How Hormones are Sabotoging Weight Loss

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Objectives

1. Discuss menopause and disruptions for weight loss.

2. Discuss polycystic ovarian syndrome and the implications for weight loss.

3. Management of menopause and polycystic ovarian syndrome from a medical and functional standpoint.

Obesity Trends

- Adult obesity 39.8%
- Hispanic 47.0%
- Non-Hispanic black 46.8%
- Hispanic women 50.6%
- Non-Hispanic black women 54.8%

Menopause and Obesity

- Between the age of 40-59 obesity in women is 75%
- Over age of 60, obesity in women is 73%

Menopause

- Premenopause: One or more periods in previous 3 months, no perceived change in cycle interval
- Early perimenopause: One or more periods within the past 3 months, with a perceived change in cycle interval
- Late perimenopause: no bleeding in the previous 3 months but bleeding in the last 11 months
- Postmenopause: 12 or more consecutive months of amenorrhea

Do hormones cause weight gain?

- According to Health Women Study, average weight gain in perimenopausal women was 5 pounds
- 20% of the population they studied gained 10 pounds or more
- Weight increase is from drop in estrogen, and decrease in energy expenditure

Do Hormones Cause Weight Gain?

- Longitudinal cohort of 5119 perimenopausal women
- Follow-up for 20 years
- Obesity doubled from 14% to 28%
- 69% of participants were overweight or obese
- Greater than 70% gained >5% of their baseline BMI
- No change in energy intake and physical activity levels
- Conclusion: Overweight and obesity increased by over 50% in 20 years

Yang, et al. J. Epidemiol Comm Health 2017; 71: 499-504

Do Hormones Cause Weight Gain?

- Meta-analysis of 107 trials showed that HRT reduced abdominal fat, HOMA-IR and new onset DM2
- HRT increase lean body mass and reduced waist circumference and abdominal fat compared with placebo or no treatment
- Thus reduced risk of metabolic syndrome with HRT

Saltpeter, et al Diabetes Obes Metab. 2006 Sept 8(5): 538-54

Causes of weight gain

- Low estrogen is obesity triggering factor
- Estrogen deficiency enhances metabolic dysfunction predisposing to DMII, metabolic syndrome, and CVD
- Estrogen plays role in fat storage and distribution
- Before menopause, estrogen deposits fat on thighs, hips, and buootcks
- After menopause, fat distributed to midsection
- Increase in visceral fat is linked to insulin resistance, DM, and inflammatory diseases

Obesity and Menopause

- Low estrogen may impair function of leptin and neuropeptice Y, hormones that control fullness and appetite
- Therefore women in late states of perimenopause who have low estrogen levels may be driven to eat more calories and store fat.

Estrogen

- Estrogen control distribution of adipose tissue
- Estrogen control adipose centrally
- Estrogen receptors are throughout the adipose tissue
- Estrogens control hunger/appetite
- Estrogens influence insulin secretion and sensitivity

Estrogen and Visceral Adipose Tissue (VAT)

- BMI and weight increase in menopause, but VAT increases at least 3 x faster than BMI
- Associated in some studies with low E2 and in some studies with higher testosterone environment

Estrogen and VAT

- Higher VAT and increased risk of CVD
- Decrease E2-decreased SHBG-increased bioavailable T
- Shift from estrogen dominant to testosterone dominant environment
- Increased bioavailable T associate with higher levels of VAT in menopause in SWAN data

Janssen, et al. Obesity. 2015 Feb; 23(2): 488-94

Central Effects Estrogen

- Estrogens mediate almost every aspect of metabolism by regulating insulin sensitivity in many tissues.
- Estrogen regulate distribution pattern of adipose tissue
- Estrogens regulate thermogenic potential of brown adipose tissue

Lopez and Tena-Sempere. Trends Endocrinol Metabl. 2015 Augu; 26(8): 411-21

Central Effects Estrogen

- ERs are expressed throughout the CNS
- Central Era are required for optimal weight control
- Estrogens act on the arcuate nucleus of hypothalamus to regulate feeding
- Estrogens act on ventral medial hypothalamus to control energy expenditure

Lopez and Tena-Sempere. Trends Endocrinol Metab. 2015 Aug; 26(8): 411-21

Estrogen & Fatty Heart

- Cardiovascular Fat (CF) role in pathogenesis of CHD
- CF=Epidcardial Adipose Tissue (EAT)
- CF is influence by sex hormones in women
- SWAN (Study of Women's Health Across the Nation) CF Study
  - Late peri/menopausal women almost 20% more EAT than premenopausal women
  - 20% more paracardial adipose tissue (PAT)
  - Lower levels of E2 were associated with higher volumes of PAT

El Kahoudary, et al., J. Clinical Endo Metab. 2015 Sept; 100(9);3301-12

Estrogen and ER receptors

- E2 receptors alpha and beta are expressed in human VAT
- SNPs of the ER's are associated with increased risk for obesity in humans
- E2 facilitates uptake of glucose in skeletal muscle
- E2 via ERa and ERb in pancreas facilitates synthesis and release of insulin

Michopoulous. Physiol Behav. 2016 May 13

Estrogen & Food Metabolism

- E2 attenuates food intake
- E2 prevents obesity and IR
- E2 increases energy expenditure and physical activity levels
- E2 suppresses lipogenesis

Michopoulous. Physiol Behav. 2016 May 13

Estrogen & Hunger

- E2 facilitates anorexigenic signals
- E2 inhibits actions of orexigenic molecules
  - Hypothalamic NPY (neuropeptide Y) is orexigenic-decreased by E2
  - Actions of ghrelin and Melanin concentrating hormone) are both orexigenic and are decreased with E2 replacement in OVX rodents

