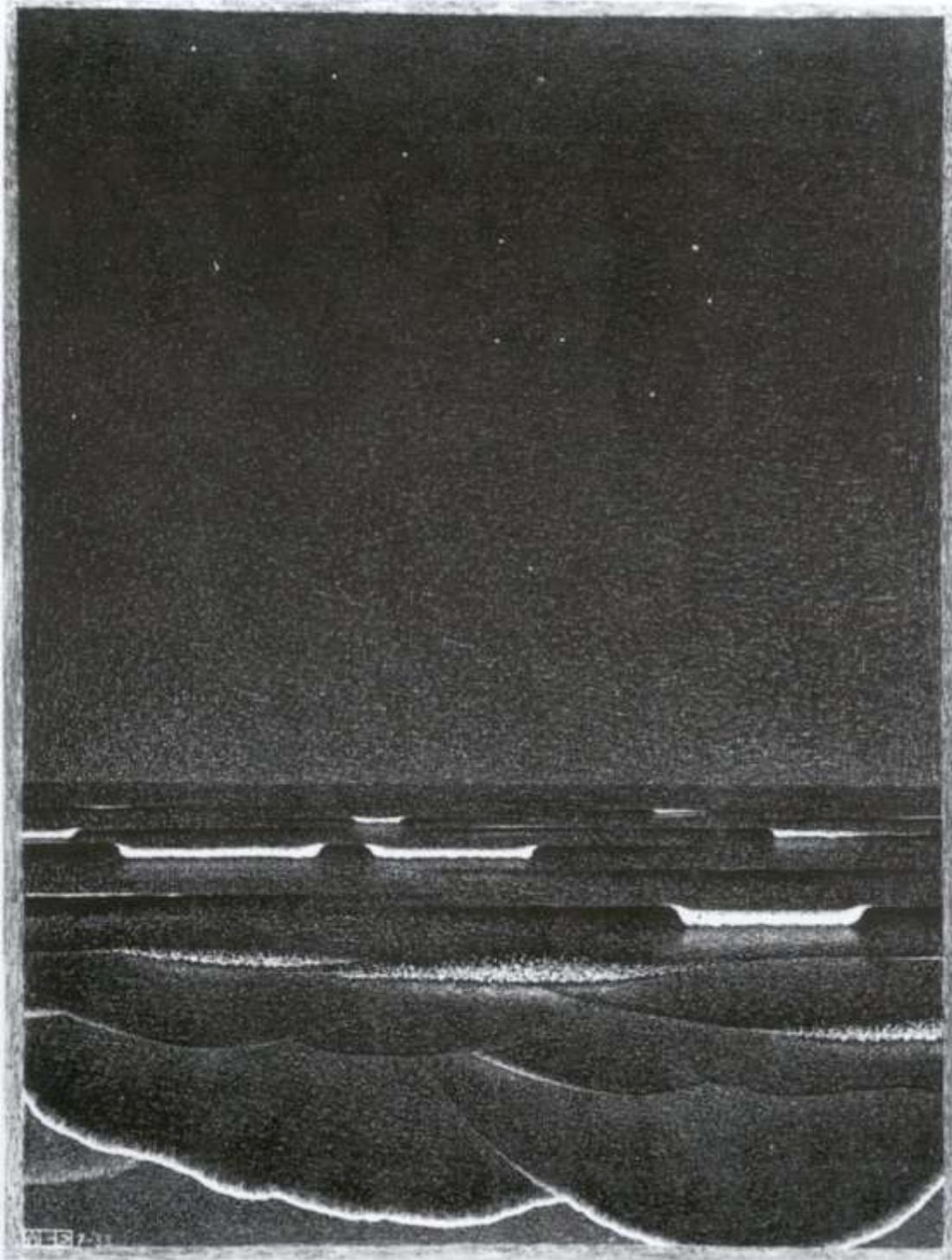


BACLOFEN OVERDOSE



“Fluorescent Sea”, lithographic print, M.C Escher, 1933.

He fitted the rope lashings of the oars onto the thole pins and, leaning forward against the thrust of the blades in the water, he began to row out of the harbour in the dark. There were other boats from other beaches going out to sea and the old man heard the dip and push of their oars even though he could not see them now the Moon was below the hills.

Sometimes someone would speak in a boat. But most of the boats were silent expect for the dip of the oars. They spread apart after they were out of the mouth of the harbour and each one headed for the part of the ocean where he hoped to find fish. The old man knew he was going far out and he left the smell of the land behind and rowed out into the clean early morning smell of the ocean. He saw the phosphorescence of the Gulf weed in the water as he rowed over the part of the ocean that the fishermen called the great well because there was a sudden deep of seven hundred fathoms where all sorts of fish congregated because of the swirl the current made against the steep walls of the floor of the ocean. Here there were concentrations of shrimp and bait fish and sometimes schools of squid in the deepest holes and these rose close to the surface at night where all the wandering fish fed on them.

In the dark the old man could feel the morning coming and as he rowed he heard the trembling sound as flying fish left the water and the hissing that their stiff set wings made as they soared away in the darkness. He was very fond of flying fish as they were his principle friends on the ocean. He was sorry for the birds, especially the small dark =delicate terns that were always flying and looking and almost never finding, and he thought, the birds have a harder life than we do except for the robber birds and the heavy strong ones. Why did they make birds so delicate and fine as those sea swallows when the ocean can be so cruel? She is kind and very beautiful. But she can be so cruel and it comes so suddenly and such birds that fly, dipping and hunting, with their small sad voices are made too delicately for the sea.

