Sertraline in the Treatment of Premature Ejaculation: A Double-Blind Placebo Controlled Study

PREMATURE EJAKÜLASYON TEDAVİSİNDE SERTRALİN: ÇİFT-KÖR PLASEBO KONTROLLÜ BİR ÇALIŞMA

Hasan BİRİ*, Kenan İSEN**, Zafer SINIK***, Metin ONARAN**, Bora KÜPELİ***, İbrahim BOZKIRLI****

* Yrd.Doç.Dr.,Gazi Üniversitesi Tıp Fakültesi Üroloji AD,
** Araş.Gör.Dr.,Gazi Üniversitesi Tıp Fakültesi Üroloji AD,
*** Uz.Dr.,Gazi Üniversitesi Tıp Fakültesi Üroloji AD,
**** Prof.Dr.,Gazi Üniversitesi Tıp Fakültesi Üroloji AD, ANKARA

Summary

This study investigated the efficacy and the adverse effects of sertraline in the treatment of premature ejaculation (PE). Thirty-seven patients with PE were randomly assigned to receive either sertraline or a placebo. The study group excluded those with psychiatric and neurological disorders, urogenital infections and drug or alcohol abuse. In this double-blind study, twenty-two of them were given 50 mg of sertraline perday and the another 15 patients were given an identical placebo one perday. After 4 weeks, they were evaluated for latency to ejaculation and side effects of the drug. The latency to ejaculation in the sertraline group was found to be significantly longer than that of the placebo group ($p<0.01$). No patients discontinued therapyy due to adverse effects. Four weeks after the end of the therapy, PE recurred in 19 (86.36%) patients who received sertraline. These result indicate that sertraline is an effective therapy for PE.

Key Words: Sertraline, Premature ejaculation, Antidepressant drug

T Klin J Med Sci 1998, 18:176-179

Özet

Bu çalışmada Sertralin'nin prematüre ejakülasyondaki etkinliği ve yan etkileri araştırıldı. Erken boşalma şikayeti olan 37 hasta çalışmaya alındı. Psikiatrik ve nörolojik hastalık, ürogenital enfeksiyon, ilaç yada alkol bağımlılığı saptanan hastalarda çalışma dışı bırakıldı. Hastaların 22'sine sertraline 50 mg/gün, 15'ine plasebo 1/gün verildi. Dört hafta sonra hastalar ejakülasyon oluşma süresi ve ilacın yan etkileri açısından değerlendirildi. Ejakülasyon oluşma süresi sertralin tedavisi alan grupta plasebo grubuna göre daha uzun saptandı ($p<0.01$). Hiçbir hasta yan etki nedeniyle tedaviyi kesmedi. Tedavi bitiminden 4 hafta sonra sertraline tedavisi alan hastaların 19(%86.36)'unda rekürrens görüldü. Sonuç olarak, sertralin premature ejakülasyon tedavisinde başarılı bulundu.

Anahtar Kelimeler: Sertralin, Premature ejakülasyon, Antidepresan ilaç

T Klin Tıp Bilimleri 1998, 18:176-179

Premature ejaculation is one of the most common complaints, estimated to affect up to 30% of men (1). It is defined as a disorder in which ejaculation occurs before or soon after vaginal intercourse (2,3). Recently, it has been defined as persistent or recurrent ejaculation with minimal sexual stimulation before, during or after intromission and before the patient wishes it (3). A diagnosis can be based on history, because a definitive desciption is impossible due to the differences in the level of arousal and sexual activity of the patients and their partners.

Experimental and clinical investigation have shown various neurotransmitters as important mediators of the ejaculatory response. In the rat, dopaminergic, α-adrenerjic and seratonergic systems all play a role in male sexual function (4).

Geliş Tarihi: 11.08.1997

Yazışma Adresi: Dr.Kenan İSEN
Kenedy Cd. 34/6
Kavaklıdere, ANKARA

Recent studies in humans provide additional evidence for the role of seratonergic mechanisms in delaying ejaculation (5,6). Sertraline is a highly potent and selective inhibitor of seratonin reuptake that has recently been approved for the treatment of depression or premature ejaculation (7-9).

The objective of thiss study was to determine the efficacy of sertraline in patients with premature ejaculation.

