Testosterone Patch Improves Sexual Function in Postmenopausal Women

BY MARY ANN MOON
Contributing Writer

The testosterone patch improves sexual function and decreases emotional distress in postmenopausal women who have hypoactive sexual desire disorder, but the patch's long-term safety needs to be assessed, according to an international study of more than 800 women.

"The increase in the frequency of satisfying sexual episodes was modest but appeared to be clinically meaningful," said Dr. Susan R. Davis of Monash University, Prahran, Victoria, Australia, and her associates.

Compared with the placebo group, both groups on active treatment reported increases in sexual desire and frequency of satisfying sexual episodes.

This is the first large-scale, phase III clinical trial of testosterone therapy that involved postmenopausal women who were not taking concomitant estrogen. The results "indicate that exogenous estrogen or combined estrogen plus progestin are not required for testosterone to be effective in the treatment of hypoactive sexual disorder," the authors wrote.

However, "additional data are needed to assess the long-term safety of testosterone use in women with estrogen depletion," they added.

Of particular concern is the possibility that testosterone without concomitant estrogen may have adverse effects on the breast and endometrium. In this study, four cases of breast cancer occurred in women on active treatment, compared with no cases in women taking placebo, and vaginal bleeding also was significantly more common with active treatment.

The study involved women aged 20-70 years who had surgically induced menopause of at least 1 year's duration, and women aged 40-70 years who had natural menopause of at least 2 years' duration. These subjects all had hypoactive sexual desire and were treated at 65 medical centers throughout the United States, Canada, Australia, the United Kingdom, and Sweden between 2004 and 2006.

The study was sponsored by Procter & Gamble Pharmaceuticals Inc., which also was involved in study design and data collection, and conducted the data analysis. Procter & Gamble makes Intrinsa, a testosterone patch that has been approved by the European Medicines Agency for treatment of hypoactive sexual desire. A Food and Drug Administration advisory committee recommended against approval of the drug for the U.S. market in 2004.

In the study, 814 women were randomly assigned to use a 150-mcg testosterone patch, a 300-mcg testosterone patch, or a placebo patch every day for 1 year. The efficacy analysis was performed at 24 weeks, after which the effect of testosterone tends to plateau; the safety analysis was performed at 1 year. A total of 71% of the study subjects completed 24 weeks, and only 57% completed the full year.

Compared with the placebo group, both groups on active treatment reported significant increases in sexual desire and frequency of satisfying sexual episodes, as well as decreases in personal distress related to sexual function.

The improvement in frequency of satisfying sexual episodes was "numerically modest," at only 1.4 more such episodes per month. However, this amount has been shown to be clinically meaningful in previous studies, Dr. Davis and her associates said (N. Engl. J. Med. 2008;359:2005-17).

Treatment effects did not differ between women who had undergone surgical menopause and those who had undergone natural menopause.

The overall incidence of adverse effects was similar among the three groups. The most common reasons for withdrawal from the study were patch-site reactions and androgenic events, principally the growth of facial hair.

Four women receiving active treatment developed breast cancer, compared with none receiving placebo. The size of the study groups was too small to allow for analysis, and this excess could be the result of chance. But "the possibility of a causal relationship must be considered," the researchers noted.

Nearly 11% of women with an intact uterus who used the higher dose patch reported vaginal bleeding, compared with fewer than 3% of the other two groups. All women with vaginal bleeding had ultrasonography and/or endometrial biopsy. There were no cases of endometrial hyperplasia or carcinoma.

In an accompanying editorial comment, Julia R. Heiman, Ph.D., of the Kinsey Institute for Sex, Gender, and Reproduction at Indiana University, Bloomington, said that it is reasonable to wonder whether an absolute increase in satisfying sexual episodes of only 1.4 per month is worthwhile.

"Although the report does not indicate whether the women were asked whether this change was meaningful for them, a review of the baseline data suggests it probably was, since the mean number of such episodes almost doubled for the high-dose group," she said (N. Engl. J. Med. 2008;359:2047-9).

The "potentially worrisome" excess of breast cancer cases "cannot be ignored," Dr. Heiman added.

They "suggest the need for caution in using testosterone until we understand more about its possible link with breast cancer and are better able to predict which patients are more likely to be subject to negative effects."

