Clomipramine May Aid Premature Ejaculation

BY ROBERT FINN
San Francisco Bureau

SANTA FE, N.M. — Men with premature ejaculation appear to have weaker erections and abnormal heart-rate responses in addition to their shortened ejaculatory latency, according to a study presented by Wendi L. Tai at the annual meeting of the Society for Psychophysiological Research.

Clomipramine, which delays ejaculation, also results in more normal penile and heart-rate responses, said Ms. Tai, who worked with David L. Rowland, Ph.D., of Valparaiso (Ind.) University on the study. Ms. Tai is currently at Indiana University, Bloomington.

The double-blind, placebo-controlled study involved 33 men with previously identified premature ejaculation (PE), along with 12 control subjects. The men viewed an erotic film and experienced vibrotactile stimulation 4-6 hours after taking clomipramine or placebo.

When taking placebo, control subjects achieved a full erection in about 4.5 minutes and maintained that erection for the entire 9 minutes of the session. Men with PE, however, reached a significantly smaller penile circumference 2.5 minutes into the session.

Some of the men with PE ejaculated between 2.5 and 4 minutes into the session, but even among the men who maintained their erections for the full 9 minutes, erections were significantly weaker than those of controls. Despite that, the investigators found no evidence that the men with PE had any significant differences in maximal erect penis size, compared with that of the control subjects.

On placebo, control subjects had a heart-rate decrease of about 4 beats/min during the session, whereas men with PE had a heart-rate increase of 2 beats/min.

The erectile and heart-rate responses of men with PE and controls were more alike when they took clomipramine, known to retard ejaculation. Although some men with PE did ejaculate early, those who did not had as strong a penile response as the control subjects—significantly stronger than with placebo. The control subjects had just as strong an erection with clomipramine as with placebo.

Likewise, men with PE and controls did not have significantly different heart-rate responses. Both groups had a heart-rate decrease between 0 and 1 beats/min while taking clomipramine.

Ms. Tai said that her study supported the hypothesis that anxiety plays a role in premature ejaculation and that clomipramine's antianxiety effects may be responsible for its efficacy in retarding ejaculation. ■

Androgen Deficit Linked To QT Prolongation in Men

BY MITCHEL L. ZOLER
Philadelphia Bureau

MUNICH — Hormone therapies that produced androgen deficiency in men were associated with significant prolongation of the QT interval in three different prostate-cancer studies.

"These findings should be considered when assessing the risk-to-benefit ratio of hormone therapy [in men], especially in patients with a baseline QT interval of more than 450 msec and in patients who are treated with class IA or class III anti-arrhythmic drugs," Craig M. Pratt, M.D., said in a poster at the annual congress of the European Society of Cardiology. QT interval prolongation is associated with an increased risk of life-threatening arrhythmia and torsades de pointes ventricular tachycardia.

The data are consistent with testosterone having an important role in cardiac repolarization and possibly having a cardioprotective effect, said Dr. Pratt, a professor of medicine at Baylor College of Medicine in Houston.

He and his associates reviewed the results from three phase III studies that assessed several drugs in men with prostate cancer. All the drugs induced androgen deficiency.

In the first study, 177 men were treated with abarelix or with goserelin plus bicalutamide. In the second study, abarelix was compared with leuprolide, and in the third study, abarelix was compared with leuprolide plus bicalutamide. The second and third studies involved a total of 295 men.

All of the regimens studied were effective at reducing plasma levels of testosterone to 35 ng/ml or less, and all of the regimens led to prolongation of the QT interval, said Dr. Pratt, who is also director of the coronary care unit at the Methodist Hospital in Houston.

The extent of prolongation ranged from an average of 9 msec, when leuprolide plus bicalutamide were used, to an average of 20 msec, with leuprolide alone. ■

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Premature Ejaculation

BY NEIL SKOLNIK, M.D., AND CHRISTOPHER NOTTE, M.D.

Many studies suggest that premature ejaculation is the most common male sexual disorder, and according to the National Health and Social Life Survey, the prevalence of premature ejaculation in the United States is 21% in men aged 18-59. Although there is no universally accepted definition of premature ejaculation, the American Urological Association (AUA), defines it as "ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners."

