HORMONAL CONTRACEPTION

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Classification

A. Combined preparation(estrogen and progesterone)

B. Progesteron only preparation

Combined hormonal contraception(CHC)

It contains two hormones:

- ☐ Synthetic estrogen
- Progestogen

Mechanism of action Centrally:

Inhibition of ovulation by suppress release of FSH& LH.

Peripherally:

- Making endometerium atrophic and hostile to an implanting embryo.
- Altering cervical mucos(scanty &thick) to prevent sperm ascending into uterine cavity.

Methods of administration

- ☐ Oral (combined oral contraceptive pill,cocp)
- ☐ Transdermal (patch)
- ☐ Vaginally (vaginal ring)

Formulations of COCP:



estrogen compenent is either:

- Ethinyloestradiol (15,20, 30,35,50)mcg
- Some newer pills contain oestradiol valerate or oestradiol hemihydrate, which is more similar in structure to the 'naturally occurring' oestradiol, but confers no other proven benefits

Formulations of COCP:

- Progestogen compenents is either
- 2nd generation: norethisterone acetate, levonorgestrel
- 3th generation: gestodene, desogestrel, norgestimate
- 4th generation; dienogest ,drospirenone : e.g, yasmine the newest one , contains drospirenone 3mg & ethionyloestradiol 30mcg.

Newer (third-and fourth-generation) progestogens were developed to have advantages due to *less androgenic activity*, but seem to be associated with a higher risk of venous thrombosis than pills containing second-generation progestogens. In view of this, COCPs containing second-generation progestogens are generally recommended as first choice.

regimens of COCP:

■ Most 'traditional' preparations contain 21 pills, one pill daily followed by a 7-day pill-free interval (or 7 placebo tablets in place of a 7-day pill-free interval



Some preparations contain 24 days of pills with a shorter pill-free interval. Preparations are commonly monophasic (i.e. same dose of hormones throughout), but some are phasic (dose varies). There is no advantage of phasic preparations over monophasic preparations. Although traditional 21 days on and 7 days off usually results in a withdrawal bleed during the pill-free interval, there is no reason why women cannot take the pill

Women with dysmenorrhoea or headaches during the pill-free interval, are often advised to do so to avoid recurrence of symptoms during the hormone-free interval by tricycling (taking three packets without any break).

continuously.

Transdermal Patch

- it releases norelgestromin 150 μg and ethinylestradiol 20 μg per 24 hours.
- It is applied on the skin of the lower abdomen, buttock or arm, weekly for 3 weeks, after which there is a patch-free week.
- Contraceptive patches have the same risks and benefits as COC.
- They are relatively more expensive, may have better compliance.



Vaginal ring

- It is a flexible ring of 54 mm diameter, made of latex-free plastic.
- It releases 15 μg ethinyloestradiol and 120 μg etonorgestrel daily
- The ring is self inserted and worn in the vagina for 21 days, followed by a
 7-day hormone-free interval
- Women should not feel discomfort from the ring and it can be removed for a short time (less than 3 hours),
- It can be cleaned and replaced.
- It has the same risks and benefits as COC but is those capensive.

Minor Side effects of combined contraception

- <u>Central nervous system</u>: Depressed mood, Mood swings,
 Headaches, Loss of libido.
- Gastrointestinal: Nausea, Perceived weight gain, Bloatedness.
- Reproductive system: Break through bleeding ,Increased vaginal discharge.
- Breasts :Breast pain, Enlarged breasts.
- Miscellaneous : Chloasma (facial pigmentation which worsens with time on COC)

Major risks of combined

contraception I-Venous thromboembolism

1-venous thromboembolism

- COC increases risk of venous thromboembolism (VTE) three- to five-fold.
- This risk depend on:

1-Dose of estrogen: it The effect appears independent of dose of EE dose below 50 μg (but is significantly increased with higher dosages above this).

