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Baclofen Overdose

Purpose: To inform healthcare professionals in Saskatchewan about the recent baclofen overdoses, to review appropriate prescribing practices of baclofen and to briefly describe the manifestations and management of baclofen toxicity.

Background: Over the past three months, the Battlefords' Union Hospital has seen approximately seven baclofen-related overdoses. This has been a concern for Prince Albert emergency room physicians for some time as well. The prevalence of baclofen-related overdoses is currently unknown in Saskatchewan. These baclofen-related overdoses rarely appeared to be intentional, but rather the result of a multi-drug recreational cocktail. These overdoses can be very difficult to manage and may result in an ICU admission for respiratory depression and severe agitation or paradoxical sedation. It is important to be aware that baclofen is a medication that is known to be diverted and therefore may not appear on a patient's PIP profile. Do not be too quick to exclude it as a possible contributor to a patient's presenting signs and symptoms. Baclofen misuse is not well understood and few reports of misuse appear in the literature, though publications tend to lag in describing anecdotal reports. However, literature out of England has described growing recreational baclofen use between 2009-2015.[1,2]

Reducing Overdose Potential through Appropriate Prescribing

Evidence-Based Use of Baclofen

- **Spasticity** (e.g. MS or spinal cord injury)[3-5]

Limited or No Evidence Uses of Baclofen

- **Alcohol use disorder:** off-label use to ↓ withdrawal symptoms and ↑abstinence[6]
- **Short term (≤2 weeks)** pain relief at ***onset*** of **low back pain** – limited evidence[7]
- Persistent hiccups – limited evidence[8,9]
- **No evidence for use in chronic low back pain[7]**

Prescribing Tips

- ✓ Keep oral daily doses < 80 mg
- ✓ Adjust dose for renal insufficiency (> 70% excreted renally unchanged)
- ✓ Monitor for behaviours of substance use disorder (e.g. CAGE-AID tool)
- ✓ Exercise caution when considering for alcohol use disorder
- ✓ Counsel patients to store securely
- ✓ Do not use baclofen for chronic low back pain

Potential Reasons for Overdose

- Therapeutic use
  - reports of increasingly higher doses being prescribed for alcohol use disorder[10]
  - anecdotally, has been prescribed inappropriately for chronic pain in excessive amounts
  - pump malfunction during intrathecal infusions[11]
- Recreational use
- Intentional

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Baclofen Toxicity

Mechanisms of Action

Baclofen is an agonist of the gamma aminobutyric acid $(GABA)_B$ receptor,[11-13] unlike benzodiazepines, ethanol, and barbiturates, which are $GABA_A$ receptor agonists.[13] It has presynaptic and postsynaptic effects.

Presynaptic inhibitory effects[14]

- Prevents Ca^{2+} influx and provides feedback inhibition of GABA release
- In overdose, greater inhibition of GABA release (negative feedback) results in seizure potential

Postsynaptic inhibitory effects[14]

- Increases K^+ efflux with inhibitory effects similar to GABA.
- Seizure potential in withdrawal due to loss of inhibitory effects.

In other words, **seizures may be seen in overdose as well as withdrawal**.

Presentation and Management

Toxic dose varies; stupor or coma may occur at doses ~3-5x usual therapeutic dose.[15]

Symptoms[11,12,15-19]

Symptom Onset can be rapid (30-120 minutes following ingestion[15]) but may also be prolonged[11]; **duration** may persist several days[11, 17, 18]

***All symptomatic patients should be admitted to acute care**

CNS: spectrum of lethargy to coma; ataxia, agitation (patient may exhibit both CNS depression and stimulation throughout admission)
CV: hypotension, bradycardia, AV block
Respiratory: respiratory depression, respiratory failure
GI: nausea/vomiting
Other: hypothermia, mydriasis, flaccidity, hyporeflexivity

***Important note: "coma, flaccidity and loss of reflexes can last several days after severe overdose and should not be mistaken for brain death."**[11]

Management[11, 12, 15]

Symptomatic/Supportive

- **airway management;** baclofen is a CNS and respiratory depressant**.** Patients must be intubated if they are unable to protect their own airway
- **mechanical ventilation** may be required.
- treat **agitation or seizures** with benzodiazepines
- treat **hypotension** with fluids and pressors
- treat **bradycardia** with O_2 (if hypoxic) and per ACLS symptomatic bradycardia algorithm[20]

Decontamination

- baclofen binds to **activated charcoal**. A dose of 1g/kg PO can be given if the GCS is 15 or the patient is intubated

For more information, as well as for support in the management of individual patient cases, please consult PADIS 1-866-454-1212

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