BROMOCRIPTINE

Introduction

Bromocriptine is a dopamine agonist that may on *theoretical* grounds be used for cases of moderate to severe **neuroleptic malignant syndrome.**

Autonomic instability and fever usually resolve within 24 hours of commencing bromocriptine therapy, but neuromuscular changes may take 1-2days to resolve and delirium may take several days to resolve.

See also separate Document on Neuroleptic Malignant Syndrome, (Toxicology Folder).

Chemistry

Bromocriptine mesylate is a **peptide ergot alkaloid.**

Classification

Dopamine agonists act directly on dopamine receptors:

They can be classified into two principle groups: [2]

1. Ergot-derived:
    - **Bromocriptine**
    - Cabergoline
    - Pergolide
2. Non - ergot derived:
    - Apomorphine
    - Pramipexole
    - Ropinirole
    - Rotigotine
    - Quinagolide

The dopamine agonists currently available in Australia are bromocriptine, cabergoline and quinagolide.

Preparation

Tablets: 2.5 mg

Mechanism of Action

Bromocriptine is a dopamine agonist

It inhibits prolactin secretion

Pharmacodynamics

Bromocriptine is primarily a dopamine receptor antagonist.

Unlike other classical ergot compounds, bromocriptine has **no** uterotonic and very little vasoconstrictor activity.

Pharmacokinetics

Absorption:

- Bromocriptine can be given orally or via nasogastric tube.
- About 7% of the dose reaches the systemic circulation unchanged. This is due to a high hepatic extraction rate and first pass metabolism.

Distribution:

- Plasma protein binding is high at around 96%.

Metabolism and excretion:

- Bromocriptine is extensively metabolized in the liver.

  The active parent drug and the metabolites are primarily excreted via the liver into the bile; only 6% is eliminated via the kidney

Indications

In the Emergency Department:

1. Neuroleptic malignant syndrome
   - In moderate to severe cases.

Other indications include:

2. Prolactinomas:

    - Dopamine agonists are first-line treatment in prolactinomas.

3. Acromegaly:

    - Where surgery or radiotherapy are contraindicated or have failed to control disease, or until radiotherapy becomes fully effective.

4. Parkinson's disease

In the past bromocriptine was used for the prevention of the onset of lactation in the puerperium for clearly defined medical reasons - however **cabergoline** is now the preferred agent

Contra-indications / Precautions

1. Known hypersensitivity to bromocriptine or other ergot alkaloids.

2. Breast feeding:

    - Prolactin is the crucial hormone for the preparation of the mammary gland for lactation and for the initiation and maintenance of milk secretion.

    - During pregnancy and after childbirth (through suckling stimuli) prolactin levels are elevated.

    - Reduction of circulating prolactin levels will thus prevent or suppress lactation.

3. Uncontrolled hypertension:

    - Including hypertensive disorders of pregnancy (eclampsia, pre-eclampsia or pregnancy induced hypertension)

      Bromocriptine should not be used in women with a history of pre-eclampsia.

4. Treatment with ergometrine, or other vasoconstrictive sympathomimetics - possible increased risk of cardiovascular adverse effects; avoid combination.

5. Treatment with **dopamine antagonists** (e.g. antipsychotics, metoclopramide) - avoid combined use (mutual antagonism).

6. Higher doses may cause CNS effects, including delirium, hallucinations or psychiatric disturbances:

- It is not recommended in patients with a history of serious psychiatric disorders.

7. Monitor for symptoms of progressive fibrotic disorders in patients on long-term treatment with ergot-derived dopamine agonists.

Pregnancy

Bromocriptine is a class A drug with respect to pregnancy

Category 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.

Breast feeding:

Contraindicated: Inhibits lactation.

Adverse Reactions

These may include:

1 Headache

2 Postural hypotension

3 GIT upset:

- Nausea and vomiting

4 Dyskinesia

5. Erythromelalgia

- This is painful erythematous lower limbs.

Dosing

Bromocriptine is the best treatment for neuroleptic malignant syndrome on theoretical grounds however it is not currently proven to be effective. [1]

- It should be considered, especially if the patient is not responding to more conservative measures or is very unwell.

- **2.5 mg orally**, (or by nasogastric tube) **8 hourly**, increasing to a maximum of **5 mg** every **4 hours** (i.e. 30 mg per day). [1]

- It should be continued for 1-2 weeks, before **tapering** the dose.
    - ♥ Do not stop bromocriptine abruptly; reduce dose gradually because of the risk of symptoms resembling the neuroleptic malignant syndrome

References:

1. Neuroleptic Malignant Syndrome: L Murray et al. Toxicology Handbook 3rd ed 2015.

2 eTG - March 2015

- Antibiotic Therapeutic Guidelines 15th ed 2014.

3. Bromocriptine in Australian Medicines Handbook, accessed November 2014

4. Bromocriptine in MIMs 1 October 2013.

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