He always thought of the sea as la mar which is what some people call her in Spanish when they love her. Sometimes those who love her say bad things of her but they are always said as though she were a woman. Some of the younger fishermen, those who used buoys as floats for their lines and had motor-boats, bought when the shark livers had brought much money, spoke of her as el mar which is masculine. They spoke of her as a contestant or a place or even an enemy. But the old man always thought of her as feminine and as something that gave or withheld great favours, and if she did wild or wicked things it was because she could not help them. The Moon affects her as it does a woman, he thought.

*Ernest Hemmingway,
"The Old Man and the Sea", (Pulitzer Prize) 1952.*

Like the wild Sea itself, Baclofen, can be a friend or a foe. In normal therapeutic doses, it can most definitely be a friend – but in massive overdose - most definitely a foe!

BACLOFEN OVERDOSE

Introduction

Most **baclofen** overdoses are minor and benign.

Large overdoses however are potentially lethal without timely intervention and present with rapid onset delirium, which can be prolonged, coma, seizures and respiratory depression.

Treatment is supportive, and the majority of cases will do well with this.

History

Baclofen was initially designed as an anti-epilepsy agent.

It was developed by the Swiss chemist **Heinrich Keberle**, in 1962.

It was not satisfactory as an anti-epilepsy agent, but it was found that in some people, spasticity was decreased, and so it gained value for this indication.

Preparations

Baclofen as:

Tablets:

- 10 mg
- 25 mg

Ampoules:

- 0.05 mg/mL, 1 mL
- 0.5 mg/mL, 20 mL
- 2 mg/mL, 5 mL
- 2 mg/mL, 5 mL
- 2 mg/mL, 20 mL

Toxicology

Baclofen is synthetic derivative of GABA.

At therapeutic doses, it acts principally on spinal GABA-**B** receptors, *inhibiting the release* of the excitatory amino acids - glutamate and aspartate.

In overdose it causes effects on brain GABA receptors resulting in *inhibition* of CNS excitatory neurotransmitters leading to sedation and coma.

Pharmacokinetics

Absorption

- Baclofen is rapidly and completely absorbed following ingestion.
- Peak serum concentrations occur within 2 hours.

Distribution

- The volume of distribution is 0.7 L/Kg.
- Baclofen readily crosses the blood brain barrier.

Metabolism and excretion

- About 15% is metabolised in the liver to inactive metabolites.
- About 85% is excreted unchanged in the urine.
- The mean elimination half life is 3.5 hours.

Risk Assessment

Good supportive care should result in favourable outcomes.

Dose	Clinical effects
< 200 mg orally	Usually minor CNS symptoms only.
> 200 mg orally	May result in significant CNS symptoms, with severity increasing with increasing dose
Intrathecal > 10 mg	Can result in coma

Clinical Features

Toxic features generally develop within **2 hours** and include:

1. CNS:

- Confusion/ delirium.
- Sedation - **Coma**:

This can be **profound** and **prolonged, (24 - 48 hours)**

Note that there may also be significant depression of **brain stem function and reflexes** - including **fixed** and **dilated pupils**, making a diagnosis of brain death problematic.

There can also be generalized hypotonia, hyporeflexia, and pupillary abnormalities (miosis or mydriasis) as well as hypothermia.³

- **Seizures.**

2. Respiratory:

- Respiratory depression.

3. Cardiovascular:

- Sinus bradycardia or tachycardia.
- First degree heart block
- QT prolongation, (rare)
- Hypertension, (less commonly hypotension).

Investigations

There are no specific investigations other than those pertaining to “generic” overdose issues, such as:

1. BSL
2. Consideration of coingestion - serum paracetamol and blood alcohol levels
3. ECG assessment.

Management

1. Immediate attention to any ABC issues
 - This will be the mainstay of supportive management.
 - **Intubation should be instituted early in baclofen overdoses in view of the potential for a *protracted* course (i.e. > 72 hours) as well as for seizures and respiratory depression.**
2. Charcoal:
 - This should be **avoided** in view of the risk of **deep coma** and **seizures**.
 - It may be given in patients who have been intubated.
3. Seizures:
 - Seizures are generally self-limiting, but if persistent or recurrent they should be treated with IV diazepam titrated to effect.

Give 5 mg IV, 5 minutely as required. ⁴
4. Delirium:
 - Delirium can be difficult to treat.

Initial management should be with benzodiazepines or a sedating antipsychotic such as droperidol. ³
5. Hypotension:
 - Usually responds to fluids. Inotropes are not usually required.
6. Hemodialysis:
 - This may reduce duration of toxicity in patients with **significant renal impairment**.

Baclofen withdrawal syndrome:

This may occur between 24 and 48 hours post **abrupt** cessation of baclofen.

Baclofen withdrawal can be **life-threatening**

It is characterised by:

- Delirium / hallucinations

- Visual disturbances
- Seizures
- Dyskinesia
- Hyperthermia

Management essentially involves reinstating baclofen. This should be discussed with a clinical Toxicologist.

Note that failure to reinstitute baclofen therapy, following recovery from overdose may precipitate a withdrawal syndrome, which may be mistaken for ongoing toxicity.

Disposition:

Asymptomatic patients or those who have ingested < **200 mg** of baclofen can be discharged **4 hours** after ingestion.

Patients with mild symptoms should be observed in hospital until all symptoms have resolved.

If ingestion is associated with coma, delirium or seizures, HDU/ICU/ admission and a prolonged length of stay is required.

Patients should not drive for at least 72 hours post exposure. ⁴

References

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3. eTG - October 2019.
4. Baclofen in Austin Health Clinical Toxicology Service Guidelines, September 2019.

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