PROCHLORPERAZINE

Introduction

Prochlorperazine (better known in Australia by one of its common trade names – "**Stemeti**l") is a phenothiazine with a side chain containing a piperazine moiety.

It possesses strong antiemetic activity but is much less sedating than chlorpromazine making it useful as an antiemetic agent.

It also useful for conditions of vertigo, of both central and peripheral origin.

See also separate document on Dystonic Reactions (in Toxicology folder).

Chemistry

Prochlorperazine is a phenothiazine with a piperazine moiety in the side chain.

Preparation

Tablets: Prochlorperazine maleate: 5 mg, 10 mg, 25 mg.

Ampoules: Prochlorperazine mesylate: 12.5 mg/mL

Suppositories: Prochlorperazine base: 5 mg, 25 mg.

Mechanism of Action

It possesses strong antiemetic and antipsychotic activity with less sedative action than chlorpromazine.

Pharmacokinetics

Absorption:

- Prochlorperazine is well absorbed from the GIT

  It can also be given IM, IV and as a suppository.

Distribution:

- Prochlorperazine is widely distributed to tissues including the brain, fat, kidney, heart and skin and is stored in reticuloendothelial tissues.

Metabolism and excretion:

- Phenothiazines are metabolised primarily in the liver and are subject to enterohepatic circulation. Excretion is mainly in the faeces.

  Only a very small amount (approximately 0.1%) of prochlorperazine and its metabolites is excreted in the first 24 hours in the urine and the drug may continue to be excreted in the urine for up to three weeks after cessation of long-term therapy.

  The elimination half-life is long at approximately 24 hours, presumably due to its enterohepatic circulation

Pharmacodynamics

As with other phenothiazines, prochlorperazine has actions on several neurotransmitter systems as follows:

1. Anti-dopamine action:

   - Prochlorperazine's main antiemetic effect is centrally mediated, probably by blockade of dopamine receptors.

   - Dopamine blockade contributes to unwanted effects including extrapyramidal disorders and endocrine disturbances.

2. Alpha-adrenoreceptor antagonism:

   - Which contributes to cardiovascular side effects, e.g. orthostatic hypotension and reflex tachycardia.

3. Potentiation of noradrenaline by blocking its reuptake into nerve terminals.

4. A weak anticholinergic action.

5. Weak antihistamine action.

6. Weak serotonin antagonism.

Indications

1. Nausea and vomiting in general.

2. Vertigo:

   From a wide range of causes, including both central and peripheral vertigo.

It is effective in:

- Migraine

And peripheral causes of nausea and vertigo including:

- BPPV
- Meniere's syndrome
- Labyrinthitis
- Vestibular neuritis

Contraindications/ Precautions

Precautions include:

- Parkinson's disease: avoid if possible as symptoms may worsen
- Hypotension, although this if much less troublesome than those of other phenothiazines.
- Known hypersensitivity to phenothiazines.
  - ♥ This can include allergic reactions or idiosyncratic cholestatic jaundice
- It is avoided in children (especially below the age of 2 years) due to side effects, including extrapyramidal reactions, which are more commonly seen in children than in adults.
- Prochlorperazine may enhance the CNS depressant effects of alcohol and other depressant drugs

Pregnancy

Prochlorperazine is a **category C** drug with respect to pregnancy.

Category C drugs are those drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Specialized texts should be consulted for further details.

Adverse Effects

These primarily include:

1. Sedation:

- This is usually only mild, however.

2. Postural hypotension.

3. Anticholinergic effects:

   - Prochlorperazine can cause problems due to anticholinergic effects, especially in the elderly (urinary difficulties, constipation and precipitation of acute narrow angle glaucoma), but to a lesser extent than with other phenothiazines.

4. Acute dystonias:

   - Especially in children.

   See also separate document on Dystonic Reactions (in Toxicology folder).

5. Prolonged use:

   Use should be short term only; the risk of neurological disorders increases with cumulative dose and length of treatment.

   Prolonged use of prochlorperazine can lead to:

   - Tardive dyskinesia

   - Drug-induced parkinsonism

Dosing

Orally:

- Prochlorperazine **5 to 10 mg orally, 4 - 8 hourly** as required. [1]

Parenterally, IV or IM:

- Prochlorperazine **12.5 mg IM or IV, 4 - 8 hourly** as required. [1]

Suppository:

- Prochlorperazine **25 mg rectally, 12 hourly** as required.

References

1. eTG - July 2013

2. Australian Medicines Handbook, October 2013

4. MIMs October 2013.

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2 November 2013.