Genitourinary System Module

Pharmacology

Drugs acting on the pregnant uterus

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هسة احنا في عنا ادوية بتعمل تحفيز للرحم عشان يصير انقباض ، و هاي الادوية احنا بنعطيها بثلاث حالات ، الاولى انه اجى وقت الولادة و فش طلق و الثانية انه في طلق و انقباضات بس ضعيفة و بدنا نقويها ، الحالة الثالثة انه في نزيف بعد الولادة لهيك بنعطي هاي الادوية مشان يصير في انقباض فبنضغط على الاوعية الدموية و نمنع النزيف و بس كدة يمؤمن

و عنا ادوية ثانية بتعمل العكس ، طيب ليش بنستخدمها ؟
جاتك وحدة عندها انقباضات و بدها تولد بدري ، مش بفترة طويلة لانه عملها تقريبا ٧ ايام بتعطيها هاي الادوية عشان تمنع هاي الانقباضات ، بس كدة اعمل سكيب عن السلايد الجاي

Drugs acting on uterus smooth muscles

A. **Uterine Stimulants (uterotonics):** are used to stimulate the uterus in three main clinical scenarios:

1. To initiate uterine activity for induction of labor or termination
2. To augment slowly progressing labors
3. To stimulate delivery of the placenta and prevent post-partum hemorrhage

B. **Uterine relaxant (tocolytics):** are used to relax the uterus in cases of **preterm labor; to delay preterm (before the aga of 37-week gestation) delivery.**

***Both classes of drugs target the pathways that initiate and produce uterine contractions.**

Uterine Stimulants

These drugs increase **uterine contraction:**

1. **Posterior pituitary hormone :** Oxytocin, Desaminooxytocin
2. **Ergot alkaloids:** Ergometrine, Methylergometrine
3. **Prostaglandins (E2, F2α) analogues:** Dinoprostone, Dinoprost, Misoprostol.

يا حلو ، بدنا نبلش بالادوية يلي بتعمل تحفيز الانقباضات ، اول اشي عنا ال oxytocin و هذا موجود طبيعي بالجسم ، يعني احنا بنستخدم الطريقة يلي موجودة بجسم الانسان بشكل طبيعي ، و في كمان نوع من الfungi اسمه ergot بنستخدمه برضه و في اخر اشي ممكن نستخدم ال PG ، يلي اكيد كلنا بنعرف انها بتعمل انقباضات ،، alkaloids اغششكم اشي ؟
ترا حتى الادوية يلي بتعمل تثبيط هي عبارة عن مضادات لهاي المواد يعني ، فالمحاضرة سالكة الحمدلله

نيجي على الاوكسيتوسن ، بتعرف انه هرمون ينفرز من ال p.pitutry gland ، بنعرف وظائفه ، اعرف انه بشتغل على G protein ، فيزيد ال intracellular calcium ، فبتزيد الانقباضات، اعرف انه اله ADH effect ، و VD effect مهمممم اعرف انه اله positive feedback ، يعني لما يصير في انقباضات بعمل تحفيز انه يتم افراز الهرمون ، و الهرمون نفسه بعمل تحفيز للغدة انها تنتج منه اكثر ، يعني بحفز زيادة افرازه ، اخذنا الحكي هاظ

Posterior pituitary hormone uterotonic: Oxytocin

- Oxytocin is a nonapeptide hormone (contains nine amino acid residues).
- It is generated in the hypothalamus but stored and released from the posterior pituitary gland.
- Oxytocin is one of the few that exhibit positive feedback loops, i.e., release of oxytocin stimulates even more of a release of oxytocin.
- Stimulates uterine contractions in the myometrium by causing G-protein coupled receptors to stimulate a rise in intracellular calcium in uterine myofibrils.
- Uterine contractions, cause more oxytocin to be release leading to increase in both the intensity and frequency of contractions and enables a mother to carry out vaginal delivery completely.
- Causes contractions of the myoepithelial cells in the female breasts to enable milk expulsion.
- Oxytocin also has both antidiuretic and vasodilatory effects, increasing cerebral, coronary, and even renal blood flow.

ال oxytocin بتاخذ بوقتين اما قبل الولادة او بعد الولادة عشان نزيف ما بعد الولادة

Oxytocin: clinical use

- Oxytocin is indicated and approved by the FDA for two specific time frames: antepartum and postpartum.

- In the antepartum period, exogenous oxytocin used for strengthening uterine contractions with the aim of successful vaginal delivery of the fetus; For mothers who have:

1. inactive uteri that require stimulation to start labor
2. preeclampsia (high blood pressure in late stage of pregnancy), maternal diabetes, premature rupture of the membranes: these conditions require delivery before labor has begun
3. inevitable or incomplete abortions in their second trimester

- Indication in the postpartum period include delivery of the placenta and control postpartum hemorrhage.

- Cervical status must be favorable (soft and dilated) for oxytocin use.

