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Review Article

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ORAL CONTRACEPTIVES

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ABSTRACT

The birth control pill is the most commonly prescribed contraception method in the US, with 25% of women aged 15 to 44 preferring it. This hormonal tablet, containing estrogen and progesterone, is used to prevent conception and regulate monthly bleeding. However, due to their negative effects on at-risk groups, other methods of contraception are also employed. Contraception prevents pregnancy by blocking sperm interaction with the developed ovum. They help the menstrual cycle and some medical disorders. Non-pharmacological treatments include periodic abstinence and barriers, whereas pharmaceutical treatments include spermicide, spermicide-implanted barrier method, and hormonal contraception. The combination treatment of estrogen and progesterone suppresses gonadotropin production by negative feedback inhibition. Combining estrogen and progesterone lowers Luteinizing hormone production, which inhibits the mid cycle surge. Treatment options include combination and phased tablets.

KEYWORDS: Birth pills, contraception, sexually transmitted diseases.

INTRODUCTION

Generally contraceptives are used in prevention of pregnancy. Fertilization is the process the sperm contact with the mature ovum. This process is stopped by using the contraception. contraceptives are given according to the patient acceptability. The effectiveness of contraceptives is difficult to determine because the many factors affects contraceptives and in some patients the contraception may failed. The directions should be followed correctly. The clinicians give opportunity to educate the patient and prevent Sexually transmitted diseases physical examination may delays access to contraception. Contraception used in the pregnancy and it is harmful too. Since some national organization allow provision of contraception. Contraceptives improves menstrual cycle and certain health conditions management of menopause.

Non pharmacological therapy include

1. Periodic abstinence
2. Barriers

Periodic abstinence: This avoid sexual intercourse at the time of fertile period (day- 14to17) by this pregnancy is avoided.

Barriers: These are primary contraception. condoms, diaphragms, cervical cups and sponges are under barriers. these have high rate of failure and the chances of getting pregnancy are more Pharmacological therapy include

1. Spermicide
2. Spermicide- Implanted barrier technique
3. Hormonal contraception.

Spermicide: It contains nonoxynol- 9 and it is a chemical surfactant. Spermicide is in the form of cream, films, foams, gels, suppositories, sponges and tablets. it has no protection against Sexually transmitted diseases. Spermicide has increased risk of transmission of HIV.

Spermicide- Implanted barrier technique: It contains 1gm of nonoxynol-9. It is in the form of sponge. It should be inserted for 6 hours before intercourse and protected for 24 hours.

Hormonal contraception: It is available from 1960s. It contains estrogen & progestin or alone progestin. Available in the form of transdermal patch, intrauterine contraceptive, vaginal ring, injectables, implantable.

Estrogen: It has two synthetic estrogens they are ethinyl estradiol & mestranol. Mestranol is converted in liver and form ethinyl estradiol. Estrogens are mostly combined oral contraceptives, transdermal patch, vaginal ring contains approximately 20 to 50mcg of ethinyl

estradiol.

Progestins: It differs with respect to inhert estrogenic, anti estrogen and androgenic effect. These are secondary to extent progestin.[1]

Oral contraceptive pills (OCPs) are a popular reversible contraception method in the U.S., available as progestin-only pills (POPs) or combined oral contraceptives (COCs). POPs, like norethindrone, lack estrogen and thus have fewer contraindications but require strict daily timing and may cause irregular bleeding. Newer POPs, such as Slynd, offer more flexible dosing but may have limited insurance coverage. COCs, containing synthetic estrogen (ethinyl estradiol) and progestin, provide better bleeding control and flexible dosing but have more contraindications and varying side effects.[3]

Estrogens

- Estrogens are 3 types they are estradiol, estriol, estrone
- It promotes development and maintenance of female reproductive structure, female secondary sex characters and breasts.
- Increase in protein anabolism.
- Lowering blood cholesterol.
- Moderate levels of estrogens stop the release of GnRH, LH, FSH.[2]

Progesterone

- Produced by adrenal glands, gonads, brain, placenta.
- It works with estrogens to prepare endometrium for implantation and it prepares mammary glands to secrete milk. It inhibits the release of GnRH, LH.[2]

