PRILOCAINE

Introduction

Prilocaine (trade name in Australia, "**Citanest"**) is an **amide** local anaesthetic agent.

It is less toxic than other amide local anaesthetics.

It has **lower cardiac and lower CNS toxicity**, than lignocaine and so is the preferred agent for **intravenous regional anaesthesia, (Bier's Block)**.

See also separate documents on:

- **Bier's block (in Critical Care & Anaesthetics folder).)**
- **Intralipid Therapy (in Toxicology folder)**
- **Methemoglobinemia (in Toxicology folder)**

History

The Nobel Prize in Physiology or Medicine for 1963 was awarded jointly to **Sir John Carew Eccles, Alan Lloyd Hodgkin** and **Andrew Fielding Huxley.**

By studying the giant axons of two squid species ***Loligo forbesii*** and ***Doryteuthis pealeii,*** they were able to determine the nature of the nerve action potential. Their discoveries remain one of the greatest in the history of biology, and rank among the most significant conceptual breakthroughs in the neurosciences.

Later studies utilized tetrodotoxin to further understand the nature of the action potential in excitable tissue.

Tetrodotoxin is a natural lethal toxin found in **pufferfish** that specifically inhibits the voltage-sensitive sodium channel, responsible for the initiation and propagation action potentials.

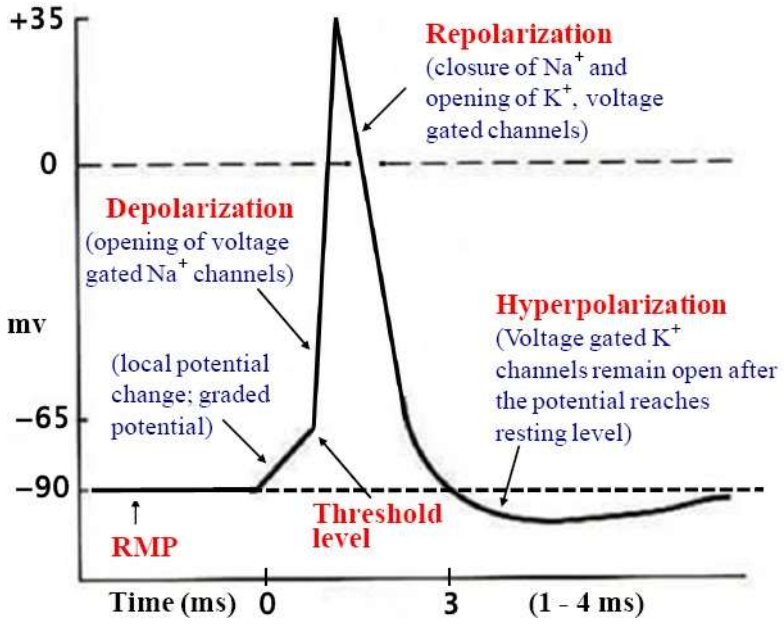
Nils Löfgren (1913 - 1967) was a Swedish chemist who developed the local anaesthetic agent lignocaine (marketed under the name trade name of Xylocaine) in 1943.

Later, in partnership with Claes Tegner, he developed the local anaesthetic agent prilocaine.

Chemistry

Prilocaine is an **amide** local anaesthetic agent.

Physiology



The nerve action potential. Local anaesthetic drugs are sodium channel blocking agents.

Classification

Local anaesthetic agents are classically divided into two principal classes:

1. Amides:
    - Bupivacaine
    - Levobupivacaine
    - Lignocaine
    - **Prilocaine**
    - Ropivacaine
2. Esters:
    - Amethocaine
    - Oxybuprocaine

- Cocaine

Preparations

Prilocaine hydrochloride as:

- Ampoules:
  - ♥ 0.5%, in 50 mL, (“Citanest”).
- Fixed combinations with lignocaine:
  - ♥ Cream, prilocaine 2.5%, + lignocaine 2.5% (“EMLA”)
  - ♥ Patch, prilocaine 2.5%, + lignocaine 2.5% (“EMLA”)

Note that Citanest for local infiltration is not currently available in Australia.

Mechanism of Action

Local anesthetics block nerve conduction by preventing the increase in membrane permeability to sodium ions that normally leads to a nerve impulse.

As for other local anaesthetic agents prilocaine acts by the reversible blockade of fast sodium channels.

The progression of local anaesthetic block relates to:

- Nerve fiber diameter
- Myelination
- Conduction velocity.

In general, loss of nerve function occurs in the following order:

- Loss of autonomic activity
- Loss of pain sensation.
- Loss of other sensory modalities
- Motor activity.