Brown and Clegg. J Steroid Biochem and Mol Bio. 2010 Oct; 122(1-2):65-73

Estrogen Induces Pancreatic Insulin Secretions

- E2 increases anorectic actions of leptin
- E2 increases expression of insulin receptors in adipose tissue
- Leptin receptors abd Ers are seen together in the hypothalamus and E2 seems to have direct effect on leptin sensitivity

Brown and Clegg. J Steroid Biochem and Mo Bio 2010 oct;122(1-2);65-73

Chronic Stress and Modulation of E2

- Exposure to chronic stress and dysregulation of the LHPA (Limbic HPA) axis
- May result in loss and or reversal of the protective effects of E2 on metabolism and food intake

Estrogen, E2 & Obesity

- E2 normally anorexigenic with chronic stress can become orexigenic
  - May be due to changes in ERa and ERb expression
  - ERa expression in hypothalamus stimulates anorexigenic actions
  - ERb expression PVN stimulates hyperphagia
  - Cortisol administration has been shown to decrease Era and increase Erb expression

Michopoulous. Physiol Behav. 2016 May 13

Estrogen Therapy & IR

- Years since menopause shows difference in HT effect on IR
- Early menopausal women (less than 6 years) have lower risk of T2D with MHT
- Later menopausal women (over 10 years have higher risk of T2D with MHT than without MHT
- Effect seen with and without progestins

Pereira RI, et al. J Clin Endocrinol Metab. 2015 Dec; 100(12):4456-62

Excess Estrogens in Women

- Can cause weight gain
- Increase in PMS symptoms
- Fibroids, breast cancer
- Allergies
- Infertility
- Sluggish metabolism

Mechanisms of Estrogen Dominance

- Increased estrogen production
- Increased estrogen exposure
- Progesterone resistance
- Poor elimination/detoxification
- Bottom line=inflammation

Avoid Overdosing Estrogen

- Watch for s/s estrogen excess
- Patches and pellets deliver more estrogen overall
- Testosterone aromatization

Improve Estrogen Metabolism

- Aerobic Exercise 30 min 5 times per week
- Flax
- Green Tea
- Resveratrol
- Cruciferous vegetables
- I3 and DIM
- Omega 3-fatty acids
- Rosemary
- Turmeric
- Avoidance of EDC’s

Androgens in Women

- Hyperadrogenism and PCOS
- Hyperinsulinemia
- Hirsuitism
- Acne
- Male pattern hair loss
- Oligo or amenorrhea
- High testosterone
- Insulin resistance
- Acanthosis nigricans
- Polycystic ovaries on ultrasound

Diagnostic criteria

- Nov 2015 guidelines for diagnosis, must include 2/3
- Anovulation
- Hyperandrogenism
- Polycysitc ovaries on u/s

Diagnosis to exclude

- Adrenal or ovarian tumors
  - Suspect with Serum T >150 ng/dL and DHEAS > 800 mcg/dL
- Thyroid dysfunction
- Congenital adrenal hyperlplasia-17OHP
- Hyperprolactinemia-fasting prolactin level
- Cushing syndrome-24 hour urine cortisol, spot urine cortisol
- Primary ovarian failure- FSH, LH

Additional workup

- Evaluate for insulin resistance
- Evaluate lipids
- U/S of ovaries

Treatment options

- First line-address insulin resistance
  - Metformin
  - Botanicals
    - Berberine 500 mg TID
    - Selenium 200 mcg daily
    - Zinc 50 mg
    - Vit D3 replection
    - Folic acid 5 mg
    - Inositol 500 mg

Treatment for PCOS

- Address progesterone deficinency
- Address estrogen dominance
- Improve estrogen metabolism
- Address testosterone excess symptoms
  - Hair loss-finasteride 0.5 mg-1 mg per day
  - Acne-spironolactone 25-50 mg
- Consider gut-lactobacilli

PCOS Problems

- Similar factors trigger the 2 disorders
- Recent study of women with PCOS vx controls showed that PCOS patients had
  - Highe TSH
  - Lower progesterone
  - Anti-TPO
  - Higher T, DHEAS and more insulin resistance
  - Estrogen higher in PCOS + AT

Gaberscek, et al. Eur J Endocrinol. 2015 Jan; 173(1): r9-21

Androgen Def

- Low free or low bioavailable testosterone is associated with loss of lean mass in women
- Muscle loss associated with lower metabolism
- Androgen replacement in obese women produces greater weight loss and maintenance of lean mass

NAMS Guidelines for HT

- Hormone therapy is the most effective treatment for vasomotor symptoms and genitourinary syndrome of menopause and has been shown to prevent bone loss and fracture.
- Risks associated with hormone therapy differ among women, depending on type, dose, duration, route of administration, timing of initiation, and whether a progestogen is needed. Treatment should be individualized using the best available evidence to maximize benefits and minimize risks, with periodic reevaluation for the benefits and risks of continuing hormone therapy.
- For women aged younger than 60 years who are within 10 years of menopause onset and have no other contraindicatins, the benefit-risk ration appears favorable for treatment of bothersome vasomotor symptoms and for those at elevated risk for bone loss or fracture. Longer duration may be more favorable for estrogen therapy than for estrogen progestogen therapy, based on the Women's Health Inititative RCTs.
- For women who initiate hormone therapy more than 10 to 20 years from menopause onset or when aged 60 years or older, the benefit-risk ration appears less favorable compared with younger women because of greater absolute risks for coronary heart disease, stroke, venous thrombemoblism, and dementia.
- For GSM symptoms not relieved with over-the-counter or other therapies, low-dose vaginal estrogen therapy is recommended.

Thank you!!

- Questions?

References

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- Pinkerton, J.V., Aguirre, F.S., Blake J., et al. (2017). The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 24(7): 728-753.