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USE OF BACLOFEN IN TREATMENT OF VARIOUS MEDICAL CONDITIONS

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ABSTRACT

Baclofen, sold under the brand name Lioresal among others, is a central nervous system depressant used as a skeletal muscle relaxant. It is primarily used to treat spasticity. It is also used in topical creams to help with pain. It is a GABA receptor agonist, specifically of the GABAB receptors. Its beneficial effects in spasticity result from actions at spinal and supraspinal sites. It is a derivative of γ-aminobutyric acid (GABA). The drug is rapidly absorbed after oral administration and is widely distributed throughout the body. Biotransformation is low and the drug is predominantly excreted unchanged by the kidneys. The half life of baclofen is roughly 2–4 hours and it therefore needs to be administered frequently throughout the day to control spasticity appropriately. Baclofen comes in tablets of 10 and 20 milligrams (mg), and you'll usually take an equally divided dose three times a day. The most common side effect experienced by people taking baclofen is drowsiness. Other drugs that depress the central nervous system may make some side effects of baclofen worse.

KEYWORDS: GABA, spasticity, supraspinal sites, drowsiness.

INTRODUCTION

Baclofen, sold under the brand name Lioresal among others, is a central nervous system depressant used as a skeletal muscle relaxant. It is primarily used to treat spasticity. It is also used in topical creams to help with pain.[1]

It is a GABA receptor agonist, specifically of the $GABA_B$ receptors.[2][3] Its beneficial effects in spasticity result from actions at spinal and supraspinal sites. It is a derivative of γ-aminobutyric acid (GABA).

A beneficial property of baclofen is that tolerance to its muscle-related therapeutic benefits does not seem to occur to a significant degree — baclofen retains its therapeutic anti-spasmodic effects even after many years of continued use.[4] Newer studies, however, indicate that tolerance may develop in some people receiving intrathecal baclofen treatment.[5][6][7] As of 2015 the cost for a typical course of treatment in the United States is less than 25 USD.[8]

Baclofen is a muscle relaxer and an antispastic agent. Baclofen is used to treat muscle symptoms caused by multiple sclerosis, including spasm, pain, and stiffness. Baclofen is sometimes used to treat muscle spasms and other symptoms in people with injury or disease of the spinal cord.

MEDICINAL USES

Spasticity

Baclofen is primarily used for the treatment of spastic movement disorders, especially in instances of spinal cord injury, cerebral palsy, and multiple sclerosis.[9] Its use in people with stroke or Parkinson's disease is not recommended.[9]

Alcoholism

Baclofen is being studied for the treatment of alcoholism.[10] While evidence is promising that it may help with alcohol withdrawal syndrome, as of 2015 it is not strong enough to recommend its use for this purpose.[10,11]

In 2014 the French drug agency ANSM issued a 3-year temporary recommendation allowing the use of baclofen in alcoholism.[12]

Other

It is being studied along with naltrexone and sorbitol for Charcot-Marie-Tooth disease (CMT), a hereditary disease that causes peripheral neuropathy.[13] It is also being studied for cocaine addiction.[14]

Pharmacokinetics

The drug is rapidly absorbed after oral administration and is widely distributed throughout the body. Biotransformation is low and the drug is predominantly

excreted unchanged by the kidneys.[15] The half life of baclofen is roughly 2–4 hours and it therefore needs to be administered frequently throughout the day to control spasticity appropriately.

Baclofen produces its effects by activating the $GABA_B$ receptor, similar to the drug phenibut which also activates this receptor and shares some of its effects. Baclofen is postulated to block mono-and-polysynaptic reflexes by acting as an inhibitory neurotransmitter, blocking the release of excitatory transmitters. However, baclofen does not have significant affinity for the GHB receptor, and has no known abuse potential.[16] The modulation of the $GABA_B$ receptor is what produces baclofen's range of therapeutic properties.

