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Effect of Anti-inflammatory Treatment On Depression, Depressive Symptoms and Side Effects: a Systematic Review and Meta-analysis of Randomized Clinical Trials

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## Introduction:

Studies have indicated antidepressant effects of anti-inflammatory treatment; however, results have been conflicting and side effects may contraindicate anti-inflammatory treatment.

# **Objectives:**

To systematically review the antidepressant and possible side effects of anti-inflammatory interventions.

## Aims:

To include trials published prior to December, 31<sup>st</sup> 2013, and evaluate depression scores after treatment and side effects.

# Methods:

We identified randomized, placebo-controlled trials assessing efficacy and side effects of pharmacological anti-inflammatory treatment in adults with depressive symptoms including adults fulfilling depression-criteria. We calculated standard mean difference (SMD) and Odds ratios (OR).

# **Results:**

10 publications covering 14 trials (n=6,262) were included: 10 on non-steroidal anti-inflammatory drugs (NSAIDs) (n=4,258) and four on cytokine-inhibitors (n=2,004). Anti-inflammatory treatment reduced depression (SMD=-0.54; 95%-CI:-1.08 to -0.01; I<sup>2</sup>=68%) and depressive symptoms (SMD=-0.27; 95%-CI:-0.53 to -0.01; I<sup>2</sup>=93%). Sub-analyses particularly emphasized antidepressant properties for the selective cyclooxygenase-2 inhibitor celecoxib in general (SMD=-0.29; 95%-CI: -0.49 to -0.08; I<sup>2</sup>=73%), on remission (OR=7.89; 95%-CI: 2.94 to 21.17; I<sup>2</sup>=0%) and response (OR=6.59; 95%-CI: 2.24 to 19.42; I<sup>2</sup>=0%). Among 6 studies (n=2,523), we found no evidence of an increased number of gastrointestinalor cardiovascular events after 6 weeks nor infections after 12 weeks of anti-inflammatory treatment. All trials were associated with high risk of bias.

# **Conclusions:**

Anti-inflammatory treatment, in particular celecoxib, decreased depressive symptoms without increased risks of side effects. However, a high risk of bias and high heterogeneity made the mean estimate uncertain. This study supports a proof-of-concept concerning use of anti-inflammatory treatment in depression. Identification of subgroups that could benefit hereof might be warranted.