Dr.Saba jassim

Its steroid hormone synthesized by the ovary, testis, adrenal cortex. Estrogens include the natural hormones and synthetic, most estrogen in the female is produced in the ovaries

Classification

Natural Estrogens: Estradiol, estriol, estrone

Synthetic estrogen:

Steroidal: Ethinylestradiol, mestranol

Non steroidal: Diethylstilbestrol, dienestrol

NATURAL ESTROGENS

1-Estradiol- also known as 17β-estradiol, principle estrogen in premenopausal women.

2-Estrone is a metabolite of estradiol that has less estrogenic potency . Estrone is the primary circulating estrogen after menopause. isolated from the urine of pregnant.

3-Estriol-significantly less potent than estradiol

present in significant amounts during pregnancy,

because its principal estrogen produced by placenta.

2.Synthetic

-steroidal estrogens:-Ethinylestradiol ,mestranol (prodrug), & tibolone

-non-steroidal estrogens:-Stilbestrol, Dienestrol.

-long duration of action ,slow metabolic rate.

Work via a steroid hormone mechanism.

-Entering the target cells and binding to specific cytosolic receptors

-The steroid-receptor complex is then translocated to the nucleus, Where it alters gene expression

Estrogen receptors

2 estrogen -receptor subtypes mediate the effects of the hormone

1.α receptor -the classic estrogen receptor. Found in breasts, hypothalamus, uterus ,vagina ,endothelial cells and vascular smooth muscle.

2.β receptor-highly homologous to the α receptor. found in bone, brain, ovaries, prostate

Pharmacokinetic of estrogens

- Synthetic estrogens-active orally. Available as oral, parental, TDS ,creams.

-Natural E are not effective orally due to 1st pass effect, and undergo glucuronide & conjugation.

-Excreted through urine.

Natural Estrogen: Preparations

-Estradiol:2.5-10mg intramuscular injection(depot) and transdermal patch.

-Estriol: 4-8 mg/day initially then 1-2 mg/day, oral

-Estriol succinate: cream

Synthetic Estrogen: Preparations

-Ethinylestradiol: oral

-Mestranol: oral ,convert to EE

-Fosfestrol: intravenous preparation

-Dienestrol: topical preparation

-Conjugated Estrogens: oral (DUB) or injections 25 mg/ml

Therapeutic uses of estrogens

1.HRT- for post menopausal symptoms

a) Prevention of osteoporosis and fractures

b) Vasomotor symptoms(hot flash)

c) protection against CV diseases

d) Urogenital atrophy

e) Neuroprotective & CNS effects

2.ERT in primary ovarian failure

3.Dysfunctional uterine bleeding

4.Dysmenorrhoea

5.Acne & Hirsutism

6.Prostrate carcinoma, Migraine & Colon cancer

"H..has your hot flush gone yet, c..can we close the window now?"

The principal hormone used in HRT is estrogen. This is ideal for a woman who had her uterus removed (hysterectomy) already.

But in a woman with an intact uterus, only estrogen therapy leads to endometrial hyperplasia and even endometrial carcinoma.

-Addition of progestin for last 12–14 days each month can prevent this problem

Considering the risks, hormone therapy should be used with the lowest effective dose and for a short period of time.

-Low dose oral conjugated estrogen 0.3 mg daily

is effective and has got minimal side effects.

-Dose interval may be modified as daily for initial 2-3 months then it may be changed to every other day for another 2–3 months and then every third day for the next 2–3 months.

It may be stopped after symptoms are controlled

there may be irregular bleeding with this regimen

In patients with history of breast carcinoma, or endometrial carcinoma, progestins may be used. It may be effective in suppressing hot flushes and it prevents osteoporosis.

-Medroxyprogesterone acetate 2.5–5 mg/day can be used.

-Levonorgestren intrauterine system with daily release of 10 microgram of levonorgestrel per 24 hours, it protects the endometrium from hyperplasia and cancer. At the same time it has got no systemic progestin side effects.

-It can serve as contraception and HRT when given in a premenopausal women.

