

Abstract

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Effect of folic acid combined with fluoxetine in patients with major depression on plasma homocysteine and vitamin B12, and serotonin levels in lymphocytes.

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OBJECTIVE: Folic acid, a micronutrient supporting the natural defense system, may elevate antidepressant responses, although the lymphocyte serotonergic system has not been explored in folate-supplemented depressed patients.

METHODS: Twenty-seven patients were randomly assigned to groups receiving fluoxetine (20 mg) and folic acid (10 mg/day) or fluoxetine and placebo for 6 weeks. Clinical outcome was assessed according to the Hamilton Depression Rating Scale (HDRS) at the beginning, during and at the end of treatment. Blood samples were taken, plasma was separated, and lymphocytes were obtained by density gradient centrifugation with Ficoll/Hypaque and differential adhesion to plastic dishes. Fifteen healthy subjects served as controls. Plasma folate, homocysteine and vitamin B12, and serotonin concentration in lymphocytes were determined by HPLC.

RESULTS: The HDRS score was significantly lower in patients receiving fluoxetine and folic acid compared with those receiving fluoxetine and placebo after 6 weeks of treatment (7.43 +/- 1.65 vs. 11.43 +/- 1.31, respectively; $p = 0.04$). Plasma homocysteine statistically significant decreased after folic acid ($p = 0.02$), but no significant changes were observed in vitamin B12. Serotonin was significantly reduced after fluoxetine either with folate ($p = 0.03$) or placebo ($p = 0.01$) probably by the effect of transporter blockade. 5-Hydroxyindoleacetic acid was lower in lymphocytes of patients receiving folate ($p = 0.04$), indicating a reduced turnover rate, thus accumulating serotonin in the cells. A significant negative correlation was noted between homocysteine and folate. No significant correlations were present among biochemical parameters and depression severity.

CONCLUSION: Modifications due to treatment with fluoxetine and folic acid may alter lymphocyte function in depression probably indirectly by reducing homocysteine levels and directly on lymphocytes by modifying the serotonergic system.

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