



DRUGS ACTING ON UTERUS

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Uterine contractions

- Uterine smooth muscle is characterized by high level of spontaneous contractile activity.
- It is innervated by autonomic nervous system
- Uterine contractions are muscle contractions of the uterine smooth muscle that occur during the menstrual cycle and labor, during ovulation and during pregnancy.

Drugs affecting uterus

Stimulatory

- Muscarinic agonists
- Alph_1 - Adrenoceptor agonists
- Oxytocin
- PGE_2 or $\text{PGF}_{2\alpha}$
- 5-HT_2 agonists

Inhibitory

- B_2 - adrenoceptor agonists
- Calcium channel blockers

The main drugs used *clinically* to increase uterine motility and contractility include **Oxytocin**, **PGs**, and **Ergot derivatives** (Ergonovine)

1. **Oxytocin (Pitocin, Syntocinon) :**

Oxytocin and vasopressin are nonapeptide hormones, synthesized in hypothalamus, then transported to posterior pituitary where they are stored and released.

Actions of oxytocin include :

1. **Oxytocin causes contraction of myoepithelial cells surrounding secretory alveoli of breast leading to milk ejection in lactating females.**

2. In pharmacological doses, it induces intermittent uterine contractions, and maintains labor; but at physiological blood levels, reaches peak during pushing phase of labor and it contributes to initiation of parturition.

These contractions can be inhibited by B_2 -adrenoceptor agonists or by general anesthetics.

3. Oxytocin has weak antidiuretic or pressor activity.

PKs of oxytocin

- It is not given orally since it is destroyed by proteolytic enzymes stomach, and intestine (trypsin and chymotrypsin).
- It is not bound to plasma proteins
- Eliminated by liver and kidney (plasma $t_{\frac{1}{2}} \sim 5$ min).

Therapeutic uses :

Induction of labor given by IV infusion in:

1- Conditions requiring early vaginal delivery at 37-38 weeks: maternal diabetes, pre-eclampsia, Rh-isoimmunization

2- Delayed onset of labor at term: post-maturity

3- Primary uterine inertia, and to enhance uterine contractions in incomplete abortion and full-term labor

4- Control of post-partum hemorrhage (PPH):
(by IV infusion or IM injection with ergonovine)

5- To induce milk let-down after labor: by nasal spray.

N.B. Clinically oxytocin is given only when uterine cervix is soft and dilated

Adverse effects: rare with proper supervision.

1- With large IV infusion doses, tetanic uterine contractions can occur which obstructs intramural uterine blood flow causing

- fetal distress or death.
- Uterine rupture may occur esp. with obstructed labor.

2- with large doses , blood pressure increases due to vasoconstriction

3- Water intoxication can rarely occur due to large volume of IV infused fluid.

4- Increased incidence of neonatal jaundice due to increased osmotic fragility of RBC

Contra-indications:

1- Fetal distress.

2- Prematurity of fetus.

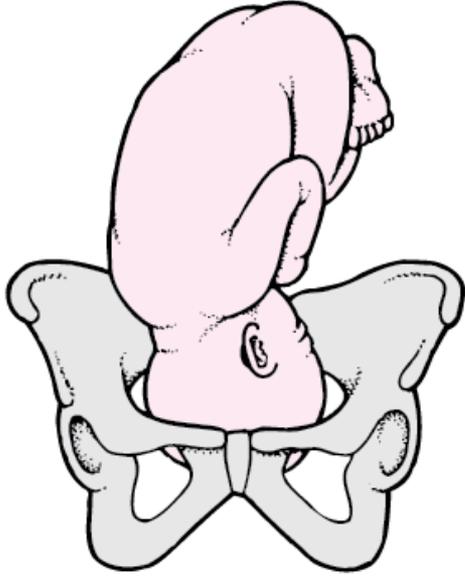
3- Fetal malpresentation e.g. breech presentation & Cephalopelvic disproportion i.e. contracted pelvis: both predispose to uterine rupture.

4- Prolapse of umbilical cord following rupture of fetal membranes.