<u>2-The type of progestogen</u> also affects the risk of VTE:

- -5/100,000 normal population,
- -15/100,000 in 2nd generation OCCP,
- -30/100,000 in 3rd generation OCCP,
- 60/100,000 in pregnant women,
- **3- age**: increase the risk
- **4- obesity**:increase the risk

5-acquired or congenital thrombophilia::increase the risk

The risk of VTE is greatest during the first year of use, possibly due to the unmasking of inherited thrombophilias. Screening for known thrombophilias is not cost effective, but women should be asked about a personal and family history of VTE if considering using this method, as these are contraindications to using a CHC method.

Women who are using CHC and making long-distance travel (>3 h of immobility) should take appropriate exercise on the journey and consider wearing graduated compression socks.

2-Arterial disease:

• The risk of myocardial infarction and thrombotic stroke in young, healthy women using low-dose COC is extremely small.

• Cigarette smoking and high blood pressure will both increase the risk, and any woman who smokes must be advised to stop COC at the age of 35 years.

• Around 1 per cent of women taking COC will become significantly hypertensive and they should be advised to stop taking it.

3- Breast cancer:

- All data show a slight increase in the risk of developing breast cancer among current COC users (relative risk around 1.24).
- This is not of great significance to young women
- For a woman in her forties or one with a strong family history, these are more relevant data, as their background rate of breast cancer is higher.
- Most data also show that any effect of COC on breast cancer risk has disappeared ten years after stopping COC.

Drug interaction: This occur with:

- enzyme-inducing agents as anti-epileptics, Higher dose estrogen pill combinations of 50 μg EE may need to be prescribed.
- Some broad-spectrum antibiotics can alter intestinal absorption of COC and reduce its efficacy.
- Additional contraceptive measures should therefore be recommended during antibiotic therapy and for 1 week thereafter.

Positive health benefits:

- 1-light pain free regular bleeding, so used for heavy painful cycle.
- 2- improve PMS.
- 3-decrease PID
- 4-long term protection against ovarian & endometrial cancer
- 5- also to treat acne & huirsutism.

Absolute contraindications:

- 1-Breastfeeding < 6 weeks postpartum
- 2-Smoking ≥15 cigarettes/day and age ≥35
- 3- Multiple risk factors for cardiovascular disease
- 4- Hypertension: systolic pressure ≥160 or diastolic ≥100 mmHg
- 5- Hypertension with vascular disease
- 6- Current or history of deep-vein thrombosis/ pulmonary embolism
- 7-Major surgery with prolonged immobilization
- 8- Known thrombogenic mutations
- 9- Current or history of ischaemic heart disease

- 10- Current or history of stroke
- 11-Complicated valvular heart disease
- 12Migraine with aura
- 13-Migraine without aura and age \geq 35 (continuation)
- 14- Current breast cancer
- 15-Diabetes for ≥20 years or with severe vascular disease or with severe nephropathy, retinopathy or neuropathy
- 16-Active viral hepatitis
- 17-Severe cirrhosis
- 18-Benign or malignant liver tumours.

Relative contraindications

- 1-Multiple risk factors for arterial disease
- 2-Hypertension: systolic blood pressure 140–159 or diastolic pressure 90–99 mmHg, or adequately treated to below 140/90 mmHg
- 3-Some known hyperlipidemias
- 4-Diabetes mellitus with vascular disease
- 5-Smoking, <15 cigarettes/day, and age \ge 35
- 6-Obesity
- 7-Migraine, without aura, and \geq 35
- 8-Breast cancer >5 years ago without recurrence
- 9-Breastfeeding until 6 months post-partum
- 10-Post-partum and not breastfeeding, until 21 days after childbirth
- 11-Current or medically treated gallbladder disease
- 12- Hx of cholestasis related to combined oral contraceptives
- 13-Mild cirrhosis
- 14-Taking rifampicin (rifampin) or certain anticonvulsants

Management of missed pill of COCP

If one pill has been missed (more than 24 hours and up to 48 hours late)

Continuing contraceptive cover

The missed pill should be taken as soon as it is remembered

The remaining pills should be continued at the usual time

Minimizing the risk of pregnancy

Emergency contraception (EC) is not usually required but may need to be considered if pills have been missed earlier in the packet or in the last week of the previous packet

If two or more pills have been missed (more than 48 hours late)

