01-oxytocics & tocolytics

DRUGS PRODUCING UTERINE CONTRACTIONS (oxytocics)

Drug	Uses	MOA	Pharmacokinetics	ADRs & contraindication
1-Oxytocin(Pitocin® / Syntocinon®) -Oxytocin is synthesized in hypothalamus, then stored & released from posterior pituitary gland. -At term, the uterus is highly sensitive to oxytocin. -Oxytocin stimulates both the frequency & amplitude (force) of uterine contractility (both are related to the dose) -These events are highly dependent on estrogen & antagonized by progesterone -Oxytocin causes regular coordinated contractions that resemble the normal physiological contractions of uterus that travel from fundus to cervix. Then contraction is followed by relaxation.	• drug of choice to induce or augment labor at term when the uterine muscle is not functioning adequately and only when uterine cervix is soft & dilated. -Following incomplete abortion (but PGs are preferred). • In Induction of labor in cases of: - Intrauterine growth retardation - Placental insufficiency as in (diabetes, pre - eclampsia) - Uterine inertia - Incomplete abortion - Post maturity. Dosage : Slow I.V infusion 1-2 mU /min then gradually. - increase the dose to 5-30 mU/min. • Postpartum uterine hemorrhage Given slow I.V injection 5 units followed by I.V infusion of 5-200 in severe cases.(ergometrine is often used) • Impaired milk ejection: One puff in each nostril 2-3 min before nursing. (Taken in the form of Nasal spray)	-The interaction of endogenous or administered oxytocin, with myometrial cell membrane oxytocin receptor promotes : -influx of Ca2 + from extra cellular fluid & from S.R in to the cell , -This increase in cytoplasmic Ca2+, stimulates uterine contraction by activation of MLCK. *Other actions of oxytocin: -Oxytocin contracts myoepithelial cells in the mammary gland ⟶ breast feeding, (Letdown /milk ejection) -Weak antidiuretic action.	▪Not absorbed orally ▪Administered by i.v, i.m, & most often given by i.v. infusion to induce labor. ▪Not bound to plasma proteins ▪tl/2: 5- 15 minutes ▪Metabolized in liver & kidney	-Maternal death (Due to HTN) -Uterine rupture -Fetal death -Water intoxication (weak anti-diuretic effect) & hyponatremia -Hypertension (due to water retention) -Allergic reactions. Overdose: Rupture of the uterus, fetal distress, & maternal injury. **Contraindications:** - Hypersensitivity - Prematurity -Abnormal positioning of the fetus - Cephalopelvic disproportion - Incompletely dilated cervix. **Precautions:** • Monitor mother & fetus, because over stimulation interferes with blood flow thru the placenta & causes fetal distress/ death. • previous uterine surgery (C-section) • Multiple pregnancy • Hypertension
2-ERGOT ALKALOIDS • Ergometrine (Ergonovine) • Dihydroergotamine • Methylergonovine • Alkaloid derivatives induce TETANIC CONTRACTION of uterus without relaxing in between; NOT like the normal physiological contractions. • It causes contractions of uterus as a whole i.e. fundus & cervix (Tend to compress rather than expel).	▪Post partum hemorrhage (3rd stage labor) ▪Administered immediately postpartum to obtain marked uterine response. Preparation: Syntometrine (ergometrine 0.5 mg + oxytocin 5.0 I.U, IM).		Rapid oral absorption (tablet) Both ergonovine & methylergonovine can be given im / iv. Duration of action 24 hrs with half life: 2hrs Metabolized extensively in liver 90% metabolites are excreted in bile.	-Nausea, vomiting & diarrhea (ergots has an effect on D2 receptors in chemoreceptor trigger zone) -Hypertension -Vasoconstriction of peripheral blood vessels (toes & fingers) -Gangrene -Headache. Contraindications: -1st and 2nd stage of labor - Induction of labor -vascular disease, HTN, toxemia - Impaired hepatic functions.