Materials And Methods

Between January 1995 - April 1997, 37 normally potent men with the complaint of PE were enrolled in this study. They were al married and the ages ranged from 21 to 54 (mean age 31.1) years. PE was descibed as involuntary ejaculation during foreplay or within 1 minute from the begining of intercourse during the previous 6 months (9). The patients were assessed for concomittant neurological or psyhitaric disorders and for alcohol or drug abuse. All patients underwent a physical examination, a digital rectal examination, and urine-sperm samples were coltured to detect urinary tract infection. Latency to ejaculation before treatment was recorded in all patients. Petients were randomized to 4 weeks of douple-blind treatment with sertraline or placebo. Twenty two of them received 50 mg sertraline tablets while the other 15 received one identical placebo. The tablets were taken orally each evening. They were encouraged to have sex twice a week and record the time between intercourse and ejaculation by a clock with a second hand at home. The average time of four consecuative intercourses and the side effects of the therapy reported by the patients were recorded. One month after the end of therapy, the patients were evaluated for recurrence of PE.

Differences between the groups was assessed using the independent-samples t test and the paired-samples t test.

Results

In this study with sertraline, to ejaculation noticably increased after 4 weeks of the treatment. Latency to ejaculation before treatment was 40.93±12.6 seconds and 43.53±20.2 seconds in the sertraline and placebo group respectively. The difference between these groups were negligible (t=0.50, p>0.05). Latency to ejaculation increased to 325.4±261.7 seconds in the sertraline group and to 114.4±93.7 seconds in placebo group. The difference was found statistically significant in the sertraline and placebo groups (t=5.72, p<0.01, t=2.07 p<0.05). sertraline treatment produced significant improvement relative to the placebo in time to ejaculation (t=2.96, p>0.01) (Figure 1).

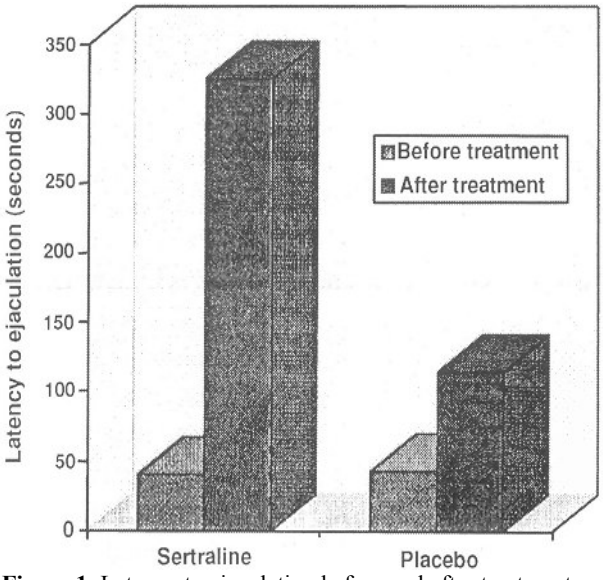

Figure 1. Latency to ejaculation before and after treatment.

Adverse effects of the treatment and placebo in this study are represented in Table 1. Adverse effects were found in 12(54.54%) who received sertraline and in 7(46.66%) in the placebo groups. The differance between the 2 groups was not statistically significant (t=0.23, p>0.05). No patients were discontinued from therapy due to severe adverse effects. Moreover, the adverse effects disappeared in

Tablo 1. Adverse effects o sertraline and placebo

Adverse effects	Sertraline n (%)	Placebo n (%)
Headache	6 (27.27)	3 (20.0)
Sleepiness	5 (22.72)	3(20.0)
Diarrhea	3 (13.63)	1.(6.66)
Dry mouth	2 (9.09)	0
Total	12 (54.54)	7 (46.66)

most of the patients after 15-20 days of thearpy. Four weeks after the therapy ceased, the premature ejaculation recurred in 19 (86.36%) patients who received sertraline.

Discussion

Since the early 1970's PE has most commonly been treated with partner-oriented sex therapy derived from behavioral techniques. Masters and Johnson have reported a succes rate>90% at their clinics (10). Other authors have recorded success rates that are substantially lower-at around 60% (11,12). Although PE responds to behavioral therapy in a couples format, it is far more difficult to treat without the willingness of a female sexual partner (13).

Antidepressant drugs frequently have associated side-effects on sexual function, some of which may be adventageous. Increased use of these medications, however, has revealed that fluoxetin, paroxetine, and sertraline all have sexual side effects, the most being lowered libido and inhibited ejaculation (9,14,15). Recently, their use in thee treatment of PE is based on the adverse effects of delayed ejaculation. The mechanism for these side effects is not fully delinated, but both central and peripheral serotonergic neurotransmitter pathways diminish sexuel behavior in animal models (16). Clinical evidence further suggests thet increased seratonergic receptor activation inhibits orgastic potantial (17). Utilization of these side effect may be a cost-effective method of treating PE, one of the most common sexual dysfunctions in clinical practice.

