Title: Clinical Utility of Inflammatory Biomarkers in Personalizing Treatment of Depressed Patients: Findings from CO-MED Trial

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The Methodological Question Being Addressed

Can inflammatory biomarkers guide treatment selection for major depressive disorder patients?

Introduction

Lack of objective markers for treatment selection is one of the biggest challenges in managing depressed patients. Even the practice guidelines recommend use of subjective factors such as cost or provider preference when making treatment decisions. Unsurprisingly, depressed patients go through multiple treatment trials before finding an effective medication. Uher et al. recently reported that pre-treatment level of C-reactive protein (CRP) <1 mg/L favored improved outcomes with escitalopram while higher levels predicted better outcomes with nortriptyline. The goal of this study was to replicate the role of CRP, and develop a paradigm for future research studies that demonstrate superiority of biomarker-informed clinical decision making over current standard of care.

Methods

Analytic sample for this study included participants of Combining Medications to Enhance Depression Outcomes (CO-MED) trial who provided plasma samples and were treated with either escitalopram-plus-placebo (SSRI monotherapy, n=51) or bupropion-plus-escitalopram (bupropion-SSRI combination, n=55). Multiplex immunoassays were used to measure levels of CRP and other inflammatory biomarkers (serum amyloid P component, and alpha-2-macroglobulin). Logistic regression analysis was used to evaluate if remission rates in the two treatment arms differed based on a priori defined CRP threshold of 1 mg/L. The remission rate if participants were assigned based on CRP threshold was estimated: [(remission rate with SSRI monotherapy)*(proportion of participants with CRP <1 mg/L)+(remission rate with bupropion-SSRI combination)*(proportion of participants with CRP ≥1 mg/L)]. Using remission rates in the first step of Sequenced Treatment Alternative to Relieve Depression (STAR*D) study as current standard of care, we estimated number needed to treat (NNT): 1/[(estimated remission rate with a CRP threshold based assignment)-(remission rate in STAR*D)].

Results

The treatment arms did not differ in overall treatment outcomes. Most participants (74/106, 69.8%) had CRP ≥1 mg/L. We found that in contrast to the bupropion-SSRI treatment arm, where ≥1 mg/L CRP level was associated with higher rates of remission (remission rate=51.35%) as compared to <1 mg/L CRP level (remission rate=33.33%), participants in SSRI monotherapy treatment arm with CRP level <1 mg/L had higher rates of remission (remission rate=57.14%) as compared to those with ≥1 mg/L CRP level

(remission rate=29.73%). The estimated remission rate with CRP threshold based treatment assignment was 53.10%. When compared to the remission rate of 32.9% in first step of STAR*D, CRP threshold based treatment assignment had NNT=5. In other words, treatment of five depressed patients using CRP informed treatment assignment will result in 1 additional remission when compared to current standard of care.

Conclusions

We found that depressed patients with pre-treatment CRP level less than 1 mg/L do better with SSRI monotherapy whereas those with higher levels respond better to SSRI-bupropion combination. Additionally, we found that using such a CRP threshold based treatment assignment, as compared to the current standard of care, will result in 1 additional remission for every 5 patients treated. As these findings are based on secondary analysis of previously collected data, they should be considered preliminary with future prospective studies needed that compare treatment assignment based on "high" or "low" inflammation as compared to current standard of care.

Disclosures

One or more authors report potential conflicts which are described in the program.

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