Drugs used in Obstetrics and Gynaecology

[1] Drugs acting on uterus

[a] Stimulants
- Oxytocin
- Prostaglandins & analogs
- Ergot alkaloids

[b] Relaxants
- β2-adrenoceptor stimulants
- Others

[2] Drugs inducing Ovulation

[3] Respiratory Surfactants For Infants

Clinical uses of Oxytocin

[1] Induction & maintenance of labour.

Oxytocin

1 unit = ~ 2 µg
[Ineffective orally]

Generally infused as 10 units / L [in 5% dextrose]

Start with 10 drops / min

Increase by 10 drops every 20-min [if no response]

Max. 60 drops / min.

Prior amniotomy should be carried out in Hydramnios
Use low doses in multipara / grand multipara*

Primigravida & women with dead foetus require higher doses

[2] Control of postpartum haemorrhage

Oxytocin 2.5 - 5 units i.m.
Usually in combination with 0.25 - 0.5 mg Ergometrine

[3] **Promotion of milk ejection**

Nasal spray 40 units / ml  [1 spray = 4 mg]
Dose 1 spray 2 - 3 times / day

[4] **Management of missed (incomplete) abortion.**

Oxytocin 20 units / litre  [sometimes higher concentrations]
Dose 15 - 30 drops / min.

[5] **Control of postpartum hypertonicity** [Rare use]

**Contraindications for Oxytocin in Labour**

**Absolute**
Cervix pathology
Foetal malposition
Disproportionate foetal head
Foetal distress
Placental abnormality/ Prolapse
Grand multipara
Uterine hypertonus  **[pre-partum]**
Pre-eclampsia
Ectopic pregnancy

**Relative**
Diabetes mellitus
One previous low segment caesarean section
Placenta praevia

**Side Effects of Oxytocin**

1. Increased resting uterine tone [even sustained tetanic contractions] may interfere in placental circulation - foetal bradycardia/arrhythmia.

2. Water retention / increased BP

3. GID
Clinical uses of Prostaglandins.

[1] Induction & maintenance of labour
PGE₂ Generally infused as 5 mg / litre [in 5% dextrose]
Start with 2-6 drops /min [0.67-2.1 µg]
Increase by 2-6 drops every 2 hr [if no response]
Total max. 600 µg [normally 100 - 400 µg]
PGF₂α dose is 5 times higher than PGE₂
Multipara requires low doses while primigravida & women with dead foetus require higher doses.

[2] Missed (incomplete) abortion

[3] Hydatiform mole


Available preparations:
PGF₂α [Dinoprost: Prostin-F₂α]
PGE₂ [Dinoprostone: Prostin-E₂]
15-methyl-PGF₂α [Carboprost: Prostin-15M]
16–16 Dimethyl trans delta PGE₁ [Gemeprost]
16–16 Phenoxy-PGE₂ methyl sulphonamide [Sulprostone]

These are more potent stimulants of uterine muscle than oxytocin. Their onset of action slower than oxytocin, but their onset of action is slower than oxytocin but they have a longer duration of action.

Carboprost is about 500 times more potent & therefore has a bigger risk of uterine over-stimulation. Its main use is in missed abortion. Rarely also used for the control of PPH unresponsive to oxytocin or ergot alkaloids,

Side effects of Prostaglandins

Phlebitis [painful but usually disappears soon]
GID.
Transient CV Symptom [flushing / shivering/ headache/ dizziness]
Bronchoconstriction with PGF2α
Temporary Pyrexia / Increased WBC count
Overstimulation of uterus [Higher risk with previous CS/ grand multipara*]

* Five or more viably delivered babies: PPH= post partum haemorrhage.

**Ergot Alkaloids**

Ergometrine [Ergonovine]
Methylergonovine

Clinical uses

Post partum / Post abortion Haemorrhage
Haemorrhage due to caesarean section
Delayed uterine involution

**Uterine Relaxants**

Clinical uses

[1] Uncomplicated Premature Labour [gestation >20 wk <34 wk. Not useful if membranes have ruptured or Cervix > 4 cm or foetal Hr is abnormal]
[2] Control of powerful uterine contractions [Threatening Foetal Asphyxia]

**Drugs used**

- β2 Adrenoceptor Simulants
  - Terbutaline [Bricanyl] 10 µg/min i.v. with gradual increase to 25 µg/ min max.
  - Ritodrine [Yutopar]

SE: VD, Sweating, ↓BP , ↑BSL [may require insulin]
Tremors, aldosterone [Na+/ H2O retention] K+ excretion
Rarely oedema, pulmonary overload

- Others

**Ethanol** [10% @ 7.5 ml/Kg low infusion [to give plasma levels 120-180 mg / 100 ml
After 24 hr the dose is reduced to 1.5 mg / Kg for further 10 hr.
SE: Phlebitis, foetal distress.

**Atosiban** [Tractocile] it is a blocker of oxytocin receptors but can also block Vasopressin receptors. A bolus dose of 6.75 mg followed by 100-300 µg / min for 2-3 hr.
SE: GID, Headache, Chest pain, Reduced ability to maintain BP due to V₁α receptor block in blood vessels.

