

Drugs Acting on the Uterine Smooth Muscle

Uterotonics (Oxytocics, Uterine Stimulants): Oxytocin, Prostaglandin, Ergometrine

Drugs that stimulate the contraction of the uterus, or to increase the frequency and intensity of the contractions. They are mainly used to:

- A. Induce (start) or augment (speed) labor.
- B. Facilitate uterine contractions following a miscarriage
- C. Induce abortion
- D. Reduce hemorrhage following childbirth or abortion.

Uterine contractions are rhythmical or sustained

- ✓ For induction of labour rhythmic contractions are important
- ✓ After delivery sustained contractions in order to minimise bleeding.

Tocolytics (Uterine Inhibitors):

- Calcium channel blockers
- Magnesium Sulfate (MgSO₄)
- Ritodrine, Salbutamol & Terbutaline
- Oxytocin antagonists (Atosiban)
- NSAIDs (ibuprofen, indomethacin and naproxen)
- General anaesthetics, particularly halothane
- Papaverine & amyl nitrite.

Drugs that relax the uterus, they use mainly to stop preterm labour Prevention or treatment of dysmenorrhea (uterine cramps).

Normally uterine smooth muscle is

- Stimulated by
 - α 1-adrenoceptors
 - Oxytocin
- Inhibited by β 2-adrenoceptors.

Uterotonics (Oxytocin)

Physiological Effects:

- Stimulation of milk ejection (milk letdown)
- Stimulation of uterine smooth muscle contraction during birth
- Establishment of maternal behavior

The release of oxytocin is governed by neuronal mechanisms elicited by:

- Cervical dilatation
- Coitus
- Suckling
- Emotional stimuli
- Some drugs (e.g. morphine & nicotine)

Pharmacologic Effects

- Stimulation of uterine contraction
- Frequency and force all enhanced
- Affected by sexual hormone levels in blood plasma:
 - Estrogen sensitizes
 - Progesterone oppresses it
- Different dosages lead to different contractions
 - Low dosage: rhythmic contraction (uterine fundus contracts while cervix relaxes)
 - High dosage: sustained contraction in whole uterus
- Milk letdown effect
- weak antidiuretic effect
- Dilation of vessels at high doses (controversy)

pharmacokinetics

- Null swallowed
- IM or IV usually used
- Not bound to plasma protein
- $T_{1/2}$: 5 min

Indications:

- Induction/augmentation of labor
- Management of inevitable or incomplete abortion
- Control postpartum hemorrhage

- Stimulate milk letdown (intranasal)

Contraindications:

- Malposition
- Cephalopelvic disproportion
- Birth canal abnormality

Uterotonics (Prostaglandins): Dinoprostone (PGE₂), Dinoprost (PGF_{2α})

PGF_{2α} and PGE₂ induce labour at any time during pregnancy and therefore are used mainly as *abortifacient*.

Clinical use

- Stimulating the uterine contractions at the beginning of labor (inducing abortion)
- May be used to ripen the cervix prior to induction.

Adverse Effects

- Abdominal cramps (both PGF_{2α} and PGE₂)
- Bronchospasm (PGF_{2α})

Contraindications

- Similar to oxytocin
- PGF_{2α} is banned for patient with asthma
- PGE₂ is banned for patient with glaucoma

Uterotonics (Ergot alkaloids): Ergometrine (ergonovine), Methylergonovine maleate (Methergine®)

Stimulation of uterine smooth muscle contraction through α and dopamine receptors.

Adverse Effects

- Nausea
- Hypertension
- Decrease lactation (being ergot alkaloid, it interferes on the level of the hypothalamus, like bromocriptine, reducing the release of prolactin and thus decrease lactation)

Tocolytics (Calcium channel blockers)

- ⊙ Calcium is blocked from entering the smooth muscle cells, thus preventing contractions
- ⊙ Nifedipine and Verapamil commonly used
- ⊙ Dizziness, flushing and headaches are among side effects

Tocolytics (Magnesium Sulfate (MgSO₄))

- ⊙ Acts as a calcium antagonist and membrane stabilizer, thus decreasing the force of contractions
- ⊙ Used prophylactically in patients with preeclampsia to prevent seizures
- ⊙ Side effects include fatigue, headaches, diplopia and flushing
- ⊙ Toxicity is associated with hypoxia, respiratory depression and cardiac arrest

Tocolytics (Beta 2 receptor agonist) Ritodrine, Salbutamol & Terbutaline

- ⊙ Acts on smooth muscle cells to increase levels of cAMP (via adenylate cyclase), which decreases levels of free calcium ions and reduces contractions.
- ⊙ Side effects include tachycardia, headaches, and anxiety.
- ⊙ Verapamil is commonly used to alleviate the side effects of tachycardia.

Tocolytics (Oxytocin antagonists) Atosiban

- ⊙ Oxytocin is a hormone that stimulates the uterus to contract .
- ⊙ The drug blocks the effect of Oxytocin by binding to the Oxytocin Receptor.
- ⊙ Mild side effects compared to other tocolytic agents.