Menopause and Hormone Replacement Therapy (HRT)

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Hormone Replacement Therapy

Terminology

- Estrogen Replacement Therapy (ERT)
- Hormone Replacement Therapy (HRT)
- Hormone Therapy (HT, UK)
- Combination Hormone Therapy (i.e. estrogen and progesterone)
- Unopposed Estrogen Therapy (i.e. no progesterone; hysterectomy)
- Bio-identical hormone replacement therapy (BHRT, BHT)
Case Presentation

- N.I. is a 51-year-old woman with hot flashes and vaginal irritation.
- She has tried exercise, diet and antidepressants to help relieve her hot flashes, but has been unsuccessful.
- She is otherwise healthy with no history of cancer and no surgical procedures.
- She states her hot flashes are interfering with her daily activities and wants to try HRT.

Case Presentation Con’t

- When counseling N.I. on the use of HRT and explaining the WHI trial, which one of the following has been proven statistically significant with conjugated estrogen and medroxyprogesterone acetate and should be mentioned to N.I.?

Answer?

- A. Decreased risk of stroke
- B. Decreased risk of MI
- C. Increased risk of fractures
- D. Increased risk of DVT
Question?

• Which treatment should be recommended to N.I.?

Answer?

• A. Alora patch 0.025 mg; change patch twice weekly
• B. Climara 0.025 mg; change patch once weekly
• C. Prempro 0.3 mg/1.5 mg; take one tablet daily
• D. Premarin 0.625 mg; take one tablet daily

Reproductive Aging

• Decline in reproductive potential
• Puberty → Peak reproduction → Decline in fertility → Anovulation (menstrual irregularity) → Menopause
• Due to ovarian aging (physiology)
• Progresses with the decline in oocyte/follicular pool
Reproductive Aging

*Oocytes and Follicles*

- Process begins in embryonic life.
- 20 weeks gestation - 6 - 7 million follicles.
- At birth - 1.5-2 million follicles.
- At menarche - 300,000-400,000 follicles.
- Follicular atresia continues throughout life.
- Follicular loss accelerates when the total number of follicles is ~25,000.
- When follicles are sufficiently depleted (<1000), menopause occurs.

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Reproductive Aging

*Hormonal Changes*

![Diagram of Hormonal Changes]

- Hypothalamus
- FSH
- GnRH
- Inhibin B

Normal Ovary

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Reproductive Aging

*Hormonal Changes*

![Diagram of Hormonal Changes]

- Hypothalamus
- FSH
- GnRH
- Estradiol / Inhibin B

Aging Ovary
Reproductive Aging
Hormonal Changes

Hypothalamus

FSH

GnRH

Estradiol / Inhibin B

Ovary

Menopausal Ovary

Perimenopause

- Follows period of declining fertility
- Precedes menopause
- Characterized by
  - cycle irregularity (shortening then lengthening)
  - increasing symptoms
- Duration 2 to 8 years (average 5 years)
Perimenopause -- Symptoms:

*Highly Variable*

- Vasomotor instability (85%)
- Sleep disturbances
- Mood disturbances.
- Somatic symptoms:
  - Fatigue, palpitations, headache, increased migraine, breast pain and enlargement.
- Oligo- Anovulation
  - Heavier or irregular cycles.

Menopause

- Marks the end of reproductive life
- Cessation of menses for 12 months
- Clinical diagnosis (not labs)
- Result of egg depletion and estrogen production by the ovary due to:
  - Natural aging or surgery

Summary of Key Physical Changes

- Vasomotor instability
- Metabolic Changes
- Coronary Artery Disease
- Accelerated bone loss
- Skin changes
- Urogenital atrophy
- Cognition
- Libido
- Irritability, mood
Vasomotor Symptoms

- Hot flashes (most common reason treatment is sought)
- May interrupt sleep (insomnia)
- Occurs in 75% - 85% of women
- Cause increased skin temperature, nausea, dizziness, headache, diaphoresis, night sweats, palpitations
- Increase in norepinephrine and serotonin released from hypothalamus

STRAW: Stages of Reproductive Aging

Ethnic Differences: SWAN Study

VMS less frequently experienced
- Japanese and Chinese women (OR, 0.47-0.67)*

VMS more frequently experienced
- African-American women (OR, 1.17-1.63)*

Results of SWAN study “suggest that lifestyle, menstrual status, race/ethnicity, and socioeconomic status affect symptoms…”

