

# Hormonal Contraceptives

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# Hormonal Contraceptives

- Most effective methods of contraception
- Used for reversible suppression of fertility
- Three different methods have been employed
  - 1) Oral
  - 2) Parenteral
  - 3) Intra-uterine Devices

# Hormonal Contraceptives

## 1) ORAL CONTRACEPTIVES :-

### a) *Combined Oestrogen and Progestin preparations* :-

i) Monophasic

ii) **Biphasic**

iii) **Triphasic**

### b) *Progestin – only pill* :-

i) **Minipill**

\* **Norethindrone**

\* **Norgestrol**

### c) *Emergency (Postcoital) contraceptives* :-

• **Levonorgesterol**

• **Ulipristal**

# Hormonal Contraceptives

## *II) Parenteral contraceptives :-*

### **a) Injections :-**

**\*Depot Medroxy Progesterone Acetate( DMPA)**

**\*Nor-Ethesterone Enanthate ( NET – EN)**

## *III) Intra-uterine devices :-*

**-\* Progesterone (Progestestastert)**

**-\* Levonorgestrel**

# Oral Contraceptive Pills

- **3 types :-**
- A) Combined Oestrogen & Progestin Preparations:-
- B) Progestin Only Pill (Minipill)
- C) Emergency (Postcoital) Contraceptive pills

Most commonly used method is combined oral pills

# Combined Oestrogen + Progestin Oral Preparations

- Most effective reversible method
- Success rate up to 98%
- Most commonly used :-
- Oestrogen is ethinyl estradiol (30 to 50 mcg)
- Progestins are Norethindrone, Levonorgestrel
- And Third Generation Progestins such as Desogestrel, Gestodene and Norgestimate

## Combined Oestrogen + Progestin Oral Preparations

- Combined Oral Contraceptives are available as :
  - *A) Monophasic combination tablets :*
    - \* Ethinyl Estradiol (50 mcg) + Norethisterone (1mg)
    - \* Ethinyl Estradiol (30 mcg) + Levonorgestrel (0.15mg)
  - *B) Biphasic combination tablets :*
    - \* Days 1-10 Ethinyl estradiol (35 mcg) + norethindrone (0.5)
    - \* Days 11-21 Ethinyl estradiol (35 mcg) + norethindrone (1.0)
  - *C) Triphasic combination tablets :*
    - \* Days 1-7 Ethinyl estradiol (35 mcg) + norethindrone (0.5)
    - Days 8-14 Ethinyl estradiol (40 mcg) + norethindrone (0.75)
    - Days 15–21 Ethinyl estradiol (35 mcg) + norethindrone (1.0)

## Combined Oestrogen + Progestin Oral Preparations

- Monophasic pills contain fixed amount of oestrogen and Progestins
- Biphasic pills contain fixed amount of oestrogen but progestin amounts varies
- Triphasic pills contain more amount of oestrogen in mid cycle but doses of progestin increases in 3 successive phases
- Preparations containing less than 35 mcg of oestrogen are referred as 'low-dose' pills
- 3<sup>rd</sup> generation progestin pills (Desogestrel, gestodene, norgestimate) are 'lipid friendly' as they increases HDL level & reduces atherogenic risk



# Principles for use of Combined Oestrogen + Progestin Oral Preparations

## 1) Schedule for use of oral combined pill :-

- Start one tablet daily from fifth day of menstrual cycle & continue till 21 days
- Keep seven days (Days 22-28) drug free period
- The Next course is started after 7 days drug free interval during which the bleeding occur, so that a cycle of 28 days is maintained.

2) If a lady on combined oral contraceptive pills misses to take a tablet, she should take two tablets the next day and continue rest of the pills as prescribed.

3) If more than 2 tablets are missed , then the course should be interrupted, and an alternative method of contraception should be used and next course started on the 5<sup>th</sup> day of bleeding.

