Men and women with chronic major depression responded differently to sertraline and imipramine

Kornstein SG, Schatzberg AF, Thase ME, et al. *Gender differences in treatment response to sertraline versus imipramine in chronic depression. Am J Psychiatry* 2000 Sep;157:1445–52.

QUESTION: Do men and women with chronic depression have different treatment responses to selective serotonin reuptake inhibitors (SSRIs) (eg, sertraline) and tricyclic antidepressants (TCAs) (eg, imipramine)?

Design

Randomised [allocation concealed*]†, blinded [clinicians, patients, and outcome assessors]†*, controlled trial with 12 weeks of follow up.

Setting

10 university medical centres and 2 clinical research centres in the US.

Patients

400 women (mean age 40 y) and 235 men (mean age 43 y) who were 21–65 years of age and met *DSM-III-R* criteria for chronic major depression or double depression. Follow up was 80%; analysis of all patients was done using last observation carried forward.

Intervention

Patients were allocated to sertraline, 50 mg/day initially (n = 264 women and 162 men) or imipramine, 50 mg/day initially (n = 136 women and 73 men). Doses could be increased to a maximum of 200 mg/day for sertraline (mean dose 139.6 mg/d for women; 143.2 mg/d for men) and a maximum of 300 mg/day for imipramine (mean dose 196.3 mg/d for women; 207.5 mg/d for men).

Main outcome measures

Dropout rates and treatment response (50% decrease in Hamilton Depression Rating Scale [HDRS] score, HDRS score ≤ 15, a Clinical Global Impression [CGI] severity scale score ≤ 3, and a CGI improvement scale score of 1 or 2).

Main results

A statistically significant interaction effect was found between treatment and sex for rates of dropout (p = 0.009) and treatment response (p = 0.001). Women taking sertraline had lower dropout rates than women taking imipramine (p = 0.002), whereas no difference was seen between groups among men (table 1 and 2). Women had a greater response rate in the sertraline group than in the imipramine group (p = 0.02), and men had a greater response rate in the imipramine group than in the sertraline group (p = 0.04) (table 1 and 2).

Conclusions

In patients with chronic depression, sertraline was more effective than imipramine and led to fewer dropouts in women; imipramine was more effective than sertraline in men.

*See glossary.

†Information provided by author.

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Sertraline and imipramine for chronic major depression at 12 weeks†
Table 1 Sertraline v imipramine in women

Outcomes	Sertraline	Imipramine	RRR (95% CI)	NNT (CI)
Dropout rate	14%	26%	47% (20 to 65)	9 (5 to 24)
			RBI (CI)	
Treatment response	57%	46%	23% (0.46 to 54)	10 (5 to 435)

Table 2 Imipramine v sertraline in men

Outcomes	Imipramine	Sertraline	RRR (CI)	NNT (CI)
Dropout rate	19%	24%	20% (–34 to 54)	Not significant
			RBI (CI)	
Treatment response	62%	45%	37% (6.2 to 75)	6 (4 to 35)

†Abbreviations defined in glossary; RRR, RBI, NNT, and CI calculated from data in article.

COMMENTARY

As we all know, men and women are different. One of these sex differences occurs in mood disorders: depression is approximately twice as common in women as men. Mood disorder in women is also a subject of serious academic study and the focus of a major new textbook.¹ The increase in depression rates in women becomes evident after puberty, and it is argued that the difference lessens after menopause. Given these findings, sex based differences in treatment response are of great interest. Such differences are important because unipolar depression is such a large public health problem, ranking second in developed market economies in recent global burden of disease studies.²

Previous studies have suggested that women might be more responsive to serotonergic agents, and the study by Kornstein *et al* is a timely addition to this literature. It shows fairly convincingly that women have a better response to SSRIs and men a better response to TCAs. The authors comment on the possible reasons for this, especially because the differing response rate was observed primarily in premenopausal women. Obviously, the female sex hormones and the menstrual cycle may play a role in determining this phenomenon.

This finding has potentially important implications for clinical practice. Although reasons still exist (eg, side effect profile, safety in overdose) to choose an SSRI as a first line agent in men, this study reminds us that TCAs may still have a place in psychiatry, and that sex should be added to the list of factors to consider when selecting an antidepressant. This study was completed under contract from Pfizer Pharmaceuticals, the makers of sertraline, and this article may enhance the sales profile of sertraline. The relationship between the pharmaceutical industry and medical academics has recently come under the spotlight.³ Because of the clear commercial implications and potentially increased healthcare costs, it is important that this study be independently replicated.

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1 Steiner M, Yonkers KA, Eriksson E. *Mood disorders in women*. London: Martin Dunitz, 2000;573.

2 Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: global burden of disease study. *Lancet* 1997;349:1436–42.

3 Jackson T. Marketing: are you being duped? *BMJ* 2001;322:1312.