J Clin Psychiatry. 2007 Dec;68(12):1867-75.

# Ethyl-eicosapentaenoic acid in first-episode psychosis: a randomized, placebo-controlled trial.

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## Abstract

**OBJECTIVE:** To investigate if ethyl-eicosapentaenoic acid (E-EPA) augmentation improves antipsychotic efficacy and tolerability in first-episode psychosis (FEP).

**METHOD:** We performed a 12-week, randomized, double-blind, placebo-controlled trial of 2-g E-EPA augmentation in 80 FEP patients. Sixty-nine patients were eligible for analysis; a post hoc analysis was computed for a subgroup of nonaffective FEP patients (N = 53). The first participant was included in November 2000 and the last participant completed the trial in August 2003. Primary outcome measures were symptom change scores and time to first response, while tolerability measures and cumulative antipsychotic dose were secondary outcome measures.

**RESULTS:** Analysis of covariance controlling for baseline symptoms found no significant mean difference between E-EPA and placebo at week 12 for symptom change scores. Cox regression analysis revealed a significant treatment by diagnosis interaction (p = .024) for time to first response favoring E-EPA in nonaffective psychosis. Post hoc analysis for cumulative response rates further confirmed a higher response rate at week 6 (42.9% [15/35] vs. 17.6% [6/34] for all participants, p = .036; 54.2% [13/24] vs. 17.2% [5/29] for the nonaffective psychosis subset, p = .008); however, the difference at week 12 was no longer significant. Analysis of secondary outcome measures revealed that E-EPA-augmented participants needed 20% less antipsychotic medication between weeks 4 through 6 (p = .03), had less extrapyramidal side effects in the initial 9 weeks (p < .05 for all participants and for all timepoints), and reported less constipation (p = .011) and fewer sexual side effects (p = .016) than those treated with antipsychotic medication alone.

**CONCLUSION:** The findings suggest that E-EPA may accelerate treatment response and improve the tolerability of antipsychotic medications. However, it was not possible to demonstrate a sustained symptomatic benefit of E-EPA in early psychosis, possibly due to a ceiling effect, since a high proportion of first-episode patients already achieve symptomatic remission with antipsychotic medication alone. Further controlled trials in nonaffective early psychosis seem warranted.

**TRIAL REGISTRATION:** Australian Clinical Trials Registry identifier 12605000267651 (http://actr.org.au).

PMID: 18162017 [PubMed - indexed for MEDLINE]