Current Topics in Hormone Replacement Therapy

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Outline

• Why is this Important?
• Review Hormone Replacement Nomenclature
• Evaluate Current Indications for Therapies
• Discuss Proper Prescribing for Hormone Replacement Therapy
Conflict of Interest Disclosures

- Speaker’s Bureau: AMAG Pharmaceuticals, Valeant Pharmaceuticals
What is Hormone Replacement Therapy?

- Hormone Replacement Therapy (HRT) is?
  - A.) A means of restoring deficient hormone levels to physiologic values
  - B.) A way to greatly improve patient’s quality of life
  - C.) A way to cause significant morbidity and/or mortality if not performed correctly
  - D.) All of the above
Why is this Important?

• Public Confusion about HRT
  • Types, safety, etc
• Who could benefit from HRT?
  • Men, women, transgendered?
• Who should be prescribing HRT?
  • Physicians?
  • Chiropractors?
  • Dentists?
  • APRNs?
• Training in HRT?
Global Effects

The Global Hormone Replacement Therapy Market (MCP-6453)
Trends, Drivers & Projections

May 2016

Research Insights & Findings

- Lack of Proven, Effective Alternatives
- Rise in the Number of Women in Menopause
- Growing Demand for Transdermal HRT Products
- Increasing Sales of Approved Bioidentical Therapies
- Regulatory Controls Over Unapproved Bioidentical Drugs

Sizing the Global Market

Global Market to Reach US$3.5 Billion by 2022

Key Players

Bayer
Teva
Pfizer/Wyeth
Allergan
TherapeuticsMD, Inc.
Novo Nordisk

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Nomenclature
“Synthetics”

- FDA-Approved form of HRT
  - Only type studied in WHI
  - Lab-made compounded that are similar in structure to endogenous hormones

- Examples:
  - Conjugated Equine Estrogens, Ethinylestradiol
    - ex. Premarin, Tulane
  - Medroxyprogesterone Acetate
    - ex. Provera
“Bioidenticals Type 1”

- FDA-Approved form of HRT
- Lab-made compounds that are *identical* in structure to endogenous hormones
- Examples:
  - Estradiol, Estradiol Acetate
    - ex. Estrace, Climara, Femring
  - Micronized Progesterone
    - ex. Prometrium

“Bioidenticals Type 2”

- NOT FDA-Approved
- May be listed as nutritional supplements
- Multiple routes of delivery
- “Individualized Dosing”
- Often based off of salivary testing
- Examples:
  - BioTe
  - Multiple pharmacy formulations
A Note about Bioidenticals...

- The term “bioidentical” is a marketing, not medical, term
- Coined by physicians John R. Lee and Jonathan Wright
  - Believed progesterone panacea
- Consumer scare of HRT from WHI lead to propagation of BHRT compounds
- Suzanne Somers popularized it in print form in 2006
In January 2008, the FDA ordered seven compounding pharmacies...to stop making illegal claims about "bio-identical hormone replacement therapy (BHRT)" products. The companies were told that the FDA regards "bio-identical" as a marketing term that implies a benefit for which there is no medical or scientific basis [7]. Some were also making unsupportable claims that their drugs are better than FDA-approved menopausal hormone therapy drugs and can be used to prevent and treat serious diseases such as Alzheimer's disease, stroke, and various forms of cancer.
A Little More Minutia...

- Sex Hormones are Cholesterol Based Steroids
  - Estrogens
    - 18-carbon ringed structures
    - Hydroxyl group vs. Ketone on C17
  - Progestogens
    - 20-carbon ringed structures
      - Progesterone MC type
      - Progestins are synthetic progestogens
  - Androgens
    - 19-carbon ringed structures
    - Testosterone precursor to Dihydrotestosterone
You Knew This Was Coming...
Current Indications for HRT

Click to learn more about hormone replacement therapy.
Indications Con’t

- FDA-Approved (and NAMS codified)
Indications for HRT in Women
  - Vasomotor Symptoms
    - Should be bothersome
  - Genitourinary Symptoms
    - VVA, recurrent UTI, dyspareunia
  - Prevention of Bone Loss
  - Premature Hypoestrogenism
    - Chemotherapy, POI, surgical menopause
Would You Like to Know More?

