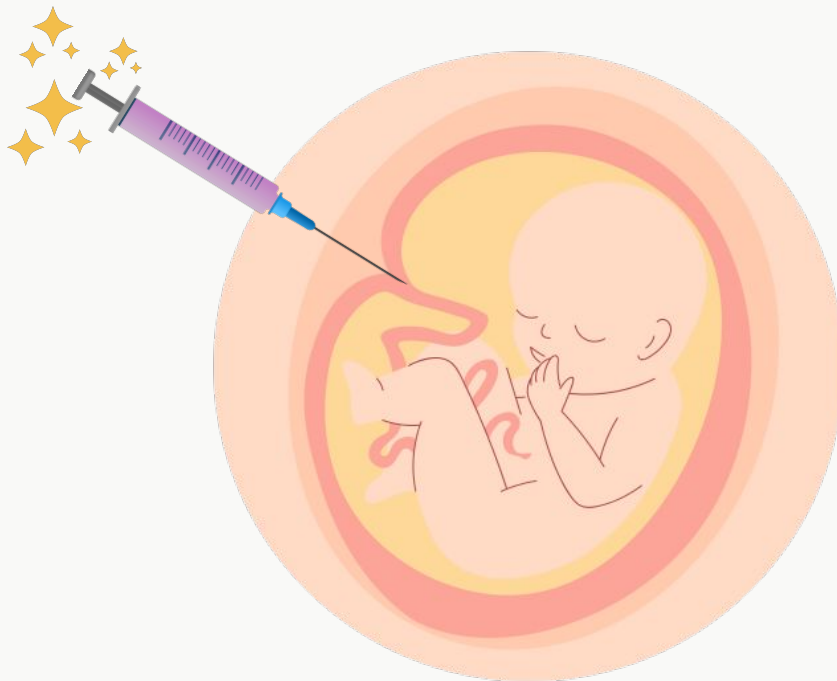




Tocolytics and oxytocin

Dr. Alia Alshanwani | Dr. Mohammed Almutairi



- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

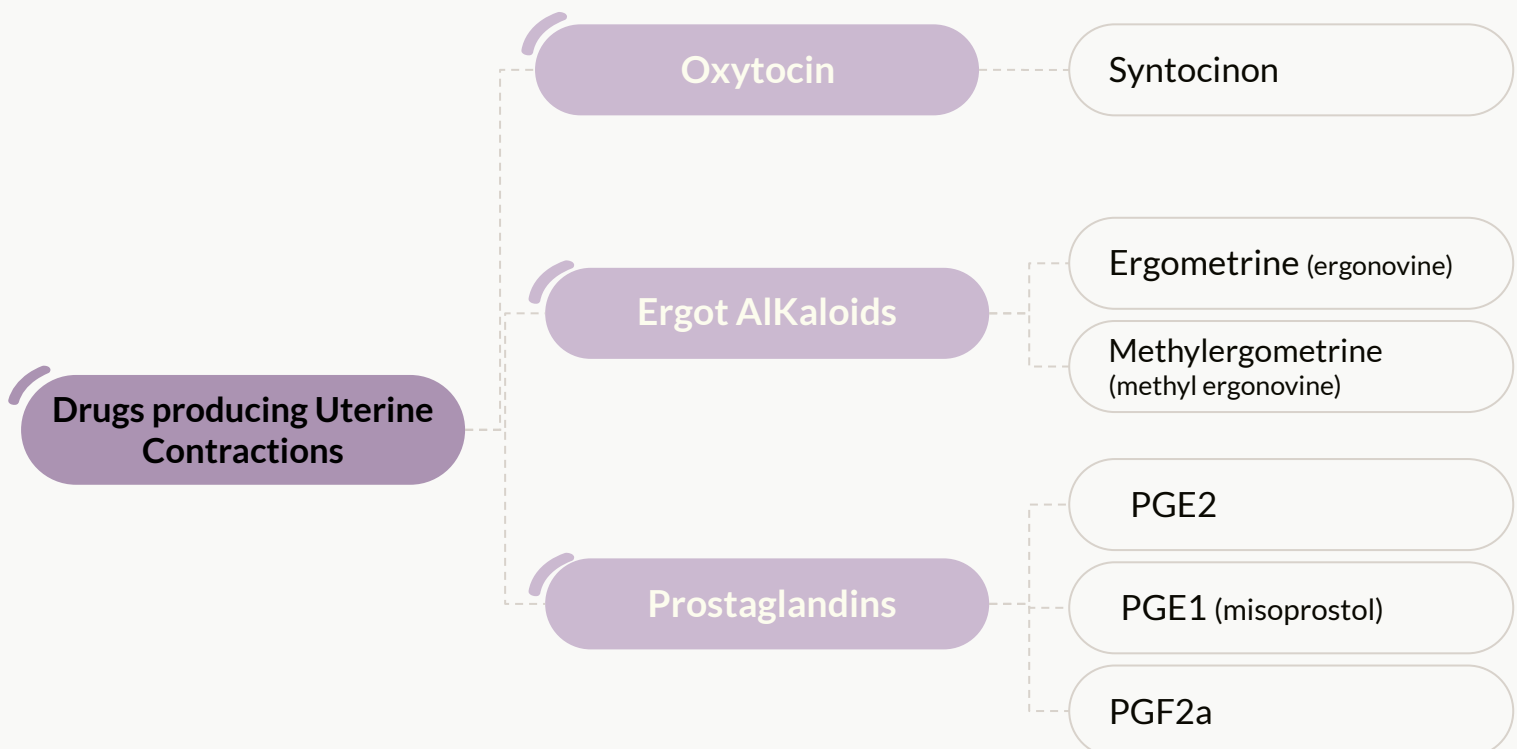
EDITING FILE

Objective

- Drugs used to induce & augment labor.
- Drugs used to control postpartum hemorrhage.
- Drugs used to induce pathological abortion.
- Drugs used to arrest premature labor.
- The mechanism of action and adverse effects of each drug.



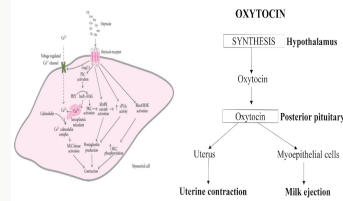
Oxytocics:



Oxytocin (Syntocinon)

M.O.A

- The interaction of endogenous or administered oxytocin with **myometrial cell membrane receptor promotes the influx of Ca^{2+}** from extracellular fluid and from sarcoplasmic reticulum into the cell: \uparrow in cytoplasmic calcium \rightarrow **stimulates uterine contraction**



Actions

1. Effect on uterus:

- **Stimulates** both the **frequency and force** of uterine contractility particularly of the **fundus** segment of the uterus.
- These contractions resemble the **normal physiological contractions of uterus (contractions followed by relaxation** "coordinated")
- **Immature** uterus is **resistant** to oxytocin.
- Contract uterine smooth muscle **only at term**
 - Sensitivity **increases** to 8 fold in **last 9 weeks** and 30 times in **early labor** (term specific)
 - Clinically oxytocin is **given** only when uterine **cervix is soft and dilated** (ready for delivery)

2. Effect on Myoepithelial cells: Oxytocin contracts myoepithelial cells surrounding mammary alveoli in the breast & leads to milk ejection.

P.K.

- **Not effective orally (destroyed in GIT)**
- Administered **I.V. to augment labor** or as **nasal spray** in impaired milk ejection
- Not bound to plasma proteins
- **Catabolized by liver & kidneys**
- $T_{1/2} = 5$ min **very short (disadvantage)**

Uses

Synthetic preparations of oxytocin (e.g. syntocinon) are preferred.

1. Induction & augmentation of labor (slow I.V infusion):

- Mild **preeclampsia** near term