Guidelines are most useful when they are available to answer questions at the point of care. A concise yet complete handheld computer version of this guideline is available for download, compliments of FAMILY PRACTICE NEWS, *at www.redi-reference.com.*

Clinical Evaluation

The AUA emphasizes that "the diagnosis of premature ejaculation (PE) is based on sexual history alone." As a result, a detailed history should be obtained from all patients with ejaculatory complaints, with particular attention paid to time to ejaculation. Additional relevant details include frequency and pattern of PE, relationship to specific partners, degree of stimulus resulting in ejaculation, nature and frequency of sexual activity (including masturbation and intercourse), relationship to drug use or abuse, and psychosocial impact of PE. It is valuable to obtain input from sexual partners as well.

It's also imperative to distinguish PE from erectile dysfunction (ED), the inability to sustain a sufficient erection prior to ejaculation, though the conditions often coexist. In patients with concomitant PE and ED, the erectile dysfunction should be treated first, and PE may improve if the ED is effectively treated. It is not necessary to perform laboratory or physiologic testing unless history and physical exam reveal specific indications for doing so.

Recommendations for Treatment

The AUA makes it clear that "patient and partner satisfaction is the primary target outcome for the treatment of PE." Because PE is not life-threatening, the safety of a treatment should be the most important concern. Certain treatments, such as neurectomy and prosthetic implants, have risks that far outweigh their benefits. It is also important to note that no pharmacologic treatments have FDA-approved indications for PE, but the following agents have been studied:

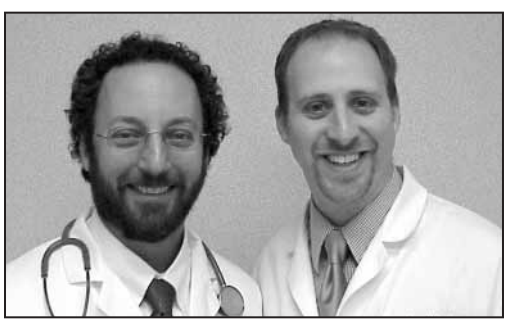
► **Serotonin reuptake inhibitors.** In clinical trials, SRIs have proven to be more effective than placebo in treating PE. SRI options include fluoxetine, paroxetine, and sertraline (selective SRIs), as well as clomipramine (a nonselective SRI). Many dosages and dosing regimens have been evaluated, and it is unclear whether continuous daily dosing or situational dosing is superior for managing all patients. It is therefore recommended that dosage regimens be based on patient needs, compliance concerns, and frequency of sexual activity. Doses of SRIs used in treating PE tend to be lower than those recommended in the treatment of depression, and duration of therapy has not been established. SRI use will most likely be needed on a continuing basis; experience has shown that PE returns when treatment with SRIs is terminated. Adverse effects from SRI use for PE are similar to those seen in treating depression and are considered acceptable for the benefits seen in patients with PE.

► **Topical anesthetic agents.** According to the AUA, topical anesthetic agents may be applied to the penis prior to intercourse to delay ejaculation. Approximately 2.5 g of lidocaine/prilocaine cream applied 20-30 minutes before intercourse has been shown to increase latency time without significant side effects. It is important to note that topical agents may be used with or without a condom and may be wiped off immediately prior to intercourse to prevent transfer of product to the partner's vaginal wall. One concern when using these products, however, is increased numbness in the penis after prolonged periods of time, leading to loss of erection. This loss in penile sensation may make topical treatment unacceptable to many patients and thereby limit its use.

► **Other pharmacologic therapies.** There have been other agents proposed for the treatment of PE. These involve therapies typically used in the management of erectile dysfunction. There is a small amount of evidence suggesting intracorporal injection of a vasoactive agent, such as alprostadil, or use of sildenafil may increase latency in patients with PE. There is also evidence to suggest that combined use of sildenafil and paroxetine on a situational basis is more effective than paroxetine alone, albeit with an increase in the frequency of headaches and flushing. One other possibility for treatment involves medications that effect adrenergic blockade, as ejaculation is modulated by the sympathetic nervous system. One study using alfuzosin and terazosin showed mild efficacy at increasing ejaculation latency.

The Bottom Line

Premature ejaculation is diagnosed exclusively by patient history, so a detailed sexual history should be obtained from all patients with ejaculatory complaints. Serotonin reuptake inhibitors have become the mainstay of medical treatment, but other possibilities, including topical anesthetics, sildenafil, and adrenergic blockers, have been studied.



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