# DRUGS ACTING ON UTERUS

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Drugs acting on uterus can primarily affect the endometrium or the myometrium.

-The most important drugs affecting endometrium are estrogens, progestins and their antagonists.

-Myometrium receives both sympathetic and parasympathetic innervation: autonomic drugs can affect its motility.

Uterine stimulants

These drugs increase uterine motility, especially at term

1-Posterior pituitary hormones

Oxytocin, Desamino oxytocin

2-Ergot alkaloids

Ergometrine ,Methylergometrine

3-Prostaglandins

PGE2 , PGF2α ,Misoprostol

4-Miscellaneous agents

Ethacridine, Quinine

# OXYTOCIN

Oxytocin is a non peptide secreted by the posterior pituitary along with vasopressin (ADH)

1- main effects on uterus: Increases force and frequency of uterine contraction

2-Milk ejection from breast

3- fall in blood pressure, reflex tachycardia

4-Kidney: ADH like action at high doses

**Mechanism of Action**: Oxytocin action is mediated through specific G-protein coupled oxytocin receptors. When these receptors are activated, they mediate response through:

1-Depolarization of muscle fibers and influx of Ca++ ions (main mechanism)

2-Through phosphoinsitide hydrolysis and Phosphatidyl inositol IP3mediated intracellular release of Ca++ ions.

3-Number of oxytocin receptors increases markedly during later part of pregnancy

4-Also increases Prostaglandin (PG) synthesis and release by the endometrium

**Pharmacokinetics**

- Inactive orally because peptide in nature so destroy by proteolytic enzyme in Gut.

-I.V. infusion , I.M, intranasal spray

-Metabolized in kidney and liver

-Plasma t ½ ~6min

-Destroyed by oxytocinase

-secreted by pregnant uterus & placenta

USES

1.Induction of labor:

In case of post maturity ,prematurely in toxemia of pregnancy, diabetic mother, ruptured membranes or placental insufficiency.

Oxytocin is given by slow i.v. infusion: 5 IU is diluted in 500 ml of glucose or saline solution.

2.Uterine inertia

When uterine contractions are feeble and labor is not progressing satisfactorily

Oxytocin is the drug of choice and is preferred over Ergometrine and PGs for the above two purposes:

A-It has short t½ and slow i.v. infusion

B-Low concentrations allow normal relaxation in between contractions-foetal oxygenation does not suffer.

C-Lower segment is not contracted: fetal descent is not compromised.

d-Uterine contractions are consistently augmented

3-Postpartum hemorrhage, Caesarean section

Oxytocin 5 IU may be injected i.m. or by i.v. infusion for an immediate response, especially in hypertensive women in whom ergometrine is contraindicated

4.Breast engorgement

Adverse effects

1-Produce too strong uterine contractions forcing the presenting part through incompletely dilated birth canal, causing maternal and fetal soft tissue injury, rupture of uterus, fetal asphyxia and death.

2-Water intoxication: This occurs due to ADH like action of large doses given along with i.v. fluids, especially in toxemia of pregnancy and renal insufficiency

**Desamino-oxytocin:-**

-Buccal formulation of oxytocin

-Action is similar to oxytocin

Indications

-Induction of labor:-50 IU buccal tabs , every 30 min ,max 10 tabs.

-uterine inertia:-25 IU , every 30mis , 5times for 7days

-Breast engorgement:-25-50IU

-It is also preferred in hypertensive women in which ergometrine is contraindicated

**ERGOMETRINE, METHYLERGOMETRINE**

Ergometrine (ergonovine), methylergometrine

Both have similar pharmacological property.

1-Uterus:

-They increase force, frequency and duration of uterine contractions.

-Gravid uterus is more sensitive, Their stimulant action involves the lower segment also.

-partial agonistic action on 5-HT2 and α adrenergic receptors.

2-Are much weaker vasoconstrictors than ergotamine.

3-High doses produce complex actions

◦Partial agonistic/antagonistic interaction with adrenergic, serotonergic and dopaminergic receptors in the brain

4-High doses can increase peristalsis

Pharmacokinetics

-Rapidly and nearly completely absorbed from the oral route.