## **Principles of use of Combined Oestrogen + Progestin Oral Preparations**

- 4) If pregnancy occurs during use of hormonal contraceptives – it should be terminated by suction aspiration because of increased risk of congenital malformations in new born babies.
- 5) Average weight having lady require low dose eostrogen- 30mcg ethinyl estradiol, over weight and obese women may require 50 mcg ethinyl estradiol.
- 6) In case of break through bleeding or spotting in between, then switch over to a pill containing higher eostrogen dose.
- 7) If eostrogen is contraindicated, then use a progestin only contraceptive pill.
- 8) Discontinuation of oral combined contraceptive pills results in full return of fertility within 1-2 months.

# Mechanism of Action of OC combination Pill

- OC combination pills acts by different mechanisms:-
  - 1) Both oestrogen and progestin act synergistically on Hypothalamo-pituitary axis by enforcement of negative feedback mechanism and inhibit the release of FSH & LH, which leads to inhibition of ovulation.
  - 2) Causes strong tubal and uterine contractions that may interfere with fertilization
  - 3) Makes the endometrium less suitable for implantation (progestins)
  - 4) Thick, viscid cervical mucus secretion prevents sperm penetration (progestins)

# Adverse Effects of OC combined pills

- A) Non-serious side effects (within 1-3 cycles):
- N, V, Headache, Break through bleeding or spotting with progestin alone pills, breast discomfort.
- B) Side effects occurring later :-
- Weight gain, acne, increased body hair due to androgenic action of older 19-nortestosterone progestins.
- Chloasma, pigmentation of cheeks, nose and forehead
- Mood swings, abdominal distension

# Adverse Effects of OC combined pills

- C) Serious complications :-
- A) Leg vein thrombosis and pulmonary embolism risk in women > 35 yrs of age, diabetics, hypertensives & in smokers.
- B) Coronary and cerebral thrombosis resulting in myocardial infarction and stroke.
- Oestrogen component is responsible for venous thromboembolism, while both are responsible for arterial phenomena.
- Rise in blood pressure
- Estrogen raise HDL/LDL ratio (Beneficial) while progestins nullify it.

# Adverse Effects of OC combined pills

- 5) Increase risk of vaginal, cervical and breast cancer in high risk women. Endometrial carcinoma more with progestin component.
- 6) Benign Hepatomas
- 7) Gallstones – estrogen increases biliary cholesterol excretion.

# Contraindications of OC pills

I) Absolute contraindications :-

- \* Thromboembolic disorder, coronary & cerebrovascular disease
- Moderate to severe hypertension, hyperlipidaemia
- Active liver disease, hepatoma or H/O Jaundice during last pregnancy
- subsequent malignancy of breast or genitals
- Porphyria
- Impending major surgery to avoid risk of postoperative thromboembolism

# Contraindications of OC pills

II) Relative contraindications :-

Diabetes, obesity, smoking, hypertension

Vaginal bleeding, uterine leiomyoma

Gall bladder disease, migraine.

Age > 35 yrs, mentally ill



# Drug – Interactions

- 1) OC combined pills + tetracyclines/ampicillin → suppresses intestinal microflora → deconjugation of estrogens excreted in bile fails to occur → enterohepatic circulation of OC pills interrupted → blood levels of OC pills falls.
- 2) OC pills + Rifampicin / Phenytoin / Phenobarbitone → Rifampicin and others are microsomal enzyme-inducer drugs → enhances metabolism & excretion of OC pills → Treatment failure occur → pt. may conceive.
- In such cases, either switch on to preparation containing 50 mcg of ethinyl estradiol or use other method of contraception.

# Beneficial Effects Of OC combined pill

- Lowers the risk of endometrial, ovarian and colorectal carcinoma.
- Reduces menstrual blood loss, hence reduces risk of anaemia
- Regulizes abnormal cycles, dysmenorrhoea
- Improves endometriosis & PID
- Reduces risk of fibrocystic breast disease & ovarian cysts.