*Compared to white women

Genitourinary Atrophy

- Shrinkage of labia minora
- Atrophy of vulva – pruritis and pain
- Vaginal pH – more basic
- Loss of lubrication – dyspareunia
- Recurrent episodes of urinary frequency and urgency with dysuria

The Menopause Transition: Clinical Manifestations

- VMS
- VVA
  - Menstrual cycle changes
  - Breast tenderness
  - Sleep disturbances
  - Mood disorders
  - Changes in sexual interest
  - Metabolic changes

Epidemiological and Clinical Trials
Background: Late 1980s

- In 40 retrospective observational studies, both EPT and ET reduced the risk of heart attack by 50%
- Most studies included women in their 50s
- Women were self-selected for hormone use (or not); studies were subject to selection bias
- Conventional wisdom
  - All women should use HT for heart protection, unless there was a reason not to do so
  - Women with CVD risk factors, especially previous MI, stroke, HTN or diabetes, should use HT

Background: 1990s

- 1990: Wyeth requested that FDA add labeling to HT products that included cardioprotection
- FDA insisted that RCTs be performed to prove that HT improved CVD outcomes vs. placebo
- PEPI Trial: Effects of HT on Cholesterol and BMD
- Two RCTs initiated to evaluate cardioprotection
  - HERS: secondary prevention trial
  - WHI: primary prevention trial

PEPI (Postmenopausal Estrogen/Progestin Interventions) – Effects on cholesterol

- Postmenopausal Women: n=875, age 45-64; 1/3 hysterectomy:
  - (1) placebo
  - (2) conjugated equine estrogen (CEE), 0.625 mg/d
  - (3) CEE, 0.625 mg/d plus cyclic medroxyprogesterone acetate (MPA), 10 mg/d for 12 d/mo
  - (4) CEE, 0.625 mg/d plus consecutive MPA, 2.5 mg/d
  - (5) CEE, 0.625 mg/d plus cyclic micronized progesterone (MP), 200 mg/d for 12 d/mo

PEPI Results

- Unopposed estrogen – associated with a significantly increased risk of adenomatous or atypical hyperplasia (34% vs 1%)
- Estrogen alone or in combination with progestin – improves lipoproteins and lowers fibrinogen levels
- Unopposed estrogen – optimal regimen for elevation of HDL-C, but the high rate of endometrial hyperplasia restricts use to women without a uterus
- CEE + cyclic MP had the most favorable effect on HDL-C and no excess risk of endometrial hyperplasia.

JAMA 1995; 273(3):199-208

HERS Study: 1998

- Does EPT reduce MIs in women with CHD?
- 2,763 women randomized to CC-EPT or placebo
  - Entry: MI, CABG, balloon angioplasty, + angiogram
  - Menopausal, intact uterus, 44-80 years of age
  - Average follow up: 4.1 years
- Study findings
  - EPT had no value in reduction of MIs or CHD deaths
  - More deaths in year 1; neutral thru year 8
  - Not seen in prior observational studies
  - 3-fold increased risk of VTE events

Hulley, JAMA 1998:280:605

Women’s Health Initiative (1991-2005)

Postmenopausal Women
(age=50-79), mean=64 yrs

Prempro
(CEE 0.625mg/2.5mgMP A)
Combined HRT
N=16,608

Premarin
(0.625mgCEE); Unopposed Estrogen
N=10,739
Estrogen Plus Progestin Replacement (Prempro);
Rousseau, JAMA 2002

Good Effects

- Strengthens Bones
- Decreases colon cancer risks
- Reduces menopausal Sx (hot flashes)

Bad Effects

- Increases invasive breast cancer risk
- Increases blood clots
- Increases heart attacks
- Increases strokes

Estrogen Replacement in Menopause

Good effects:
- Strengthens bones
- Lowers LDL cholesterol
- Increases uterine cancer risk
- Reduces musculoskeletal symptoms, e.g., hot flashes

Bad effects:
- Increases breast cancer risk
- Increases uterine cancer risk
- Increases blood clot risk

Medroxyprogesterone acetate (Provera)

Natural Progesterone
Women's Health Initiative......

• 2006 Reanalysis of data:
  • 44% lower risk of heart disease in the “Younger Women” – (age: 50 – 59)
  • Estrogen only group
  • HRT less than 10 years after menopause

Goldstein et al. / Women's Health. JAMA 2006.