- Uterine inertia (inefficient contractions)
- Incomplete abortion
- Post maturity (late delivery)
- Maternal diabetes (can lead to preeclampsia)

2. Postpartum uterine hemorrhage (IV drip): but **ergometrine is often used (1stline)**

3. Impaired milk ejection (one puff in each nostril 2-3 min before nursing) **fast onset of action**

ADRs

- **Maternal death due to hypertension**
- Uterine rupture
- **Fetal death (ischemia)**
- **Water intoxication:** if oxytocin is given with relatively large volumes of electrolyte-free aqueous fluid intravenously (antidiuretic effect)

#

- Hypersensitivity
- Cephalopelvic disproportion (head of fetus larger than pelvis)
- Prematurity
- Incompletely dilated cervix (must be soft and dilated)
- Abnormal fetal position
- Evidence of fetal distress

Pre-cautions

- Multiple pregnancy
- previous C-section
- Hypertension

Ergot Alkaloids

| Drug | Natural: Ergometrine (Ergonovine) | Synthetic: Methylergometrine (Methylergonovine) |
|--------|---|---|
| M.O.A. | <ul style="list-style-type: none"> Ergot alkaloids induce Tetanic contraction of uterus without relaxation in between (not like normal physiological contractions) <small>tetanic = continuous</small> It causes contractions of uterus as a whole i.e. fundus and cervix (tend to compress rather than to expel the fetus) | |
| P.K. | <ul style="list-style-type: none"> Usually given I.M Extensively metabolized in liver (90% of metabolites are excreted in bile) | <p><u>Preparations:</u> Syntometrine (ergometrine 0.5 mg + oxytocin 5.0 I.U), I.M. "for postpartum hemorrhage"</p> |
| Uses | Postpartum hemorrhage (3 rd stage of labor) | |
| ADRs | <ul style="list-style-type: none"> NVD (<u>N</u>ausea, <u>V</u>omiting, <u>D</u>iarrhea) Hypertension | <ul style="list-style-type: none"> Vasoconstriction of peripheral blood vessels (toes & fingers) → Gangrene |
| # | <p>Induction of labor:</p> <p>a) 1st and 2nd stages of labor b) vascular disease</p> | <p>c) Severe hepatic and renal impairment d) Severe hypertension</p> |

