REGEN MED

ARTICLE

BIO-IDENTICAL HORMONES AND THERAPIES

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ABSTRACT: BHRT treatments and products are increasingly utilized to address menopause, sexual dysfunction and other conditions. Products are typically prepared by compounding pharmacists from plant and other natural extracts. They are often marketed as safer than traditional hormone therapies and, with careful dosage and other management by the treating physicians, more effective for a given patient. However, bio-identical hormones are not approved by the FDA. Most clinicians and patients are seeking more and better data on safety and efficacy.

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BACKGROUND

BHRT's are estimated to account for one third of menopausal hormone therapy prescriptions. [1] Since the Women's Health Initiative Hormone Therapy Trials, [2] the debate over relative safety and efficacy between conventional hormone therapeutic approaches and BHRT's for women remains vibrant. Similar discussion surrounds BHRT's andropause and other male-specific conditions.

As stated by The American College of Obstetricians and Gynecologists [3]:

> "Compounded preparations are not regulated by the FDA. Although technically all compounded prescription drug preparations could be considered unapproved new drugs, the FDA has adopted a policy of enforcement discretion, allowing legitimate preparation of compounded formulations to be regulated by state boards of pharmacy, with a provision of stepping in when dangerous practices must be addressed and when drug manufacturing occurs under the guise of compounding. There are currently no specific regulations by the FDA on what constitutes a legitimate claim for compounded drug preparations. In general, states regard compounding to be part of the practice of pharmacy. In addition, individual states' pharmacy acts usually permit other licensed practitioners (e.g., physicians, nurse practitioners, and others with prescriptive authority) to engage in the practice of pharmacy compounding for their own patients."

BHRT's are thus an important manifestation of a broader healthcare trend -- personalized/precision medicine. [4]

However, developing statistically significant safety and efficacy data for personalized medicine interventions through traditional clinical trials is challenging. Time constraints, administrative burden and cost are significant impediments.

THE NEED FOR BHRT STUDIES

RWE studies and registries are needed to focus on many safety and efficacy issues specific to bio-identical hormone products and interventions. Examples include:

- Testosterone Replacement Therapy ("TRT) for symptomatic hypogonadism.
- Other TRT claims such as beneficial effects on bone density, strength, muscle, cardioprotective effects.
- Potential TRT side-effects such as polycythemia, peripheral edema, cardiac and hepatic dysfunction.
- Comparison of bio-identical estradiol, estriol and progesterone with synthetic and animal derived versions.
- Specific compounding ingredients and

proportions for a given product as used for a specific indication, and with reported long-term outcomes.

- Long-term outcome assessments capturing increased incidence of breast cancer, cardiovascular disease, venous thromboembolism, hirsutism, and other for specific dosages of specific products.
- Identification of outcomes, including adverse events, against various administration routes – subcutaneous pellets, injections, oral, other.
- Dosage measurement of key compounded ingredients in the context of specific indications and long-term outcomes assessments.
- Integrating longitudinal laboratory blood, saliva, and other analyses into the study protocol.

Publications such as *The Clinical Utility of Compounded Bioidentical Hormone Therapy: A Review*, by the National Academies of Science, Engineering and Medicine suggest other important real-world study topics regarding BHRT

PRACTICAL CONSIDERATIONS

The need for clinically significant datasets addressing many BHRT issues is evident. Patients, providers, and regulators will increasingly require such evidence. Equally clear is that such datasets will ultimately depend on busy clinicians designing and executing such studies.

Those clinicians will also need to enroll their BHRT patients into their studies, and ensure maximum compliance with long-term outcomes reporting. These factors normally imply cost, time, administrative burden, and distraction from patient care.

Circles eliminate these traditional obstacles. At the same time, they enable providers to support clinical decision making with relevant aggregated datasets. They provide the foundation for evidence-based communications with patients.

Circles also allow compounding pharmacies and other manufacturers to develop auditable, statistically significant product and treatment registries to support marketing claims.

ILLUSTRATIVE USE CASE

Dr. Grant Pagdin is utilizing two Circles – one for men and a second for women – to develop BHRT clinical decision support.

Pre-treatment and long-term outcomes assessments include the Cervantes Short-Form Scale and the Aging Males' Symptom

Scale. Aggregated outcomes are explained and shared with patients, as described on the Outcomes Page on Dr. Pagdin's website.

Dr. Pagdin's initial BHRT Circles and associated datasets will focus on standardized outcomes assessments and patient compliance. Subsequent Circles will also collect data on specific types, dosages and other characteristics of bio-identical product used.

FOR FURTHER INFORMATION

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FOOTNOTES

1 Compounded Bioidentical Hormones: Myths and Realities. Santoro and Liss. Clin. Obstet. Gynecol. 2021 Dec 1;64(4):793-802.

2 See The Women's Health Initiative Hormone Therapy Trials: Update and Overview of Health Outcomes During the Intervention and Post-Stopping Phases, Manson et al.

3 Committee on Gynecologic Practice and the American Society for Reproductive Medicine Practice Committee.

4 See for example From Hype to Reality: Data Science Enabling Personalized Medicine, Froehlich et al.