Oxytocic & Tocolytic drugs

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Learning Outcomes

By the end of the lecture, the students will be able to:

- List different drugs used as oxytocic agents
- Describe mechanisms of action, indications and side effects of oxytocic drugs
- List different drugs used as tocolytic agents
- Describe mechanisms of action, indications and side effects of tocolytcic drugs

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Lecture outline

Oxytocics

- Mechanism of action
- Indications
- Side effects

Tocolytics

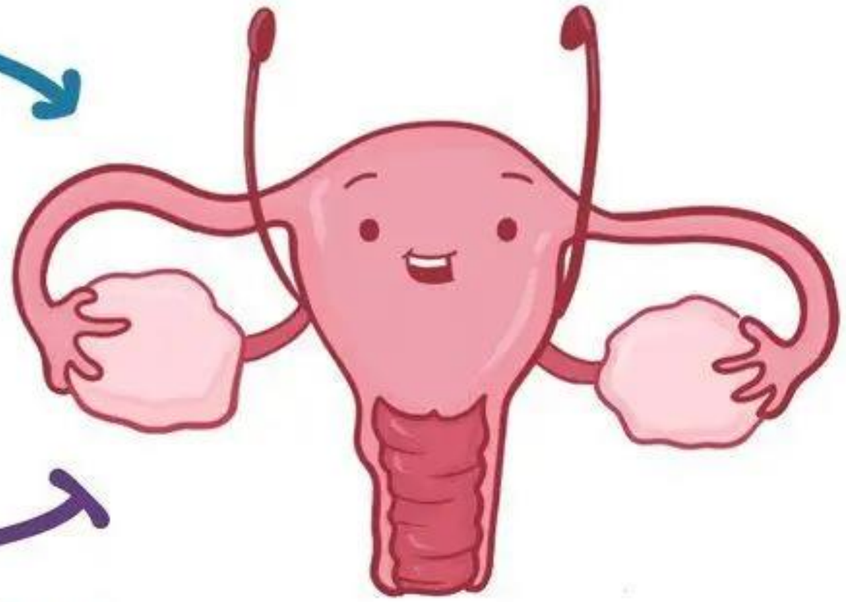
- Mechanism of action
- Indications
- Side effects