Prostaglandins

| Drug | PGE ₂ Dinoprostone | PGE ₂ α Dinoprost, Carboprost | Synthetic PGE ₁ Misoprostol | |
|----------------|--|--|--|---|
| Administration | <ul style="list-style-type: none"> Vaginal suppository Extra-amniotic solution | Intra-amniotic injection | - | |
| Uses | <ul style="list-style-type: none"> Induction of abortion (<i>pathological</i>) in cases of fetal deformity Induction of labor (fetal death in utero) Postpartum hemorrhage | | | |
| ADRs | <ul style="list-style-type: none"> NVD (<u>N</u>ausea, <u>V</u>omiting, <u>D</u>iarrhea) Abdominal pain | | | |
| | Flushing <small>vasodilation of tissues</small> | Bronchospasm | - | |
| # | <ul style="list-style-type: none"> Mechanical obstruction of delivery Predisposition to uterine rupture Fetal distress | | | |
| caution | <ul style="list-style-type: none"> Multiple pregnancy | <ul style="list-style-type: none"> Glaucoma | <ul style="list-style-type: none"> Asthma | <ul style="list-style-type: none"> Uterine rupture |

Oxytocics Comparison

| group | Oxytocin | Ergometrine | Prostaglandins |
|-----------------------------|---|--|--|
| Contractions | <ul style="list-style-type: none"> ● Coordinated contractions that resemble normal physiological contractions ● Only at term | <p>Tetanic contractions; doesn't resemble normal physiological contractions</p> | <ul style="list-style-type: none"> ● Coordinated contractions ● Throughout pregnancy |
| Cervix | Does not soften the cervix | - | soften/relax the cervix |
| Onset & duration | <ul style="list-style-type: none"> ● Rapid onset ● Shorter duration of action | <ul style="list-style-type: none"> ● Moderate onset ● Longer duration of action (compared to oxytocin) | Longer duration of action (compared to oxytocin) |
| Uses | <ul style="list-style-type: none"> ● To induce & augment labor ● Postpartum hemorrhage | Only in postpartum hemorrhage | <ul style="list-style-type: none"> ● Induce abortion in 2nd trimester of pregnancy. ● Used as vaginal suppository for labor induction |

Tocolytics

Drugs Producing Uterine Relaxation

| Drug | Ritodrine (β adrenoceptor agonists) | Nifedipine (Ca channel blockers) | Atosiban oxytocin antagonist (New tocolytic agent) |
|---------------|---|--|---|
| M.O.A. | <p>Selective β_2 receptor agonist used specifically as a uterine relaxant : bind to β-adrenoceptors, activate enzyme Adenylate cyclase \rightarrow \uparrow cAMP \rightarrow \downarrow intracellular calcium level \rightarrow relaxation of uterine smooth muscle</p> | <ul style="list-style-type: none"> ● Causes relaxation of myometrium ● Markedly inhibits the amplitude of spontaneous and oxytocin-induced contractions | <p>Compete with oxytocin at its receptors on the uterus.</p> |
| P.K. | IV drip | - | Given by IV infusion for 48 hrs |
| Uses | Relax the uterus and arrest threatened abortion or delay premature labor . | | |
| ADRs | <ul style="list-style-type: none"> ● Tachycardia (high dose) act on β_1 ● Flushing ● Tremor ● Nausea, vomiting ● Sweating ● Hypotension ● Hyperglycemia ● Hypokalemia | <ul style="list-style-type: none"> ● Tachycardia ● Hypotension ● Flushing ● Headache, dizziness ● Constipation ● Ankle edema ● Coughing ● Wheezing | - |

Team leaders

Sarah Alajaji

Maryam Alghannam

Team members

Sarah Aldossary

Sultan Almishrafi

Lama Hazzaa

Omar Banjar

Aroub Almahmoud

Fatimah Alghamdi

Layan Al-Ruwaili

Naif Alateeq

Mohammed Alhudaithi

Rahaf Alslimah

Mansour Alotaibi

Wasan Alanazi

Lama Alotaibi

Sultan Albaqami



Ghaida Aldossary



Fahad Aldhafian

Zeyad Alotaibi

Alanoud Alolaywah

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