THE NORTHERN HOSPITAL

IVERMECTIN

Introduction

Ivermectin is a semi-synthetic **broad-spectrum antiparasitic** drug in the avermectin family.

It currently plays a vital role in the elimination of Onchocerciasis (or river blindness).

Ivermectin is on the World Health Organization's List of Essential Medicines, a list of the most important medication needed in a basic health system.

History

The discovery of the avermectin family of compounds, from which ivermectin is chemically derived, was made by Satoshi Omura of Kitasato University, Tokyo and William C. Campbell of the Merck Institute.

Omura identified avermectin from the bacterium *Streptomyces avermitilis*.

Campbell purified avermectin from cultures obtained from Omura and led efforts leading to the discovery of ivermectin, a derivative of greater potency and lower toxicity.

Ivermectin was introduced to clinical therapeutics in 1981.

Half of the 2015 Nobel Prize in Physiology or Medicine was awarded jointly to Campbell and Omura for discovering avermectin, "the derivatives of which have radically lowered the incidence of river blindness and lymphatic filariasis, as well as showing efficacy against an expanding number of other parasitic diseases".

Chemistry

Ivermectin is a semi-synthetic agent derived from the **avermectins**, a class of highly active broad spectrum antiparasitic agents isolated from fermentation broths of *Streptomyces avermitilis.*

Preparation

Tablets:

- 3 mg.

Mechanism of Action

Ivermectin alters chloride channel function by binding to glutamate-gated chloride ion channels and acting as a **GABA agonist** in parasites, leading to its paralysis and death.

By this action ivermectin inhibits signal transmission from the ventral cord interneurons to the excitatory motor neurones in nematodes by stimulating release of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA) from presynaptic nerve terminals.

In arthropods, a similar mechanism inhibits signal transmission at the neuromuscular junction.

Ivermectin does not readily penetrate the CNS of mammals, and thus does not interfere with mammalian GABA dependent neurotransmission.

Pharmacodynamics

Ivermectin is a **broad-spectrum antiparasitic** agent that is effective against a wide range of **helminths** (or parasitic worms).

Pharmacokinetics

Absorption:

- Ivermectin is given orally but is incompletely absorbed with about 50 % bioavailability

  Following a high fat meal there is an approximate 2.5 fold increase in bioavailability

Distribution:

- Ivermectin has 93% protein binding.
- Ivermectin does not readily penetrate the CNS of mammals, and thus does not interfere with mammalian GABA dependent neurotransmission.

Metabolism and excretion:

- Ivermectin is primarily metabolised in humans by the CYP450 enzyme system.
- Ivermectin and its metabolites are excreted almost exclusively in the faeces over an estimated 12 days with less than 1% of the administered dose being excreted in the urine.
- The plasma half-life of ivermectin in man is about 12 hours and that of the metabolites is about 3 days.

Indications

For use over the age of **5 years** and/or **15 kgs weight.**

Indications include:

1. Strongyloidiasis (the current preferred treatment)
2. Scabies (crusted or if topical treatment has failed or is contraindicated)
3. Onchocerciasis (river blindness):
    - Ivermectin does not kill the adult worm only the larval stage microfilae.
4. Cutaneous larva migrans
5. Lymphatic filariasis, usually with albendazole (seek specialist advice)
6. Other intestinal nematode infections
7. Bot fly infection
8. Refractory head lice. [1]

Contra-indications/precautions

1. Is not recommended for use in children under the age of **5 years** and/or **15 kgs** weight.
2. Known hypersensitivity to ivermectin
3. Loiasis coinfection:
    - May develop life-threatening encephalopathy.
4. Hyper-reactive onchodermatitis:
    - More likely to have serious adverse reactions, especially oedema, transient worsening of onchodermatitis.

Pregnancy

Ivermectin is classified as a category B3 class drug with respect to pregnancy.

Category B3 drugs are those drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been

observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans

Ivermectin should not be used during pregnancy since safety in pregnancy has not been established

Breast feeding:

Safe for use in pregnancy.

Adverse Effects

1. Hypersensitivity reactions:
    - Rarely these can be severe e.g. TEN
2. GIT upset
3. Mazzotti reaction:
    - May occur during the treatment of Onchocerciasis due to allergic or inflammatory responses to the death of the parasite (Mazzotti reaction).

      They occur in at least one-third of patients, are most severe if there is high microfilariae count, and lessen with repeated courses.

      They include arthralgia, lymphadenopathy, itch, oedema, rash, fever, tachycardia, hypotension, temporary worsening of ocular symptoms.

Dosing

Exact doing and the duration of dosing depends on the condition being treated as well as the severity of the condition and illness.

In general terms:

Ivermectin (adult and child 15 kg or more) 200 micrograms/kg orally with fatty food, per dose. [1]

See specialized texts for exact dosing regimes.

References

1. eTG - July 2015

2. Ivermectin in Australian Medicines Handbook Website, Accessed December 2015.

3. Ivermectin in MIMs Website, 1 September 2015.

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