

Correcting Misconceptions About Compounding Bioidentical Hormones: A Review of the Literature

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Abstract

There are many misconceptions about the profession of pharmaceutical compounding and the preparation of bioidentical hormones used in hormone replacement therapy. These misconceptions are unfounded, because compounding is regulated by individual state boards of pharmacy, and compounded bioidentical hormones are prepared only when prescribed by a physician who has made a professional judgment in the interest of the patient. Physicians and the pharmacists who compound bioidentical hormones have not only the right but also the responsibility to be aware of current information published in the scientific literature concerning any prescribed medication.

Prescriptions for bioidentical hormone replacement therapy (BHRT) are prepared by compounding pharmacists. Compounding involves providing individualized and customized therapy that does not meet the definition of manufacturing as described by state boards of pharmacy, the U.S. Food and Drug Administration (FDA), the U.S. Drug Enforcement Administration (DEA), and the Supreme Court. It is undisputable that there are concerns related to statements in advertisements for manufactured pharmaceutical products and that the information provided to practitioners and the public is lacking in total disclosure of the truth.

Compounding is a component of the profession of pharmacy that is and has always been regulated by individual state boards of pharmacy. Information provided to patients about compounded prescriptions must comply with all state pharmacy laws. All compounding pharmacies are strongly urged to comply with the law and to provide necessary written information as well as verbal consultation to all patients for all prescriptions, compounded or otherwise.

Compounded bioidentical hormones must be prescribed by a physician, who has the right and the responsibility to be aware of current information published in the scientific literature about any prescribed medication. The choice to prescribe compounded bioidentical hormone preparations is a professional judgment made in the interest of the patient.

Compounding pharmacists do not and should not make claims regarding BHRT. There is a major difference between making a claim and portraying a possible benefit. For example, some advertisements suggest that the new “low-dose” conjugated estrogens/medroxyprogesterone acetate tablets (Prempro) are safer than other Prempro tablets manufactured in higher standard doses. However, the manufacturer of low-dose Prempro is very careful not to make such a claim. This is certainly wise because there is absolutely no scientific evidence indicating that the newer lower dose has an improved safety profile. Unproven claims about safety and efficacy should not be made for any product, including compounded bioidentical hormones. However, it is standard practice in the medical field to imply what evidence supports.

In our opinion, the efficacy and safety of bioidentical hormones could be proven if all evidence-based literature were reviewed. Because the drug-manufacturer-controlled medical economy will not fund studies on BHRT, no specific medical claims should be made pertaining to bioidentical hormones.

The following information refers only to facts presented in the scientific literature. One of the foremost references on the subject of BHRT is the textbook titled *The Clinical Gynecologic Endocrinology and Infertility* by Speroff and Fritz. This book lists many positive benefits of endogenous estradiol, including multiple mechanisms by which estradiol protects the cardiovascular system. Failure of commercial products to provide these benefits clearly should not be confused with the literature that supports exogenous use of low doses of bioidentical estrogens.

A comparison of the evidence suggesting that bioidentical progesterone may be more effective and safer than synthetic progestins shows that most synthetic progestins imitate the action of natural progesterone only in their effect on the uterus. A comparison of the effects of medroxyprogesterone acetate (MPA), which is the most commonly prescribed progestin, with those of bioidentical progesterone shows that the synthetic agent causes weight gain, irritability, acne, fluid retention, migraines, and a worsened cholesterol ratio, but treatment with natural progesterone produces improved mood and a reduction in anxiety, depression, somatic complaints, and hot flashes.¹ In another direct comparison, bioidentical progesterone produced less bleeding and breast tenderness than did treatment with MPA.² In other research, bioidentical progesterone produced better sleep than did placebo, but MPA had no effect on the quality of sleep.³

The literature suggests that the use of natural progesterone reduces the risk of cardiovascular disease. Research has shown that although MPA increased the level of low-density lipoprotein and decreased the level of high-density lipoprotein, bioidentical progesterone produced the opposite (and hence positive) effect.⁴ Although MPA stimulates vascular smooth muscles (VSMs) in coronary arteries, bioidentical progesterone inhibits VSM proliferation.⁵ Bioidentical progesterone has been shown to enhance the vasodilating effect of estrogen on exercise-induced myocardial infarction (MI) in postmenopausal women, but MPA produced the opposite effect.^{6,7} Miyagawa and colleagues demonstrated that MPA does not prevent vasospasm (an effect opposite that produced by progesterone).⁸ Progesterone increases blood flow and the level of nitric oxide; MPA decreases nitric oxide induced by estradiol.⁹ The level of C-reactive protein (CRP) is increased by MPA, but progesterone produces no increase in the level of CRP beyond that which is induced by treatment with oral estrogen alone.¹⁰

Numerous studies have shown that MPA therapy significantly increases the risk of breast cancer.¹¹⁻¹⁶ Evidence has revealed that bioidentical progesterone does not increase the risk of breast cancer and may instead be protective against it. Bioidentical progesterone has been shown to inhibit breast cells and to increase overall survival,^{17,18} but MPA stimulates breast cells (Women’s Health Initiative, Breast and Cervical Cancer Detection Program) and increases cell adhesion.¹⁹ Only progesterone has been shown to reduce the uptake of estrogen by breast cells.¹⁸ Cowan and colleagues showed that low progesterone levels resulted in a 5.4-fold increase in premenopausal breast cancer.²⁰ Bioidentical progesterone, however, has been shown not to increase the risk of breast cancer.^{21,22} Progesterone also stimulates Bcl-2, an antiapoptotic protein, and is protective against glutamate toxicity (effects that are not produced by MPA).²³

Bioidentical progesterone stimulates osteoblasts, which increase bone formation and bone mineral density, but MPA has no such effect.²⁴⁻²⁶ Bioidentical progesterone produced fewer adverse effects and less bleeding than did MPA and was preferred to MPA by study subjects in a variety of research investigations.^{1,2,27-29}

The literature clearly shows that bioidentical progesterone provides more protection for the cardiovascular system, the brain, and bone and greater protection against cancer than does MPA, which antagonizes many of the potential benefits of both estrogen and bioidentical progesterone. Many human studies have demonstrated that treatment with estradiol causes vasodilation; a decrease in sympathetic flow, vascular proliferation, and vascular inflammatory response; and lower blood pressure.³⁰⁻³⁵

Evidence also suggests that estriol may provide protection against cancer.³⁶⁻³⁸ Estriol has been shown to reduce thrombosis³⁹ and may exert neuroprotective or neuroenhancing effects, including a greater propensity for inducing ganglion nerve cell proliferation in the brain than does either estradiol or estrone.⁴⁰ Treatment with estriol has been beneficial in reducing the effects of autoimmune demyelinating disease⁴¹ and in treating patients with multiple sclerosis.⁴² Estriol has also been shown to reduce bone loss, reverse vaginal atrophy, and resolve chronic urinary tract infections caused by atrophy.^{39,43-45}

Conclusion

All medical disciplines should seek and provide a better therapeutic outcome for the individual patient. Expert advisory groups often state opinion rather than fact, and the FDA should be wary of such opinions, especially when they are not supported by the scientific literature.

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Resource

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