- Vasomotor symptoms

-Hot flushes are most common in P.M.W

-Short term RX with conjugated equine estrogen.

-Medroxy progesterone - is effective.

-Clonidine-in E dependent tumors.

Tibolone:

Tibolone is a steroid (19 nortestosterone derivative) having weakly estrogenic, progestogenic and androgenic properties. It prevents osteoporosis, atrophic changes of vagina and hot flushes. It increases libido . dose of 2.5 mg per day is given.

Adverse Effects

Males :Suppression of libido, gynecomastia and feminization

Children :Fusion of epiphyses and reduction of adult stature

Postmenopausal women/ on HRT

-Risk of irregular bleeding and endometrial carcinoma

-Growth of existing breast cancer

Women under long term estrogen therapy

-Increased incidence of gallstones, benign hepatoma thromboembolism, hepatic adenomas

-Co-morbidity worsening of Migraine, epilepsy, endometriosis

Pregnant Women(esp. first trimester)

-Vaginal and cervical carcinoma in female offspring in childhood or early adulthood

Antiestrogen and selective estrogen receptor modulator (SERMs)

Clomiphene Citrate (Antiestrogen)

The "**Fertility pill**" - pure antagonist of estrogen receptor in all human tissues

- MOA: By acting as a partial estrogen agonist and blocks the negative feedback of estrogens on the hypothalamus, so increases the secretion of gonadotropin-releasing hormone and gonadotropins, Increase in amount of secretion of FSH/LH at each secretary pulse ,leading to a stimulation of ovulation. The drug has been used successfully to treat infertility associated with an ovulatory cycles.

-Bind to both, ERα and ER β receptors

Dosage:

-50 mg oral dose from 5th day of cycle for 5 days

-Continued for 2-3 cycles

-Conception occurs within 4-6 cycles

-If no, dose increased

Other Uses:

-Assisted reproduction (to develop multiple eggs)

-Oligospermia (25 mg daily for 6 months - 6 days rest)

selective estrogen receptor modulator (SERMs)

Exerts both estrogenic and anti-estrogenic actions in a tissue selective manner

-**Tamoxifen**:

-Is a competitive antagonist to estrogen at receptors in the breast.

-Partial agonist at other estrogen receptors bone, uterus, liver and pituitary(thus minimizing side effects)

-Decrease in LDL level but no change in HDL level

-Improvement in bone mass and lipid profile

-Kinetics: Absorbed orally and has half life-10 Hrs and 7 days – long duration of action

-Excreted in Bile

-Dose is 10 to 20 mg BD

Uses:

-Breast carcinoma of pre and post menopause

-Adjuvant therapy in early cases

-Palliative therapy

-Side effects.

-The drug has a low incidence of adverse reactions

-Hot flashes, menstrual irregularities and bleeding, headache, hypercalcemia , and blood dyscrasias

-Less toxic than anticancer drugs

-Other SERM – Raloxifene, ormeloxifene etc.

-Raloxifene is estrogen antagonist of breast and endometrium while partial agonist of bone and CVS

Used as **second line** drug for prevention and treatment of osteoporosis in postmenopausal women

Aromatase Inhibitors

-Letrozole, Anastrozole

Letrozole is an aromatase inhibitor used in the treatment of breast cancer. Aromatase inhibitors work by inhibiting the action of the enzyme aromatase, which converts androgens into estrogens by a process called aromatization. As breast tissue is stimulated by estrogens, decreasing their production is a way of suppressing recurrence of the breast tumor tissue.