Million Women Study

• National study of women's health (1996-2001)
• ~1 million UK women (50-64 yrs)
• Cancer Research UK and National Health Service
• Main focus = effects of HRT use
  - Increased risk of incident breast cancer users of estrogen only (1.3X) and combine HRT (2X)
  - HRT taken over 5 years – 1 extra ovarian cancer/2500 HRT users and 1 extra ovarian death/3300 users = 1.2 increased risk 1.2 fold
  - Risk of fracture in current users of HRT = 40% lower than in non-users
  - TBD: heart attacks, stroke, and blood clots

Beral V. J Natl Cancer Inst 2011; www.millionwomenstudy.org

KEEPS: Kronos Early Estrogen Prevention Study

• Does initiating HRT in women at the menopausal transition provide significant protection against the major cause of heart attacks, atherosclerosis?
KEEPS

- 2 types of estrogen
  - Low-dose oral conjugate estrogen (0.45mg/d)
  - Transdermal patch estradiol (50 mcg/d)
- Progesterone
- Both groups - bioidentical

KEEPS Results

- Improvement in hot flashes, night sweats, mood, sexual function and bone density.
- No significant differences in adverse events!!


North American Menopause Society (NAMS)

- Current evidence supports the use of HT for perimenopausal and postmenopausal women when the balance of potential benefits and risks is favorable for the individual woman.
- Recent data support the initiation of HT around the time of menopause to treat menopause-related symptoms and to prevent osteoporosis in women at high risk of fracture.
- The most favorable benefit-risk ratio for ET allows more flexibility in extending the duration of use compared with EPT, where the earlier appearance of increased breast cancer risk precludes a recommendation for use beyond 3-5 years.

Therapy Options

- Non-pharmacological Treatment
- Pharmacological Treatment
  - Hormonal therapies
  - Non-hormonal (prescription) therapies
  - Alternative medicine (herbals)

Life-Style Changes – Hot Flashes

- Keep core body temperature as cool as possible
  - Layered clothing, lowered thermostat
- Avoid perceived personal hot flash triggers
  - Smoking, alcohol, coffee, hot beverages, spicy foods, emotional stress
  - Maintain a healthy body weight
  - Exercise regularly
  - Practice relaxation techniques
  - Try paced respirations

Mind-Body Techniques

- Cognitive-Behavioral Therapy – trained in paced breathing and relaxation as well as sleep hygiene.
- Paced Respiration – taking 6-8 slow deep breaths per minute while inhaling through the nose and exhaling through the mouth
- Relaxation – limited and inconsistent
- Clinical hypnosis – limited evidence
Treatments for VMS: Prescription Therapy (Hormonal)

Estrogen used for many decades for VMS
- Most effective treatment
  - Numerous randomized, placebo-controlled trials
  - 75% reduction in VMS frequency
  - Significant reduction in VMS severity

Oral and transdermal estrogen have similar efficacy

Contraindications to HT

- Undiagnosed vaginal bleeding
- History of stroke or MI
- History of DVT or PE
- Estrogen-sensitive cancers
- Liver dysfunction or disease (eg, hepatitis)

Assessing CVD Risk

<table>
<thead>
<tr>
<th>Years Since Last Menstrual Period</th>
<th>&lt; 6</th>
<th>6 to 10</th>
<th>&gt; 10</th>
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</thead>
<tbody>
<tr>
<td>Very low (&lt; 5%)</td>
<td>HT OK</td>
<td>HT OK</td>
<td>No HT</td>
</tr>
<tr>
<td>Low (5% to &lt; 10%)</td>
<td>HT OK</td>
<td>HT OK (Choose transdermal)</td>
<td>No HT</td>
</tr>
<tr>
<td>Moderate (10% to 20%)</td>
<td>HT OK (Choose transdermal)</td>
<td>HT OK (Choose transdermal)</td>
<td>No HT</td>
</tr>
<tr>
<td>High (more than 20%)</td>
<td>No HT</td>
<td>No HT</td>
<td>No HT</td>
</tr>
</tbody>
</table>

DECISION ABOUT DURATION OF USE:
Continued moderate-to-severe symptoms; patient preference; weigh baseline risks for breast cancer vs osteoporosis

Lower Doses of Estrogen for VMS

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogens</td>
<td>0.3 mg oral</td>
</tr>
<tr>
<td>Miconized 17β-estradiol</td>
<td>0.5 mg oral</td>
</tr>
<tr>
<td>17β-estradiol patch (gel, spray)*</td>
<td>0.025, 0.0375 mg</td>
</tr>
</tbody>
</table>

*Please see package labeling or NAMS Website for gel and spray dosages.

