Hormone Dosing

A Pharmacist's Perspective

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AARM
Association for the Advancement of Restorative Medicine

Objectives

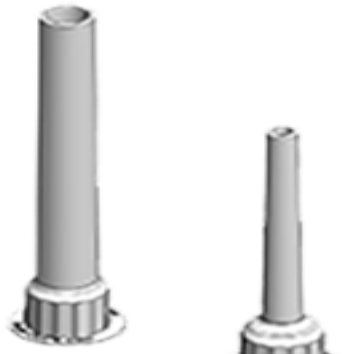
1. Dispensing devices for compounded BHRT
2. BHRT and Evidence base studies
3. Quality and Safety of BHRT
4. Case studies

Dispensing Devices

- **Oral syringes**
  Dispenses **0.1-0.2ml**

Dispensing devices

EMP jars
Dispenses 1-1.25ml



Dispensing devices

Mega Pumps
Dispense 0.5-1ml

Dispensing devices

Topi-Click
Dispenses 0.23ml

Turn the base to dispense the number of clicks specified on label.

When rotating base, <u>watch</u> the Visual Indicators

Indicator Node on Body is fixed at the Click Point

Indicator Column moves with Base. This shows Node in line with column.

<u>LEAVE IN THIS POSITION AFTER EVERY CLICK</u>
(The Home Position)

Dispensing devices

Tickers

Dispenses **0.05ml** increment

Dispensing devices
For vaginal products

Studies

ESTHER Study
Conclusion: “Oral but not transdermal estrogen is associated with an increased VTE risk”

KEEPS Study
Hormone Therapy has many favorable effects in newly menopausal women
http://www.keepstudy.org/news/pr_100312_a.cfm

Studies

Stanczyk FZ, Paulson RJ, Roy S. Menopause. 2005 Mar;12(2):232-7.

".. anti-proliferative effects on the endometrium have been demonstrated with progesterone creams when circulating levels of progesterone are low. Despite the low serum progesterone levels achieved with the creams, salivary progesterone levels are very high, indicating that progesterone levels in serum do not necessarily reflect those in tissues

Studies

Vashisht A, Wadsworth F, Carey A, Carey B, Studd J.Gynacological Endocrinology, 2005;21(2):101-5

"..PE40mg/ E2 "1mg" cream, highly significant reduction in symptoms of anxiety, depression, vasomotor symptoms and
libido issues when compared with baseline after12/24/48 weeks.."

Studies

Holtorf K. Postgrad Med. 2009 Jan;121(1):73-85

Conclusion: “..Physiological data and clinical outcomes demonstrate that BHRT are associated with lower risks,
including the risk of breast cancer and cardiovascular disease, and more effecaious than their synthetic and animal derived counterparts”

Studies

Andres D Ruiz, et al.BMC Women's Health 2011, 11:27

The most common compounded BHRT dosage forms utilized is topical 71%. The study demonstrates that compounded BHRT improves mood symptoms. Women experienced a 25% decrease in emotional lability ($p<0.01$), a 25% decrease in irritability ($p<0.01$), and a 22% reduction in night sweats ($p=0.09$) and a 6% reduction in hot flashes ($p=0.50$).

Visit your Compounding Pharmacy, Ask the right questions:

1. Do they have the right **equipment**?
2. Do they have the right **sourcing for chemicals**?
3. Do they have the right **SOP**?
4. Are they updated in their knowledge **(training / certificates)?**

Equipment

1. Containment hood

2. Ointment mill

3. Unguator mixer

4. RAM Mixer

Resonance Acoustic Mixer

Sourcing API

We source all of our hormones from **PCCA-Professional Compounding Centers of America**

Bases

Does the **topical** cream base have the ability to **transport** hormones deep into the dermis?

Bases

Does the **vaginal** cream base have the ability to **bond** to mucosal membranes for increased contact time?

Continuing Education

USP <800> and NAPRA guidelines
What's next?

Clinical pearls & Nuggets

Estriol, is the least potent of physiological hormones, and it acts as an agonist and antagonist at the receptor site an in essence balance the Estradiol

Bi-est ratio, 80:20 or 50:50?

Clinical Pearls

Estradiol deficiency may have a role in developing Alzheimer's disease
Helps maintain memory
increases cerebral blood flow
Influences neurotransmitter systems

Lumsden MA, Benefits of treatment:local and general menopause symptoms. Chapter 53, IN:Fraser IS, Jansen RPS Lobo RA, Whitehead MI eds. Estrogens and Progesterones in Clinical Practice London UK: Churchill Livingstone 2000

Clinical Pearls & Nuggets

Phytoestrogens (Black cohosh, soy containing products, Flaxseed, Chaste berry, Red Clover) can be helpful with symptoms of menopause, specifically hot flashes.
A patient that has a diet that is rich in phytoestrogen like soy or tofu, will have a higher estrogen burden, and should be counseled about this effect. This also should be considered when dosing BHRT.

https://naturalmedicines.therapeuticresearch.com

Clinical Pearls & Nuggets

Continued vasomotor symptoms such as **hot flashes** and **night sweats**;

1. Increase the estrogen
2. Make sure the patient is applying the hormones properly
3. Monitor hormonal levels

Clinical Pearls & Nuggets

Breakthrough bleeding or Heavy menses;

1. May need to increase progesterone or decrease estrogen specially if estrogen dominance symptoms are present
2. If persistent, comprehensive management requires a pelvic ultrasound to evaluate the endometrial lining

Clinical Pearls & Nuggets

Weight gain

1. It is not unusual, just like other hormone replacement to see some fluid retention with the addition of BHRT. It is usually **transient**.
2. Be sure exercise, diet, supplements are in place in life style, along with adequate sleep.
3. Reassessment of **thyroid** may be required.
4. **Reassurance** that this is all will improve as hormones are optimized; energy will return, motivation will improve and weight will come off.