# Minipill (Progestin – Only Pill)

- Method of contraception less popular in females
- Does not contain Oestrogen to eliminate adverse effects associated with oestrogen
- Minipill contains very low dose Progestin (Norethindrone or Norgestrel) only.
- One tablet is taken continuously without any break from 1<sup>st</sup> day of menstruation and continue the course without a gap till required
- Lower efficacy as compared to OC combined pills
- Useful in females in whom OC oestrogen is C/I.
- Menstrual cycle becomes irregular.
- Eg. Tab. Norethindrone 0.35 mg
- Tab. Norgestrel 75 mcg

## Emergency (Postcoital) Pill

- Taken orally, an useful emergency (postcoital) pill following rape, unprotected sex or accidental rupture of condom during intercourse to prevent unwanted pregnancy.
- Drugs used for post-coital contraception are Levonorgestrel, Mifepristone & Ulipristal
- **Standard regimens used are :-**
  - i) Levonorgestrel 0.75mg two doses 12 hours apart (or) 1.5mg single dose taken as soon as possible, but before 72 hrs of unprotected sex.
  - ii) **Yuzpe Method :-** Levonorgestrel 0.5 mg + Ethinyl estradiol 0.1mg, two doses at 12 hrs interval within 72 hrs of exposure

# Emergency (Postcoital) Pill

- iii) Mifepristone 600mg single dose taken within 72 hrs of intercourse. It is anti-progestin with less side effects.
- iv) Ulipristal 30 mg single dose as soon as possible within 120 hrs of intercourse. It is 'Selective Progesterone receptor modulator' (SPRM). Has advantage, if the woman misses to take the drug within 3 days.

# Parenteral (Injectable) Contraceptives

- 1) Depot Medroxyprogesterone Acetate (DMPA): 150 mg deep i.m. inj during 1<sup>st</sup> 5 days of menstrual cycle , once in 3 months.
- 2) Norethindrone enanthate (NET-EN) : 200 mg i.m. once in 2 months.
- **Advantages :-**
  - 1. Avoids daily use of oral medication. Hence, better patient compliance
  - 2. Can be used safely during lactation
  - 3. Decreased risk of endometrial cancer on prolonged administration
  - 4. No increase in risk of cervical, ovarian or hepatic cancer.

# Parenteral (Injectable) Contraceptives

- Disadvantages :
- Complete disruption of menstrual bleeding pattern or total amenorrhoea (with DMPA)
- Not suitable in adolescent girls
- Return of fertility may take 6-30 months after discontinuation. May cause permanent sterility in some women.
- Weight gain, headache occur
- Decrease in BMD (Bone Mineral Density) , produce menopause like symptoms( hot flushes, vaginal dryness, reduced libido) on long term use

# Implants & Devices as Contraceptives

- **Implants :-**
- Implants are newer drug Delivery System
- Implanted under skin from which the steroid is released slowly over a period of 1-5 yrs.
- **Consists either of :-**
- **1) Biodegradable polymeric matrices** – do not need to be removed on expiry
- **2) Non-Biodegradable rubber membranes** – have to be removed on expiry
- **Eg.**
- **A) Norplant** : A set of 6 flexible rods each containing 36 mg Levonorgestrel (total 216 mg) for subcutaneous implantation
- **B) Implanon** : A single rod containing 36mg of Desogestrel. Have contraceptive effect lasting upto 3 yrs.
- **Side effects of implants are:-** Local infections at site of implant, local irritation & pain, headache, mood changes, weight gain and acne.



# Implants & Devices as Contraceptives

- **Devices** :- are impregnated (coated) with progesterone for continuous release up to 3-5 yrs
- **1) Intrauterine devices** :
- **(a) Levonorgestrel device**: It is a 'T'- shaped device inserted into the uterine cavity and the contraceptive effect lasts upto 5 yrs.
- **(b) Progestasert** : Intrauterine device containing Progestogen inserted into uterine cavity. Short acting and the device needs to be replaced every one year.
- **2) Transdermal Patch** : containing oestrogen and progesterone is applied over the buttocks , upper arm, lower abdomen, etc. Is applied weekly for 3 weeks followed by a patch – free week to get withdrawal bleeding.

