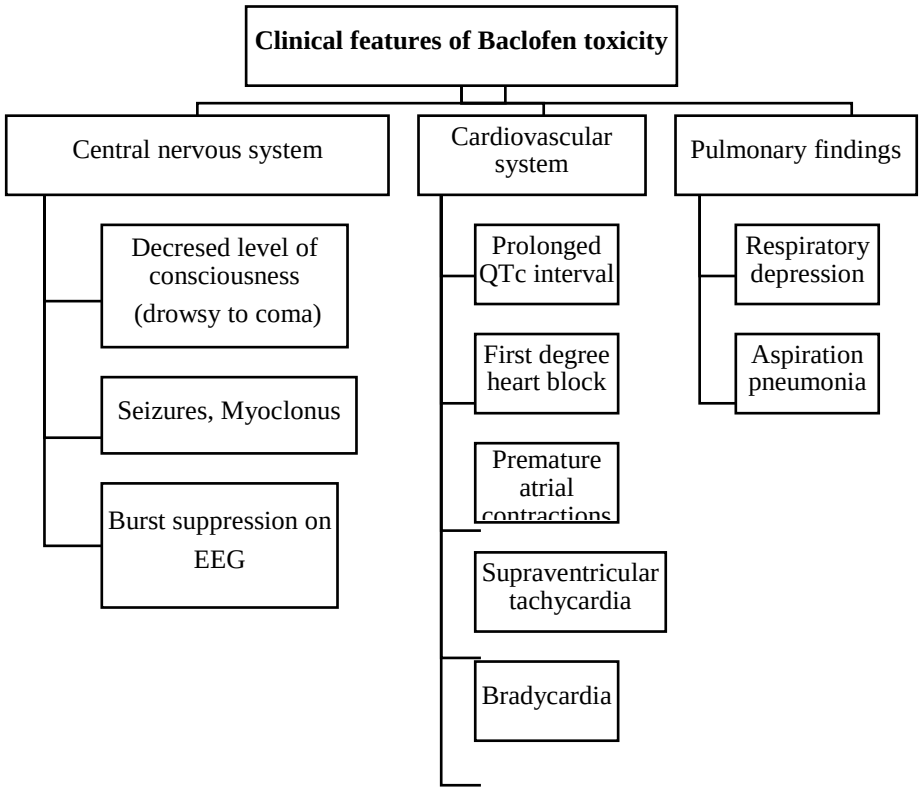


**Figure-1 Clinical features of Baclofen toxicity**

### Case report

A 47 years old gentleman was admitted to our tertiary care hospital in ICU with a history of altered sensorium of 6 hours duration. There was no history of fever, vomiting, headache, double vision, seizures, weakness in limbs or sensory complaints associated with impaired awareness. He was a known hypertensive, hypothyroid, diabetic with diabetic retinopathy, neuropathy and nephropathy (baseline creatinine-3mg/dl), old ischemic cerebrovascular accident, vascular Parkinsonism on oral syndopa. He was recently prescribed oral baclofen 10 mg twice daily for spasticity which he started two days before admission to the hospital.

On clinical examination, his heart rate was 90/ minute, Blood Pressure -120/70 mm Hg, Respiratory rate - 16/minute, and oxygen saturation of 97% at room air. He was drowsy with a GCS of E3V4M5, Pupils were bilaterally normal in size and reaction; the tone was increased in all limbs; deep tendon reflexes were absent and plantar reflex was extensor bilaterally' Also clinically he had asterixis. His cardiovascular system, abdominal system and respiratory system were normal on examination.

Lab evaluation showed Hb 8.4 g/dl, total cell count- 7600 cells/$mm^3$ and platelets 341000 cells/dl. Blood Urea - 137 mg/dl, creatinine 4.5 mg/dl, sodium - 137 meq/dl and potassium - 4.5 meq/dl. Liver function tests, S. calcium, S. magnesium. S. Creatine Phosphokinase and S. ammonia were within normal limits. Electroencephalogram showed generalized slowing with the background

showing theta (5-6Hz) rhythm. His MRI Brain showed mild diffuse cerebral atrophy with chronic ischemic changes. His ABG analysis showed metabolic alkalosis.