Are Transdermal Preparations Safer?*

- **VTE**: French systematic review and meta-analysis¹
  - Increased risk with oral ET (OR, 2.4)
- **Stroke**: Nested case-control study from the UK General Practice Research Database²
  - No increased risk with transdermal HRT (OR, 1.7)
- **MI**: Danish National Registry³
  - Significantly lower risk found with transdermal oral ET (RR = 0.62, 95% CI: 0.42-0.93)

*Data based on observational trials

Bioidentical Hormones
Bioidentical Hormones

- “Compounds that have exactly the same chemical and molecular structure as hormones that are produced in the body”
- Come from: Soy or Wild Yams
- FDA-approved estradiol patches, gels, sprays, emulsions
- FDA-approved progesterone capsules and gel
- Custom blends of hormones prepared by compounding pharmacies without FDA oversight or required testing or labeling
- Estradiol, Estrone, Estriol

The Problems with BHT

- No tested in good clinical trials, and no endometrial safety data
- “Natural” does not really equal “safer”
- No clinician or patient package inserts documenting safety/efficacy, and no black box warnings
- No uniform manufacturing standards. In one study 25% of compounded products tested failed quality control testing vs. 2% of commercially manufactured drug products
- No formal review of accuracy of advertised claims

This is A LOT of “Nots”. Will it even matter to those determined to take these products?

Products containing Estradiol

- **Activella** (estradiol/norethindrone acetate tablet)
  - 0.5 mg estradiol and 0.1 mg norethindrone, 1 mg estradiol and 0.5 mg norethindron, Human
- **Alora** (estradiol transdermal system (twice weekly))
  - 0.025 mg/24 hr, 0.05 mg/24 hr, 0.075 mg/24 hr, 0.1 mg/24 hr, Human
- **Angeliq** (estradiol/drospirenone tablet)
  - 0.5 mg estradiol and 0.25 mg drospirenone, 1 mg estradiol and 0.5 mg drospirenone
Products Containing Estradiol

- **Climara** (estradiol transdermal system (once weekly))
  - 0.025 mg/24 hr, 0.0375 mg/24 hr
- **Climara Pro** (estradiol/levonorgestrel transdermal system (once weekly))
  - 0.045 mg estradiol and 0.015 mg levonorgestrel/24 hr
- **CombiPatch** (estradiol/norethindrone acetate transdermal system (twice weekly))
  - 0.05 mg estradiol and 0.14 mg norethindrone/24 hr
- **Divigel** (17-beta-estradiol transdermal gel (once daily))
  - 0.1%

Products containing Estradiol

- **Elestrin** - Estradiol gel (once daily) - 0.06% (estradiol 0.53 mg/metered dose)
- **Estrace** - 17-beta-estradiol, micronized tablet
- **Estrasorb** - estradiol topical emulsion (once daily) - 0.25%
- **Evamist** - 17-beta-estradiol transdermal spray (once daily)
- **Minivelle** (estradiol transdermal system (twice weekly))
  - 0.0375 mg/24 hr, 0.05 mg/24 hr
- **Vivelle-Dot** (estradiol transdermal system (twice weekly))
  - 0.025 mg/24 hr, 0.0375 mg/24 hr, 0.05 mg/24 hr
**Conjugated Estrogen-Containing Products**

- **Cenestin** – (conjugated estrogen tablet); 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg
- **Enjuvia** – (conjugated estrogen tablet); 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg
- **Esterified estrogens** – estrone + equilin
- **Premarin** (conjugated estrogens tablet) 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg
- **Premphase** (conjugated estrogens/medroxyprogesterone acetate)
- **Prempro** (conjugated estrogens/medroxyprogesterone acetate tablet)

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**Other Hormones**

- Progestogens
- Medroxyprogesterone acetate – Provera
- Micronized progesterone – Prometrium

**Compounded Estrogen Products** (in pharmacies):
- **Biest (biestrogen)** containing 20% estradiol and 80% estriol
- **Triest (triestrogen)** containing 10% estradiol, 10% estrone and 80% estriol, expressed on a mg per mg basis, prepared by compounding pharmacies for patients.
- Biest, available as capsules, sublingual compounds and transdermal cream or gel - most common preparation used

