

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Novel alternatives for treatment-resistant schizophrenia

Schizophrenia is a complex brain disorder characterised by abnormal social behaviour and a distorted perception of reality. Many patients continue to be symptomatic despite receiving recommended treatment, including clozapine (which is generally reserved for refractory schizophrenia). A number of unconventional therapies have been studied for treatment-resistant schizophrenia, including adjunct allopurinol, minocycline, omega-3 fatty acids and other therapies.

Allopurinol

Allopurinol inhibits purine degradation and enhances adenosinergic activity. This produces effects similar to dopamine antagonists, a mechanism for antipsychotic action in schizophrenia. There have been multiple studies and case reports investigating the addition of allopurinol (300 mg daily or twice daily) to antipsychotics for the treatment of refractory schizophrenia. In particular, a double-blind, placebo-controlled, crossover trial involving 22 patients explored the addition of allopurinol (300 mg twice daily) to an antipsychotic for poorly responsive schizophrenia or schizoaffective disorder. Allopurinol was found to be well tolerated and produced significant improvement in Positive and Negative Syndrome Scale (PANSS) scores. Another double-blind, placebo-controlled trial involving 46 patients over eight weeks assessed the addition of allopurinol (300 mg daily) or placebo to haloperidol (15 mg daily). The researchers concluded that allopurinol may be an effective adjuvant agent in chronic schizophrenia. A review article addressing available literature concluded that allopurinol in doses of 300 mg once or twice daily may improve psychotic symptoms, especially refractory positive symptoms. However, the authors suggest the need for larger, randomized clinical trials for more conclusive data.

Minocycline

Studies evaluating the use of minocycline in neurological disorders suggest benefit associated with anti-inflammatory and neuro-protective properties. While a study is currently being undertaken to investigate the role of minocycline in treatment resistant schizophrenia, the current place in therapy of minocycline is unclear.

Omega-3 fatty acids

Omega-3 fatty acids may have a role in the management of a range of psychiatric conditions. This may involve various biological mechanisms, including alterations in dopaminergic function, which is of particular interest in schizophrenia. A double-blind, placebo-controlled trial assessing 87 patients concluded that the augmentation of neuroleptics with ethyl eicosapentaenoic acid (EPA) 3000 mg daily, did not result in significant changes in symptoms of schizophrenia.

Others

Other 'unconventional' therapies for treatment resistant schizophrenia include the complementary medicine ginkgo biloba, and also ondansetron. It has been proposed that Ginkgo biloba (which may act as a free radical scavenger), may be effective in schizophrenia. Serotonin (5-HT₃) receptors are involved in the pathogenesis of schizophrenia: ondansetron, which is a serotonin (5-HT₃) antagonist, has been studied in schizophrenia. However, the role of either one of these agents in refractory schizophrenia remains unclear.

Clozapine remains the treatment of choice in refractory schizophrenia. While several alternatives to clozapine have been studied, larger, randomized trials are required to determine the magnitude of benefit from alternative agents in treatment resistant schizophrenia.

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