UTERINE STIMULANTS

INDUCE

"UTEROTONICS" - ↑ TONE of MUSCLES

- ~ INDUCE/FACILITATE LABOR
- ~ ↓ POSTPARTUM HEMORRHAGE
- ~ INDUCE ABORTION



UTERINE RELAXANTS

INHIBIT

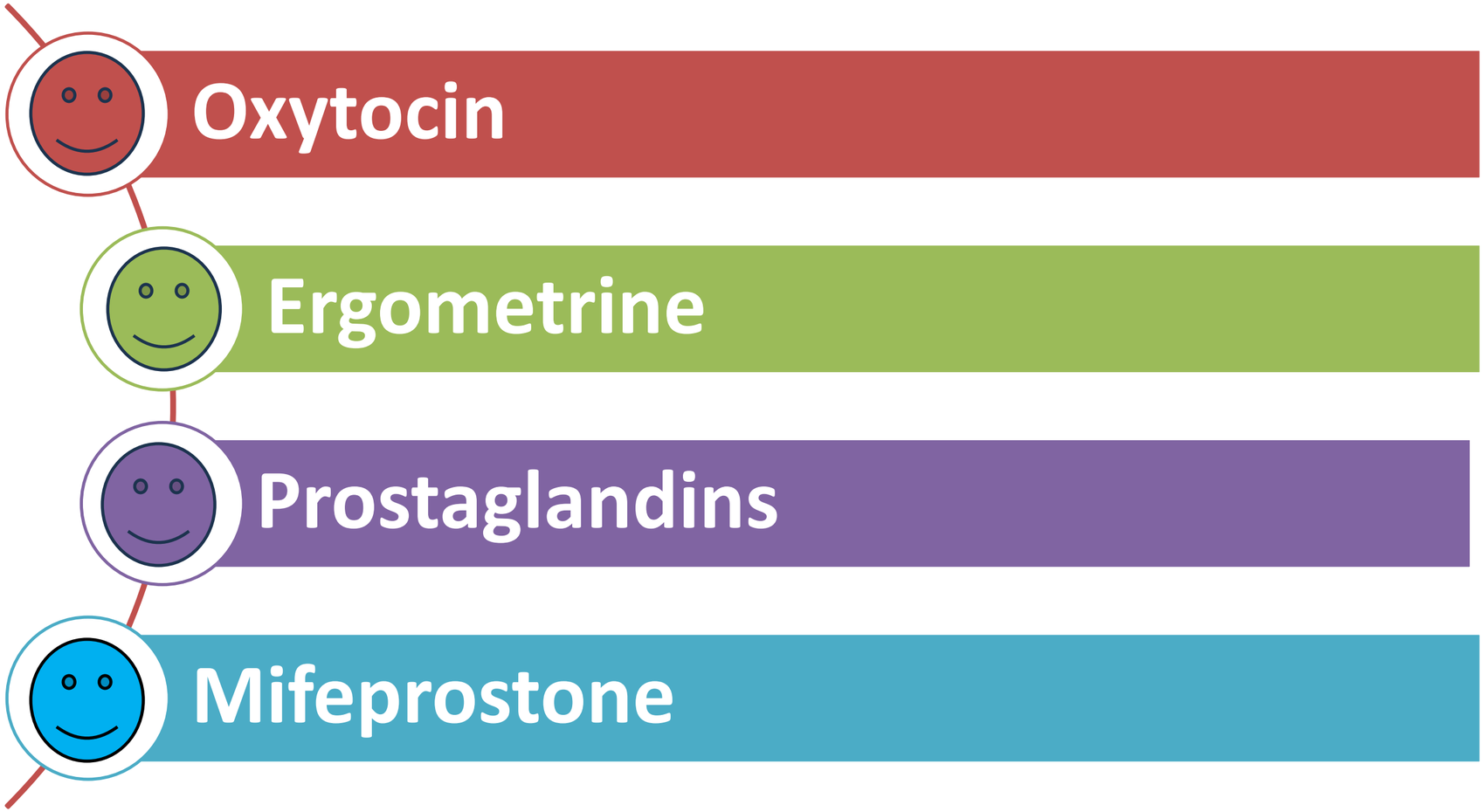
"TOCOLYTICS"