-Orally active, Rapid oral absorption – 100% bioavailability, large Vd, t1/2 – 40 Hrs

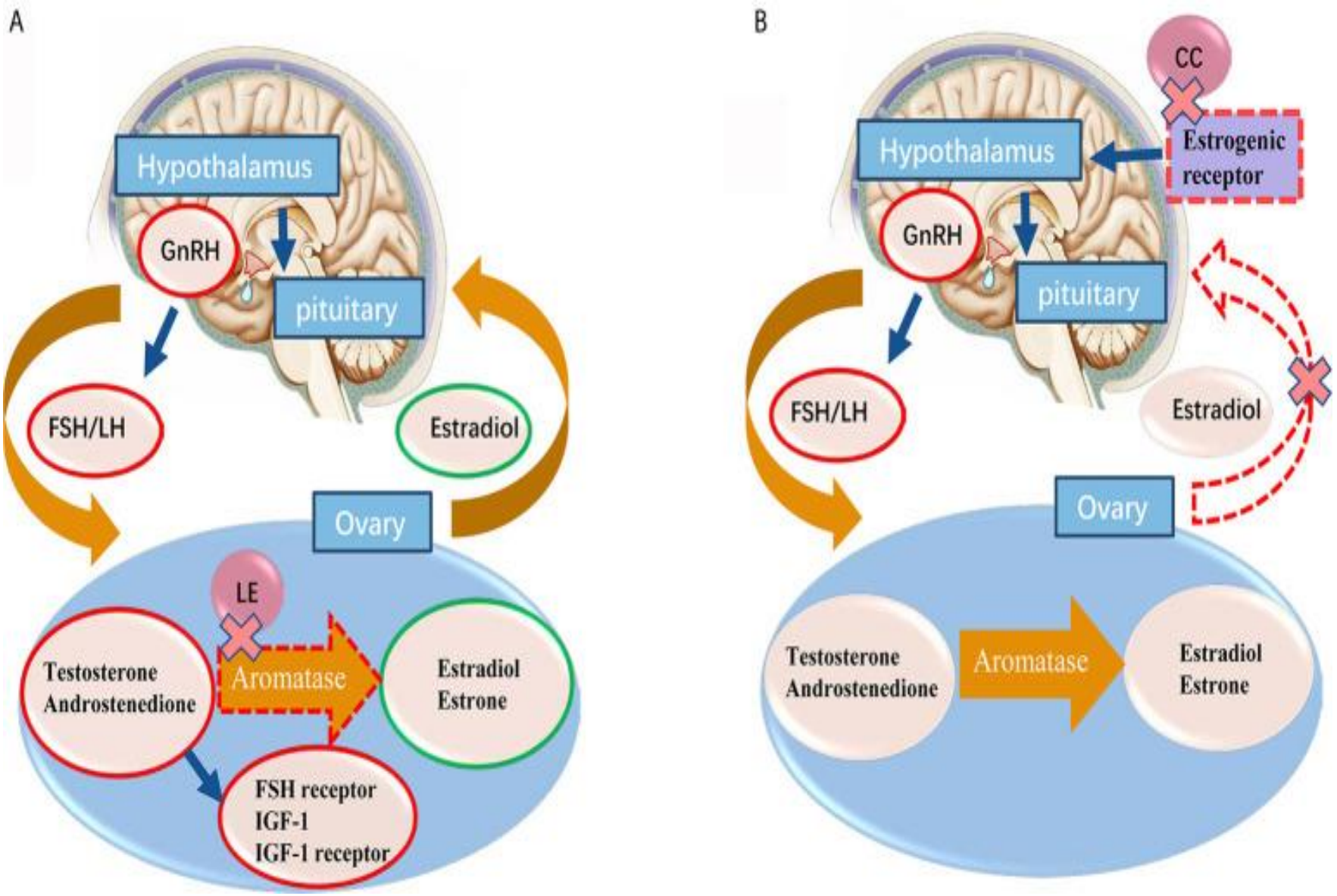
-Reversibly inhibits aromatization of testosterone and androstenedione all over body total estrogen deprivation

-Used in Early breast cancer (first line adjuvant therapy post mastectomy)

-in ER in postmenopausal women

-Advanced breast cancer (first line as well as tamoxifen failure cases)

