Menopause

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Menopause

- Natural menopause is defined as the permanent cessation of menstrual periods, determined retrospectively after a woman has experienced 12 months of amenorrhea without any other obvious pathological or physiological cause. It occurs at a median age of 51.4 years in normal women, and is a reflection of complete, or near complete, ovarian follicular depletion, with resulting hypoestrogenemia and high follicle-stimulating hormone (FSH) concentrations
- Menopause before age 40 years is considered to be abnormal and is referred to as primary ovarian insufficiency (premature ovarian failure).
- The menopausal transition, or perimenopause, occurs after the reproductive years, but before menopause, and is characterized by irregular menstrual cycles, endocrine changes, and symptoms.

Diagnosis

History

FSH

- Before 45 years
- Before 40 years

Difficult

- PCOS, hypothalamic amenorrhoea
- Pills
- Hysterectomy/ endometrial ablation

Implications of menopause (Short term)

- **Hot flashes**
- **Sleep disturbance**
- **Depression**
- **Vaginal dryness**
- **Sexual function**
- **Cognitive changes**
- **Joint pain**
- It is unclear if the pain is related to estrogen deficiency or a rheumatologic disorder, but in the Women's Health Initiative, women with joint pain or stiffness at baseline were more likely to get relief with either combined estrogen-progestin therapy or unopposed estrogen than with placebo.

Long-term consequences of estrogen deficiency

- **Bone loss -** Bone loss begins during the menopausal transition
- **Cardiovascular disease** – The risk of cardiovascular disease increases after menopause, thought to be at least in part due to estrogen deficiency.
- **Dementia** – There is limited epidemiologic support for the hypothesis that estrogen preserves overall cognitive function in non-demented women. However, in the Women's Health Initiative (WHI), both unopposed estrogen and combined estrogen-progestin therapy had no global cognitive benefits in older, non-demented postmenopausal women
- **Degenerative arthritis** – Estrogen deficiency after menopause may contribute to the development of osteoarthritis, but data are limited.
- **Body composition** – In the early postmenopausal years, women who do not take estrogen therapy typically gain fat mass and lose lean mass. Some, but not all, studies, suggest that postmenopausal hormone therapy is associated with a decrease in central fat distribution.
- **Skin changes** – The collagen content of the skin and bones is reduced by estrogen deficiency. Decreased cutaneous collagen may lead to increased aging and wrinkling of the skin. Limited data suggest that collagen changes may be minimized with estrogen.
- **Balance** – Impaired balance in postmenopausal women may be a central effect of estrogen deficiency

Management

- When
- What are the concerns
- What to start
- HRT and contraception

Case scenario

- 50 years old, nulliparous, Professor, demanding job, worried about dementia,no symptoms wants to start HRT.

Case scenario

- 60 years old, on Norethisterone? for many years as started during perimenopause, arthritis, does not want to stop HRT.

Case scenario

- 50 years old , had TLH,BSO, severe symptoms of hot flushes/sweats.

Treatment/ management

- Estrogen is the most effective treatment available for relief of menopausal symptoms, most importantly hot flashes. Menopausal hormone therapy (MHT; estrogen alone or combined with a progestin) is currently indicated for management of menopausal symptoms.

- Long-term use for prevention of disease is no longer recommended.

What are the concerns/ side effects?

Case scenario

- 55 years old, Nulliparous, BMI 35, strong family history of CAD, Hypertensive, suffering from hot flushes and works in city.

Concerns

Cardiovascular

Coronary artery disease

Stroke

slightly increased with Oral (not TD) and incidence as such is very low before 60.

DM

- Explain to women that taking HRT (either orally or transdermally) is not associated with an increased risk of developing type 2 diabetes.
- Ensure that women with type 2 diabetes and all healthcare professionals involved in their care are aware that HRT is not generally associated with an adverse effect on blood glucose control.
- Consider HRT for menopausal symptoms in women with type 2 diabetes after taking comorbidities into account and seeking specialist advice if needed.

Case scenario

- 52 years old, multiparous, BMI 29, had breast cysts, no family history of breast cancers, symptomatic, wants to start HRT

Breast cancer

- HRT with oestrogen alone is associated with little or no change in the risk of breast cancer
- HRT with oestrogen and progestogen can be associated with an increase in the risk of breast cancer
- Any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT.