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**Conjugated estrogens + bazedoxifene**

- FDA-approved – 2014
- Moderate to severe vasomotor symptoms
- 0.45 mg estrogen and 20 mg bazedoxifene
- Bazedoxifene – SERM; added just to inhibit estrogen’s endometrial effects...as an alternative to a progestin
**Vulvovaginal Atrophy**

**Treatment**
- **Nonprescription**
- Vaginal lubricants and moisturizers
- **Prescription**
- Creams – Estrogen
  - Estrace (17β-estradiol)
  - Premarin (conjugated estrogen)
- Rings
  - Estring (17β-estradiol) – 2 mg (releases 7.5mcg/d) for 90 days
  - Femring (Estradiol acetate) – 0.05mg/d and 0.1 mg/d for 90 days
- Vaginal Tablet - Vagifem

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**Vulvovaginal Atrophy**

**Treatment**
- Premarin Cream – used cyclically (21 days of use, 7 days of no use)
- Estradiol Cream (Estrace) – used daily for the first 1-2 weeks, then 1-3 times weekly for maintenance
- Estring vaginal ring – contains reservoir of estradiol, provides 90 days of continuous use once inserted
- Femring vaginal ring – secretes higher dosages
- Vagifem tablet – contains an ultra-low dose of estradiol (10 mcg); one tablet is inserted daily for two weeks, then one tablet twice weekly for maintenance.

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**Ospemifene (Osphena)**

- FDA-approved in 2013
- Treatment of menopausal-related dyspareunia, or pain with intercourse
- Selective estrogen receptor modifier (SERM) - serves as an agonist and antagonist on different tissue estrogen receptors.
- 60 mg PO QD
- Metabolized through CYP3A4
- Side effects: hot flashes, leg cramps
- $160/month
Non-hormonal Prescription Therapies

• Limited evidence – Less effective for hot flashes than HT
• Head-to-head RCT are limited
• Nonhormonal Agents studied:
  - SSRIs and SNRIs
  - Gabapentin
  - Clonidine

SSRIs and SNRIs

• Modulate serotonin and norepinephrine levels in the hypothalamus where body temperature is regulated.
• Venlafaxine and paroxetine (low doses) – most studied in relation to frequency/severity of hot flashes
• Lesser effects with sertraline and fluoxetine
• Paroxetine capsules (Brisdelle) – 7.5 mg – FDA-approved for the treatment of moderate to severe hot flashes and night sweats
  - Take at bedtime, $135/month vs. $8/month for paroxetine 10mg
  
Caution not to use paroxetine or fluoxetine in women on tamoxifen...these SSRIs may decrease tamoxifen’s efficacy.

Gabapentin (Neurontin)

• Antiepileptic
• 300mg 3x/d, improved frequency and severity of hot flashes
• SE: dizziness, drowsiness at week 1
• Higher doses (2400mg/d) were more effective in studies, but caused more disorientation and dizziness
• More recent studies have shown no benefits
• Pregabalin is effective, but less well studied

Clonidine (Catapres)

- Centrally-acting alpha adrenergic agonist
- Less effective than SSRIs, SNRIs and gabapentin
- Older trials: 0.1 mg once daily or a weekly transdermal patch were found to reduce hot flashes moderately
- Inconsistent results
- Used infrequently due to hypotension, headache, dizziness, and anticholinergic side effects

Question

- Which of the following is the most potent and most common phytoestrogen?
  - A. Coumestans
  - B. Flaxseed
  - C. Isoflavones
  - D. Lignans

Dietary Management and Supplements - Phytoestrogens

- Most commonly used group of natural products for vasomotor symptoms are phytoestrogens or "plant estrogens."
- The three main kinds of phytoestrogens are isoflavones, lignans, and coumestans.
- Isoflavones are the most potent and the most common phytoestrogens in supplements.
- Phytoestrogens are also found in many common food sources.
Phytoestrogen Class | Food Source
---|---
Isoflavones | Legumes (soy, chickpeas or garbanzo, red clover, lentils)
Lignans | Flaxseeds, whole grains, fruits and vegetables
Coumestans | Red clover, sunflower seeds, sprouts

**Phytoestrogens**

- Not structurally related to estrogen
- Contain a phenolic ring that allows them to bind to estrogen receptors
- 100 to 10,000 times weaker than endogenous estrogen.
- Depending on the tissue type and location in the body, can act as estrogens OR antiestrogens.
- Activity similar to tamoxifen and raloxifene
- Estrogenic activity of soy varies with the level of endogenous estrogen