Relaxin

It stops contractions of uterine smooth muscles, increase of flexibility in pubic symphysis and dilation in uterine cervix.[2]

Inhibin

It inhibits the release of Follicle stimulating hormone (FSH), Luteinizing hormone (LH).[2]

Synthetic estrogens

- 17α ethinyl estradiol
- 3 methyl ether
- Ethinyl estradiol.[2]

Progestins

It is two types

C19- derived from testosterone C21-derived from progesterone

In adequate doses it inhibits ovulation and reduces levels of FSH, LH.[2]

Mechanism of action of combination therapy

Combination therapy of both estrogen and progesterone works by preventing ovulation by suppressing the secretion of gonadotropin through negative feedback inhibition.

It also changes the lining of the uterus to prevent pregnancy from developing and changes mucous to prevent sperm. Low doses of progesterone alter the endometrium and put it out of phase with ovulation there is no disruption of cycle and ovulation continues. Large doses of estrogen in case of post coitus pills alters the motility of Fallopian tube and character. therefore there is no chance of fertilization.[2]

Estrogen and progesterone combination

This combination is taken from day-5 to day-25 remaining 7days are free from therapy on repeating this schedule the cycle becomes an ovulatory with regular cyclic bleeding this is 100% effective in preventing pregnancy or conception.[2]

Sequential estrogen-progesterone preparation

It is administered from day-5 to day-25 of the menstrual cycle in between 7 pills free days during which withdrawal bleeds occur. serial packs available having 16 pills of estrogen, 5 estrogen progesterone pills and 7 placebo pills. inhibition of ovulation is due to estrogen and progesterone is added for satisfactory bleeding.[2]

Low doses progesterone preparation

It contains only progesterone take daily to control fertility and it is less effective than combined or sequential therapy.[2]

Adverse effects

Mild: Nausea, vomiting, lethargy, discomfort of breast.
Moderate: Pigmentation, increased weight, amenorrhoea (no menses).
Severe: DVT, PE, all types of thrombosis, hypertension, liver disease.[2]

Some Adverse drug reactions includes- abdominal cramps (15), ischemic stroke (17), follicular ovarian cyst.(19) The patient history should be taken to suggest the oral contraceptives (20).

PROGESTIN	DOSE	ESTROGEN	DOSE
Combined pills			
Norgestrel	0.3mg	Ethinyl estradiol	30µg
Norgestrel	0.5mg	Ethinyl estradiol	50µg
Levonorgestrel	0.25mg	Ethinyl estradiol	50µg
Levonorgestrel	0.15mg	Ethinyl estradiol	30µg
Desogestrel	0.15mg	Ethinyl estradiol	30µg

Desogestrel	0.15mg	Ethinyl estradiol	20µg
Phased pill			
Levonorgestrel	50-75-125µg	Ethinyl estradiol	30-40-30µg
Norethindrone	0.5-0.75-1.0mg	Ethinyl estradiol	35-35-35µg
Postcoital pill			
Levonorgestrel	0.25mg	Ethinyl estradiol	50µg
Levonorgestrel	0.75mg & 1.5mg	Nil	-
Mini pills			
Norethindrone	0.35mg	Nil	-
norgestrel	75µg	Nil	-

Mechanism of action

By the normal feedback mechanism the Gonadotropin hormone releases by the pituitary gland. Pulse is reduced by the progestin. FSH secretion is reduced by the estrogen. Both synergise and inhibits the mid cycle. Both estrogen and progesterone is combined taken in reduces the LH secretion so the mid cycle surge is abolished as a results follicles development decreases and fails to rupture.

Mini-pill and progestin only is attenuated by LH surge ovulation may occur irregularly in ⅓ cycle post cortical pill is taken after the intercourse inhibits the ovulation. Thick cervical mucous secretion to sperm penetration evoked by progestin action. Even the ovulation and fertilization occur the blastocyst fail to implant because the endometrium is proliferate or hyper secretory or atrophic it is mostly seen in the mini pill and post coital pill.

Uterine and tubular secretion are modified as the unfavour fertilization contributes the efficacy of the mini pill and post coital pill.