# Male Contraceptives

- Suppresses male fertility by drugs by inhibiting spermatogenesis. Has reversible effect on discontinuation
- **Drugs used are :-**
- **1) Gossypol:** obtained from cotton seed
- **2) Antiandrogens**
- **3) Estrogens and progestins**
- **4) Superactive GnRH analogues**
- **5) Cytotoxic drugs :** cadmium, nitrofurans

**They all acts by :-**

- i) Inhibiting spermatogenesis
- ii) Decrease sperm count
- iii) Decrease sperm motility

# ANDROGENS (Testosterone)

- Testosterone is main androgen in men.
- Is synthesized by Leydig cells (interstitial cells) of the testes by Interstitial cell stimulating hormone (ICSH;LH) of anterior pituitary gland.
- FSH is responsible for spermatogenesis.
- **Classification of Androgens:-**
- ***1) Natural androgens*** : Testosterone, Dihydrotestosterone
- ***2) Synthetic androgens*** :
- ***i) Methyltestosterone*** – Given orally, slowly metabolized, longer acting than testosterone
- ***ii) Esters of testosterone*** :- Testosterone proprionate (i.m), Enanthate (i.m.) & undecanoate (oral,i.m) – slowly absorbed, long acting.

# Therapeutic Uses Of Androgen (Testosterone)

- 1) As a replacement therapy in men with hypogonadism → Transdermal patches are used.
- 2) Carcinoma of breast in postmenopausal women :- testosterone is physiological antagonist of oestrogen. Hence, tumors containing oestrogen receptors (ERs) respond to androgens.
- 3) Senile osteoporosis in male
- 4) Hypopituitarism
- 5) AIDS related muscle wasting
- 6) Hereditary angioneurotic edema
- 7) Ageing

# Adverse Effects of Testosterone

- **1) In female**, cause virilization leading to hirsutism, menstrual irregularities, breast atrophy, acne and deepening of voice.
- **2) In children**, impairment of growth due to premature closure of epiphyses
- 3) Oedema due to sodium & water retention
- 4) Cholestatic jaundice with methyltestosterone

# ANTI - ANDROGENS

- Examples :-
- **1) Physiological antagonists** : Oestrogens
- **2) Testosterone synthesis inhibitors** : Ketoconazole, spironolactone
- **3) Androgen receptor antagonists** : Flutamide, Cyproterone, Bicalutamide
- **4) 5-alpha reductase inhibitors** : Finasteride, dutasteride
- Therapeutic uses of Antiandrogens :-
- 1) Carcinoma of prostate (Cyproterone & Flutamide), Hirsutism in females and acne.
- 2) Benign prostatic Hyperplasia (BPH) in males (Finasteride)
- 3) Precocious puberty in children
- Adverse effects :- impotence, Gynaecomastia, hepatic damage, Hyperkalaemia (spironolactone)

# Anabolic Steroids

- *Promote protein synthesis*
- *Increase muscle mass, weight gain*
- *Synthetic androgens with greater anabolic & lesser androgenic effects.*
  
- *Examples :*
- *Nandrolone phenylpropionate(i.m.), Nandrolone decanoate(i.m), Stanazolol(Oral).*
  
- *Uses of Anabolic steroids :-*
- *1) In chronic illness to improve appetite & feeling of well being*
- *2) During recovery from prolonged illness, surgery, burns, trauma or chronic debilitating diseases*
- *3) To counteract catabolic effects of exogenously administered adrenal cortical hormones*
- *4) In postmenopausal and senile osteoporosis*
- *5) To control itching in chronic biliary obstruction*