**Soy Isoflavones**

- Most studied
- Difficulty to quantify isoflavone content (due to crop variety)
- Potency is dependent on purity and dosing
- 40-160mg/d
- Randomized, blinded, comparative trials – no more effective than placebo:
  - Manufacturing processes are uncontrolled (batch-to-batch variation)
  - Benefits seen much slower than traditional medicine
- **Laboratory evidence suggests that phytoestrogens from soy can stimulate proliferation of normal human breast tissue.**

Red Clover

• 1st discovery of phytoestrogens ~ 1950
• 40 mg/day
• Promensil (82mg/d isoflavones), Rimostil (57mg/d isoflavones)
• Most trials – no significant difference compared to placebo
• Practice Pear:
• Caution women on warfarin:
  • Red clover contains coumarins which can have anticoagulant effects. Taking high doses of red clover might have additive effects with warfarin and potentially increase the risk of bleeding.

Black Cohosh

• What should you tell a patient who wants to take black cohosh for hot flashes?
  • A. It’s more effective than soy for hot flashes.
  • B. It does not work for hot flashes.
  • C. Liver function tests are needed.
  • D. It decreases the risk of breast cancer.
Black Cohosh

- Brand “Remifemin”
- Binds to serotonin-receptor, not ER; suppresses the release of LH – reduces hot flashes
- 500 – 1000 mg extract, standardized to 2.5% triterpene glycosides
- Insufficient evidence for control of hot flashes
- Hepatotoxicity

Cochrane Database Sys Rev. 2012

Don Quai

- “Female tonic”
- Promotes release of progesterone
- 50 mg/day
- Does not seem to be effective for relieving hot flashes.
- There are also safety concerns; Dong quai contains constituents considered to be carcinogenic.


Other Herbs

- **Flaxseed**
  - Rich source of lignan phytoestrogens, omega-3 fatty acid, alpha-linolenic acid, and fiber.
  - Consuming dietary flaxseed 40 grams/day in place of other dietary fats significantly improves MILD menopausal symptoms such as hot flashes.
  - Mixed results

- **Gamma-Linolenic Acid (GLA)**
  - Evening Primrose Oil
  - 200-400 mg/d
  - Not efficacious based on current evidence
A Decade After WHI – Where are we now?

- **TWO concepts:**
  - HT for treatment of menopausal symptoms
  - HT for prevention of chronic diseases

Recommendations - NAMS

- **For younger women:**
  - HT is an acceptable option for treating moderate-severe menopausal symptoms (up to age 59 or within 10 years of menopause)
  - Women with vaginal symptoms only:
    - Most effective treatment is low-dose, local vaginal ET.
  - Women with a uterus:
    - They need to take a progesterone along with the estrogen to prevent cancer of uterus
  - Risk of breast cancer:
    - An increased risk in breast cancer is seen in 3-5 years of continuous estrogen/progesterone therapy

Recommendations - NAMS

- **Risk of blood clots/stroke:**
  - Both ET and EPT increase the risk of blood clots in the legs and lungs
  - Although the risks of blood clots and strokes increases with either of HT, the risk is much less in the 50-59 year-old age group.
  - Both transdermal and low-dose oral estrogens have been associated with lower risks of VTE and stroke than standard doses of oral estrogen.
Role of Pharmacist

• Can help women understand that the menopause is not a disease, but a natural transition that signals the end of fertility.
• Should convey the message that perimenopause does not have to signify loss, instead emphasizing the positive aspects of impending menopause, such as relief from menstruation and an end to the potential inconvenience of contraceptive methods.
• Proper health education and drug therapy can help women prevent the illnesses associated with menopause, such as osteoporosis and heart disease.
• Pharmacist-led counseling can help women understand their treatment options and weigh the advantages and disadvantages of these therapies.

Conclusion

• Growing body of evidence – HT formulation, route of administration, and the timing of therapy produce different effects.
• Benefit-risk profile is essential for every woman considering HT regimen
• Absolute risks known to date for use of HT in healthy women 50-59 years of age are low.
• ET has a more favorable safety profile and could be considered for longer duration of therapy in the absence of adverse effects and risk factors
• Additional research is needed to understand the different effects of ET and EPT and how they apply to individual women.