ERGOMETRINE

Introduction

Ergometrine (also known as **ergonovine**) is an **oxytocic** agent that stimulates the contraction of **uterine smooth muscle.**

In the ED it is used in the prevention and control of postpartum hemorrhage after delivery of the placenta, and the control of post abortion hemorrhage.

It can be used as a stand alone agent, but is also often combined with **oxytocin**.

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

It has a number of important contraindications.

History

The pharmacological properties of **ergot** were known and utilized by midwives for centuries.

Ergometrine was first isolated by the chemists C Moir and H W Dudley in 1935.

Chemistry

Ergometrine is an **amine ergot alkaloid,** derived from the ergot fungus, *Claviceps purpurea*.

Classification

Principle ergot alkaloid drugs include:

- Ergometrine:
  - ♥ A parenteral form used in obstetrics
  - ♥ An oral form used in vascular headaches.
- Dihydroergotamine:
  - ♥ An oral form used in vascular headaches.

Preparation

Ergometrine maleate can be used as a stand alone agent, but is also often combined with **oxytocin**.

Ampoules:

- **Ergometrine** as 500 micrograms / mL, in 1 ml ampoule.

Combination preparations with oxytocin:

- **Syntometrine** - ergometrine 0.5 mg + oxytocin (synthetic) 5 IU.

Combination with caffeine:

- **Cafergot** - Caffeine and ergotamine (an oral preparation used for vascular headaches).

Mechanism of Action

Ergometrine stimulates contraction of uterine and vascular smooth muscle.

Pharmacodynamics

Ergometrine stimulates the contraction of:

1. Uterine smooth muscle:
    - Intense contractions of the uterus occur which are usually followed by periods of relaxation.
    - Larger doses of the drug, however, produces more **sustained,** forceful contractions followed by only short or no periods of relaxation.
    - There is increased amplitude and frequency of uterine contractions and uterine tone which in turn impedes uterine blood flow.
    - Contraction of the uterine wall around bleeding vessels at the placental site assists in haemostasis.
    - Ergometrine also increases contractions of the cervix.
2. Vascular smooth muscle:
    - Ergometrine produces vasoconstriction, capacitance vessels resulting in increased central venous pressures.

- Like other ergot alkaloids, ergometrine produces arterial vasoconstriction by stimulation of alpha-adrenergic and serotonin receptors and inhibition of endothelial derived relaxation factor release, resulting in elevated blood pressure.

Pharmacokinetics

Absorption:

- Ergometrine is given IV or IM:

  Ergometrine has a an onset of action following IV injection of 1 minute or even less.

  Ergometrine is rapidly and completely absorbed after IM injection with uterine contractions initiated within 2-5 minutes.

Distribution:

- The distribution of ergometrine has not been fully characterized.

Metabolism and excretion:

- Little is known about the elimination of ergometrine, but it appears to be principally by metabolism in the liver.

Indications

Obstetric indications include: [1]

As stand alone agent:

1. Prevention or postpartum haemorrhage:

   - Ergometrine is administered *after* the delivery of the placenta for the purpose of contracting the uterus in order to help prevent postpartum haemorrhage.

2. Treatment of postpartum haemorrhage:

   - Ergometrine is administered after the delivery of the placenta to promote involution of the uterus.

3. **Post** abortion haemorrhage due to uterine atony.

In Fixed-dose combination with oxytocin:

1. Active management of third stage of labour

2. Prevention or treatment of postpartum haemorrhage

Contraindications/ Precautions

These include:

Pregnancy related contraindications:

1. Ergometrine is **not** appropriate for induction of labour
2. Ergometrine should not be used if there is any suspicion of **retained placenta.**
3. Ergometrine should not be in cases of **threatened** spontaneous abortion
4. Hypertension (may be exacerbated by vasoconstriction).
    - Including pre-eclampsia / eclampsia (contraindicated)
5. Multiple pregnancy:
    - Ergometrine may result in the death of a second fetus due to excessive uterine contraction.

Non-pregnancy related contraindications:

6. Moderate to severe cardiac disease / IHD (contraindicated)
7. The vasoconstrictor effects of ergometrine is potentiated by sympathomimetics.
8. Severe peripheral vascular disease (contraindicated)
9. Severe hepatic impairment.
10. Drug reactions:
    - The concurrent use of sumatriptan and ergotamine should be avoided because of the theoretical risk of additive vasospastic reaction, in particular coronary vasoconstriction.
    - The concurrent use of ergot alkaloids and methysergide can increase the risk of severe and persistent spasm of major arteries in some patients. The combination should be used with great caution.

Pregnancy:

Not indicated

Breast feeding;

Ergot preparations are frequently given as a single dose postpartum to control haemorrhage. A **single** dose of ergometrine does not prevent the mother from breastfeeding.

Adverse Effects

These include:

1. Nausea and vomiting:
    - More common with IV route than with the IM route.
2. Abdominal cramps
3. Hypertension:
    - Especially when administered IV undiluted or too rapidly
4. Headache
5. High doses of ergometrine administered *prior* to delivery if may cause
    - Uterine tetany with consequent infant hypoxia.
    - Retention of the placenta
    - Missed diagnosis of a second twin infant (due to excessive uterine contraction).

    The placenta should be delivered, and the possibility of twin pregnancy should be ruled out, before ergometrine is administered.
6. Uterine overstimulation during labour may:
    - Uterine tetany with uterine rupture.
    - Amniotic fluid embolism.
7. Rarely, peripheral arterial ischaemia and gangrene may result, (excessive/ prolonged use).

Dosing

After IV injection uterine contractions are usually initiated within 1 minute or even less and can persist for 45 minutes.

After IM injection uterine contractions are usually initiated within 2 - 5 minutes and can persist for 3 hours or longer.

Exact dosing regimens vary according to local protocols, but in *general terms:* [1]

Prevention of postpartum haemorrhage:

- IM: 200 micrograms following delivery of the placenta.

Treatment of postpartum haemorrhage:

- IV: 250 micrograms *slow* push, dose may be repeated after 2 - 3 minutes.

  IV doses should be given *slowly*, over a period of at least 1 minute.

  It is best *diluted* to a volume of 5 mL with normal saline before administration.

- IM: 250 micrograms.

References

1. Ergometrine in Australian Medicines Handbook, Accessed April 2015

2. Ergometrine in MIMs 1 July 2014.

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