N-acetylcysteine augmentation therapy for moderate-to-severe obsessive-compulsive disorder: randomized, double-blind, placebo-controlled trial

Background
- The etiology of obsessive-compulsive disorder (OCD), an anxiety disorder that can be debilitating, is currently unknown. It has recently been suggested that abnormalities in the glutamate system may be to blame.
- N-acetylcysteine (NAC) has been proposed as a potential treatment for OCD because it may help to prevent glutamate's pre-oxidant effects and regulate its exchange.

Objective
- To determine the efficacy and tolerability of NAC augmentation in the treatment of moderate-to-severe OCD.

Methods
- **Design**: Randomized, double-blind, placebo-controlled, parallel study; Duration: 10 weeks
- **Inclusion criteria**: Met the Diagnostic and Statistical Manual-IV Text Revision (DSM-IV TR) criteria of moderate-to-severe OCD, scored ≥21 in Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), 18 and 60 years old, and did not receive any psychotropic medications 6 weeks prior to the study.
- **Exclusion criteria**: Suicidal ideation, substance dependence, other comorbid DSM-IV axis I disorders, seizure, intelligence quotient <70, concomitant neurologic, as well as, severe cardiac, renal, hepatic or other serious medical illnesses, history of psychosurgery, significant head trauma, pregnancy, and breast feeding.
- **Primary outcome measure**: The difference in the Y-BOCS total score from baseline to week 10
- **Secondary outcome measures**: The difference in Y-BOCS obsession score and Y-BOCS compulsion score from baseline to week 10, partial and complete response rate (≥ 25% or ≥35% reduction in Y-BOCS score, respectively), and remission rates (score <16).
- 46 patients were randomized into two groups
  - 23 patients assigned to fluvoxamine + NAC
  - 23 patients assigned to fluvoxamine + placebo
- Power was calculated to be 80%, based on a needed sample size of 46 (23 per group)
- Data handling method was intent-to-treat

Results
- 44 patients completed the study (22 in each group)
- **Primary outcome measure**: ANOVA showed a significant effect for time treatment interaction (P=.012). No significant differences were seen in mean difference for total Y-BOCS score.
- **Secondary outcome measures**:
  - Obsessive Y-BOCS score --- ANOVA showed a significant effect for time (P=0.011). No significant differences were seen in mean difference for obsessive Y-BOCS score.
  - Compulsive Y-BOCS score --- ANOVA showed no significant difference in the compulsion scale (P=0.095). No significant differences were seen in mean difference for compulsive Y-BOCS score.
S- partial/complete --- 11 patients in NAC compared with 8 in placebo met criteria for partial or complete response (P=.54)

S- remission --- 12 patients in NAC achieved remission after 10 weeks, compared to 5 in placebo group (P=.062)

**Authors’ conclusion:** Their results showed that NAC might be effective as an adjunct for the treatment of moderate-to-severe OCD. They state that its good safety profile and lack of significant interactions highlight its potential benefits as add-on therapy.

Strengths

- Gold standard study design – randomized, placebo-controlled, double-blind study
- Good concept and a solid starting point to research the potential use of NAC for the treatment of OCD

Limitations

- Not sufficiently powered, due to unaccounted drop-outs
- Short duration
- Small sample size
- No follow-up period
- Compliance was not addressed
- Inclusion criteria was a Y-BOCS score of 21 or more (the classification for moderate OCD is a score of 16 or more)
- Remission was defined as a Y-BOCS score less than 16 (the classification for subclinical is a Y-BOCS score of 7 or less)
- There was no mention of the history of previous OCD treatment (i.e., failed treatments, partial responses, complete responses, etc.)

Conclusion

- This study is a good starting point for research on NAC use as an adjunct in OCD treatment. With the recent proposals of glutamate abnormalities playing a role in OCD pathophysiology, NAC may have the potential for benefit.
- Future Research:
  - Studies that account for treatment history and response
  - Studies that measure compliance, have a longer duration, and are appropriately powered.


Tamra L. Little, Doctor of Pharmacy Candidate
08.25.2016