childbirth terminate

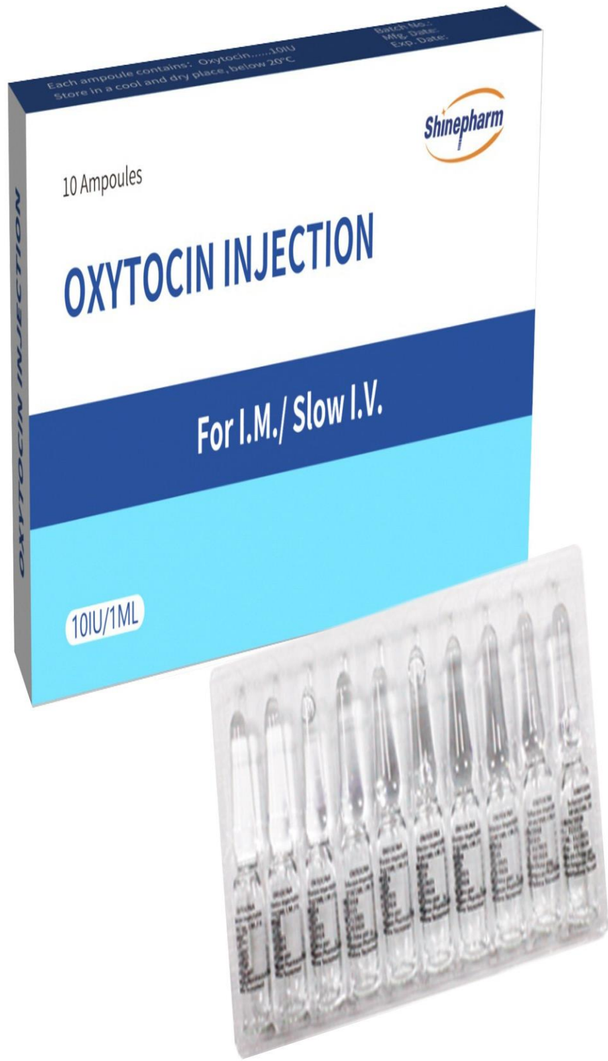
- ~ STOP PREMATURE LABOR

Oxytocic drugs

Drugs that stimulate the pregnant uterus and are important in obstetrics include :



Oxytocin



- Oxytocin is a posterior pituitary hormone that induces powerful contractions of uterine muscle and induces milk ejection from the breast (a nasal spray preparation of oxytocin is available to **stimulate milk let-down in nursing mothers**)

❖ Mechanism of action:

- By stimulation of Oxytocin receptors (G protein coupled receptors)
- It acts synergistically with prostaglandins to release Ca^{2+} from intracellular stores in the myometrial cells and promote muscle contraction.

Ergometrine

❖ **Mechanism of action:**

- It also causes vasoconstriction by α-adrenoceptor stimulation, which further limits hemorrhage.
- It also causes prolonged and forceful contraction of uterine smooth muscles**.**

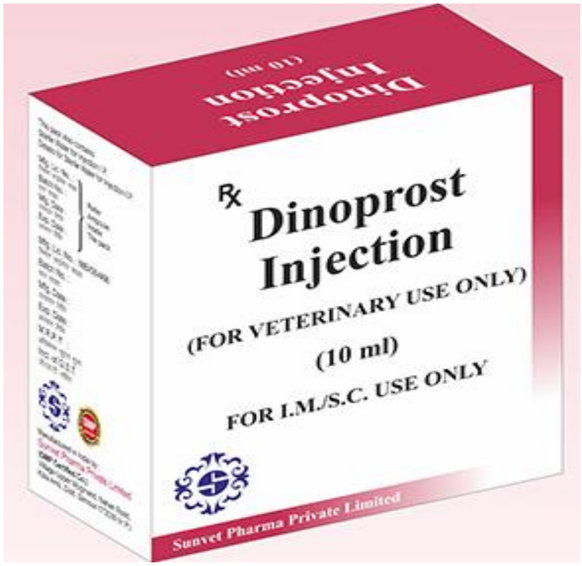
N.B– Ergometrine should **not be used to induce labor**. It should be given at the time of placenta delivery (3rd stage of labor) and never before that. If it is given before delivery of the placenta, it causes severe spasm of uterine smooth muscles and retained placenta.

Prostaglandins

Production of PGF and PGE by the cells of the amnion and decidua is increased near term.

Synthetic PGs E and F are used as oxytocic agents e.g.

1. Gemeprost and Misoprostol [PGE_1 analogues]
2. Dinoprostone [PGE_2]
3. Carboprost [$PGF_{2}\alpha$]



❖Mechanism of action:

- The PGs act at PG receptors ➡ release Ca^{2+} from intracellular stores in the myometrial cells ➡ promote muscle contraction.
- prostaglandins ripen and soften the cervix, further aiding the expulsion of uterine contents.
- Prostaglandins also upregulate oxytocin receptors.

N.B. PGs are contraindicated with uterine scar.

Indications of oxytocics

1- Induction of abortion: **Gemeprost** (intravaginally)

or **Misoprostol** (following Mifepristone) are used.

2- Induction of labour: **Dinoprostone** and **Oxytocin** are used

3- Bleeding due to incomplete abortion:

Ergometrine and ***Oxytocin*** (**Syntometrine**) given intramuscularly, before surgery.

4-Prevention and treatment of postpartum hemorrhage:

Oxytocin, **Ergometrine** and **Carboprost** (in those unresponsive to **oxytocin** and **ergometrine**) are used.

