A New View of Women's Sexual Problems

for FDA Advisory Committee Hearing on Intrinsa, December 2, 2004

The Potential for Adverse Drug Reactions (ADRs)

Problem 1: Dosage and Dosing Indications

- Groups of Women in the Phase III clinical trials were surgically menopausal.
    - Presently available clinical assays make it impossible to recommend a serum testosterone level at which treatment should be undertaken. It is very difficult to measure total testosterone at low levels (Morley and Perry, 2003, p. 409).
    - There is currently no readily available inexpensive assay which reliably measure free testosterone levels in the female range (Rivera-Woll et al, 2004, p. 421).
    - There is a lack of data demonstrating a minimum serum free testosterone level which, if below this, correlates with the symptoms of androgen insufficiency (Ibid., p. 421).
    - Testosterone levels kept close to and within the normal physiological range for women does not appear to have undesirable metabolic consequences. However, there is no reliable, inexpensive test to determine the appropriate level and no indication of how frequently such a test should be repeated.
    - In different clinical trials, women were administered 150 micrograms/day, 300 micrograms/day or 450 micrograms/day. The group receiving 300 micrograms/day experienced the most benefit. Which group of menopausal women (surgical v. natural) should receive which dose?
    - Women in the clinical trials were also taking estrogen. This is a "general rule" for postmenopausal women (Davis). What happens to women who do not take estrogen together with testosterone?
    - What additional risks do women assume by taking the estrogen? Estrogens may increase the risk of heart attack, stroke, breast cancer, endometrial cancer and blood clots in the lungs or legs.
    - Women who have used testosterone products designed for men (with acknowledged higher doses than women need) have experienced the following masculinizing effects:
        - hoarseness or deepening of the voice,
        - unnatural hair growth or loss,
        - acne or oily skin,
        - decreased breast size,
        - increase in the size of the clitoris and
        - irregular menstrual cycles.

Problem 2: There have been no long-term trials.

- In the past, users of testosterone products have experienced liver cancer. How can the possibility of that be known in this population without a long term trial?
- We have learned about the elevated risk of malignancies (cancers) of various tissues in women who were on hormone replacement therapy. Can we assume, without evidence, that testosterone will be benign? (Somboonporn & Davis, 2004, p. 374).
- Desirable effects and lack of negative side effects has been concluded by researchers for women who received testosterone in a 14-24 week range. The only way to gain information about adverse drug reaction in the "real world" based on this short duration, would be to expect testosterone users to become the equivalent of guinea pigs, like women were in the 1960s with the early birth control pill.
- Once drugs are approved for the marketplace, there is no method for tracking users in the "real world." Health privacy regulations (HIPAA) make this even more problematic.

Problem 3: "Real world" women will have a variety of other factors and may be taking other prescription and nonprescription remedies that could make them vulnerable to unanticipated adverse drug reactions.

- Large age differences (younger, middle-aged, and older)
- Cardiovascular disease or precursors (hypertension, etc.)
- Diabetes and other chronic conditions
- Auto-immune disorders
- Cancers
- Different ethnic backgrounds
- Weight issues and body morphology
- Depression and other mood disorders

References:

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