



Tocolytics and Oxytocin

Objectives:

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

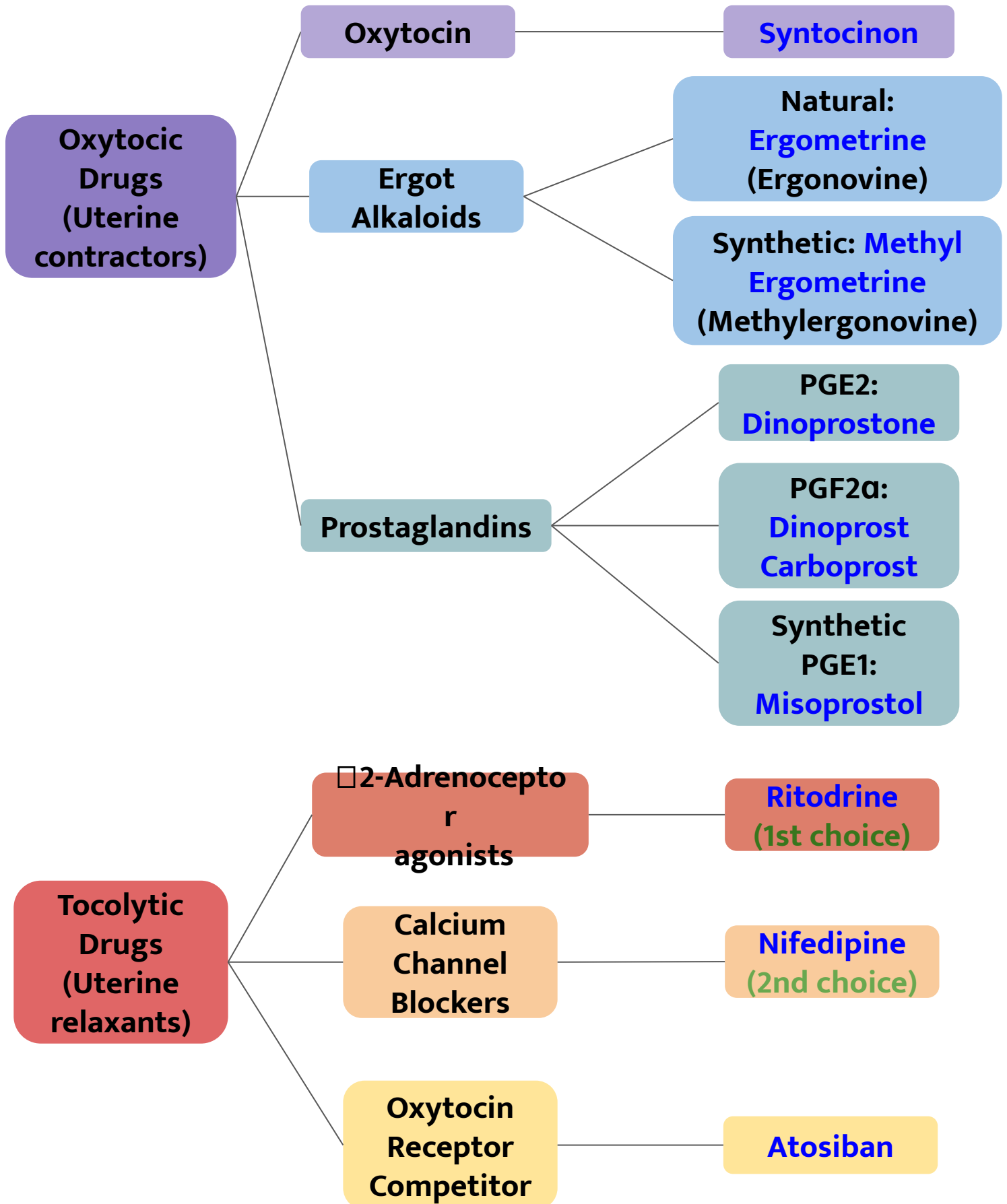
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Important Note Extra

