



Clinical Pharmacology & Toxicology Pearl of the Week

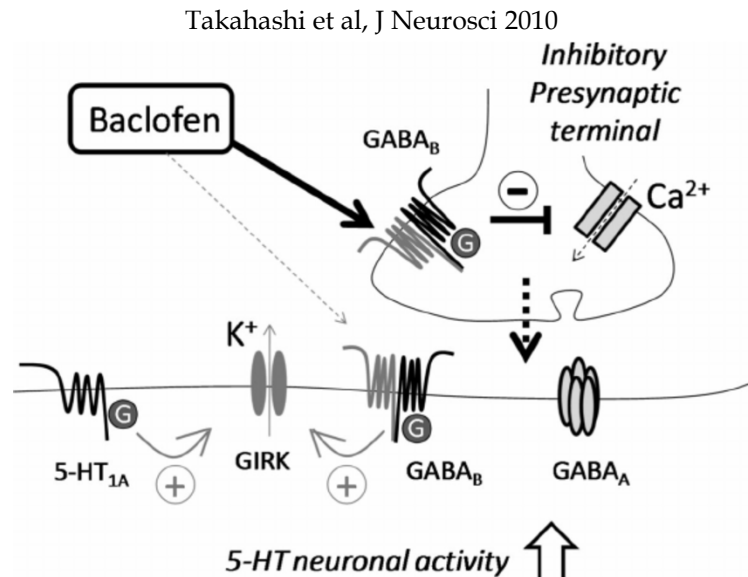
Baclofen

Case

- A 40 year old female was found unresponsive by family members with empty bottles of baclofen, diphenhydramine, an NSAID and alprazolam on scene. Family members believed that baclofen was the primary drug involved. Narcan was ineffective and she was intubated on scene.
- She had a GCS of 3, fixed dilated pupils, and was flaccid with no corneal or ocular reflexes.
- ASA, APAP and Ethanol were negative, urine drug screen was positive for opiates and benzos. She was in sinus rhythm with a QTc of 500msec. She developed some hypotension and some seizure like activity and was started on vasopressors and propofol.
- On day 3, the propofol was discontinued and no further seizure activity was noted. The patient remained deeply comatose with an EEG that showed “burst suppression pattern with occasional sharp waves on a flat background” suggesting poor prognosis.
- On Day 4, Neurology found her unresponsive to all stimuli, absent of corneal and oculocephalic reflexes, with no response to caloric testing and flaccid extremities. She did have a spontaneous breath during a 5 minute apnea test and the neurologist noted she didn’t meet criteria for brain death. Despite this, they felt her prognosis was poor and plans to withdraw care were made.
- On Day 5, “with organ procurement imminent”, eye opening and extremity movement was noted.
- The patient was discharged to psychiatry on Day 15, admitted to having taken a large baclofen overdose, then went home.

Pharmacology

- Baclofen is an agonist at GABA-B receptors, similar to GHB. Benzodiazepines, Barbiturates, Ethanol, and Propofol are all GABA-A agonists.
- GABA B receptors are found post synaptically, pre-synaptically and extra-synaptically (i.e. a different neuron’s pre-synaptic terminal).
- Presynaptic GABA-B receptors function to inhibit the release of neurotransmitters – be it excitatory glutamate or to act as a shut off valve to GABA release itself. Inhibiting neurons that are normally inhibitory themselves (i.e. GABA releasing neurons) results in stimulation.



- Baclofen is rapidly absorbed from the GI tract.
- Peak absorption occurs within 2 hours of oral ingestion.
- The usual elimination half-life is 2.5–4 hours in therapeutic dosing, but may be prolonged in overdose.

Clinical features

- Baclofen intoxication
 - Nausea, vomiting, confusion, somnolence, lethargy.
 - Occasionally paradoxical hallucinations, agitation, and seizures (from GABA-B inhibition).
 - More severe toxicity = coma, respiratory failure, bradycardia, hypotension, flaccidity, mydriasis, and hypothermia.
 - Deep coma can mimic brain death and may persist for several days postingestion.
- Baclofen withdrawal
 - Usually with abrupt discontinuation of an intrathecal pump but may also occur after cessation of oral dosing.
 - The onset is typically 24–48 hours after the dose reduction.
 - Symptoms include agitation, seizures, tachycardia, hyperthermia, hyper- or hypotension, muscle rigidity, and hallucinations.
 - Severe withdrawal has been reported to cause rhabdomyolysis, multi-organ system failure, and death.

Management

- Maintain an open airway and assist ventilation if necessary. Activated charcoal 1g/kg PO/NG is appropriate if the airway is protected.
- Treat coma, seizures, arrhythmias, hypothermia, and hyperthermia if they occur.
 - Seizures respond to IV benzodiazepines
 - Hypotension is usually responsive to supine position and IV fluid resuscitation.
- There is no specific antidote.
- Withdrawal symptoms may respond to benzodiazepines but definitive treatment is re-institution of baclofen followed later by gradually tapering the dose if indicated.
- While most patients do well with supportive care, hemodialysis may be warranted in patients with renal compromise as baclofen is excreted largely by the kidneys.



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.