Pharmacodynamics

For local infiltration:

Average onset of action is around **5 - 10 minutes**

Duration of action **1 - 2 hours**

In Bier's Blocks:

Maximum anaesthesia occurs in Bier's Block within **5-10 minutes.**

Effective for as long as the Bier's Block cuff is inflated (this should not be less than **20 minutes** or more than **60 minutes**).

Pharmacokinetics

Absorption:

- Prilocaine can be administered by local infiltration or can be used in intravenous regional anaesthetic blocks, (i.e. Bier's blocks).

Distribution

- Human placental transfer can occur with prilocaine.
- Some excretion into breast milk is thought likely to occur.

Metabolism and excretion:

- Amidases in the liver, kidneys and lungs metabolize prilocaine directly.

  One metabolite excreted in the urine is **o-toluidine** which is believed to be the cause of methaemoglobinaemia observed after large doses of prilocaine.

Indications

Prilocaine is used for:

1. Local infiltration anaesthesia (uncommonly)
2. Peripheral nerve block techniques (uncommonly)

2 IV regional anaesthesia i.e. Bier's blocks, (commonly).

Contra-indications/precautions

These include:

1. Allergic reaction to local anaesthetic of the same group (i.e. ester or amide) - contraindicated.

2. Local inflammation or infection (direct infiltration into areas affected by these is contraindicated).

3. Methaemoglobinaemia related situations:

    - Methaemoglobinaemia, (contraindicated).
    - Effects of methaemoglobinaemia are more severe in the setting of in anaemia or hypoxia; use with caution.
    - Treatment with drugs that may cause methaemoglobinaemia:
        - ♥ e.g. sulfonamides, nitrates, may worsen methaemoglobinaemia; use with caution.
    - Children:
        - ♥ Not recommended in children < 12 months taking drugs that may cause methaemoglobinaemia:
            - ♥♥ e.g. sulfonamides.
        - ♥ Preterm babies (< 37 weeks gestation).
        - ♥ Due to the risk of methaemoglobinaemia, limit EMLA application time to approximately 1 hour in babies < 3 months.

4. Neuromuscular disease (e.g. myasthenia gravis):

    - Increases sensitivity to local anaesthetic and so may increase muscle weakness and depress respiration with central neural blockade; assess risks and benefits before use.

Pregnancy

Prilocaine is classified as a class A drug with respect to pregnancy.

Class A drugs are those drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Prilocaine use in the obstetric setting has not been associated with adverse pregnancy outcomes.

However, high doses of prilocaine used as an epidural or pudendal block during labour may be associated with an increased risk of the newborn developing methaemoglobin.

Topical prilocaine use during pregnancy is unlikely to pose harm in the newborn.

Therefore, prilocaine is safe to use during pregnancy.

Breast feeding

Published reports describing the use of prilocaine during breastfeeding have not been located.

Prilocaine has a short half-life and poor oral bioavailability. **Small** amounts of prilocaine are expected to be excreted into breast milk, but infants exposed to prilocaine via breast milk are unlikely to experience harmful effects.

Prilocaine is considered safe to use during breastfeeding, but avoid application of prilocaine to the nipple areas.

Adverse Effects

These include:

1. Allergic reactions:

    - These are rare, (reactions are relatively more common with esters compared to IV amides.

      There is no cross-reactivity between the 2 groups.

      It may present as localised oedema, urticaria, bronchospasm and anaphylaxis. Rash may occur following skin application.

2. In cases of inadvertent cuff deflation during Bier's Block procedures:

    Systemic effects of prilocaine toxicity include:

    - Neurological:
        - ♥ Restlessness
        - ♥ Paraesthesia, especially circumorally.
        - ♥ Tinnitus
        - ♥ Seizures
        - ♥ Reparatory arrest
    - Cardiovascular:

- ♥ Hypotension
- ♥ Bradycardia.
- ♥ Conduction delays
- ♥ Cardiac arrest

- Methemoglobinemia

Dosing

Local Infiltration:

Maximum dose is **6 mg/kg (or with adrenaline 8 mg/kg).**

Bier's Block:

Inject the **0.5 % prilocaine** via the IV cannula in the affected limb slowly over **2 minutes.**

- **Dose for arm blocks is 2.5 mg/kg = 0.5ml/kg of the 0.5 % solution.**
- **Maximum dose= 5mg/ kg (=1ml/kg) up to 50 mls**

References

1. Prilocaine in Australian Medicines Handbook Website Accessed, February 2017.

2. Prilocaine in MIMs Website, 1 December 2011.

3. Prilocaine in RWH Pregnancy & Breastfeeding Guidelines; 15 February 2017

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