After ruling out other causes for the altered sensorium, we kept the possibility of baclofen-induced encephalopathy. The drug was immediately stopped. A femoral double lumen hemodialysis catheter was inserted and he underwent hemodialysis for three hours (blood pump speed - 180 ml/min, dialysate flow - 400 ml/ hour, ultrafiltration - nil and heparin - 5000U stat followed by 1000 u per hour x 3 hours). Following one session of dialysis, his sensorium improved notably and with the second session of dialysis the next day, his sensorium became normal. He was observed in the ward for one more day and was discharged after optimizing his medications and removal of the hemodialysis catheter. He is on regular OPD follow-up and is neurologically stable.

**Discussion**

Baclofen is a natural derivate acting at the GABA-B receptors at the cerebral cortex, thalamic and spinal level altering the muscle tone at therapeutic levels. The typical dosing for oral baclofen for spasticity starts at 5mg thrice daily which is gradually increased every third day by 5mg/dose to a maximum of 80mg/day [(13).] Toxicity with this drug occurs on acute ingestion of > 200-400mg [(14).] Suboptimal renal function is a major risk factor for baclofen intoxication as the elimination half-life of the drug may be as long as 12 to 36 h post-overdose [(15).] The symptoms usually manifest within 2-3 days of the exposure but the patient may be symptomatic within few hours of ingestion. The most common symptoms include somnolence, coma, seizures, encephalopathy, respiratory depression and cardiac conduction abnormalities [(16).]There are various differential diagnoses including septic encephalopathy, intracranial haemorrhage, hypoglycaemia, adrenal crisis and opioid intoxication. Management of baclofen encephalopathy is mainly symptomatic. It involves discontinuation of the drug, maintaining hemodynamic stability, protection of airway if needed. Hemodialysis is the treatment of choice in encephalopathic patients with impaired renal function with impending intubation and mechanical ventilation. This intervention (i.e. Hemodialysis) will reduce the hospital length of stay and avoid hospital acquired complications [(14).] Baclofen is moderately lipophilic and the filtration rate of haemodialysis is kept similar to native kidneys in clearing baclofen [(17).] This is mainly because only 30% of the circulating concentration is protein bound. Siddhartha et al treated a paediatric patient with baclofen toxicity using high flux high efficiency dialysis and had reported a good outcome [(18).] In 2011, a review of 41 reported cases of baclofen toxicity by A. El-Husseini et.al proposed that baclofen should be avoided in renal patients with a GFR<30mL/min/1.73m2 or on renal replacement therapy and its dosing should be titrated in CKD patients with a GFR > 30 to 60 mL/min/1.73 $m^2$ [(19)]. This review also highlighted that baclofen encephalopathy developed generally in elderly and mostly dialysis dependent patients because the drug gets sequestrated in CSF which requires repeated sessions of haemodialysis for clearance of the drug. Our case presents a patient of chronic renal failure with acute confusional state secondary to inappropriate baclofen dosage which resolved completely with hemodialysis.

**Conclusion**

Baclofen-induced encephalopathy is not a well-known condition among clinicians. It is a treatable cause of acute confusional state in patients on baclofen therapy, especially with suboptimal renal functions. This case report highlights the dramatic response to hemodialysis in these patients. There is a need to educate healthcare professionals about this entity so that prompt diagnosis and management of this drug toxicity can be carried out. We also highlight the fact that baclofen should be used carefully in patients with renal impairment and utilization of other non-sedative alternatives of muscle relaxants can be used for the treatment of spasticity, especially in chronic renal disease patients.

**Key learning points:**

1. Baclofen is a commonly used muscle relaxant for treating muscle spasticity.
2. Pharmacokinetics of baclofen:

a) It has 70-80% oral bioavailability
b) The half-life of baclofen is 4.5-6.5 hours which is prolonged in patients with renal dysfunction.
c) It is primarily excreted through the kidneys (80%)

3. Dose adjustment of the drug is recommended in Chronic kidney disease
4. Hemodialysis is the treatment of choice for baclofen encephalopathy with suboptimal renal dysfunction.

**Abbreviations:** GABA- Gamma-aminobutyric acid; EEG-Electroencephalogram; GCS- Glasgow Coma Scale; MRI- Magnetic resonance imaging; ABG- Arterial Blood Gas; CKD- Chronic Kidney Disease; CSF- Cerebrospinal Fluid; GFR- Glomerular Filtration Rate

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