VTE

- HRT is associated with 2-4 fold increase
- Transdermal HRT appears safe
- Choose low risk progesterone

Cochrane conclusion

For every 1000 women, when given at the right time, HRT could:

Save 6 lives

Prevent 8 women from suffering heart disease

At the cost of 5 extra women experiencing blood clots

HRT

- Offer women HRT for vasomotor symptoms after discussing with them the short-term (up to 5 years) and longer-term benefits and risks. Offer a choice of preparations as follows:
- oestrogen and progestogen to women with a uterus
- oestrogen alone to women without a uterus.

- Do not routinely offer selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms alone.

- Isoflavones or black cohosh

- Side effects — Common side effects of estrogen include breast soreness, which can often be minimized by using lower doses. As noted above, some women experience mood symptoms and bloating with progestin therapy. Vaginal bleeding occurs in almost all women receiving cyclic estrogen-progestin regimens and is common in the early months of continuous estrogen-progestin regimen.
- Estrogen, especially in combination with a progestin, is also associated with increased breast density and a higher rate of abnormal mammograms and breast biopsies.

Factors affecting oral estrogen metabolism

- The dosing suggestions may need to be increased in women taking anticonvulsant drugs.
- In women receiving T4 replacement therapy, the addition of oral estrogen therapy may increase T4 requirements.
- Concurrent acute alcohol ingestion with oral estradiol has been found to cause a threefold rise in serum estradiol concentrations, apparently by slowing the metabolism of estradiol. While it would be difficult to alter the medication dose based upon these findings, women taking exogenous estrogen should be encouraged to limit alcohol intake.
- Women with end-stage renal disease have higher serum estradiol concentrations after an oral dose of estrogen than do normal women.

HRT preparations

- Estrogens(TD)
- Estradot patches 25-100 mcg
- Oestrogel 2-4 apps(2measures 2.5g of Oestrogel-1.5mg of Estradiol)
- Sandrena gel

- Progesterone
- Oral; Utrogestan cc 100 mg, sc 200mg 12 days, day 15-26
- IUS

- Combined oral regimen
- Femoston (Estradiol, Didrogesterone)range 1:10,2:10, Femoston conti .5:2.5, 1:5

- Combined patches Evorel conti(Norethisterone), Femseven conti (LNG).

HRT and contraception

- Estradiol oral/td/IUS

Or

- Qlaira E2/Dienogest 26/2 E2 COC
- Zoely E2/Nomegestrol 24/4 E2COC

When to stop contraception

- Periods stop under 50 after 2 years
- Periods stop after 50 after 1 year
- Amenorrhoeic due to progesterone
- Over 50, FSH 2, >30, stop after 1 year
- Using sequential HRT use contraception in addition to HRT
- Stop in anyone at 55?

Testosterone?

Pink Viagra?

Testosterone preparations

- Testim gel/ testogel/tostran .5-1ml/day

- Off license in women
- Pea sized blob to abdomen daily
- FAI is less than 5 % of physiological upper limit so no beard!
- Intrinsa patches too expensive
- Livial weakly androgenic
- Testosterone implants unlicensed USA
- Pill plus (COC with DHEA) not available yet

Duavive estrogen/ SERM

Vaginal Estrogen

- Why?

- What?

Vaginal treatment Why?

- **SUI** local estrogen and PFMT provide superior improvement than PFMT or estrogen alone

- **OAB** tolterodine plus estrogen and Solifenacin plus estrogen

- **Recurrent UTIs** oral estrogen no effect/ vaginal reduced

Vaginal preparation what?

Creams Ovestin .1% estriol, Gynest .01% estriol

Rings Oestradiol Estring 7.5mcg/24 hours 2 years license

Tabs Vagifem 10 mcg 1.14 mg/annum!

In development phase

Ovules DHEA also may help libido

Tablets Ospemifene Ist SERM for this indication

Vaginal estrogen and breast cancer

- Non hormonal therapy
- Vaginal estrogen reserved for unresponsive cases
- Systemic levels are very low
- Data do not show increased recurrence of breast cancer

Alternative

Moisturisers and lubricants can be used alone or in addition to vaginal oestrogen.

Mona Lisa touch(fractional microablative CO2 laser)

Regeneration of collagen and elastic fibres/ambulatory setting/ 3 treatments over 12 weeks/ < 10 min

Sexual function, quality of life

Dyspareunia, pain, itching, burning, dysuria.

Breast cancer survivors also (Recent studies)