The post coital pill may dislodge implanted blastocyst interfere with fertilization and implantation.[2]

Types of methods

1. Combined pill

It is the mixture of estrogens and progestin at fixed dose for treatment. both estrogen and progestin is reduced in the second generation of OC pills without comprising efficacy.it reduces the side effects and complications. In the third generation pills it is with newer progestins like Desogestrel it have introduced from 1990s. Ethinylestradiol with 30µg daily to 20µg with progestin it has anti ovulatory action. Progestin is a 19-nortestosterone because it is with antiovulatory action. Currently used progestins is Levonorgestrol 60µg, Desogestrol 60µg, norgestimate 200µg, Gestodene 40µg. This pills are taken for 21days stating from 5th day of mensuration. Next treatment is started with the gap of 7days it is most common and efficacious method.[2]

2. Phased pills

It is a triphasic and it reduces in total steroid dose without compromising efficacy by exact action the normal hormonal pattern in the mensuration. Estrogen dose is common where progestin dose higher in second and third phases compared to first phase. this pills is given to women of above age 35 years. This is with no withdrawal bleeding. It has other risk factors.[2]

3. Progestin only pill

In this pill it is with only progestin it does not contain estrogen because of long-term risk. It give to the women who are contraindicated to the estrogen. It is taken without gap and the menstrual cycle became irregular and ovulation is 20-30% women. the efficacy is lower compared to the combined pill.[2] some progestin compounds have more antiandrogenic characteristics, making them more helpful for treating polycystic ovarian syndrome, hirsutism, and acne.[10] The CDC has issued guidelines for users of progesterone-only tablets (POPs) who have other medical issues. Most women can take POP, because they are contraindicated to COC or to avoid the estrogen in the contraceptive pill.[14]

4. Emergency pill

This pills are used by the women with no using of contraception with having intercourse. If there is any chance of getting pregnancy third pill is used. most commonly used regimen is- Levonorgestrol 0.75mg two doses for 12hours or 1.5mg is used as single dose it is taken before 72 hours of unprotected intercourse. According to WHO trails on postovulatory methods of controlling fertility. It is more effective and well tolerated than before. Earlier combination is Levonorgestrol 0.5mg+ethinyl estradiol 0.1mg two doses for every 12hours with in 72 hours. Ulipristal 30mg single dose is used with in 120 hours of the intercourse. Anti progestins are mainly used in china and Europe. mifeprestone 600mg is taken in with in 72hours of intercourse.[2]

Practical considerations

Discontinuation of the OC pill leads to fertility in 2-3 months. Increases the fertility chances and multiple pregnancies are more if conception is more than 2-3 cycles. If the combined pill is missed by the women the next day the 2 pills should be taken if more than 2 pills are missed leads to the interruption of the cycle and the next cycle is started after the 5th day of the bleeding. A pill contains 30µg of the ethinylestradiol. if the women is obese it can be taken upto 50µg and 20µg it may leads to the cardiac risk after the age 40.The bleeding may occur if the estrogen is taken in the high dose. If the is contraindicated to the estrogen the progesterone only pill

should be used.[1] This pill combination typically contains less than 50 mcg of ethinyl estradiol. The pills might be monophasic (the same dose of both components in the active tablets) or multiphasic. The withdrawal bleeding can be administered as cyclic (monthly), extended cyclic (every 3 months), or continuous dosage (no bleeding).[11] If a patient misses a dose, take it as soon as they remember, and then take the following tablet at the customary time. If the patient misses two tablets in a row in the first or second week, take two tablets on the day he or she remembers, two pills the next day, and thereafter one per day. Use additional kinds of contraception until the patient starts a new cycle.[13]

Considerations with combined hormonal contraception

Combined hormonal contraception have a disadvantage of increased weight. The prescriber should explain about contraception. It has disadvantages, adverse effects and risks of contraception. Before giving the contraception the medical history & blood pressure should be checked. Combined hormonal contraception also have advantage of relief of menstrual cramps, decrease of ovulation pain and decreasing the menstrual blood loss and improves menstrual regularity and decreases iron deficiency anemia. Decrease in the risk of ovarian and endometrial cancer. By using, there is no 50% of risk for 5 years or more than 5years. Decrease in risk of ovarian cyst, ectopic pregnancy, pelvic inflammatory disease. combined hormonal contraception vaginal ring is uncomfortable to women and cause discharge in vagina. combined hormonal contraception patch may cause irritation and increase potential for thromboembolism. According to ACOG and WHO there will be less risk of the complications. Women above 35 years the contraception is controversial and the dose should be less (< 30mcg). and the women age above > 40 years and smokers should contain dose >50mcg of combined hormonal contraception should be suggested.(1) if a woman is breast feeding, avoid COC for the first 42 days of postpartum since hormones affect lactation.[12]

