Bioidentical custom compounded hormone therapy

KEY POINTS:

- Conventional MHT often contains the same form of body-identical hormones as compounded therapies.
- The patient must be fully informed that custom compounded bioidentical hormone therapy is unproven and that there may be risks, particularly the lack of endometrial protection.
- In the absence of peer-reviewed scientific data, and for all the other reasons mentioned below, the Australasian Menopause Society cannot endorse the use of compounded bioidentical hormone therapies.

Many patients are attracted to the concept of using hormones that are the same as those which are produced by the ovary pre-menopause. This gained traction after the publication of the Women's Health Initiative study. There was a suggestion from some that the adverse findings were secondary to the "synthetic" hormones used in that study and that the same would not occur with the use of natural hormones. This has led to an industry of the compounding of 'bioidentical' hormones which are often in the form of creams, troches and pessaries. These are widely used by many women at considerable expense.

'**Bioidentical' hormone therapy** refers to compounded products which are marketed as hormones that are identical to those produced by the body. The production of these products is not subject to the regulatory conditions of approved pharmaceutical products (1).

In contrast 'body-identical' hormone therapy refers to pharmaceutical products that have the same chemical structure as those produced in the human body (1).

It is important to realise that no hormone used in any preparation of pharmaceutical grade menopausal hormone therapy (MHT) or compounded "bioidentical therapy" is 'natural'. They are all synthesised in the laboratory from some precursor by enzymatic manipulation.

Furthermore, oestrogens all act through the same receptors, although different progestogens interact with other steroid receptors as well as with the progesterone receptor.

Do compounded bio-identical hormones work?

The efficacy of oestrogen preparations for menopausal symptoms may be measured by

the resolution of vasomotor symptoms. There are no data on the efficacy of compounded oestrogen therapies for the maintenance of bone density and prevention of osteoporosis.

For progestogens, the measure of efficacy is the prevention of endometrial hyperplasia and neoplasia. The progestogen regimens used are variable and unregulated, and there are no data on whether they are adequate to provide endometrial protection with evidence to suggest they are not (see below).

Safety concerns about compounded bioidentical hormones

Risk of endometrial hyperplasia and neoplasia

A major concern is the question of adequate endometrial protection with compounded progestogen regimens. Here, significant failings have been documented, in that compounded progesterone delivery, both by transdermal and troche route, have been reported to be inadequate for endometrial protection when administered in combination with oestrogen, leading to endometrial cancer (2, 3).

Quality control and contaminants

Pharmaceutical grade hormone therapies are manufactured under strict conditions and are required to undergo rigorous testing of content purity and efficacy. Custom compounded hormones are produced under unregulated conditions without quality standards regarding content, efficacy, or contamination. It is impossible to know what excipients are in the preparations and how those excipients will affect pharmacokinetics (4). Contamination of compounded therapies may contain impurities which compromise sterility or those which lead to more serious consequences (5, 6).

Content of commonly prescribed compounded therapy

Oestrogens

Oestrogen in compounded therapies is often delivered as "biest" (oestradiol and oestriol) or "triest" (oestradiol, oestrone and oestriol). Although all three forms of oestrogen are naturally present in the circulation, oestrone and oestriol function as competitive inhibitors of oestradiol at the oestrogen receptor and exogenous oestradiol will be metabolised in vivo to oestrone and oestradiol. There is no evidence to support the exogenous provision of all three forms in hormone replacement.

Progestogens

Progestins (synthetic progestogens) act at different receptors of the steroid receptor family and there is some evidence that their differential effects are as a result of this, e.g. cyproterone acetate is an anti-androgenic progestin with some glucocorticoid action and drospirenone has some anti-mineralocorticoid action. There is also some

evidence that body-identical progesterone has a better risk-benefit profile, when delivered in sufficient amount, to most other members of the progestogen family (7). However, delivery of progesterone in sufficient therapeutic doses is the important issue, and neither troche nor transdermal therapy does this reliably.

Other hormones

Other hormones, such as DHEA, pregnenolone (which is a precursor for cortisol), testosterone, growth hormone, thyroxine and melatonin are commonly included in custom-compounded hormone therapy. Many of these substances are prescription medicines for specific conditions other than menopausal symptoms and have the potential for adverse events from misuse.

Salivary hormone testing

Proponents of compounded MHT often advocate salivary hormone testing in order to individualise doses and monitor adequacy of therapy. However, unlike laboratory methods for hormones in blood, laboratory methods for measuring salivary hormones are not standardised and do not have quality control programs. Reproducibility of salivary hormone methods is affected by salivary flow rates, which are in turn affected by state of hydration and food intake. Both salivary and blood hormone levels are affected by recent intake of exogenous hormone. Neither blood nor salivary hormone measures should be used to judge appropriateness of dose. The exception to this is the measurement of oestradiol in blood in users of oestradiol implants to avoid tachyphylaxis. In all other cases adequacy of oestrogen dose is judged by resolution of symptoms, and/or maintenance of bone density.

Pharmacy Board Guidelines

The Pharmacy Board of Australia has issued guidelines on the compounding of medicines. The Guidelines state that a compounded medicine should be prepared only in circumstances where: a) an appropriate commercial product is unavailable, b) a commercial product is unsuitable (e.g. if a patient experienced an allergy to an excipient in the commercial product), or c) when undertaking research sanctioned by a recognised human research ethics committee (8).

Compounded MHT is being prescribed and dispensed outside these guidelines as there are appropriate commercial products available which deliver effective therapy as guided by results from clinical trial research. Moreover, there are commercial products which deliver body-identical oestradiol and progesterone, if the prescribing doctor or the patient so wishes.

Availability of pharmaceutical grade body-identical hormones.

Pharmaceutical grade oestradiol is available in Australia and New Zealand as tablets, transdermal patches or gel. It is also available for topical vaginal treatment.

Pharmaceutical grade body-identical progesterone is now available in capsule form in Australia (as Prometrium) and NZ (as Utrogestan).

Therefore, if women and their doctors wish to use hormones that are body-identical, this can be achieved with approved regulated products. In this way women can avoid the potential dangers of compounded products, maintain appropriate monitoring of safety and efficacy, and in most cases, save money.

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See Information sheets

AMS Guide to Equivalent MHT/HRT Doses Australia only

or

AMS Guide to Equivalent MHT/HRT Doses New Zealand only

Oestrogen Only Menopausal Hormone Therapy

Combined Menopausal Hormone Therapy (MHT)

The International Menopause Society, American College of Obstetricians and Gynecologists, The Endocrine Society, the North American Menopause Society (NAMS), United States Food and Drug Administration, American Medical Association and the American Society for Reproductive Medicine Practice Committee have all released statements advising against the use of compounded therapy until evidence is produced with regard to efficacy and safety. With such diverse content mix, production sites and methods, that is unlikely to be forthcoming.

References:

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