

Bioidentical hormone therapy

What are the facts?

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Art: A 50-something woman, either in consultation with a doctor or engaged in some activity like gardening or some such?

By Jon S. Nielsen, MD, FACOG

Given all the concerns about the safety of hormone therapy (HT) over the past few years, it's no surprise that women have been seeking the alternative form of HT called "bioidentical hormones." Indeed, a high-profile marketing concept, touting a "safer and gentler" approach to hormone therapy, has developed around using bioidentical hormones produced in compounding pharmacies, where drug formulas are said to be specially tailored to individual patients. As a result, there is much confusion among women, health care professionals, and the media about the definition, safety, and utility of hormone therapy preparations available today. This article clarifies some of the terms used to describe hormone therapy preparations, and reviews the safety and utility of the hormone therapy

options available today.

Sorting out the terminology

What is meant by the terms “natural,” “synthetic,” and “bioidentical,” especially as used in the marketing of hormone products? Often, the term *natural*, denoting ingredients that are organic (meaning derived from plant or animal), is used in contrast to the term *synthetic*, denoting a product made in a laboratory. Similarly, the term *plant-based* may be used in categorizing a hormone product as natural or *bioidentical*.

In fact, all hormone products are made from plants, except for Premarin, a conjugated estrogen that is extracted from pregnant mare’s urine. This product, available since the 1940s, was a fabulous medicine in the early years, and is still too often thought of as THE estrogen in estrogen therapy. All of the other estrogen products, whether they are traditional pharmaceutical products or hormones created in compounding pharmacies, contain estradiol. Estradiol is made from yams and soybeans, as are almost all estrogens. What needs to be understood is that since the 1970s, it has been possible to produce in the laboratory an estradiol that is identical to the molecule made in the human body. This estradiol is truly bioidentical and forms the basis for almost all of the pharmaceutical-grade estrogens on the market today. Many of the “natural” claims by compound pharmacy advocates are based solely on the contrast between their plant-based products and animal-based Premarin and Prempro

(Premarin with progestin added, patented in the mid-1970s after Premarin was found to raise the risk of endometrial cancer in women who still had a uterus).

Unfortunately, patients looking for relief from hot flashes and other menopausal symptoms continue to be bombarded with information about hormone therapy that is driven by motives related more to marketing than to patient education. The trend toward patient self-education, often via the Internet, has left many vulnerable to misinformation and disinformation. Television shows, celebrities, and Web sites all are telling women that because of the Women's Health Initiative study results linking HT to breast cancer and heart disease, they should take only bioidentical hormones made at compounding pharmacies, rather than standard hormone replacement therapy. The claim is that these "bioidentical hormones" are custom-mixed to the individual, thus offering a "safe" alternative. It should, however, be understood that on reanalysis many of the negative conclusions from the WHI have been subsequently discredited.

Fact vs. fiction? Marketing vs. education? Let's look at some facts.

Sorting fact from fiction

Fact #1: A woman's body produces three forms of estrogen: estradiol, the predominant pre-menopausal estrogen; estrone, the main post-menopausal estrogen; and estriol (E3), the weakest form of estrogen, made only during pregnancy by the placenta. Even though estriol is produced almost exclusively

during pregnancy, it is present in most estrogen products created in compound pharmacies. It has not been scientifically studied for safety or efficacy as a hormone therapy product and is not FDA-approved for use in any form of hormone therapy. Estriol is such a weak estrogen that it usually has little or no hormonal effect in the woman's body.

Fact #2: There's nothing inherently wrong with the term "bioidentical" – *if* defined appropriately. All non-oral pharmaceutical estrogens are estradiol, and therefore bioidentical, whether or not they are made in compounding pharmacies. Even oral estradiol should be considered bioidentical. Though both oral estradiol and transdermal estradiol (delivered via a skin patch) are considered bioidentical, transdermal preparations are becoming the gold standard because of the steady-state delivery, constant blood levels, and the probable lower risk profile.