3-PROSTAGLANDIS	1) Oxytocic use for inducing abortion, missed abortion, repining of cervix (the cervix softens and becomes more distensible) -Stimulate uterine contraction in the 2nd trimester of pregnancy, administered IV, extra amniotic & vaginal. Initiation to abortion time is 12 to 23 hours -For softening of the cervix at term single vaginal insert or jell is administered every 6 hours. 2) For induction & augmentation of labor (In case of fetal death in the uterus) administered as vaginal tablets & vaginal jell, or as controlled release formulation. 3) in post-partum hemorrhage It is administered by I.V infusion.	Endogenous: -They are significantly synthesized in endometrium & myometrium -They cause contraction of both the non-pregnant & pregnant uterus, but sensitivity increases with gestation. -They play a significant role in dysmenorrheal (painful mensturation) & Menorrhagia (excessive blood loss). Exogenous: Dinoprostone (PGE2) & Carboprost (PGF2) -They promote a series of coordinated contraction of body of uterus along with relaxation of cervix -Increase uterine tone -Can expel uterine content in early pregnancy. -PGS contract uterine smooth muscle not only at term (as with oxytocin), but throughout pregnancy. -PGS soften the cervix; whereas oxytocin does not. -PGS have longer duration of action than oxytocin	- Nausea , vomiting & diarrhea - Abdominal pain - Bronchospasm (PGF2α effect) - Flushing. (PGE2) **Contraindications:** a)Mechanical obstruction to delivery (Cephalopelvic disproportion, abnormal pelvis) in this case a C-section is preformed. b)Fetal distress (The term fetal distress is commonly used to describe fetal hypoxia, which can result in fetal damage or death if it is not reversed or if the fetus is not promptly delivered.) c)Predisposition to uterine rupture **Precautions:** a)Asthma b)Multiple pregnancy c)Uterine rupture d)Glaucoma (PGEs increase intraocular pressure)
(Tocolytic Drugs)			
1.β-ADRENOCEPTOR AGONISTS E.g. Ritodrine & terbutaline	To prevent Premature labor (To delay labour) I.v infusion 50μg/min	-Bind to β-adrenoceptors , activate enzyme Adenylate cyclase , increase in the level of cAMP reducing intracellular calcium level, thus reducing the level of sensitivity of actin myosin contractile unit.	-Sweating ,Tachycardia (high dose),Hypotension, Hyperglycemia, Hypokalaemia, Tremor, Nausea , vomiting, Flushing **Contraindications:** Heart disease, diabetes, patients on beta blockers.
2. CALCIUM CHANNEL BLOCKERS e.g., Nifedipine	To delay or prevent preterm labor	-Reduce Ca entry⟶ Reduced tone & Cause relaxation of myometrium -Markedly inhibits the amplitude of spontaneous & oxytocin-induced contractions.	Headache, dizziness, Hypotension , Flushing, Constipation, Ankle edema, Coughing.
3. Prostaglandin synthesis inhibitors e.g. Aspirin, indomethacin, ibuprofen	The depletion of prostaglandins prevents stimulation of uterus	Administration: Given orally /rectally.	-ulceration - premature closure of ductus arterious.

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Oxytocin causes regular coordinated contractions that resemble the normal physiological contractions of uterus that travel from fundus to cervix.

- **contracts myoepithelial cells** in the mammary gland and have a **Weak antidiuretic** action.

- Administered by i.**v, i.m, & most often given by i.v.** infusion **to induce labor.**
- **Considered the drug of choice to induce or augment labor at term when the uterine muscle is not functioning adequately, but the cervix must be soft and dilated.**

- Taken in the form of Nasal spray in case of Impaired milk ejection:
- **ADRs include:** Maternal death ,Uterine rupture ,Fetal death,Water intoxication & hyponatremia ,Hypertension ,Allergic reactions.
- **Contraindicated** in case of Abnormal positioning of the fetus, Cephalopelvic disproportion, or incompletely dilated cervix.

Ergots (Ergometrine (Ergonovine),Dihydroergotamine ,and Methylergonovine)

- **induce** TETANIC CONTRACTION of uterus without relaxing in between.
- **They are used in Postpartum hemorrhage (3rd stage labor)**
- **Syntometrine (ergometrine 0.5 mg + oxytocin 5.0 I.U, IM) preparation has** The advantage of a rapid effect (Oxytocin), and an effect of long duration (ergometrine).
- **ADRs include:** Nausea, vomiting & diarrhea ,Hypertension ,Vasoconstriction of peripheral blood vessels (toes & fingers)
- **ergots are not used if the fetus is still in the uterus**

PROSTAGLANDIS(Dinoprostone (PGE_2) & Carboprost (PGF_2)

- promote a series of coordinated contraction of body of uterus along with relaxation of cervix
- PGS soften the cervix; whereas oxytocin does not.
- PGS have longer duration of action than oxytocin.

It is used for:

- **softening of the cervix at term**
- **For induction & augmentation of labor (In case of fetal death in the uterus)**

Tocolytics are used to To delay or prevent preterm labor. They include:

1.β-ADRENOCEPTOR AGONISTSE.g. Ritodrine & terbutaline

2. CALCIUM CHANNEL BLOCKERS e.g., Nifedipine

3. Prostaglandin synthesis inhibitors (Aspirin, indomethacin, ibuprofen)