في اشي اسمه preeclampsia و هي حالة بصير عند المراة الحامل ارتفاع في ضغط الدم بالمرحلة الاخيرة من الحمل ، و بصير لازم نولد المرأة بوقت مبكر

و في استخدام من استخدامات الاوكسيتوسن انه لما يصير اجهاض بس مش كامل بنعطي هذا الدوا

اخر اشي بحكيلك انه لما تستخدم هذا الدواء لازم يكون عنق الرحم طري و متوسع ، لهيك لقدام رح نعرف انه ممكن نعطي PG اول اشي بعدين نعطي OX

Oxytocin: Administration and side effects

- Oxytocin is inactive orally and is generally administered by i.m. or i.v. routes, rarely by intranasal spray.
- It is rapidly degraded in liver and kidney; **plasma t½ ~6 min.**

احسن مشان نعطي مجال للرحم يرجع يرتخي بسرعة ، وهيك احنا بنكون زي الوضع الفسيولوجي للجسم

Side effects:

1. Inappropriate dosage of oxytocin can cause uterine hyperstimulation, uterine rupture, hemorrhages, maternal death, fetal distress and fetal death.
2. Water intoxication: because of ADH like action of large doses given along with i.v. fluids.

Ergot alkaloids

- Ergometrine and methylergometrine are ergot alkaloids that increase the uterine muscle tone by causing continuous tetanic contractions (contraction lasting more than 90 seconds).

- It causes contractions of both upper and lower segments of uterus i.e.fundus and cervix (tend to compress rather than to expel the fetus).

- **Uses:**

1. Control and prevent postpartum hemorrhage(PPH)
2. After caesarean section to prevent uterine atony (weak uterus muscle, leads to postpartum hemorrhage)

- They are vasoconstrictive and increase the risk of hypertension post partum. Other side effects with ergot alkaloids are pain after birth, nausea and vomiting.

هذا الدوا ممنوع اعطيه خلال فترة الحمل او الولادة ، يعني بس بعطيه بعد الولادة عشان امنع نزيف الرحم ، بعمل انقباض قوي جدا و لمدة طويلة ، تقريبا اكثر من ساعة

Ergot alkaloids

- **Adverse effects :-**

1. Nausea, vomiting
2. Increase in blood pressure occur occasionally.
3. High doses for many days → ↓ milk secretion (due to inhibition of prolactin release).

- **They are contraindicated during pregnancy and before the delivery of the placenta (3rd stage of labor).**

Prostaglandins (E2, F2α) analogues

- PGE2, PGF2α are potent uterine stimulants and cause ripening of cervix.
- **Dinoprostonw**, **Dinoprost** and **Misoprostol** are PGs analogues.
- PGs increase tone as well as amplitude of uterine contractions.
- **Uses:**

1. Induction of labour
2. Cervical ripening
3. Therapeutic abortion (proceeded 2 days by Mifepristone (anti-progestin))
4. Postpartum haemorrhage

****Should be stopped before administering oxytocin.**

هسة بدنا نحكي عن الادوية يلي بتعمل تثبيط الانقباضات ، هاي الادوية بتأخر موعد الولادة ، بس مش فترة كبيرة ، بس ٧ ايام ، طيب ابو حميد شو استفدنا اذا اخترناه ٧ ايام ، تعال اقلك ، اذا وحدة اجت بدها تولد الشهر السابع ، احنا بنعرف انه الرئة عند الطفل ما بتكون جاهزة و لازم اعطيه corticosteroid قبل ما اولد الحامل ، لهيك بنأخر الولادة فترة ٧ ايام و بنجهز المراة انها تولد باحسن ظروف ممكنة عشان نحافظ على حياة البيبي

السلايد الجاي اقرأ انواع الادوية يلي بنستخدمها

Uterine relaxant (tocolytics)

- Tocolysis is intended to prolong gestation for two to seven days in case of premature labor
- This allows for transportation to a higher care facility and to administer of corticosteroids (for fetal lung maturity)
- Tocolysis is beneficial in patients having preterm labor before 34 weeks gestation.
- Tocolysis is not intended to increase gestation of the fetus to term but is focused on providing a window of time to support treatments that to improve outcomes for delivery.
- Different medications currently used are:
  - Beta-Adrenergic receptor agonists
  - Calcium channel blockers
  - Nonsteroidal antiinflammatories
  - Oxytocin inhibitors

β Adrenoceptor agonists

- **Ritodrine** and **terbutaline**
- Selective β2 receptor agonist used specifically as a uterine relaxant.
- Mechanism of action: Bind to β adrenoceptors, which increases in level of cAMP reducing intracellular calcium level leading to smooth muscle relaxation.
- Side effects: Cardiac arrhythmias, Tachycardia, Hypotension, Hyperglycemia, Hypokalemia, Sweating,, nausea , vomiting.

Calcium channel blockers

Nifedipine:

- Decrease the influx of Ca2+ ions →↓ uterine contractions
- Adverse effects: Tachycardia, hypotension, Constipation, ankle edema, coughing and wheezing (be careful with asthmatic pts).
- Administration: oral and sublingual. Recent literature has shown sublingual nifedipine achieved faster tocolysis
- Compared to other tocolytic agents, calcium channel blockers significantly delay birth (7 days)

*Be careful with asthmatic patients

Oxytocin antagonist: Atosiban

- Is a peptide analogue of oxytocin that acts as antagonist at the oxytocin receptors.
- May be less effective as tocolytic than β 2 agonists.
- Postpone preterm labour with fewer cardiovascular and metabolic complications than β2 adrenergic agonists.