Adverse effects

Estrogen excess: Nausea, breast tenderness, headache, cyclic weight gain due to fluid retention, dysmenorrhea, menorrhagia, uterine fibroid growth.

Estrogen deficiency: Vasomotor symptoms, nervousness, decreased libido.

Progestin excess: Increased appetite, weight gain, blotting, acne, irritability, fatigue, constipation, oily skin, hirsutism, depression.

Progestin deficiency: Dysmenorrhea, break through bleeding and spotting.

Indications

The COC tablet is the most widely prescribed. Progesterone inhibits pregnancy, whereas estrogen controls monthly bleeding.[4] The majority of women take OCPs to avoid pregnancy, although 14% use them for non-contraceptive purposes. OCPs can be used to treat a variety of health issues, including menstrual discomfort, irregular menstruation, fibroids, endometriosis- related pain, and menstrual migraines.[5,6] The FDA has formally approved specific brands of acne-treatment combination tablets.[7] Strong epidemiologic evidence suggests that women who have used COCs are 50% less likely to develop endometrial cancer than those who have never used COCs. This effect can endure for up to twenty years. COC use reduces the risk of ovarian cancer by 27%; the longer the treatment, the greater the risk reduction. OCs have also been shown to lower the risk of colon cancer by 18%. Some formulations are recommended for the treatment of acne and hirsutism.[8,9]

Contraindications

However, OCPs are contraindicated in smokers (more than 15 cigarettes per day) over age 35 due to a significant risk for cardiovascular events, specifically deep vein thromboembolism. The risk of VTE increases among OC users 3 to 9/10,000 woman-years compared with nonusers who are not pregnant and not taking hormones (1-5/10,000 woman-years). The risk is more significant in those aged over 35 and smoking.[21]

Women with hypertension (systolic BP greater than or equal to 140 mm Hg or diastolic BP ≥90 mmHg as per the CDC), breast cancer, known ischemic heart disease, migraines with auras, endometrial cancer, cirrhosis, hepatocellular adenoma, or malignant hepatoma are contraindicated to use combined hormone contraceptive pill.[22]

Monitoring

A healthy woman taking COCs should see her primary care physician once a year for a blood pressure check and other routine medical care. Monitor blood pressure in women who have well- controlled hypertension that is being treated medically. Pre-Diabetic and diabetic women should be monitored on a regular basis, as hormone contraceptives can impair glucose tolerance and are typically dose-dependent. It has an anti-mineral corticoid activity and also cause hyperkalemia in patients. The patient use the medicine for hyperkalemia can increase the level of potassium.

Potent CYP3A4 inhibitors, such as indinavir, should be monitored for serum potassium levels. Potassium supplementation, potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, angiotensin-II receptor antagonists, aldosterone antagonists, heparin, and non- steroidal anti-inflammatory drugs can all raise serum potassium levels.[23]

Toxicity

if a patient use too many OCPs, the common side effects are severe headaches, nausea, and vomiting. There is no antidote for this illness; antiemetics and analgesics are

used to treat its symptoms. If the patient has other risk factors for increased VTE, a preventive anticoagulant drug may be considered. Severe or symptomatic anemia caused by hemorrhage can be treated with high doses of estrogen and progesterone.[24,25,26]

There have been no reports of significant side effects from an overdose, including intake by minors. However, overdosage in females might result in withdrawal bleeding and nausea. Drospirenone is a spironolactone analog with anti-mineralocorticoid characteristics, therefore keep an eye on serum potassium and sodium levels, as well as any signs of metabolic acidosis in overdose instances. If an overdose is suspected or confirmed, contact your local poison control center for the protocol.[27]

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