- Available oral, i.m, i.v.

-They are partly metabolized in liver

-Excreted in urine.

-Plasma t½ is 1–2 hours.effects of a single dose last 3–4 hours

Adverse effects

-Less toxic than ergotamine

-Nausea, vomiting and rise in BP occur occasionally

-Inhibition of prolactin release (dopaminergic action).

**Ergometrine should be avoided in**

1-patients with vascular disease, hypertension, toxemia.

2-presence of sepsis-may cause gangrene.

3-liver and kidney disease.

They are contraindicated during pregnancy and before 3$^{rd}$ stage of labor

Use

1-To control and prevent postpartum hemorrhage (PPH):

-If PPH is occurring-0.5 mg i.v. is recommended.

-A combination of 0.5 mg ergometrine with oxytocin 5 IU i.m./i.v. may be used in severe bleeding

2.After caesarean section and instrumental delivery to prevent uterine atony.

3-Diagnosis of variant angina: A small dose of ergometrine injected i.v. during coronary angiography causes prompt constriction of reactive segments of coronary artery that are responsible for variant angina.

**Prostaglandins**

- Local Hormones, derived from breakdown of membrane phospholipid (yielding arachidonic acid)
- PGE2 and PGF2α: commonly used clinically
- Dinoprostone (PGE2): cervical maturation and ripening
- 5 times potent than and less toxic than PGF2α
- Dinoprost trone thammine (PGF2α): promotes myometrial contraction irrespective of duration of gestation
- Change in myometrial cell membrane permeability and alteration of membrane bound Ca++.
- Also sensitizes uterus to oxytocin

**Uses:**

- **Misoprostol or PGE1**:
- Induction of labor poor pre-induction as in Intrauterine Fetal Death, shorter period of gestation, prim gravida.
- Acceleration of labor
- Cervical ripening for induction of labor or abortion
- Management of atonic postpartum hemorrhage
- Medical management of tubal ectopic pregnancy

**Side effects:**

- On systemic use:

Nausea, vomiting, diarrhea, pyrexia, bronchospasm

- Cervical laceration when used as an abortifacient
- Tachysystole of uterus during induction
- Fetal Distress
- Rupture of uterus: Rare
- **Should not be used in patients with previous history of Caesarean Section**

UTERINE RELAXANTS (Tocolytics)

These are drugs which decrease uterine motility.

They have been used to delay or postpone labor, arrest threatened abortion and in dysmenorrhea

Contraindications:

- Membranes have ruptured,
- Antepartum hemorrhage is occurring,
- In severe toxemia of pregnancy,
- Intrauterine infection or fetal death

- Adrenergic (β2) agonist: Ritodrine, Isoxsuprine, Terbutaline, Salbutamol
- Calcium channel blockers: Nifedipine
- Oxytocin Antagonist: Atosiban
- Magnesium sulfate ($MgSO_4$)
- Miscellaneous: Ethyl alcohol, nitrates, progesterone, general anaesthetics, indomethacin, Halothane

**Ritodrine**

Mechanism of action: acts as selective β2 agonist on uterus & causes uterine relaxation

-Use:-Suppress premature labor , Delay delivery

-Started as 50 μg/min i.v. infusion, increased gradually

-Side Effects: hypotension, tachycardia, arrhythmia, metabolic complications (hyperglycemia, hypokalemia) ,anxiety, fetal pulmonary edema

-Contraindication: Mother having diabetes or heart disease, or receiving β blockers or steroids

**Nifedipine**

- Mechanism of Action: Nifedipine is L-type Ca++ Channel Blocker. It Reduces the tone of myometrium and opposes contraction. It has prominent smooth muscle relaxant action.
- Uses: Postpone labor
- Oral nifedipine 10 mg repeated once or twice after 20–30 min, followed by 10 mg 6 hourly has been used.
- Side Effects:
- Maternal - Tachycardia, Hypotension
- Fetal – Fetal Hypoxia due to placental perfusion

# Thank you