Letrozole vs. Clomiphene citrate


A
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Testosterone
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Aromatase
Estradiol
Estrone
FSH receptor
IGF-1
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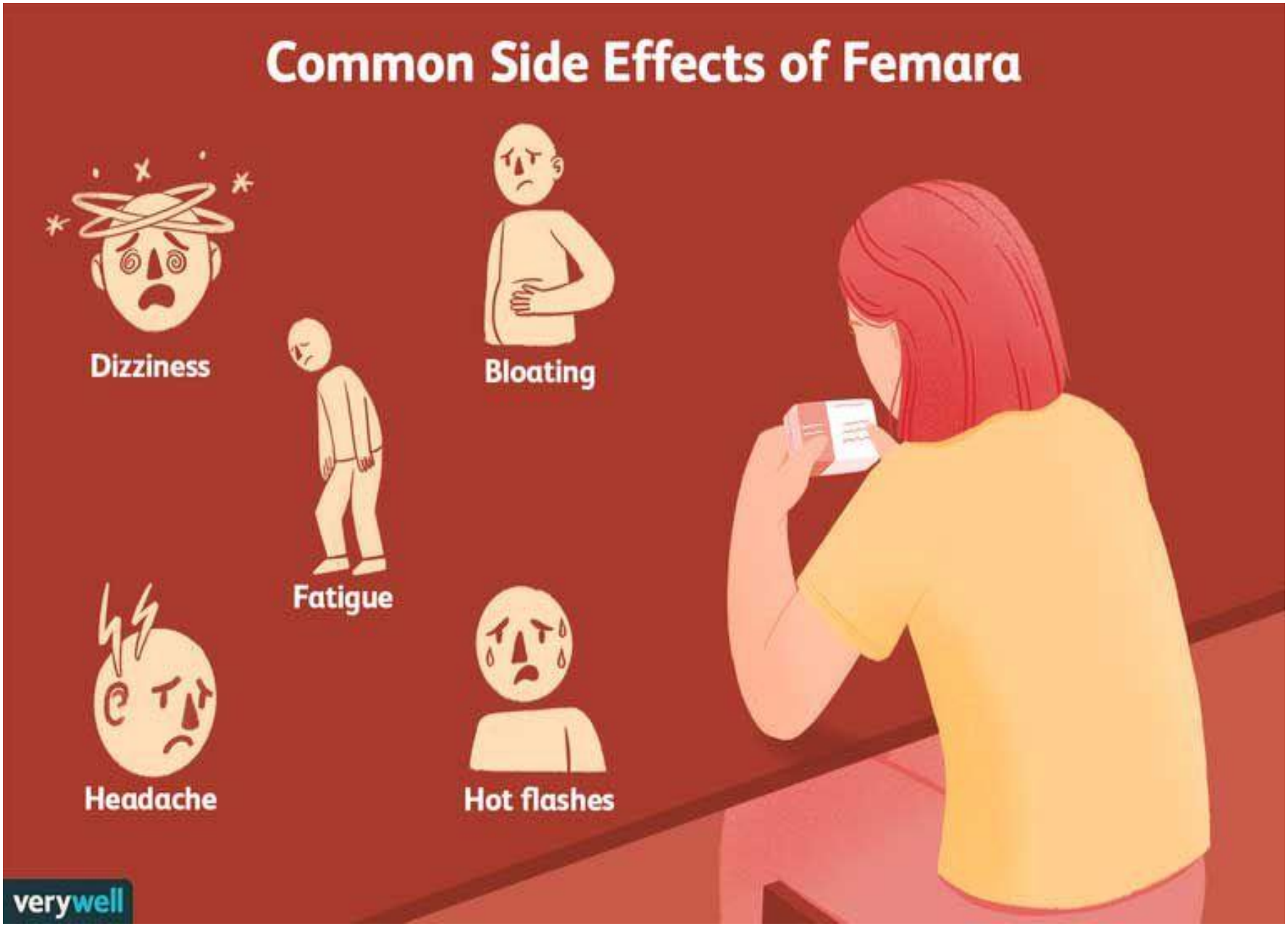
Common Side Effects of Femara
Dizziness
Bloating
Fatigue
Headache
Hot flashes
verywell

Thank you