

# Abstract

J Affect Disord. 2000 Nov;60(2):121-30.

## Enhancement of the antidepressant action of fluoxetine by folic acid: a randomised, placebo controlled trial.

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**BACKGROUND:** A consistent finding in major depression has been a low plasma and red cell folate which has also been linked to poor response to antidepressants. The present investigation was designed to investigate whether the co-administration of folic acid would enhance the antidepressant action of fluoxetine.

**METHODS:** 127 patients were randomly assigned to receive either 500 microg folic acid or an identical looking placebo in addition to 20 mg fluoxetine daily. All patients met the DSM-III-R criteria for major depression and had a baseline Hamilton Rating Scale (17 item version) score for depression of 20 or more. Baseline and 10-week estimations of plasma folate and homocysteine were carried out.

**RESULTS:** Patients receiving folate showed a significant increase in plasma folate. This was less in men than in women. Plasma homocysteine was significantly decreased in women by 20.6%, but there was no significant change in men. Overall there was a significantly greater improvement in the fluoxetine plus folic acid group. This was confined to women where the mean Hamilton Rating Scale score on completion was 6.8 (S.D. 4. 1) in the fluoxetine plus folate group, as compared to 11.7 (S.D. 6. 7) in the fluoxetine plus placebo group ( $P < 0.001$ ). A percentage of 93. 9 of women, who received the folic acid supplement, showed a good response (>50% reduction in score) as compared to 61.1% of women who received placebo supplement ( $P < 0.005$ ). Eight (12.9%) patients in the fluoxetine plus folic acid group reported symptoms possibly or probably related to medication, whereas in the fluoxetine plus placebo group 19 (29.7%) patients reported such symptoms ( $P < 0.05$ ).

**LIMITATIONS AND CONCLUSIONS:** Folic acid is a simple method of greatly improving the antidepressant action of fluoxetine and probably other antidepressants. Folic acid should be given in doses sufficient to decrease plasma homocysteine. Men require a higher dose of folic acid to achieve this than women, but more work is required to ascertain the optimum dose of folic acid.

PMID: 10967371