Women’s Health Issues and Trends in Pharmacology

Elizabeth A. VandeWaa, Ph. D.
Professor, University of South Alabama
Lecturer, Barkley and Associates
College of Nursing

Pharmacologic Categories Important to Women’s Health

- Hormones!
  - Hormone replacement therapy (HRT), contraception
- Drugs in pregnancy
- Tocolytic agents
- Treatment of common STDs
- Drugs for osteoporosis
- Thyroid issues
- Drugs for other conditions

Are Women Unique?
- With respect to hormones, YES
- With respect to pharmacology….MAYBE!
  - Historically, drug trials have been conducted in males
  - In 1997, the FDA urged inclusion of women in drug studies.
  - Of course, some drugs are fairly “female-specific”…

Some Interesting Differences
- Digoxin is more likely to cause mortality in females than in males.
- Alcohol is metabolized more slowly in females than in males.
- Women get pain relief from certain opioid analgesics at lower doses than do men.
- Quinidine is more likely to cause QT interval prolongation in women than men.

Sex Hormones

- Estrogens and progestins
  - Promote maturation, regulate reproduction
  - Estrogens affect bone mineralization and lipid metabolism.
  - Estradiol and progesterone are main endogenous sex steroids.
  - Used for contraception and for HRT

Sex Hormones

- Hypothalamus
- Pituitary
- FSH & LH
- Ovary
- Uterus
- Vagina
- Estrogen & Progesterone
Estrogens

- Cause development and maturation of female reproductive tract and secondary sex characteristics
- Block bone resorption; high levels promote epiphyseal closure at the end of puberty
- Decrease low-density lipoprotein and elevate high-density lipoprotein
- Affect coagulability of the blood

When used ALONE by postmenopausal women, it can increase the risk of endometrial hyperplasia and carcinoma.

When used WITH a progestin in postmenopausal women, the risk of breast cancer is increased.

Risk of ovarian cancer increases in postmenopausal women

When used ALONE or WITH a progestin in postmenopausal women, the risk for PE, VTE or stroke is increased. Used ALONE, or in combination, the MI risk is equivocal. In premenopausal women, risk of VTE is seen with combination agents.

Physiologic doses of estrogen with or without a progestin

- Add progestin to offset the estrogen-mediated stimulation of the lining of the uterus which could be cancerous
- Short-term HRT is considered useful and safe.
- Long-term HRT is associated with risks—most notably, cancer.

Benefits of HRT

- Reduction in vasomotor symptoms
  - Sweating, skin flushing
- Prevention of urogenital atrophy
  - Dryness, itching, burning
- Prevention of osteoporosis
  - Reduction in fractures, too
- Prevention of colorectal cancer
  - Risk decreased by 34%, but only as long as HRT is continued.

Vasomotor symptoms

- Cause decreased sleep, irritability, difficulty concentrating, and decreased quality of life.
- Treatment of vasomotor symptoms is primary indication for HRT.
- Almost all systemic HT products except for the ultra-low dose estradiol patch are indicated.
- Progestins are not as effective as estrogen.

James Hellman

Benefits Explained
**Benefits Explained**

- **Vaginal Symptoms**
  - Estrogen is the most effective.
  - Many systemic products and all local products are indicated, though low-dose systemic preps may require local preps to augment effects.
  - If low-dose estrogen is used, a progestin is not needed. Endometrial hyperplasia increases with increasing dose and duration of use (evaluate bleeding).

**Benefits, Explained**

- **Osteoporosis**
  - Standard-dose HRT reduces postmenopausal osteoporotic fractures of the hip, spine, and non-spine fractures—even in women without osteoporosis.
  - Women in early menopause are good candidates.
  - When HRT is discontinued, bone mass is lost quickly, so have another strategy to prevent loss and fracture in place.

**Risks of HRT**

- **Cardiovascular events**
  - Increased risk of MI, stroke, PE, DVT—although the risk is low
- **Endometrial cancer when estrogen is used alone**
- **Breast cancer with EPT**
- **Ovarian cancer with ET**
- **Gall bladder disease with both EPT and ET**
- **Increased risk of development of dementia with EPT and probably ET**
- **Urinary incontinence?**

**Conditions of Therapy**

- **Keep doses as low as possible**
- **Duration should be short—4 years or less is considered “short-term” use.**
- **Use for only approved indications**
- **If osteoporosis is the only indication, consider other agents (since bone loss will quickly ensue once therapy is discontinued).**
- **Consider topical preps if vulvar symptoms are the most worrisome.**

**Discontinuing HRT**

- **Sudden discontinuance may cause return of symptoms so consider slow taper.**
- **Dose tapering**
  - Dosing is done every day but dosage is gradually reduced.
  - If symptoms are intolerable, taper can be slowed.
- **Day tapering**
  - Dosage remains the same but days in between doses increases.
  - Estrogen dose is reduced; progestin dose remains the same.

**Preparations**

- **Vaginal creams**
  - Conjugated estrogens (Premarin) 62 mcg conjugated estrogens/day
- **Vaginal rings**
  - Estradiol (Estring) 2 mg ring releases 7.5 mcg/day for 90 days
- **Vaginal tablets**
  - Estradiol hemihydrate (Vagifem) 25 mcg tablet inserted twice/week
Preparations
- Conjugated estrogens, equine
  - Premarin, 0.3-0.625 mg/day
- Conjugated estrogens A, synthetic
  - Cenestin, 0.3-1.25 mg/day
- Estradiol acetate
  - Femara, 0.45-1.8 mg/day
- Conjugated estrogens/medroxyprogesterone acetate
  - Prempro, 0.3/1.5-0.625/2.5 mg/day

Questions Remaining for HRT
- Only Prempro and Premarin were tested in the WHI and HERS—how do other preps compare?
- Are topical estrogens really safer than per os (PO) preps?
- If progestin is used, should it be used continuously or sequentially?
- What is duration of therapy?
- Are there genetic factors that influence HRT?
- Do the results of HERS and WHI apply to perimenopausal women as well as postmenopausal women?

Topical Preparations
- Transdermal Patches
  - Estradiol: Alora, Climara, Esclim, Estraderm, Menostar, Vivelle, Vivelle-Dot
- Topical Emulsion
  - Estradiol hemihydrate: Estrasorb
- Topical Gel
  - Estradiol: EstroGel, Elestrin, Divigel
- Spray mist
  - Estradiol: Evamist
- Estrogen/Progestin Patches
  - CombiPatch, ClimaraPro

Answers from NAMS
- Individualization of therapy is key.
- ET is the most effective for vulvar and vaginal atrophy; low-dose local vaginal ET for vaginal symptoms
- In premature or early menopause, HRT may be used until the median age of menopause (51 years old); longer if needed.
- What about bioidentical hormones?

Bioidentical Hormones
- Usually describes custom-compounded formulations
- May also refer to chemical estrogens and progestins
- Some of these are given by non-standard routes of administration (subdermal implants)
- Some of these hormones are NOT FDA approved, may contain dyes and preservatives
  - Salivary testing of hormones is inaccurate, unreliable
  - Use at your own risk!! Better to avoid….

Selective Estrogen Receptor Modulators (SERMs)
- Developed to activate “good” estrogen receptors while avoiding “bad” estrogen side effects
- Wanted to produce decreased osteoporosis, improved lipid profile and less urogenital atrophy without promotion of breast and uterine cancers and thromboembolism
- But SERMs do not accomplish these goals…