Precautions

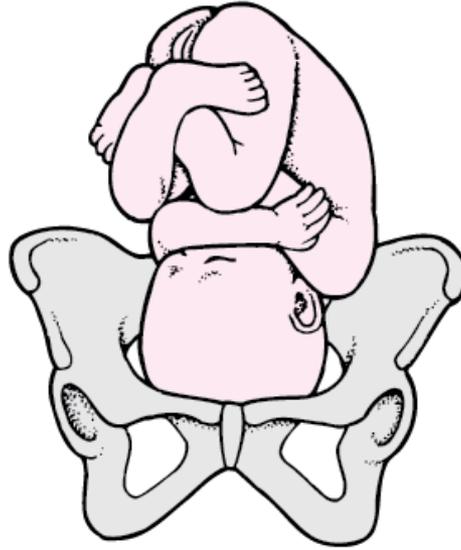
- a) Multiple pregnancy
- b) Previous c- section
- c) Hypertension

Facing Backward
Head First



Normal Position and
Presentation

Facing Forward



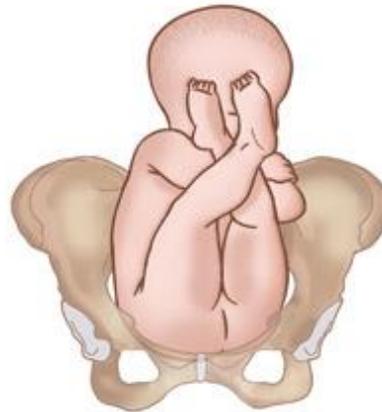
Abnormal
Position

Frank Breech



Complete Breech

Footling Breech



2. Ergonovine (Ergometrine) and methylergonovine

- more selective than other ergot alkaloids in stimulating the uterus and is the ergot alkaloid of choice in obstetrics.

Its effect on uterine muscle is the result of powerful direct action, and possibly other actions (5-HT₂ + alpha₁-adrenoceptor agonist actions).

It helps to prevent postpartum hemorrhage by causing powerful, sustained uterine contraction.

It is given IV or IM at time of delivery of placenta or after delivery of fetus but never before.

S.Es : Increased B.P

C/Is : 1- Hypertension as in pre-eclampsia
2- Peripheral vascular disease
3- Angina

3. Prostaglandins (PGs):

PGE2 (Dinoprostone): It is commonly used vaginal.

A. To stimulate uterine contractions for:

Induction of labor given as vaginal gel or insert

Note: If oxytocin is needed for induction of labor, it is given after 6 h have passed after PG use to avoid excessive uterine contractions.

Induction of abortion: vaginal suppository is used.

B. For softening the cervix at term: This shortens time to onset of labor and labor time.

PGE2 directly affects collagenase of cervix that breaks down the collagen network and softens it.

Gemeprost: PGE1 analogue

- used as vaginal suppository to induce early medical abortion during first trimester or late abortion.

Misoprostol , oral or vaginal supp. may also be used.

PGF_{2α} (Dinoprost) : less commonly used

May be given vaginally, intra-amniotically, or

IV

for induction of abortion in second trimester.

Intra-amniotic PGF_{2α} has up to 100% success rate with fewer and less severe S.Es than IV

PGF_{2α} causes more G.I. side effects (vomiting, diarrhea) than PGE₂.

Difference B/w Oxytocin and Prostaglandins

Character	Oxytocin	Prostaglandins
Contraction	Only at term	Contraction through out pregnancy
Cervix	Does not soften the cervix	soften the cervix

Difference (cont'd)

Character	Oxytocin	Prostaglandins
Duration of action	Shorter	Longer
Uses	Induce and augment labour and post partum hemorrhage	Induce abortion Used as vaginal suppository for induction of labor

Difference b/w Oxytocin and Ergometrine

Character	Oxytocin	Ergometrine
Contractions	Resembles normal physiological contractions	Tetanic contraction ; doesn't resemble normal physiological contractions
Uses	To induce & augment labor. *Post partum hemorrhage	Only in p.partum hemorrhage
Onset and Duration	Rapid onset Shorter duration of action	Moderate onset Long duration of action

Tocolytics

◦ Drugs that inhibit uterine contractions

Indications:

Delay, inhibit or prevent premature labor (< 36 weeks of pregnancy).

Usually, regular uterine contractions can stabilize on bed rest & local warmth. When this is insufficient, then a tocolytic drug is used.

N.B. Betamethasone is given IV to mother or into cord blood to stimulate maturation of fetal lung (by enhancing surfactant formation); it is preferred to dexamethasone because it is bound less to plasma proteins.

1. B₂ - adrenoceptor agonists :

- Ritodrine, Terbutaline, salbutamol
(oral or IV infusion in 5% dextrose)

S.Es: Tachycardia and increased cardiac output,
Sometimes acute left ventricular failure in mother
occurs
due to overload of infusion fluid and marked
tachycardia.

Other side effects are: Decreased plasma K and
Hyperglycemia

2. Calcium channel blocker :

The short acting Nifedipine or Nicardipine are
commonly used oral at present. Can lower BP.

3- Atosiban:

- analogue of oxytocin that act as competitive antagonist, inhibiting oxytocin binding to its receptor.
- Given IV

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THANK YOU