ركز عليه الدكتور



Mindmap



Drugs Producing uterine contractions (oxytocics)

Oxytocin

Induce location

Syntocinon

Ergot alkaloids

Induce tetanic contraction

1.Natural:

Ergometrine

(Ergonovine)

2.Synthetic:

Methyl ergometrine

(Methylergonovine)

Prostaglandins

Contraction throughout pregnancy

1.PGE2:

Dinoprostone

2.PGF2α:

Dinoprost, Carboprost

3.synthetic PGE1:

Misoprostol

Role of Oxytocin

Effect on Uterus

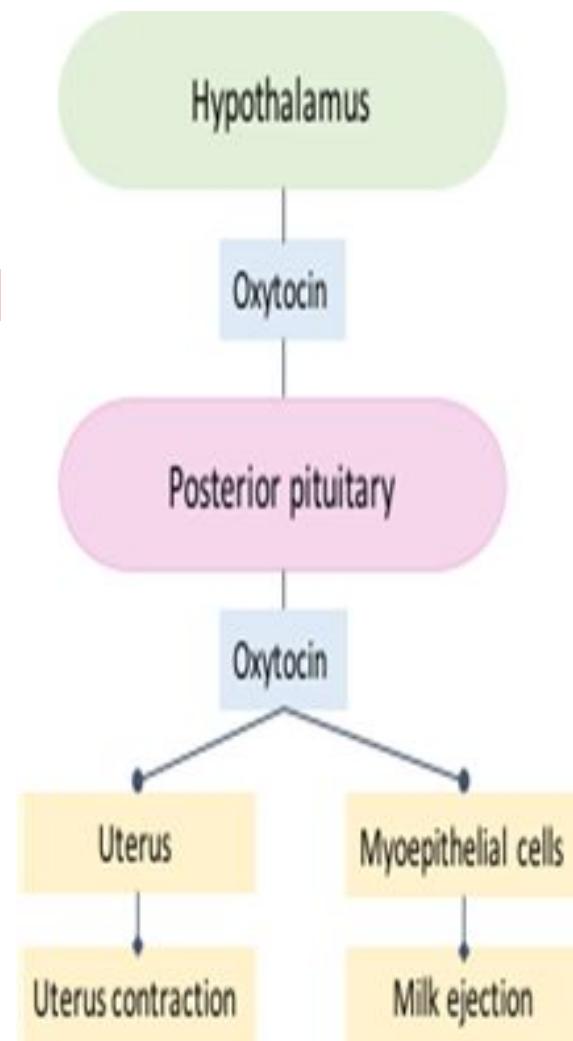
- ❖ Stimulates both the frequency and force of uterine contractility particularly of the **fundus segment** of the uterus.
- ❖ These contractions **resemble the normal physiological contractions of uterus (contractions followed by relaxation)**



- ❖ 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.
- ❖ Clinically oxytocin is given only when uterine cervix is soft and dilated. (Otherwise it might cause rupture)

Effect on Myoepithelial cells

- Oxytocin contracts myoepithelial cells surrounding mammary alveoli in the breast & leads to **milk ejection**.



Oxytocin e.g. Syntocinon

M.O.A

The binding of endogenous or administered oxytocin, with myometrial cell membrane receptor promotes the influx of Ca^{++} from extracellular fluid and from S.R into the cell, this increase in cytoplasmic calcium, stimulates uterine contraction.

P.K

- Not effective orally (destroyed in GIT)
- Administered I.V (augment labor) then we monitor its effect on the uterus
- Also as nasal spray (used in impaired milk ejection)
- Not bound to plasma proteins
- Catabolized by liver & kidneys
- Half life = 5 minutes

Indications

Synthetic preparations of oxytocin; e.g. syntocinon are preferred. (due to increased half life)

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

- Mild preeclampsia near term
- Uterine inertia
- Membranous rupture
- Incomplete abortion
- Post maturity
- Maternal diabetes