Side effects of oxytocics

1. Nausea and vomiting, vaginal bleeding, uterine pain.

2. **Oxytocin** can cause hypotension and tachycardia. Its antidiuretic hormone-like effect causes water retention and consequent hyponatraemia.

3. **Ergometrine** may cause vasoconstriction with an increase in blood pressure (angina, if vasospasm of the coronary arteries).

4. **Prostaglandins** ***(Carboprost)*** may be associated with an increased incidence of uterine rupture during labor in women who have had a previous cesarean section.

Q.1 A pregnant patient at term presents for induction of labor. The best pharmacological approach would be administration of:

A. PGE until the woman is in active labor.

B. PGE with concurrent intravenous infusion of oxytocin.

C. Oxytocin intramuscularly.

D. PGE until the cervix has ripened followed by oxytocin.

E. Ergonovine intramuscularly.

Q.2 The following drugs used in the management of post partum hemorrhage except:

a)Oxytocin

b)Ergometrine

c)Mifeprostone

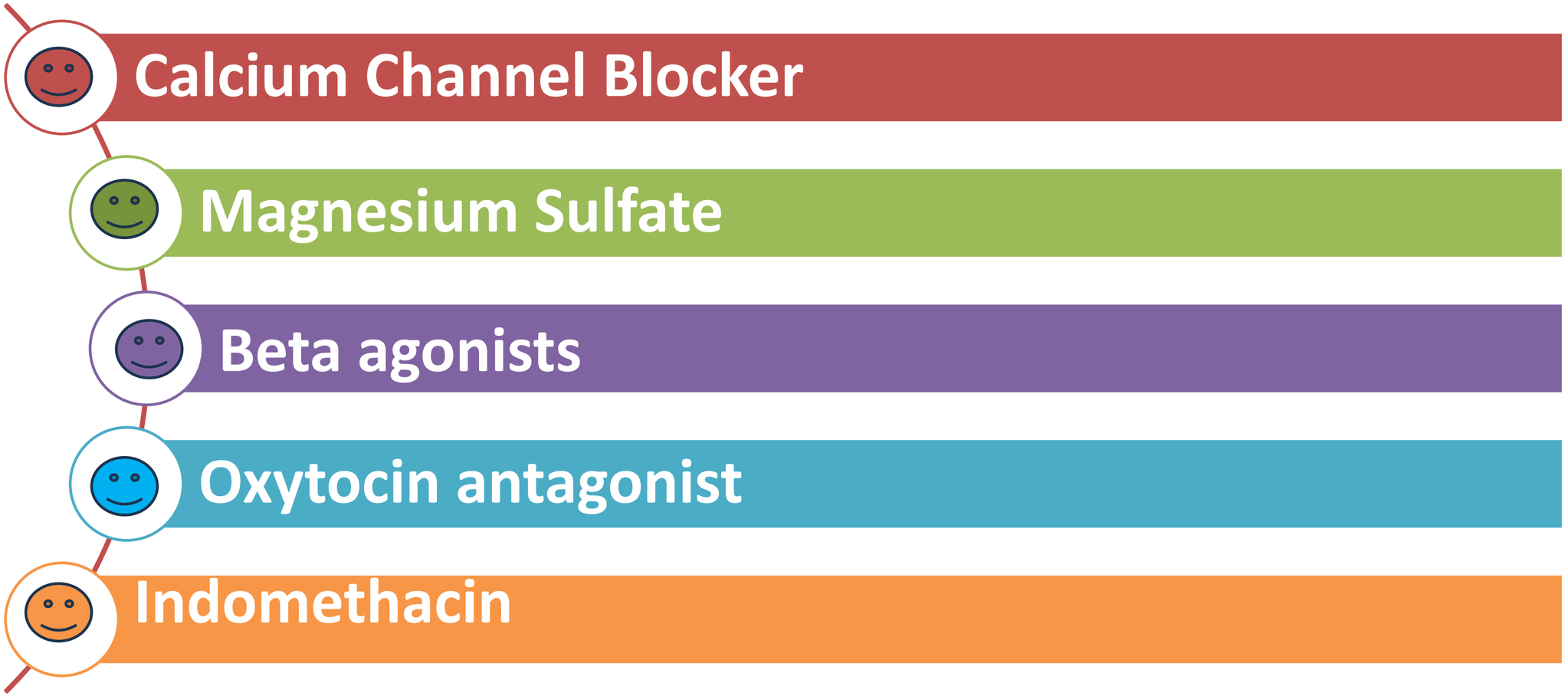
d)Carboprost

Tocolytic drugs

More than 10% of pregnancies result in preterm birth, defined as delivery before 37 weeks of gestation. Preterm birth is associated with significant complications such as neonatal respiratory distress syndrome, pulmonary hypertension, and intracranial hemorrhage.

Drugs that inhibit labor or slowdown contractions of uterus are called **tocolytics.**