Fact #3: The hormones studied in the Women's Health Initiative (WHI) were Premarin and Prempro, the animal-based products that should be considered organic but not bioidentical. The negative conclusions from the WHI study, which scared millions of women into discontinuing their hormone therapy, should not necessarily be applied to bioidentical (estradiol) hormone therapy (BHT).

Fact #4: Advocates of compound pharmacy "bioidentical hormones" have made several unsubstantiated claims about bioidentical hormone therapy. There is no evidence that BHT is safer than standard hormone therapy or has

improved efficacy. In addition, a number of concerns remain about BHT with regard to purity, quality, variation in the inactive ingredients, and variation among pharmacists and pharmacies.

Fact #5: There is essentially no scientific data to support saliva testing (typically the basis for creating “customized” BHT in compounding pharmacies) to evaluate systemic hormone levels and therefore dictate therapy decisions. With transdermal therapy, however, blood serum levels can be very helpful in managing therapy because of the steady-state, consistent levels achieved.

Fact #6: All medicines, including hormone therapies, have potential side effects. Though patients sometimes overreact to what they have read in package inserts, with BHT there is no accompanying package inset information at all for review. Therefore it is doubly important to advise patients that compound pharmacy products have no evidence of increased safety.

Fact #7: Data regarding transdermal estrogens, whether standard HT or those made in compounding pharmacies, do suggest increased safety. Transdermal estrogens go directly into the bloodstream and avoid the changes that happen when absorbed through the bowel and processed in the liver. There is less worry about heart effects or blood-clotting risk.

Other hormones: progesterone and testosterone

The use of the other hormones, progesterone and testosterone, must also be addressed from the bioidentical viewpoint. Advertising for compounding

pharmacies often contains misleading information about progesterone.

Progesterone has not been proven to prevent bone loss, prevent breast cancer, or help postmenopausal patients lose weight, as the advertising often claims.

Transdermal progesterone preparations are often helpful in perimenopausal patients because they provide low-dose progesterone during the inconsistent periods when little progesterone is being made. The oral bioidentical preparation Prometrium (synthesized from yams, and structurally identical to the natural progesterone found in a woman's body) is effective as the progesterone component in HT in patients who have a uterus and therefore need progesterone to counteract the effects of estrogen on the uterus.

Testosterone therapy, which has been touted as an effective agent for treatment of decreased libido (sex drive), is also a mainstay of most compounding bioidentical regimens. The traditional pharmaceuticals do not contain appropriate dosage formulations for libido treatment, other than the estrogen/testosterone combination product Estratest. Micronized oral testosterone products from compounding pharmacies therefore are a legitimate option for patients with libido issues. However, the anecdotal outcome results have been less than hoped. FDA approval of the transdermal product, which actually did show efficacy results, was not forthcoming because of potential cardiovascular risk associated with its use.

The bottom line

Traditional pharmaceutical estrogen therapy, in the form of transdermal estradiol, is actually “bioidentical” by definition, and the compound pharmacy-produced bioidenticals are not superior agents. More research would be necessary to confirm many of the claims made for the non-FDA-accredited BHT formulations, and more appropriate oversight of purity and production quality would be needed.

Women must aggressively seek answers from their providers about hormone therapy and how it applies to them and providers must be diligent in educating patients about hormone therapy. It must be emphasized that many of the negative conclusions about hormone therapy based on the WHI have now been appropriately challenged and in some cases discredited. Women who stopped their hormone therapy because of earlier reports are, appropriately, seeking hormone therapy again. Low-dose transdermal therapy, for as short a time as possible, is the preferred strategy. With risks lower than previously thought, longer-term usage may continue to be appropriate if symptoms persist.

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[Sidebar]

Resources

- For more information about specific drugs, a good resource is the FDA's Web site on Drug Safety and Availability, Estrogen and Estrogen with Progestin Therapies for Postmenopausal Women, at www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm135318.htm.
- The FDA also has a page of information for consumers about bioidentical hormone therapy ("Bio-Identicals: Sorting Myths from Facts"), at www.fda.gov/ForConsumers/ConsumerUpdates/ucm049311.htm.
- The North American Menopause Society Web site, www.menopause.org is also a very good source of information about this topic.