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Therapeutic Trials of Minocycline, Ondansetron and Simvastatin in Schizophrenia

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Objectives.
Immune mechanisms have been implicated in the pathogenesis of schizophrenia. This has lead to clinical trials of re-purposing drugs with off-target anti-inflammatory actions. They include the antibiotic minocycline and simvastatin (HMP-Co reductase inhibitor), which decrease microglial activation, and ondansetron a 5-HT3-receptor antagonist that has limited effects on cytokine production. This presentation will address their efficacy and mechanism of action.

Aims.
1) Update on trials with minocycline including our own positive finding on negative symptoms (PMID: 16959472)
2) Present new results with ondansetron and simvastatin summarised below.

Methods.
Ondansetron (8mg) and simvastatin (40mg) vs placebos in 2x2 design (PMID: 23782463). Patients aged 18-65, stable treatment, DSM IV schizophrenia-related diagnosis. PANSS and cognition at 0,3,6 months.

Results.
The four cells of the 2x2 design contained 302 patients. The interaction between ondansetron and simvastatin was significant at p=.006 reflecting the lower scores in the 3 active treatment groups than in the P+P group. Ondansetron improved verbal (p=.007) and visual list learning (p=.02) with no other treatment effects on cognition.

Conclusions.
Minocycline appears to benefit negative symptoms in early psychosis with a minor effect on cognition. Simvastatin had limited effects in our patients with established schizophrenia but its anti-inflammatory effects could be worth investigating in early psychosis. Ondansetron has a significant effect on new learning, which might be expected from its 5-HT3 antagonist properties. This may underlie a benefit on negative symptoms reported by others and us.

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