Pearls and Nuggets

Estrogen depletes Vitamin B12

Progesterone/Estrogen Ratio

How is the ratio calculated?
Optimal ratio of 100-500

1. Only when E2 is within a normal luteal phase range;
   (1.3-3.3 pg/mL in saliva, and 43-180 pg/mL in blood spot.
2. The ratio is calculated from the Pg value in pg/mL divided by the E2 value in pg/mL.

Saliva test example: a patient has E2 = 1.5 pg/mL and Pg = 300 pg/mL. The units are the same (pg/mL), so the ratio is 300 divided by 1.5:

Blood spot or serum example: a patient has E2 = 100 pg/mL and Pg = 20 ng/mL. The Pg units are first converted to pg/mL before calculating the ratio: 1 ng/mL is equivalent to 1000 pg/mL. Therefore, the ratio is 20 ng/mL x 1000 = 20,000 pg/mL Pg, divided by 100 pg/mL E2, ratio is pg:E2 =200
Both of these examples represent normal endogenous luteal phase levels of E2 and Pg.

Is the ratio relevant in women using hormone therapy?

With some types of hormone therapy such as topical progesterone, Pg levels in saliva are much higher than endogenous luteal phase levels, ranging from 200-3000 pg/mL at 12-24 hours after dosing, and so the ratio can appear high. However, because symptoms of both estrogen dominance and progesterone dominance can look the same, testing and assessing the ratio along with clinical symptoms can help determine the next step for treatment.

Clinical Case

Mary complains of hot flashes and night sweats. She's a 50-year-old, newly postmenopausal woman who has never been on hormones. Her BMI is normal and she has no other health issues. A saliva test finds an **E2 of 1.1 pg/mL (reported as "OK")**, but a **Pg level of 15 pg/mL (also "OK" for a postmenopausal woman)**, giving a **ratio of 13.6** which is **low.**

- Based on her symptoms and a low ratio you start her on **topical progesterone**, which immediately helps the patient symptomatically. A few months later, you test her hormone levels again in saliva. Her E2 is 1.3 pg/mL and her Pg level is now 2500 pg/mL (within range for topical treatment). Her ratio is now **1923, reported as "high"**. What do you do? The patient has no symptoms, feels great and her E2 and Pg levels are within appropriate ranges **- no adjustments in treatment are needed.**

A year later **Mary comes back reporting hot flashes and night sweats. She was doing well until about 3 months ago**. She had done a detox diet and had lost about 5 lbs. A saliva test shows that her E2 has dropped to 0.5 pg/mL: still "OK", but much lower than last year; her Pg is still within the supplementation range at 2350 pg/mL. Her **ratio is now 4700**, which is still high. Unlike the **last visit, however, Mary is now symptomatic.**

Converting Patients from Synthetic to Bioidentical Hormones

. What dose is the patient on?
. Counsel the patient that the transition may occur over weeks to months and symptoms could worsen
.Tapering the synthetic therapy

(provide a calendar with the tapering protocol clearly outlined, along with beginning date of new therapy and days to use it with taper protocol)

- **You have 3 choices: add estrogen therapy, reduce progesterone therapy, or both**. Why is her higher Pg making things worse?
- Excessive Pg when E2 is low can down-regulate estrogen receptors and worsen estrogen deficiency symptoms. If Mary chose not to start estrogen therapy, just reducing the progesterone dosage would likely normalize her symptoms.

Tapering protocol
High dose usage of oral CEE

1. Decrease the commercial oral dose by 1 daily pill, every 2 weeks
2. Start progesterone therapy upon initiation of the CEE taper
3. Start milk thistle or DIM, 250mg 2-3 times daily throughout protocol.
4. Print out calendar with doses / days marked

Tapering protocol
Low dose of oral CEE

1. Decrease commercial dose by 50% (1/2 tablet), give daily for 2 weeks
2. Discontinue medroxyprogeterone and add progesterone special micronized topical cream daily
3. On the days not using oral CEE, apply Bi-Est topical cream, Apply to genital tissue

Dose Queues

Immediate results are not usually not seen, however, some symptoms like hot flashes, may resolve faster than others such as libido and vaginal issues

Dose adjustment

Adjustment and addition are common after the first 2-3 visits, and it is better to be done in person, to ensure that the patient is using the hormones as prescribed in a manner that optimizes the hormone dose

Dose adjustment

- Should be relatively small and should be monitored for another 30 days prior to next adjustment
- Use a follow up assessment form

Navigating the Pharmacy: How it all works

- **First:** You **fax** in the patient's prescription to the pharmacy (email is not secure and not PHIPPA compliant)

- **Second**: Pharmacy **calls the patient** to confirm that the patient would like it to me made, provide pricing, get credit card info and confirm address for shipping (free shipping)

- **Third**: Prescription is **made and shipped** out

- **Fourth**: Pharmacist **Counsels** patient on how to use the prescription, in person or on the phone. A usage guide is also sent out in the delivery with details on application areas, storage and use of dispensers

- **Fifth**: **Receipt is provided to the patient**, which they can submit to their insurance. Most insurance companies cover BHRT prescriptions

Refills

- If you have not indicated refills on the prescription, and the patient requests a refill, we will fax your office to get authorization.
- If you do not want the patient to have more until blood testing or follow up appointment, You can indicate that on the fax and send back. We will let the patient know that they need to connect directly with your office.

Thank You

Please feel free to contact me with any further questions

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