

## **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  $\geq 21$  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 ( $\geq 25\%$  or  $\geq 35\%$  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.

**Reference:** 1: Paydary K, Akamaloo A, Ahmadipour A, Pishgar F, Emamzadehfard S, Akhondzadeh S. N-acetylcysteine augmentation therapy for moderate-to-severe obsessive-compulsive disorder: randomized, double-blind, placebo-controlled trial. *J Clin Pharm Ther.* 2016 Apr;41(2):214-9.

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