Pharmacodynamics

Similarly to phenibut (β-phenyl-GABA), as well as pregabalin (β-isobutyl-GABA), which are close analogues of baclofen, baclofen (β-(4-chlorophenyl)-GABA) has been found to block $\alpha_2\delta$ subunit-containing voltage-gated calcium channels (VGCCs).[17] However, it is weaker relative to phenibut in this action (K_i = 23 and 39 μM for *R*- and *S*-phenibut and 156 μM for baclofen).[17] Moreover, baclofen is in the range of 100-fold more potent by weight as an agonist of the $GABA_B$ receptor in comparison to phenibut, and in accordance, is used at far lower relative dosages. As such, the actions of baclofen on $\alpha_2\delta$ subunit-containing VDCCs are likely not clinically-relevant.[17]

Route of Administration, Dosage, Frequency

Baclofen comes in tablets of 10 and 20 milligrams (mg), and you'll usually take an equally divided dose three times a day. Tablets have a score mark, which is an indented line down the middle, so you can cut them in half if necessary.[18]

Your doctor may start you at a low dose and then gradually increase it as needed. The goal is to take the lowest effective dose.

A typical dose schedule is:

- 5 mg three times a day for the first three days;
- 10 mg three times a day for the next three days;
- 15 mg three times a day for the next three days;
- 20 mg three times a day for the next three days.

It may take a few weeks for the drug to reach the peak effectiveness. The usual daily dose is 40 to 80 mg.

The maximum dose should not be higher than 80 mg a day.

Baclofen Overdose

An overdose of baclofen can cause:

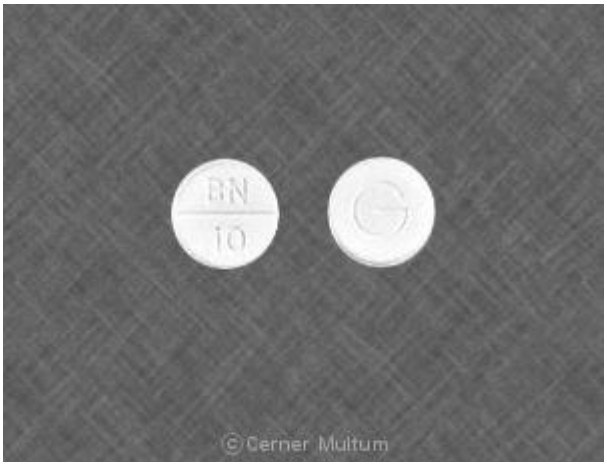
- Nausea
- Vomiting
- Severe muscle weakness
- Drowsiness
- Difficulty breathing
- Coma
- Seizure

Images of Tablets

Baclofen 10 mg-TEV, white, round.

Baclofen 20 mg-TEV, white, round.

Baclofen 10 mg-MAJ, white, round.



Baclofen 10 mg-MYL, round.

Side Effects

The most common side effect experienced by people taking baclofen is drowsiness. Other common side effects include:[19]

- Dizziness
- Weakness
- Fatigue

Less common side effects of baclofen include:

- Confusion
- Insomnia
- Headache
- Nausea
- Constipation
- Frequently passing urine
- Excitement
- Visual disturbance
- Loss of muscle coordination
- Dry mouth
- Loss of appetite
- Sexual impotence

Interactions

Some drugs may affect the way baclofen works, and baclofen may affect other drugs you're taking. It's very important to let your doctor know about all drugs you're taking, including any other prescription drugs, over-the-counter drugs, recreational or illegal drugs, herbs, vitamins, or supplements. Other drugs that depress the central nervous system may make some side effects of baclofen worse [20] These drugs may include:

- Alcohol
- Sleeping pills
- Tranquilizers
- Muscle relaxants
- Vitamins

Don't drink alcohol while taking baclofen because that can worsen side effects such as drowsiness and dizziness. Because baclofen relaxes muscles, it may cause weakness and imbalance, especially if you have muscle stiffness. Talk to your doctor about how baclofen may affect your balance [21].

Pregnancy and Lactation

Pregnancy category: C

Lactation: Enters breast milk in small amounts; not recommended

CONCLUSION

Trials are currently ongoing, and the role of baclofen should become clearer as results are made known. Clinicians should be aware of both the risks and benefits associated with baclofen and its selection over other second-line agents. Selection of an agent for this indication should be based on patient characteristics, including organ function and comorbid diseases, specifically psychiatric illnesses and seizure disorders of any type. There is some suggestion that baclofen 30–60 mg daily may be safe and effective for the treatment of alcohol-dependent individuals with normal renal function, with or without advanced liver disease, who have not been diagnosed with a psychiatric illness and do not carry a history of seizures.

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