II. Postpartum uterine hemorrhage (I.V drip) (ergometrine is often used)

III. Impaired milk ejection One puff in each nostril 2-3 min before nursing (Intranasally)

ADR

Not very common

- **Uterine rupture (Most dangerous side effect)**
- Maternal death due to hypertension
- Fetal death (ischaemia)
- Water intoxication if it is given with relatively large volumes of electrolyte free aqueous fluid


C.I

- Hypersensitivity
- Prematurity
- Abnormal fetal position
- Evidence of fetal distress
- Cephalopelvic disproportion (head is too big for mothers pelvis)
- Incompletely dilated cervix

Precautions

- ❖ Multiple pregnancy
- ❖ Previous c-section
- ❖ Hypertension

Ergot Alkaloids

	Natural E.g. Ergometrine	Synthetics E.g. Methyl ergometrine
MOA	<ul style="list-style-type: none"> ❖ Ergot alkaloids induce TETANIC CONTRACTION of uterus without relaxation in between (not like normal physiological contractions)  <ul style="list-style-type: none"> ❖ It causes contractions of uterus as a whole i.e. fundus and cervix (tend to compress rather than to expel the fetus). SO WE DON'T GIVE IT DURING LABOR <p>Main differences between oxytocin & ergots?</p> <ol style="list-style-type: none"> Type of contraction: <ul style="list-style-type: none"> ● Oxytocin: contraction followed by relaxation ● Ergot: contraction without relaxation Place of contraction: <ul style="list-style-type: none"> ● Oxytocin: only fundus. ● Ergot: the whole uterus. 	
P.K	<ul style="list-style-type: none"> ❑ Usually given I.M (if we give IV they will cause powerful hypertension) ❑ Extensively metabolized in liver ❑ 90% of metabolites are excreted in bile 	
Uses	<ul style="list-style-type: none"> ❖ Postpartum hemorrhage (3rd stage of labor) DON'T inject until you see the head of the baby ❖ Preparations: Syntometrine (ergometrine 0.5 mg + oxytocin 5.0 I.U) , I.M. When to give it? After birth, 3rd stage of labor (Don't inject until see the shoulder or head) 	
ADRs	<ul style="list-style-type: none"> ➔ Vasoconstriction of peripheral blood vessels (toes & fingers) ➔ Gangrene (due to Vasoconstriction of peripheral blood vessels 'rare') ➔ Nausea, vomiting, diarrhea ➔ Hypertension (sever) ergometrin cause less hypertension compare to Methyl ergometrine 	
C.I	<ul style="list-style-type: none"> ➤ Induction of labor: 1st and 2nd stage of labor ➤ vascular disease ➤ Severe hepatic and renal impairment ➤ Severe hypertension 	

Oxytocin Vs Ergometrine

	Oxytocin	Ergometrine
Contractions	Resembles normal physiological contractions	Tetanic contraction, doesn't resemble normal physiological contractions (without relaxation in between and causes the contraction of the uterus as a whole)
Uses	<ul style="list-style-type: none"> To induce or augment labor. Postpartum hemorrhage 	only in Postpartum hemorrhage
Onset and Duration	<ul style="list-style-type: none"> Rapid onset Shorter duration of action 	Moderate onset, Longer duration of action

Prostaglandins

	PGE ₂ e.g. Dinoprostone	PGF ₂ α e.g. Dinoprost, Carboprost	synthetic PGE ₁ e.g. Misoprostol (can be combined with mifepristone)
Route of administration	<ul style="list-style-type: none"> ❑ Vaginal suppository ❑ Extra- amniotic solution (IV) 	Intra-amniotic injection (IV)	
Uses	<ul style="list-style-type: none"> ★ Induction of abortion (pathological) ★ Induction of labor (fetal death in utero) ★ Postpartum hemorrhage 		
ADRs	<ul style="list-style-type: none"> ➤ Bronchospasm (PGF₂α) ➤ Flushing of the face and chest (PGE₂) bc it causes vasodilatation ➤ Nausea , vomiting ➤ Abdominal pain ➤ Diarrhea 		

