ADVICE BY THE AMS ON THERAPY REGIMENS INVOLVING BIOIDENTICAL HORMONE THERAPY.

Bioidentical Hormones for Menopausal Symptoms

The use of the terminology 'BIOIDENTICAL HORMONE' therapy has aroused much controversy and heated debate over the past 20 years, often with much criticism and unreferenced claims from the various protagonists.

Major concerns are directed towards a growing trend to promote the use of "Bioidentical hormone therapy" as being 'natural' and therefore superior to 'synthetic' hormone therapy. "Bioidentical hormones" are defined as compounds that have exactly the same chemical and molecular structure as hormones that are produced in the human body (US Endocrine Society definition). It is important to realise that all hormones are synthesised. No hormone used in any preparation (regular HRT or "bioidentical therapy") is 'natural' – they are all synthesised from some precursor by the action of enzymes. Both regular and compounded hormone therapies use bioidentical oestradiol but because of its rapid degradation and unsafe endometrial response, bioidentical progesterone is not used by commercial pharmaceutical companies.

This pamphlet explains why the Australasian Menopause Society does not endorse the use of compounded bioidentical hormone therapies.

What are Bioidentical Hormones?

- Bioidentical hormones are hormones synthesised to resemble identically, the natural hormones produced by the ovary. These so-called 'natural' hormones are supplied by compounding pharmacists as creams rubbed on the skin or troches placed in the buccal cavity of the cheek both of which allow the compounded bioidentical hormone to be absorbed through the buccal mucous membrane or the skin.
- .While there is evidence that these routes of delivery are viable, there is very little evidence that HRT delivered in this format is able to achieve physiological levels capable of preventing endometrial stimulation, inhibiting osteoporosis, a reduction in cardiovascular damage or a positive influence on neurological function.
- Oestradiol is rapidly metabolised by enzymes in target cells and the liver to the weaker oestrone hormone before finally being degraded to oestriol. The stepwise degradation of oestradiol occurs independently of the source or amount of the hormone and therefore the ratio of the levels of oestrone and oestriol to the parent oestradiol remains relatively constant depending on the presence and amount of enzyme in cells. For that reason, it is futile for doctors to write prescriptions for, or pharmacists to dispense, all three hormones (bi-gest, tri-gest) in an attempt to emulate what nature does naturally.
- Progesterone is very rapidly degraded in the human gut, liver and circulation so it has been difficult using oral therapy to maintain a level of progesterone sufficient to inhibit hyperplasia or prevent cancer in the endometrium. Progesterone can be absorbed through the skin but the amount circulating after a measured amount of progesterone cream has been applied to the skin, is insufficient to have any effect on the endometrial cells. There is some evidence that progesterone can be absorbed through the vaginal epithelium and through the buccal mucous membrane, but at present there are no reliable studies available to confirm that the amount absorbed from this source has a protective effect on the endometrium.
- Progesterone can be manufactured in a laboratory by a unique chemical process involving converting a precursor, called diosgenin, using a sequence of enzymatic actions which do not occur in the body. The highest amount of diosgenin is present in the Mexican wild yam. However, a cream containing Mexican wild yam will have no beneficial effect on the menopause unless the diosgenin has been converted into progesterone in the laboratory.
- The oestrogen compounds are sometimes combined with testosterone, DHEA, growth hormone, thyroxine and melatonin. Many of these substances are prescription medicines and are normally only prescribed after careful consultation with a doctor. If used inappropriately they can cause health problems.

Disadvantages to Consumers

The compounded hormones are often sold directly to the public via the Internet or through laboratories. Some doctors are also persuaded to prescribe them and as a result may receive incentives in return for doing so it is possible that women can obtain compounded bioidentical hormones without seeing or being examined by a doctor. If there is no medical consultation then safety issues may not be addressed. There is no opportunity for women to be offered, to discuss or to learn about a proven, prescribed therapy.

- Some compounding pharmacists who make the products may bypass the stringent quality standards required for prescribed drugs made by pharmaceutical companies. Bioidentical hormone ingredients may be produced outside Australia and New Zealand and the manufacture of these active ingredients may not have been audited by the Therapeutic Goods Administration (TGA) in Australia or MEDSAFE in New Zealand to see if they have met their guidelines for safe and proper manufacture.
- The compounded hormones have not been subjected to rigorous scientific trials required to produce reliable evidence that they work and are safe. For instance, research shows that DHEA is not effective to treat the menopause and DHEA is not recommended unless the patient has the serious condition affecting the adrenal glands called Addison's disease.
- Some of these compounded products contain abnormally high levels of hormones making them unsafe for women.
- Compounding pharmacists often state that these compounded bioidentical hormones are a unique mix of oestrogens but fail to add that all natural bioidentical hormones are processed in the body in the same way as regular prescribed HRT.

The compounded bioidentical products are claimed to be "tailored" to the needs of individual women based on hormonal measurements taken from their saliva. However there is inadequate scientific evidence that salivary hormone levels relate well to blood hormone levels or to menopausal symptoms. These unnecessary salivary tests are costly. It is recommended that HRT should be tailored to women's needs according to their symptoms, not to blood or salivary hormone levels. Often compounded bioidentical hormone therapy is much more expensive than prescribed HRT.

It is the doctor who writes the prescription who is legally responsible for any adverse events or legal claims from a woman who has been affected by the use troches or creams containing bioidentical hormones. For that reason it is important that the doctor must be fully aware of the benefits as well as the adverse events related to the use of pharmacological products that have not been approved by the Australian Therapeutic Goods Administration.

Australasian Menopause Society Concerns re Compounded Bioidentical Hormones

- There is inadequate scientific evidence to show that:
  - Compounded bioidentical hormones are effective.
  - these compounded hormones are safe and free of adverse side-effects.
  - these compounds are pure and free from contamination.
- There are no studies comparing the effect of doses of compounded bioidentical hormones to conventional HRT.
- The risk of cancer of the uterus may be increased with the use of compounded bioidentical hormones when estrogen is used with compounded progesterone cream, as the progesterone is poorly absorbed and therefore does not protect the uterus. (See AMS HRT pamphlets)
- There is inadequate scientific evidence documenting interactions between the compounded hormones, or between these hormones and other drugs which may be taken at the same time.
- Following reports of salivary hormone results patients may be told they have abnormal ovarian, thyroid or adrenal function and as a result may be started on a variety of unnecessary hormones. This may cause serious health problems.

Remember:

1. Conventional HRT often contains the same form of bioidentical hormones as compounded therapies.
2. If the oestrogens used in the compounded bioidentical mixtures reach similar oestrogen levels in the circulation as conventional HRT they are likely to have the same benefits but also the same risks. (see AMS pamphlets on risks and benefits of HRT)
3. If a doctor elects to prescribe an unregistered complementary or alternative therapy the woman must be fully informed that this therapy is unproven and that there may be risks.
4. In the absence of peer-reviewed scientific data, and for all the other reasons mentioned above, the Australasian Menopause Society cannot endorse the use of compounded bioidentical hormone therapies.

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 that there is a lack of evidence that the benefits and risks of compounded bioidentical hormones are any different from well-studied commercial preparations. Until such evidence is produced the risks should be treated as if they were similar.

References:

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