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L-METHYLFOLATE AUGMENTATION OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS) FOR MAJOR DEPRESSIVE DISORDER: RESULTS OF TWO RANDOMIZED, DOUBLE-BLIND TRIALS

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Introduction: Two randomized, controlled trials of L-methylfolate augmentation of SSRIs for major depressive disorder (MDD) were conducted using a novel study design (sequential parallel comparison design- SPCD).
Objectives/aims: To evaluate the efficacy of L-methylfolate augmentation using the Hamilton Depression Rating Scale.
Methods: In study one (TRD-1), 148 outpatients with SSRI-resistant MDD were enrolled in a 60-day, SPCD study, divided into two 30-day periods (phases 1 and 2). Patients were randomized 2:3:3 to receive L-methylfolate (7.5mg/d in phase 1, 15mg/d in phase 2), placebo in phase 1 followed by L-methylfolate 7.5mg/d in phase 2, or placebo for both phases. Study two (TRD-2) involved 75 patients and was identical in design to TRD-1 except for the dose of L-methylfolate (15mg only).
Results: In the TRD-1 Study, L-methylfolate 7.5 mg/d was not found to be more effective than placebo. In phase 1 of the TRD-2 Study, 37% of patients on L-methylfolate 15mg/d responded and 18% of placebo patients responded, while in phase 2 among placebo non-responders, the response rates were 28% on L-methylfolate 15mg/d and 9.5% on placebo. When phases 1 and 2 were pooled according to the SPCD model, the difference in response rates was statistically significant in favor of L-methylfolate (p=0.0399). The rates of spontaneously reported AEs and rates of study discontinuation appear r comparable between L-methylfolate and placebo in both studies. Rates of study discontinuation were also comparable
Conclusions: These studies suggest that L-methylfolate 15 mg/d may be a safe and effective augmentation strategy for inadequate response to SSRIs.

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