They include:



N.B. Hydroxyprogesterone caproate once-weekly injections are approved by the FDA to **reduce** the risk of **preterm delivery** in women with a history of at least one spontaneous preterm birth.

UTERINE RELAXANTS
(TOCOLYTICS)

It's Not My Time!

I ndomethecin (NSAID)

N ifedipine (CA Channel Blocker)

M agnesium sulfate

T erbutaune (Adrenergic Agonist)

Calcium Channel Blocker

- **Calcium channel blockers** (e.g., **Nifedipine**) reduce uterine contractions by **inhibition of** Ca^{2+} **influx** in uterine muscle cells.
- They reduce neonatal respiratory distress syndrome more than other tocolytics.

Magnesium Sulfate

- **Mg sulfate** reduces uterine contractions by **inhibition of** Ca^{2+} **influx** in uterine muscle cells related to its actions as a divalent cation to compete with Ca^{2+} in myometrial cells.
- Used also for prevention and treatment of **seizures "in preeclampsia & eclampsia".**

Beta agonists

- β_2-Adrenoceptor agonists relax the uterus and are given by intravenous infusion by obstetricians to inhibit premature labor, e.g. *terbutaline, ritodrine*.
- They can delay delivery by 48 h, time that can be used to administer glucocorticoid therapy to the mother to mature the lungs of the baby and reduce neonatal respiratory distress.
- Increases cAMP via activation of β_2-adrenoceptors leading to relaxation of uterine smooth muscle

