

MENOPAUSE

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Plan

- ❑ General considerations about aging
- ❑ Definitions
- ❑ Endocrinology of the perimenopause
- ❑ Endocrinology of the menopause
- ❑ Estrogen Deficiency –Symptoms and signs
 - The Brain
 - The Bones
 - Cardiovascular system

Aging

In the next 25 years in western countries

- People over 65 will increase from 82 %
- Newborn will increase from 3 %
- People 20 to 65 will increase from 46 %

Related to the number of ovarian follicles

- Reduction by atresia

- 7 mio of oocytes at 20 weeks of gestation

- 2.5 mio of follicles at birth

- 400 000 at the time of menarche.

- Necessity of normal hypothalamus, pituitary gland, ovary, cortex, thyroid and adrenal

Physiology & Clinical Features

- Peri-menopause – increased anovulatory cycles.
- Clinical Features: (affects 2/3rd woman)
 - Menstrual irregularity
 - Vasomotor
 - Musculoskeletal
 - Psychological
 - Urogenital
 - Cardiovascular
 - Osteoporosis
 - Breast disease

Aging and Quality of Life

o

• There is some interest to maintain our old population in good health, by

- ☐ –exercise
- ☐ –stop smocking
- ☐ –not much of alcohol
- ☐ –control obesity
- ☐ –Good Quality of Life allows Choices

Definition

Menopause:

permanent cessation of menstruation following the loss of ovarian activity. 12 months.

- Median age: 50 to 52 years old
- : FSH >30- 60 U/l
- induced menopause: surgical (Post hysterectomy)
/medical/ irradiation

Perimenopause :

- Period of time where a woman passes from the reproductive stage of life to the menopause.
- May starts about 8 years before menopause.
- Marked by irregular cycles and climacteric symptoms.

The Endocrinology of the Menopause

Postmenopausal hormonal profile:

- FSH > 30 U/l
- LH> 15 U / l
- E2< 40 pg/ml
- Ovarian production: –T stays unchanged, DHEA and A decrease
- Adrenal production: –Decreased DHEA and A

Source of estrogen at the postmenopause

Not from the ovary

- From peripheral conversion in the adipose tissue
 - Androstenedione to Estrone
 - Testosterone to Estradiol

Estrogen Deficiency

Symptoms and Signs

- ❑ Hot Flashes : Sudden sense of heat in face, neck, chest due to attacks of VD then palpitations and sweating
- ❑ Psychological functioning
- ❑ Vulvovaginal and urinary disorders

Hot Flashes

- Emblematic symptom for menopause
 - Episodic phenomenon with:
 - upper body vasodilatation
 - intense perspiration
 - Up to one every 60 minutes, timely related episodic LH elevations
 - Aggravated by hot climate

Psychological functioning

Depressive symptoms

- ❑ memory difficulties
- ❑ concentration difficulties
- ❑ sleep disorders
- ❑ decrease of sexual interest
- ❑ –30-50 % of the general menopausal population

Natural menopause doesn't increase the risk of depression
(longitudinal studies) Kaufert PMaturitas 1992

However 65 % of women attending "menopause clinics
"had varying degrees of depression

Vulvovaginal and urinary disorders

Effects of Estrogens

- ☐ E receptors found on urethral and bladder mucosa
- ☐ E₂ increase elasticity by collagen synthesis

Sexual dysfunction

- dyspareunia
 - Vaginal dryness
- decreased libido
 - Genitourinary :
 - Discharge (senile endometritis & vaginitis), pruritis
 - Frequency, urgency, SUI, recurrent cystitis

Effect of estrogen deficiency on the urogynecologic mucosa

Vaginal atrophy leading to vaginal dryness

- Urethral mucosa atrophy leading to pollakiuria
- Bladder mucosa atrophy leading to urge incontinence

285 women attending “menopause clinics”:

45 %stress

21 %urge

Effects of sex steroids on the Effects of the Brain

direct

- alteration of the electrical activity of the hypothalamus

inductive

- induction of the RNA/protein synthesis \hat{I} changes in a specific gene product, such as neurotransmitter synthesizing enzymes.

Where to find Estrogens Estrogens receptors

- ☐ Pituitary
- ☐ Hypothalamus
- ☐ Limbic Forebrain
- ☐ Cerebellum
- ☐ Cerebral Cortex
- ☐ Brain Stem
- ☐ Spinal Cord

Effect of estrogen deficiency deficiency on the CNS

- Hot flushes
- Sleep disorders
- Loss of memory
- Fatigue
- Irritability

Estrogen Deficiency and The Bones

Bone loss occurs at a rate of 2 to 3 % per year in early menopause bone loss continues during the next years bone loss accelerates in older age

decreased intestine absorption of Calcium, increased renal loss of Calcium

Gonadal failure increases

bone resorption , Bone loss leads to **osteoporosis**

the diagnosis made easy.



For osteoporosis DEXA scan , 10 million Americans currently have osteoporosis and another 33.6 million have osteopenia of the hip.

