Gender Differences in treatment response to sertraline versus imipramine in chronic depression

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Background: A recent meta-analysis of studies from 1957 to 1991 looking at treatment response in depression reported that men responded more favorably to imipramine than women did (Hamilton 1996). There is also a growing body of literature suggesting a serotoninergic role in PMS and a preferential response to SSRIs in depressed premenopausal women.

Aim: To examine gender-specific differences in treatment response to sertraline vs. imipramine for chronic depression (i.e. major depression of at least 2 years’ duration without antecedent dysthymia) and double depression (major depression superimposed on dysthymia).

Methods: A total of 235 male outpatients and 400 female outpatients with chronic or double depression were recruited from 10 university-affiliated medical centers or 2 clinical research centers. The subjects were enrolled in a 12 week, double-blind, randomized, parallel-group comparative trial of sertraline vs. imipramine. The research focus was on whether the genders differ in their response to these drugs in terms of 1) response rate at the study endpoint and 2) dropout rate.

Main Findings: Using an intent-to-treat analysis, there was a significant interaction between gender response rates. Women who took sertraline and men who took imipramine had the highest response rates at endpoint (p=0.001). Of women taking sertraline 147/260 (57%) responded as opposed to 61/133 (46%) of those women taking imipramine. The opposite was true in men. Of men taking imipramine 43/69 (62%) responded as opposed to 73/161 (45%) of men taking sertraline. When menopausal status was considered, premenopausal women were significantly more likely to respond to sertraline than imipramine (115/201 [57%] vs. 41/96 [43%]; P=0.01), whereas the response rates to sertraline and imipramine in postmenopausal women were similar. Age did not affect relative response in men or women (except for the effect of menopausal status).
Dropout rates showed a significant interaction between gender and treatment. In women assigned to take imipramine 36/136 (26%) dropped out of the study compared to 37/264 (14%) assigned to take sertraline (p=.02). In men the dropout rates were similar for sertraline (39/162 (24%)) and imipramine (14/73 (19%)). In premenopausal vs. postmenopausal women the difference in dropout rates in the imipramine group were significant (28/98 [29%] vs. 2/25 [8%]; P=0.02). This difference in drop out rates was reversed in the sertraline group (premenopausal 26/201 [13%] vs. postmenopausal 11/49 [22%]) but was not statistically significant.

Conclusions: Men and women with chronic depression have significant differences in response and dropout rates with sertraline vs. imipramine. Women responded significantly better to sertraline than to imipramine (the differences were most pronounced in premenopausal women), whereas men responded significantly better to imipramine.

Limitations: There was no placebo control. The authors chose not to have a placebo control because of low placebo response rates in chronic depression and the primary aim of the study was to compare relative efficacy. Also, this study only looked at chronic depression, one of the more severe major depressive disorders. These results may not generalize to other less severe major depressive disorders (e.g. single episode major depression).

Impact on Internal Medicine: These results have important practical implications for the treatment of premenopausal women and men with chronic depression, but caution is warranted. These data do suggest a preferential response in premenopausal women with chronic depression to sertraline (a SSRI) when compared to imipramine (a TCA). This study also supports the use of imipramine over sertraline in men with chronic depression. Before clinicians make these preferences part of standard practice, these results require replication.

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