Dr. Davis reports receiving consulting or lecture fees from Acrux Ltd., AstraZeneca Oncology Australia, Organon, and Procter & Gamble Pharmaceuticals, as well as grant support from AstraZeneca Pharmaceuticals, Novartis Oncology Australia, and Procter & Gamble Pharmaceuticals. Dr. Heiman reports receiving grant support from Pfizer, Bayer HealthCare, and Zestra Laboratories Inc. ■

Ultrasound-Guided Embryo Transfer Delivers

Chicago — Ultrasound-guided embryo transfer (US-ET) is associated with significantly higher implantation and clinical pregnancy rates than is the clinical touch method, a study of 1,700 embryo transfers at a tertiary in vitro fertilization clinic indicates.

"These data add to the available evidence supporting the use of US-ET in assisted reproductive technology," said Dr. Rubina Ali of St. Mary's Hospital, Manchester, England, in a presentation at the World Congress on Ultrasound in Obstetrics and Gynecology.

Researchers compared implantation and clinical pregnancy rates for 881 consecutive fresh (385) and frozen (496) embryo transfers performed between 2003 and 2004 using the clinical touch method with 842 consecutive fresh (394) and frozen (448) transfers performed between 2004 and 2005 using US-ET.

The US-ET group showed a significantly higher rate of implantation, compared with the clinical touch group (fresh: 20% vs. 9.5%; frozen: 13% vs. 7%) and a significantly higher clinical pregnancy rate (fresh: 26.9% vs. 12.4%; frozen: 15.6% vs. 8.8%). Women in the two groups did not differ in demographic or clinical characteristics.

The US-ET group had a higher rate of miscarriage in the frozen embryo transfers (8.9% vs. 5.6%), but no other statistically significant differences were found.

"The practice of US-ET is associated with an increased likelihood of successful pregnancy outcome," Dr. Ali concluded.

—Susan Birk

Pudendal Nerve Implant May Help Reduce Pelvic Pain

BY NANCY WALSH
New York Bureau

Lake Buena Vista, Fla. — Pudendal nerve neuromodulation may hold promise for some patients with refractory chronic pelvic pain syndrome, according to the findings of a small study.

Multiple treatment approaches have been tried for refractory chronic pelvic-perineal pain (RCPPP), but results have been suboptimal and temporary. Because sacral neuromodulation has been used with some success in refractory painful bladder syndrome/interstitial cystitis, pudendal neuromodulation has been proposed as a possible treatment for RCPPP. The procedure also has been suggested for patients with interstitial cystitis who failed sacral neuromodulation, according to Dr. Maude Carmel of the urology department at Sherbrooke (Que.) University Hospital Centre.

Ten of Dr. Carmel's patients have undergone treatment with pudendal neuromodulation (seven patients with RCPPP and three with interstitial cystitis). The patients' mean age was 53 years, and the mean duration of symptoms was 14 years. Seven patients were women; prior treatments included perineal physiotherapy, nerve and caudal blocks, and sacral neuromodulation.

"After a trial period of 3-6 weeks, one patient with interstitial cystitis and two with RCPPP reported more than 60% improvement in their symptoms and elected to have a permanent generator implanted," Dr. Carmel wrote in a poster session at the annual meeting of the International Pelvic Pain Society.

All three continued to experience improvements of more than 80% after 1 year. The remaining seven were considered treatment failures. No major complications occurred. There have been no infections and no complications after electrode removal.

The procedure involves implantation of a tined quadripolar electrode under electrophysiologic and radiologic guidance. Needle electrodes are placed at the external anal sphincter, the gluteus medius and maximus, the adductor longus, the tibialis, and the gastrocnemius muscles.

Implantation is done under fluoroscopy, using a dorsal percutaneous approach at the level of the ischial spine. The quadripolar electrode is then tunneled under the skin and connected to the external neurostimulator.

One possible etiology for RCPPP is pudendal nerve (PN) neuralgia, which is characterized by pain in the genitalia, perineum, and anorectal region. The pain is aggravated by sitting or by flexion of the hip, and is relieved by standing, lying down, or sitting on a lavatory seat or commode.

The PN arises from the S2-S4 roots of the sacral plexus, exiting the pelvis under the piriformis muscle through the greater sciatic foramen and descending ventral to the sacrotuberous ligament. It provides sensory innervation to the anal, perineal, and genital areas and motor supply to the pelvic floor muscles.

Entrapment or compression of this nerve can cause pelvic floor overactivity and perineal trauma and inflammation, according to Dr. Carmel.

No conflicts of interest were reported in Dr. Carmel's poster presentation. ■