

# Abstract

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## Folinic acid (Leucovorin) as an adjunctive treatment for SSRI-refractory depression.

Alpert JE, Mischoulon D, Rubenstein GE, Bottonari K, Nierenberg AA, Fava M.

Depression Clinical and Research Program, Department of Psychiatry, Massachusetts General Hospital, Boston 02114, USA.

**BACKGROUND:** Low folate is associated with poorer response to selective serotonin reuptake inhibitors (SSRIs) in major depressive disorder (MDD). Folate supplementation in MDD has been studied in other settings with promising results.

**OBJECTIVE:** The objective of this study was to assess the efficacy of methylfolate as an adjunctive treatment among adults with MDD and inadequate response to an SSRI.

**METHODS:** Twenty-two adults (59% female; mean age 45.2 +/- 11.0 years) with DSM-IV MDD, partial or nonresponse to an SSRI after at least 4 weeks of treatment, and a 17-item Hamilton Depression Rating Scale (HAM-D-17) score  $\geq 12$  were enrolled in this 8-week prospective open trial. Exclusion criteria included current use of anticonvulsants or psychotropics other than an SSRI, or B12 deficiency. Leucovorin (folinic acid), which is metabolized to methylfolate, was added to SSRIs at 15-30 mg/day.

**RESULTS:** Folate levels rose from 28 +/- 19 ng/mL to 301 +/- 203 ng/mL ( $p < 0.001$ ). HAM-D-17 scores among the 16 completers decreased from 19.1 +/- 3.9 to 12.8 +/- 7.0 ( $p < 0.01$ ). However only 31% of completers and 27% of the intent-to-treat (ITT) sample achieved response ( $\geq 50\%$  reduction in HAM-D-17 scores), and only 19% of completers and 18% of the ITT sample achieved remission (HAM-D-17  $\leq 7$ ).

**CONCLUSION:** Leucovorin appears to be modestly effective as an adjunct among SSRI-refractory depressed individuals with normal folate levels. The application of leucovorin as an adjunct in the setting of refractory depression deserves further study.

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