

Abstract

Biol Psychiatry. 2008 Sep 15;64(6):468-75.

N-acetyl cysteine for depressive symptoms in bipolar disorder--a double-blind randomized placebo-controlled trial.

Berk M, Copolov DL, Dean O, Lu K, Jeavons S, Schapkaitz I, Anderson-Hunt M, Bush AI.

The Mental Health Research Institute of Victoria, Victoria, Australia.

BACKGROUND: Treatment-resistant subthreshold depression is a major problem in bipolar disorder. Both depression and bipolar disorder are complicated by glutathione depletion. We hypothesized that treatment with N-acetyl cysteine (NAC), a safe, orally bioavailable precursor of glutathione, may improve the depressive component of bipolar disorder.

METHODS: A randomized, double-blind, multicenter, placebo-controlled study of individuals (n = 75) with bipolar disorder in the maintenance phase treated with NAC (1 g twice daily) adjunctive to usual medication over 24 weeks, with a 4-week washout. The two primary outcomes were the Montgomery Asberg Depression Rating Scale (MADRS) and time to a mood episode. Secondary outcomes included the Bipolar Depression Rating Scale and 11 other ratings of clinical status, quality of life, and functioning.

RESULTS: NAC treatment caused a significant improvement on the MADRS (least squares mean difference [95% confidence interval]: -8.05 [-13.16, -2.95], p = .002) and most secondary scales at end point. Benefit was evident by 8 weeks on the Global Assessment of Functioning Scale and Social and Occupational Functioning Assessment Scale and at 20 weeks on the MADRS. Improvements were lost after washout. There was no effect of NAC on time to a mood episode (log-rank test: p = .968) and no significant between-group differences in adverse events. Effect sizes at end point were medium to high for improvements in MADRS and 9 of the 12 secondary readouts.

CONCLUSIONS: NAC appears a safe and effective augmentation strategy for depressive symptoms in bipolar disorder.

PMID: 18534556