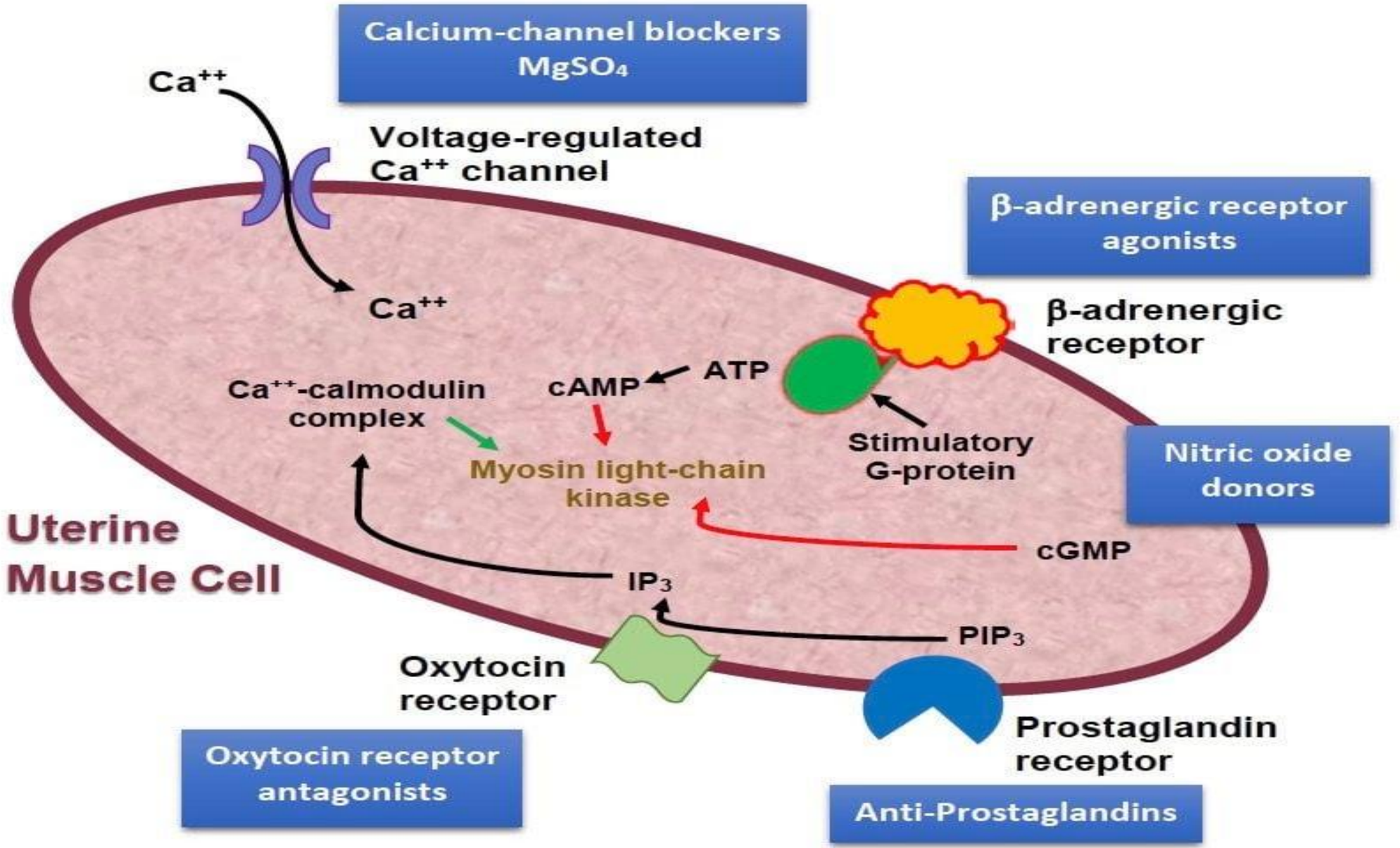
Oxytocin antagonist

- **Atosiban** is a peptide analogue of oxytocin
- It acts as an oxytocin receptor antagonist, reducing the release of intracellular Ca^{2+} .
- **Atosiban** is given initially by intravenous bolus injection followed by an infusion for not more than 48 h.

Indomethacin

- **NSAIDs** such as **indomethacin** block the production of PGs (inhibit both COX-1 and COX-2).
- used to inhibit uterine contractions based on the role of PGs in stimulating contractions.
- It is used to relieve cramps associated with menstruation (dysmenorrhea)

Tocolytic mechanism of action



Indications of Tocolytics

1. As a preventative therapy with progesterone in women with prior spontaneous preterm birth.
2. As an acute intervention to suppress established uterine contractions associated with cervical change occurring before 37th week of gestation.

Side Effects of Tocolytics

All available tocolytic agents cause maternal and/or fetal adverse effects.

1- **Maternal adverse effects:**

- ❑ Tachycardia, hypotension, and pulmonary edema (with beta agonists).
- ❑ Nausea, vomiting and hyperglycemia (with atosiban)
- ❑ Hypotension and muscle weakness (with Mg sulfate)

Side Effects of Tocolytics

2- Fetal adverse effects:

- Renal dysfunction and premature closure of the ductus arteriosus (with indomethacin).

Q.3 Which statement is true about atosiban:

A. Is oxytocin receptor antagonist

B. Is Progesterone receptor antagonist

C. Is least effective in inhibition of premature uterine contraction

D. Is an anti-tocolytic drug

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Thank You