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- DOI: 10.1097/GME.00000000000000921
- © 2017 by The North American Menopause Society
- POSITION STATEMENT
- The 2017 hormone therapy position statement of The North American Menopause Society
Indications Con’t

- TRT in Men
  - From The Cleveland Clinic...“The indications, benefits, and risks of TRT are controversial, with current data lacking long-term follow-up and consistent biochemical target values. Treatment of low testosterone is not indicated at the present time in the absence of clinical symptoms”
  - For Symptomatic Men...
  - “Recommended for symptomatic men with low or borderline total testosterone or free testosterone (< 350 ng/dL or < 65 pg/mL)”
Indications Con’t

• Contraindications for TRT in men:
  ● History of breast or prostate cancer, palpable prostate nodule or induration, or a prostate specific antigen (PSA) >4 ng/mL or PSA >3 ng/mL in men at high risk of prostate cancer, hematocrit >50%, severe lower urinary tract symptoms associated with benign prostatic hypertrophy (ie, AUA/IPSS score >19), uncontrolled or poorly controlled congestive heart failure, or uncontrolled severe obstructive sleep apnea.
Indications Con’t

• Testosterone in women?
  ● No current FDA-approved formulations for Testosterone in women
  ● Combination Estradiol/Testosterone pill does exist
    • Brand name Estratest
      ● Enteric Testosterone poorly absorbed
Indications Con’t - Transgendered Peoples

• Determined by “goal” gender
  ● Masculinizing therapies
    • Typically androgens
  ● Feminizing therapies
    • Estrogens and antiandrogens

• May or may not be covered by insurance

• Requires knowledgable practitioner
  ● Some patients will self-medicate
Proper Prescribing for HRT
Initial HRT Evaluation

• Key Points:
  ● Symptoms
  ● Indications
  ● Contraindications
  ● Desire for Therapy
Joan is a 46 y/o G2P2 who presents to your office c/o hot flashes, insomnia, and increased vaginal dryness. She reports a cessation of menses approximately one year prior. She denies any other issues, and has a benign health history. She has heard about HRT, but is concerned that “it could cause cancer!”
Case Study #1

• Symptoms: hot flashes, insomnia, vaginal dryness
• Indications: VMS, GSM
• Contraindications: None
• Desire for Therapy: Yes
Case Study #1

Key Points
- Prior to initiation of HRT, discuss diet, exercise, sleep
- VSM symptoms will often improve with environmental modalities
- GSM is progressive disorder - will most likely require medication at some point
- No demonstrable increase in CA in women using transdermal HRT within 10 years of menopause
Case Study #2

- John is an overweight, 55 y/o male executive who presents complaining of low libido and erectile dysfunction. He is very interested in testosterone therapy. His health history is pertinent for BPH, and his last PSA was 6 ng/mL. Serum total/free testosterone shows levels are 200 ng/mL and 50 ng/mL.
Case Study #2

- Symptoms: Low libido, ED
- Indications: Low serum F/T testosterone
- Contraindications: Elevated PSA
- Desire for Therapy: Yes
Case Study #2

- Key Points
  - Poor diet, lack of sleep, sedentary life can cause low T
  - High cortisol = decreased androgens
    - Sympathetic response
  - Testosterone should be AM draw
  - Contraindications for HRT should be addressed
Take Home Points

• Multiple FDA-approved formulations for HRT exist
• Multiple speciality societies express need for further investigation with longterm HRT
• HRT should only be prescribed if criteria are met
• Lifestyle modifications may reduce need for pharmacologic intervention
• Document, document, document
Questions?

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