17.5 percent for hip fracture,

15.6 percent for clinically diagnosed vertebral fracture, and
16.0 percent for distal forearm fracture (Holroyd, 2008).

Estrogen Deficiency and Cardiovascular Disease

- Lower CHD incidence in women before menopause
- After menopause, similar CHD incidence in men and women
- Ovarian function protects against CHD

Effects of Estrogen on Lipoprotein Metabolism

On LDL-lipoprotein

- Increased catabolic rate of LDL
- Increased hepatic receptors of LDL



HDL-lipoprotein –Increased HDL-lipoprotein synthesis

- Decreased HDL clearance
- Reduced hepatic receptors of HDL



Effects of Estrogen Deficiency

Effects of Estrogen Deficiency on Lipid profile

Increased total cholesterol (CHOL)

- Increased Low density lipoproteins (LDL)
- Increased triglycerides (TG)



Decreased High density lipoprotein (HDL) MORE
ATHEROGENIC

Dermatologic Changes Skin changes that may develop during menopausal transition include hyperpigmentation (age spots), wrinkles, and itching.

■ **Dental Changes**

The buccal epithelium undergoes atrophy due to estrogen deprivation, resulting in decreased saliva and sensation.

Tooth loss is also strongly associated with the use of cigarettes

Weight Gain and Fat Distribution With aging, a woman's metabolism slows, so must reducing her caloric requirements

Coagulation

Fibrinogen, plasminogen activator inhibitor-1, and factor VII levels increase and cause a relatively hypercoagulable state.

This is thought to contribute to increases in cardiovascular and cerebrovascular disease in older women.

Case Study

- 52 year old
 - Suffering from hot flushes, night sweats and loss of libido
 - Last period was 8 months ago
- Would like to discuss HRT.
 - Benefits and risks?
 - If there are things she can also adjust herself?
 - What she should start?

HRT

- Indications

- Relief of vasomotor or other menopausal symptoms
- Prevention of osteoporosis
- Premature ovarian failure

- Contraindications

- Pregnancy, undiagnosed abnormal PV bleeding
- Active thromboembolic disorder or MI
- Breast disease or endometrial cancer
- Active liver disease

HRT

- **Modifiable lifestyle factors**
 - Healthy balanced diet
 - Calcium supplements
 - Smoking, alcohol and caffeine
- **Benefits**
 - Reduce vasomotor symptoms
 - Improved sleep, joint pain, quality of life
 - Reduced psychological symptoms
 - Reduce vaginal dryness and improve sexual function
 - Improve bone mineral density

Types of hormone used

1-natural estrogens are preferred over synthetic ones eg :

conjugate equine estrogen 0.625 mg/day or estradiol valerate 1-2 mg/day.

2- synthetic gestagens are :

preferred being more effective in smaller doses. Side effects include mastalgia, mood changes, PMS like symptoms, weight gain, etc...

Non hormonal drugs

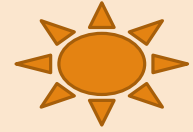
Tibolone

,Synthetic steroid with weakest, progest
androg effect 2.5 mg tablet /day

Non hormonal drugs

selective Estrogen Receptor Modulators (SERMs):

- has estrogenic actions on bone and anti-estrogenic actions on the uterus and breast.
- It is used in the prevention of osteoporosis in postmenopausal women.
- Commonest drugs are Tamoxifen (1st generation).



Screening for menopause

- mammography for breast cancer
- U/S for endometrial cancer
- pap smear for cx cancer
- LDL,HDL,triglycerides for cvs
- DEXA scan for osteoporosis

Treatments

- **osteoporosis** (prevention rather than ttt):
 - calcium 1gm/day and vit D
 - Biphosphonates decrease bone resorption.70mg Once weekly
- **hot flushes** :clonidine, Beta blocker,bromocriptine and alpha methyle dope can be used
- Oestrogen vaginal cream preparations: for local application in cases of **vaginal atrophy**

Alternative Treatments

- Vasomotor symptoms
 - Fluoxetine, citalopram, venlafaxine or clonidine
- Vaginal dryness
 - Vaginal lubricants
- Sexual dysfunction
 - Seek specialist advice re; testosterone
- Psychological symptoms
 - antidepressants
- Tibolone
- Beta blockers, gabapentin, complementary therapies

Conclusions

- Menopause is a physiologic event.
- Menopause coincides with middle age
 - increased incidence of CHD
 - increased incidence of cancer
 - increased incidence of osteoporosis



Conclusion

- Estrogen deficiency is responsible for
 - –alteration of the quality of life
 - by alteration of mood disorders
 - sleep disorders
 - urogynecologic symptoms
 - –osteoporosis
 - –more atherogenic lipid profile



Conclusion

Estrogen deficiency may be responsible for

- Increased incidence for CHD**
- decreased cognitive function**
- decreased memory**

Estrogen deficiency responsible for

- Alzheimer disease ?**
- Parkinson disease ?**

menopause is stage of life not end of life Reassurance





Thank You