Cont'D

	PGE ₂ e.g. Dinoprostone	PGF ₂ α e.g. Dinoprost	synthetic PGE1 e.g. Misoprostol
C.I	<ul style="list-style-type: none"> ● Mechanical obstruction of delivery, e.g. placenta Previa or the umbilical cord surround the baby ● Fetal distress ● Predisposition to uterine rupture 		
Precautions	<ul style="list-style-type: none"> ➤ Asthma ➤ Multiple pregnancy ➤ Glaucoma (PG increase the formation of aqueous humor, so increase IOP) ➤ Uterine rupture 		
PG Vs. Oxytocin	<p>➔ <u>Contraction:</u> Oxytocin: Only at term Prostaglandin: Contraction throughout pregnancy (used for abortion)</p> <p>➔ <u>Cervix:</u> Oxytocin: Does not soften the cervix Prostaglandin: softens the cervix</p> <p>➔ <u>Duration of action:</u> Oxytocin: Shorter Prostaglandin: longer</p> <p>➔ <u>Uses:</u> Oxytocin: Induce and augment labor and postpartum hemorrhage Prostaglandin: Induce abortion in 2nd trimester of pregnancy, used as vaginal suppository for induction of labor and postpartum hemorrhage</p>		

Uterine Relaxants (tocolytic)

"It delay pregnancy"

β_2 -Adrenoceptor agonists

Ritodrine
(1st choice)

Calcium Channel Blockers

Nifedipine
(2nd choice)

Compete with oxytocin receptors

Atosiban

Action and uses

	Ritodrine	Nifedipine	Atosiban
Use	Relax the uterus and arrest threatened abortion or delay premature labor.		
M.O.A Very IMP	<ul style="list-style-type: none"> Selective β_2 receptor agonist used specifically as a uterine relaxant. Bind to β-adrenoceptors → activate enzyme Adenylate cyclase → increase in the level of cAMP → reducing intracellular calcium level. administered IV 	<ul style="list-style-type: none"> Markedly inhibits the amplitude of spontaneous and oxytocin-induced contractions Cause relaxation of myometrium 	<ul style="list-style-type: none"> Compete with Oxytocin at its receptors on the uterus New tocolytic agent May be less effective as tocolytic as beta 2 agonist Given by IV infusion for 48 hours
ADR's	<ul style="list-style-type: none"> ❖ Hyperglycemia ❖ Hypokalemia ❖ Tremor ❖ Nausea , vomiting ❖ Flushing ❖ Sweating ❖ Reflex Tachycardia (high dose) ❖ Hypotension 	<ul style="list-style-type: none"> ❖ Ankle edema ❖ Flushing ❖ Headache, dizziness ❖ Hypotension ❖ Constipation ❖ Coughing ❖ Wheezing ❖ Reflex tachycardia <p>Dizziness is due to gravity</p>	<ul style="list-style-type: none"> ● Doesn't have the cardiovascular side effects ● It is better tolerated than beta 2 agonist because of cardiovascular side effects and may be a useful alternative

Summary

1- Oxytocin (Syntocinon)

MOA	On uterus	Stimulates both the frequency and force of uterine contractility particularly of the fundus segment of the uterus and these contractions resemble the normal physiological contractions of uterus (contractions followed by relaxation). <ul style="list-style-type: none"> Contract uterine smooth muscle only at term. Clinically oxytocin is given only when uterine cervix is soft and dilated.
	On myoepithelial cells	Oxytocin contracts myoepithelial cells surrounding mammary alveoli in the breast & leads to milk ejection.
Uses	1. Induction & augmentation of labor (slow I.V infusion). syntocinon are preferred. 2. Post-partum uterine hemorrhage (I.V drip) . ergometrine is often used. 3. Impaired milk ejection . (One puff in each nostril 2-3 min before nursing)	

2- Ergot Alkaloids (Ergometrine, Methyl ergometrine)