Sertraline is a highly potent and selective inhibitor of serotonin reuptake that has recently been approved for the treatment of PE (9,18). Serotonin has low lethality and minimal cardiovascular side effects (5). The selectivity of sertraline for serotonin in preference to norepinephine is nearly 8 times that of fluoxetine, 19 times that of clomipramine, and more than 100 times that of imipramine, amitriptyline and nortriptyline (6). Sertraline used for depression in doses of 50-200 mg per day but the optimal dosege of sertraline varies for PE (8,18). Recently, Douglas et al. reported sertraline is effective for many at a dose of 25 mg perday. In this study, the patients used 50 my sertraline perday and the treatment was tolerated very well by most of the patients. No patients were discontinued from therapy due to adverse effects (18).

This study's findings were that sertraline showed a marked increase in therapeutic effect after 4 weeks of therapy. The same results were reported by some other investigators (9,18). Improvements in latency to ejaculation within the first week of treatment, implies that it may be a direct effect of central serotonin reuptake inhibition and can not be ascribed to an antidepressive effect, since the antidepressive effect can not be seen within in the first week.

Four weeks after the treatment ceased, the PE recurred in most of the patients. It showed that sertraline is an effective treatment for PE.

Ih conclusion, the serotonin reuptake inhibitor sertraline appears to be clinically useful as a treatment for PE. The long-term effectiveness the optimal dosage of sertraline still needs to be determined.

REFERENCES

1. Derogatis LR. Aetiologic factors in premature ejaculation. Med Aspects Hum sexuality 1980; 14:1168-75.
2. Schapiro B. Premature ejaculation: a review of 1130 cases. J Urol 1943; 50:374-9.
3. Rouleu JL. Sex therapy and disorders of ejaculation. Acta Urol Belg 1993; 23:281-6.
4. Bitran D, Hull EM. Pharmacological analysisof male rat sexual behavior. Neurosci Biobehav Rev 1987; 11:365-89.
5. Stahl SM. Serotonergic mechanisms and the antidepressants. Psyhol Med 1993; 23:281-6.
6. Mcintosh TK, Barfield RJ. Brain monoaminergic control of male reproductive behavior, I: Serotonin and the post-ejaculatory period. Behav Brain Res 1984; 12:255-65.
7. Heym J, Koe BK. Pharmaclogy of sertraline: a review. Psychiatriy 1988; 49 (suppl):40-5.
8. Guthrie SK. Sertraline: a new specific serotonin reuptake blocker. Ann Pharmacother 1991; 25:925-61.
9. Mendels J, Camera A, Sıkes C. Sertraline treatment for premature ejaculation J Clin Psychopharmacol 1995; 15:341-6.
10. Masters WH, Johson VE. Human sexual inadequacy. Boston: Little, Brown&Co, 1970.

11.Boncroft J, Coles L. Three years experience in a sexual problem at clinic. Brit Med J 1976; 1:1575-81.

12.Hawton K, Catalan J. Prognostic factors in sex therapy. Bhev Res Ther 1986; 24:377-81.

13.Lawrence JS, Madakasira S. Evaluation and treatment of premature ejaculation: o critical review. Int J Psychiatry Med 1992; 22:77-97.

14.Frostier P, King J. Fluexetine for premature ejaculation (let). Am J Psychiatry 1995; 151:1523.

15.Waldinger MD, Hengevel MW, Zwinderman AH. Paroxetine in treatment of premature ejaculation: a randomized, placebo-controlled study. Am J Psychiatry 1994; 151:1377-81.

16.Gessa GL, Tagliamonte A. Role of brain serotonin and dopamine in male sexual behavior. In: Sarden M, Gessa GL, Eds. Sexual Behavioor. Pharmacology and Biochemistry. New York: NY: Raven Press, 1975: 117-28.

17.Segraues RT. Effects of psychotropic drugs on human erection and ejaculation. Arch Gen Psychiatry 1989; 46:275-84.

18.Douglas A, Swartz and Howard B. Sertraline hydrochloride for premature ejaculation: Dosing schedule (abstract):J Urol 1997; 15:182.