**MgSO₄**

A useful drug particularly when β₂ adrenoceptor stimulants are unsuitable to use. It acts by blocking the neuromuscular transmission & inhibit CNS activity. mode for inhibition of uterine activity, however not known.

A loading i.v. dose of 4-6 is given slowly over 15-30 min followed by infusion of 14 g/hr until contractions stop. And then continued for further 12 hr.

SE: Blood levels >8 mg/100 ml lead to progressive fall in cardiac conduction, neuromuscular transmission, respiratory muscle dysfunction and neonatal CNS depression. There is also inhibition of the parathyroid function.

SE are however minimal with blood levels below 7.27 mg/100 ml [6 mEq]

**Indomethacin**

Reduces uterine activity by inhibiting PG synthesis.

It has been tried in a dose of 100 mg followed by 25 mg 6 hrly. Success has been variable but indomethacin has not been found to delay labour for not more than 48 hr.

SE: Premature closure of ductus arteriosus leading to pulmonary hypertension in the newborn. Also oligydraminos & foetal distress.

**Ca ++ Channel Blockers**

May be an alternative to β₂ adrenoceptor stimulants.

Main drawback is the lack of injectable preparations and the drugs have to be given orally.

SE: Reduced placental perfusion, foetal hypoxia & acidosis

**Drugs Inducing Ovulation**

1. Anti-oestrogen: Clomiphene

It is a partial agonist of oestrogen, which is given in a dose of 50 mg orally once daily for 5-7 days starting on day 5 of the menstrual cycle. In the absence of ovulatory response the treatment should be discontinued after 3 cycles. Sometimes its oral treatment is also followed by an injection of LH.
SE Ovarian over-stimulation menstrual irregularities excessive bleeding, vaginal discharge, pruritis vulvae, headache, multiple births, Rarely luteal phase defect (LPD) leading to reduced progesterone formation.

2. Gonadotrophins: 
   - hMG [Menotrophin / Menogon]
   - Purified hMG [Follitropin]

   Human menopausal gonadotrophin [hMG] is obtained from the urine of postmenopausal women. It has the activity of both FSH [75-150 IU] and LH [75-150 IU] / ml. Purified Menotrophin [Urofillitropin] contains only FSH [75-150 IU]/ml

   Recombinant FSH [rFSH] is prepared by expression cDNA encoding the a & b units

   Human Chorionic gonadotrophin HCG [Choragon / Profasi] 1000- 10,000 units per ml is available which is mainly used to treat ovulation failure. Treatment is started with FSH on the 1st day of menstrual cycle and continued for 12-14 days when HCG injection is given.

   Purified gonadotrophins can be give by sc. injection.

   Unpurified however are given by i.m route which is believed to reduce the chances of allergic reactions.


   They are mainly used in conjunction with gonadotrophins, which are first given.

   SE: Hot flushes reduced libido, GID, sweating, weakness, vaginal dryness, rarely neuropathy.


   Used for the treatment of hyperprolactinemia related ovulatory failure. They have been shown to reduce the size of prolactin secreting tumours.

   Given orally rapidly but incompletely absorbed. All act by stimulating dopamine D2 receptors.

   Dose: Bromocriptine 2.5 mg which may be increased to 5 mg / day.

   Pergolide is given in smaller doses 0.025 mg once daily and increased gradually to 0.25 mg once daily. The dose for Carbergoline is 250 µg twice daily but is mainly used for the prevention of lactation.

   SE  
   [a] Immediate; GID postural hypotension [first dose phenomenon]  
   CV shock-like symptoms

Precautions: History of psychiatric illness, recent MI, peripheral vascular disease, peptic ulcers.

[3] **Respiratory surfactants for infants**

<table>
<thead>
<tr>
<th>Natural</th>
<th>Poractant- a  [Curosurf]</th>
<th>From porcine lung</th>
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<tr>
<td>Synthetic</td>
<td>Colfosceril [Exosurf]</td>
<td>Protein free</td>
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Two more from bovine lung have become available but yet have not been introduced here.
- Beractant  [Survanta]
- Calfactant  [Infasurf]

Clinical use of surfactants:
Premature infants [≤ 34 wk] body wt. 700 g or more [4 - 24 hr after birth and treated for RDS / HMD]

These agents act by supplementing the natural surfactants to reduce the severity and complications of pneumothorax in premature babies.

SE / Complications

Endotracheal tube obstruction
Risk of pulmonary haemorrhage / lung collapse
Blood oxygen increase [hyperoxia]

SE are more marked in infants with bradycardia / heart murmurs.
Infants treated with surfactants should be continuously monitored for heart rate/ BP and arterial blood oxygenation.

Dose 65-80 mg/kg via endotrachial tubes which may be repeated after 12 hr, if still intubated.

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HMD / RDS = Hyaline Membrane Disease / Respiratory Distress Syndrome
SE = Side Effects:
GID = Gastrointestinal disturbances [nausea vomiting ]
BSL = Blood sugar level