

Adding aspirin to antipsychotics reduces psychopathology in adults with schizophrenia spectrum disorders

QUESTION

Question: Does adjuvant aspirin benefit patients with schizophrenia spectrum disorders who are on antipsychotic therapy?

Patients: 70 adults (18–55 years of age) with DSM-IV schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder or schizophreniform disorder), who were at least moderately ill (score ≥ 60 on the Positive and Negative Syndrome Scale, PANSS, with score ≥ 4 on two items). There was a 2-week placebo run-in period, and only those who achieved over 80% compliance were randomised. Exclusion criteria: illness duration longer than 10 years (changed from 5 years because of slow recruitment), contraindications for aspirin or pantoprazole, significant somatic illness, chronic non-steroidal anti-inflammatory drug use, corticosteroid use, pregnancy or change in type or dose of antipsychotic drugs in the previous 2 weeks.

Setting: 10 psychiatric hospitals in The Netherlands; May 2004 to August 2007.

Intervention: Adjuvant aspirin (1000 mg daily) or placebo (adjuvant to antipsychotic medication). All participants received pantoprazole 40 mg daily for gastric protection.

Outcomes: Psychopathology (PANSS total, positive, negative and general psychopathology scores).

Patient follow-up: 83%.

METHODS

Design: Randomised controlled trial.

Allocation: Unclear.

Blinding: Double blind.

Follow-up period: 3 months.

MAIN RESULTS

Adjuvant aspirin reduced overall psychopathology compared with placebo in mixed effect models at 3 months (change in mean total PANSS score in last observation carried forward (LOCF) analyses: -9.27 with aspirin vs -5.46 with placebo, difference in unpaired t tests: $+3.81$, 95% CI -1.10 to $+8.73$; difference based on linear mixed model: 4.86 , 95% CI 0.91 to 8.80 ; effect size 0.47). There was also a reduction in positive symptoms with adjuvant aspirin compared with placebo in mixed effect models (change in mean total PANSS positive subscale score in LOCF analyses: -2.24 with aspirin vs -1.32 with placebo, difference in unpaired t tests: $+0.92$, 95% CI -0.98 to $+2.82$; difference based on linear mixed model: 1.57 , 95% CI 0.06 to 3.07 ; effect size 0.39). The mixed model did not show differences in negative or general PANSS subscale scores between aspirin and placebo. Aspirin had a greater effect on overall psychopathology in individuals with more altered immune function (ie, lower T_H1/T_H2 ratios; $p=0.018$). Aspirin significantly reduced overall psychopathology in individuals with the lowest T_H1/T_H2 ratios (difference in PANSS total score: 7.47 , 95% CI 1.97 to 12.98) but not in those with the highest T_H1/T_H2 ratios (difference in PANSS total score: $+2.39$, 95% CI -3.50 to $+8.28$).

CONCLUSIONS

Adding aspirin to antipsychotic treatment reduces the symptoms of schizophrenia spectrum disorders more than adding placebo.

NOTES

Randomisation was stratified based on psychiatric centre (referral or non-referral) and relative T_H1/T_H2 cytokine activity (median interferon γ /interleukin 4 ratio).

ABSTRACTED FROM

Laan W, Grobbee DE, Seltén JP, *et al.* Adjuvant aspirin therapy reduces symptoms of schizophrenia spectrum disorders: results from a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2010;**71**:520–7.

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Elevated levels of inflammatory biomarkers have been reported in patients with chronic schizophrenia as well as in patients with first episode psychosis.¹ These findings support the hypothesised role of the activation of the immune system in the aetiopathogenesis of psychosis. Indeed, cytokines have been shown to influence brain biological pathways relevant to psychosis, including neurotransmitter metabolism, neuroendocrine function and neural plasticity. In this article, Laan and colleagues have investigated the efficacy of adjuvant treatment with acetylsalicylic acid (aspirin), a well-known anti-inflammatory agent, in patients with schizophrenia spectrum disorders. The authors found that adding aspirin to an antipsychotic further reduces psychotic symptoms at 3-month follow-up, when compared with an antipsychotic combined with placebo. It is, however,

counterintuitive that the effect of aspirin is more pronounced in patients with the lowest T_H1/T_H2 cytokine balance, that is, in those with *less* evidence of inflammation before treatment.

Previous studies showing a positive effect of adjuvant anti-inflammatory treatment in patients with schizophrenia have used the selective cyclooxygenase-2 inhibitor, celecoxib,^{2,3} whereas this is the first study using acetylsalicylic acid. Both drugs have important adverse effects – cardiovascular and gastrointestinal toxicity, respectively – and therefore the balance between the clinical benefit and adverse effects needs further evaluation.

Overall, these findings support a role of immune activation in the development of psychotic symptoms and the need to develop new treatment strategies targeting inflammation in psychiatric patients. However, more extensive immunological characterisation is

required to understand the molecular mechanisms underlying these therapeutic effects.

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Competing interests None.

REFERENCES

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