Continuing contraceptive cover

The most recent missed pill should be taken as soon as possible

The remaining pills should be continued at the usual time

Condoms should be used or sex avoided until seven consecutive active pills have been taken. This advice may be overcautious in the second and third weeks, but the advice is a backup in the event that further pills are missed

Minimizing the risk of pregnancy If pills are missed If pills are missed in If pills are missed in in the first week the second week the third week (pills 8-14) (pills 1-7) (pills 15-21) EC should be No indication for OMIT THE EC if the pills in the considered if PILL-FREE INTERVAL by unprotected sex preceding 7 days have been taken occurred in the finishing the pills pill-free interval or in the current pack consistently and (or discarding any in the first week of correctly (assuming pill taking the pills thereafter placebo tablets) are taken correctly and starting a new and additional pack the next day contraceptive precautions are used)

Progesterone only contraception

Mode of administration:

1-oral

2- injectable intramuscularly

3- subdermal implant

4-hormonal releasing IUS

Mechanism of action

All progesterone-only methods work by a local effects on CX mucous making it hostile to ascending sperm, & on the endometrium making it thin & atrophic, there by preventing implantation & sperm transport.

• Higher dose progesterone- only methods will also acts centrally & inhibits ovulation as in cerrazatte and depo provera.

1-Progesterone only contraceptive pill:

Formulation:

1- mini-pills, the older form, contain a very low dose of 2ndgenerationprogesterone(norethisterone,norgestrel).

2-Cerazette, the newest POP contain 3rd generation progesterone(desogestrel).

Regimen

• The pill should be taken at the same time every day without break, failure rate (1-3)per 100 women per years.

Advantages(indications):

- 1-Breast feeding.
- 2-Older women.
- 3-Presence of cardiovascular risk factors.
- 4-Diabetes.

Disadvantages:

- 1-Menstrual disturbances & amenorrhea.
- 2-acne.
- 3-breast tenderness.
- 4- functional ovarian cyst.
- 5-loss of libido.

2-Injectable progesterone:

Two injectable progesterone are marketed:

- 1- Depoprovera (depo-medroxyprogesterone acetate) 150mg every 3 months.
- 2- Norethisteron enanthate 200 mg every 2months.

Both are given by deep IM injection in the gluteal area.

MOA: suppression of ovulation ,effect on CX mucous & endometrial effects .

Failure rate (0.1-1)per 100 women per year.



Advantages:

- 1-highly effective.
- 2-redUction in menstrual blood flow.
- 3- protection against PID.

Disadvantages:

- 1-Delaye in return to fertility (up to 18 months)
- 2-Wt. gain & increase appetite.
- 3-Menstrual disturbance & spotting.
- 4-Long term use lead to osteoporosis.
- 5-Progesterone side effects as acne, breast tenderness.

3-Subdermal implants:

• Implanon: it consist of single rode containing 68mg of 3 ketodesogesterl(metabolites of desogesterel) inserted sub dermally in the upper arm under local anesthetic, provide contraception for 3 years.



4-Intrauterine hormonal contraception(Mirena):

.it prevents pregnancy by a local hormone effects on the CX & endometrium. It contain 52mg levonorgesterl releasing 20µg of it/day for 5 years.

<u>.many women experience unpredictable bleeding</u>. Women should be advised that this usually improves with time and many women will eventually have lighter or absent periods.



Non contraception benefit of Mirena

It can be a theraputic choice in management of:

- Endomeriosis
- Adenomyosis
- Dysmenorrhia
- Endometrial protection
- Simple endometerial hyperplasia

The two oral methods of EC that are licensed for use are levonorgestrel (LNG 1.5 mg) and the progesterone receptor modulator ulipristal acetate (30 mg). LNG appears effective up to 96 hours after unprotected sex and ulipristal acetate for up to 120 hours. Both methods work by delaying ovulation, so that any sperm present in the reproductive tract will have lost the ability to fertilize the oocyte once it is eventually released. Oral EC is much less effective than the Cu-IUD for EC and is estimated to prevent only two-thirds of pregnancies. Oral EC is much less effective than regular contraception. Women should be encouraged to start an effective method of contraception immediately after EC, to protect against pregnancy from further acts of intercourse.