MOA	Induce TETANIC CONTRACTION of uterus without relaxation in between (not like normal physiological contractions). It causes contractions of uterus as a whole i.e. fundus and cervix (tend to compress rather than to expel the fetus) Preparations: Syntometrine (ergometrine + oxytocin IM) give it after birth, 3rd stage of labor.
ADRs	1. Vasoconstriction of peripheral blood vessels 2. Gangrene 3. Hypertension

3- Prostaglandins

Drug	PGE2 (Dinoprostone)	PGF2α (Dinoprost, Carboprost)	Synthetic PGE1 (Misoprostol)
ADRs	1. Bronchospasm (PGF2α) 2. Flushing (PGE2) 3. Nausea, vomiting, diarrhea. 4. Abdominal pain		
Precautions	1. Asthma 2. Multiple pregnancy 3. Glaucoma 4. Uterine rupture		

Difference b/w Oxytocin, Ergometrine, and Prostaglandins

Character	Oxytocin	Ergometrine	Prostaglandins
Contractions	Only at term and it resembles normal Physiological contractions	Tetanic contraction ; doesn't resemble normal physiological contractions	Contraction throughout pregnancy
Cervix	Does not soften the cervix	-	Softens the cervix
Uses	Induce and augment labor and postpartum hemorrhage	Only in postpartum hemorrhage	Induce abortion in 2nd trimester of pregnancy and used for induction of labor

Drugs producing uterine relaxation (tocolytic drugs)

Types	1. β-adrenoceptor agonists: Ritodrine selective β2 receptor agonist used specifically as a uterine relaxant.	2. Calcium channel blockers: Nifedipine	3. Compete with oxytocin receptors: Atosiban (oxytocin receptors antagonist)
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Quiz

Q1: in case of impaired milk ejection which of the following we should use?

- A. Oxytocin I.V
- B. Oxytocin I.M
- C. Oxytocin nasal spray
- D. none of the above

Q2: which of the following is a contraindication of Oxytocin?

- A. Incompletely dilated cervix
- B. Abnormal fetal position
- C. Multiple pregnancy
- D. A&B

Q3: Oxytocin-induced uterine contraction resemble which one of the following?

- A. physiological contractions
- B. tonic contractions
- C. none of the above

Q4: oxytocin causes contraction of which parts of the uterus?

- A. fundus
- B. body
- C. A&B
- D. none of the above

Q5: Which of the following can be used to induce labor especially in diabetic pregnant and her cervix is soft and dilated ?

- A. IV Syntocinon.
- B. Nasal spray Atosiban.
- C. I.M methyl-ergometrine.
- D. Nasal spray oxytocin

Q6: which of the following is not a contraindication of Ergot Alkaloids

- A. Induction of labor: at the third stage
- B. vascular disease
- C. Severe hepatic and renal impairment
- D. Severe hypertension

Q7: which of the following is a property of Ergometrine

- A. It is used To induce or augment labor.
- B. only can be used in Postpartum hemorrhage
- C. Rapid onset of action
- D. Shorter duration of action than oxytocin

Answers:
1) C
2) D
3) A
4) A
5) A
6) A
7) B

Quiz

Q8: which one of these could be prescribed as an Intra-amniotic injection Prostaglandin for postpartum hemorrhage ?

- A. Dinoprostone
- B. Dinoprost
- C. Misoprostol
- D. none of the above

Q9: which of the following is a side effect of Ritodrine?

- A. Ankle edema
- B. Flushing
- C. Headache,
- D. Hypokalemia

Q9: which of the following Uterine Relaxants doesn't have any cardiovascular side effects ?

- A. Ritodrine
- B. Nifedipine
- C. Atosiban
- D. Dinoprost

Answers:
1) B
2) D
3) C



Team Leader:

**Abdullah
Alsergani**

**Alanoud
Salman**

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Abdulrahman Aloajan

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Abdullah Alomar

Abduljabbar alyamani

Notes by

Sultan AlNasser

References:

- Team 436
- Doctors notes and slides



@Pharma4370



Pharm437@gmail.com