النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pharma tables

LEC NO. : Lec-3

DONE BY : Dana abudalou

وَقُل رَّبِّ زِدْنِي عِلْمًا

Female sex hormones

Estrogen

The major estrogens produced by women are estradiol, estrone, and estriol.

Estradiol is the major secretory product of the ovary and most potent estrogen.
Principal estrogen in premenopausal women. A minute amount of estradiol is synthesized in the testes.
➢ Most estrone and estriol are formed in the liver from estradiol or in peripheral tissues from androgens precursors.
Estrone is the primary circulating estrogen after menopause, and estriol, is present in significant amounts during pregnancy, because it is synthesized by the placenta.

First-pass metabolism in the gastrointestinal tract rapidly breaks down estradiol tablets before entering the systemic circulation. The bioavailability of oral estrogens is said to be 2-10% due to significant first-pass effects.

Synthetic Estrogens

estradiol valerate: The esterification of estradiol improves the administration
estradiol cypionate: sustain release from intramuscular depot injections higher lipophilicity. After absorption, the esters are cleaved, which leads to the release of estradiol.

Ethinylestradiol (EE) is a synthetic form of estradiol commonly used as the estrogenic component of most combination oral contraceptive pills. Ethinyl estradiol is different from estradiol due to its higher bioavailability and increased resistance to metabolism, rendering it more suitable for oral administration.

Estrogen uses

Primary Hypogonadism

Hypogonadism in females describes the inadequate function of the ovaries, with impaired production of germ cells and sex hormones (estrogen and progesterone).

Treatment of primary hypogonadism is usually begun at 11–13 years of age in order to stimulate the development of secondary sex characteristics and menses, to stimulate optimal growth, to prevent osteoporosis, and to avoid the psychological consequences of delayed puberty and estrogen deficiency.

Treatment attempts to mimic the physiology of puberty. It is initiated with small doses of estrogen is slowly increased to adult doses and then maintained until the age of menopause (approximately 51 years of age). A progestin is added after the first uterine bleeding. When growth is completed, chronic therapy consists mainly of the administration of adult doses of both estrogens and progestins.

Postmenopausal Hormonal Therapy

The primary indication is relief of menopausal symptoms, such as hot flashes, vaginal atrophy and dryness, insomnia and urinary urgency

If the main indication for therapy is hot flashes and sleep disturbances, therapy with the lowest dose of estrogen required for symptomatic relief is recommended.
Treatment may be required for only a limited period of time and the possible increased risk for breast cancer is avoided.

In case of premature menopause (before the age of 40) or early menopause (before the age of 45), it's particularly important to begin therapy as soon as possible for maximum protection against osteoporosis

Patients with mild atrophic vaginitis can be treated with topical preparations. The vaginal route of application is also useful in the treatment of urinary tract symptoms in these patients

The administration of an opposed estrogen is associated with an increased risk of endometrial carcinoma. However, progesterone antagonize the beneficial effect of esterogen on lipid.

For women with an intact uterus, a progestogen is included with the estrogen therapy, because the combination reduces the risk of endometrial carcinoma associated with estrogen alone. Women who have undergone a hysterectomy may use estrogen alone.

Suppression of ovulation

Estrogens combined with progestins can be used to suppress ovulation in patients with intractable dysmenorrhea (moderate to severe pain caused by menstrual periods).

or treatment of hirsutism (growth of excessive male-pattern hair in women after puberty) and amenorrhea (absence of menstruation) due to excessive secretion of androgens by the ovary.

Estrogen side effects

Uterine Bleeding:
Estrogen side effects
Estrogen therapy is a major cause of postmenopausal uterine bleeding. To avoid confusion with carcinomas, patients should be treated with the smallest amount of estrogen possible. It should be given cyclically so that bleeding, if it occurs, will be more likely to occur during the withdrawal period.
Estrogen increases the risk of both arterial and venous thrombosis

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Cancer: breast cancer and endometrial carcinoma

breast tenderness
Hyperpigmentation.
increase in frequency of migraine headaches
Cholestasis: flow of bile from the liver is slowed or blocked hypertension.

selective estrogen receptor modulator (SERM)

Tamoxifen

Tamoxifen, a competitive partial agonist inhibitor of estradiol at the estrogen receptor, was the first selective estrogen receptor modulator (SERM) to be introduced. The mechanism of its mixed agonist/antagonist is still not completely understood.

Tamoxifen is indicated for the treatment of breast cancer in a variety of settings
➢ patients with estrogen receptor-positive tumors are more likely to benefit from tamoxifen

in the breast tissue, it competes with estrogen for binding sites and causes antiestrogenic and antitumor effects. In bone, it stimulates estrogen receptors instead of blocking them, exerting an estrogenic agonist effect, and may prevent osteoporosis in postmenopausal women. It also acts as an estrogen agonist in the hypothalamus of premenopausal women, which increases gonadotropin levels and can induce ovulation

Tamoxifen- Uses

Treatment of breast cancer in both females and males.

Adjuvant treatment of breast cancer after patients have completed their primary treatment with surgery and radiation.

Treatment of female patients with ductal carcinoma in situ (non-invasive breast cancer) after surgery and radiation to reduce the risk of invasive breast cancer.

Chemoprevention of breast cancer in high-risk women

Tamoxifen-side effects

Associated with increased incidence of uterine or endometrial cancers. In patients who were already diagnosed with breast cancer, however, the benefits outweigh the risks.

Hot flashes, irregular periods, and vaginal discharge, nausea and vomiting.

Increase risk of pulmonary embolism, and stroke.

For patients taking tamoxifen for breast cancer risk reduction, it should be avoided if the patient has a history of deep vein thrombosis (DVT) or pulmonary embolism (PE). In patients that have been diagnosed with breast cancer, the benefits outweigh the risks, but it should still be used with caution in patients with a history of thromboembolic events.

Raloxifene

Partial estrogen agonist-antagonist at some but not all target tissues.

It has estrogenic effects on lipids and bone but appears not to stimulate the endometrium or breast.

Uses: prevention of postmenopausal osteoporosis and prophylaxis of breast cancer in women with risk factors.

Side effects: hot flashes, leg cramps, and increases the risk of deep-vein thrombosis and pulmonary embolism.

Progesterone

Progesterone is the most important progestin in humans. It is synthesized in the ovary, testis, and adrenal cortex from circulating cholesterol. Large amounts are also synthesized and released by the placenta during pregnancy.

Effects

Favorsfatdeposition
· Increases basal insulin levels and the insulin response to glucose.
· Compete with aldosterone for the at renal tubule, causing a decrease in Na+ reabsorption.
· Increases body temperature in humans.
· Prepares the uterus for implantation of the fertilized ovum.

Inhibit uterine contraction that would expel the fetus.
· -ve feed back effect on luteinizing hormone so, block ovulation.
· Thick cervical secretion so, block sperm penetration.

Progesterone uses

Primary use in HRT and contraception
Amenorrhea (abscense of periodes), either primary or secondary

Assisted reproductive technology treatment to enhance embryo implantation and decrease the risk of miscarriage.
Endometrial hyperplasia

Anti progesterone: MIFEPRISTONE

Mifepristone works by being an antagonist of glucocorticoid and progesterone receptors

Mifepristone has two main FDA-approved indications.:
pregnancy termination combined with misoprostol through ten weeks gestation management and treatment of hyperglycemia in patients exhibiting signs of Cushing syndrome.

Side effects: anaphylactic reactions, toxic epidermal necrolysis, peripheral edema, hypertension, hypoglycemia, vaginal bleeding, uterine contractions, nausea, abdominal pain, fever, vomiting.