doses (DDD) (OR=1.11, 95% CI, 0.85–1.46, p=0.44) or 1000–2999 DDD (OR=1.34, 95% CI, 0.76–2.34, p=0.31). However, for patients with a cumulative dose of 3000–4999 DDD and >5000 DDD, the risk of HM was significantly higher in the clozapine group (OR=2.04, 95% CI, 1.46–2.86, p<0.0001), (OR=2.45, 95% CI, 1.32–4.48, p=0.004), respectively. The association between clozapine and haematological malignancies became statistically significant after 5 years of follow-up (OR=2.32, 95% CI, 1.5–3.59, p=0.0002).
Conclusion: Despite the increased risk of HM, clozapine treatment in schizophrenia patients is associated with a significantly lower long-term all-cause mortality rate compared with other antipsychotic use. The small risk should not deter its use or not fuel "clozapine-phobia". The clinical implication of our study is to raise awareness among the psychiatrists about this risk. Haematological abnormalities could be interpreted as typical adverse effects of clozapine, leading to diagnostic bias and delays in malignancy diagnosis.

Efficacy and Safety of Ondansetron in Schizophrenia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Aims: It has been shown that 5-hydroxytryptamine3 (5-HT3) receptors are involved in the pathogenesis of schizophrenia. This systematic review and meta-analysis of randomized clinical trials (RCTs) evaluates the efficacy and safety of ondansetron, a potent 5-HT3 receptor antagonist, as adjunctive treatment for the management of schizophrenia, especially the negative symptoms and cognitive deficits.
Methods: A comprehensive search of electronic databases, including PubMed, Scopus, Cochrane, and Web of Science, was performed in October 2024. We included only randomized controlled trials (RCTs), and their data were extracted and analysed using RevMan 5.4 software. The primary outcome was the PANSS (Positive and Negative Syndrome Scale) negative subscale.
Results: Eight RCTs involving 533 patients were included in the study. Ondansetron showed a statistically significant improvement in PANSS negative subscale at 12 weeks [pooled as mean difference, MD=−2.96, 95% CI [−4.69, −1.24], p=0.00007] and in general psychopathology scale [MD= −2.71, 95% CI [−3.52, −1.90]] compared with placebo. However, ondansetron and placebo did not differ in reduction of PANSS positive subscale [MD= 0.1, 95% CI [−1.19, 1.38], p=0.88], and depression scale (SMD= 0.71, 95% [−0.35, 1.77], p=0.19). Ondansetron showed no significant difference regarding tardive dyskinesia between the two groups. However, constipation was significant in the ondansetron group over placebo.
Conclusion: The study's findings support the use of ondansetron as adjuvant therapy in the management of schizophrenia, particularly the negative symptoms and cognitive deficits.

Efficacy and Safety of Pentoxifylline in Major Depressive Disorder: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Aims: Major depressive disorder (MDD) may be linked to broader pathophysiological pathways such as oxidative stress, inflammation, vascular dysfunction, and neuroplasticity alterations. Pentoxifylline (PTX), a pleiotropic drug, targets all these pathways through non-specific phosphodiesterase (PDE) inhibition. This is the first systematic review and meta-analysis to examine the role of PTX in major depressive disorder.
Methods: A comprehensive search of electronic databases, including PubMed, Scopus, Cochrane, and Web of Science, was performed in October 2024. We included only randomized controlled trials (RCTs), and their data were extracted and analysed using Reman 5.4 software. The inclusion criteria as follows: adult patients diagnosed with MDD were included as the population. The intervention considered was pentoxifylline, either alone or in combination with selective serotonin reuptake inhibitors. Comparators included placebo, either alone or combined with SSRIs. Eligible studies needed to report outcomes such as the Hamilton Depression Rating Scale (HAM-D).
Results: Four RCTs with 318 patients were included in the study. PTX showed a statistically significant improvement in HAM-D scores at the primary endpoint compared with the placebo (MD= −3.84, 95% CI [−4.87 to −2.81], p<0.00001). Moreover, PTX showed a statistically significant increase in serotonin and BDNF levels (MD=20.76 ng/mL, 95% CI [5.49 to 36.04], p=0.008; and MD=10.83 ng/mL, 95% CI [−0.22 to 21.88], p=0.05, respectively) and a statistically significant decrease in TNF-α and IL-6 levels (MD=−3.24 pg./mL, 95% CI [−4.12 to −2.36], p<0.00001; and MD= −2.64 pig/mL, 95% CI [−3.79 to −1.48], p<0.00001, respectively). There was no statistically significant difference between the PTX and placebo in any of the reported side effects including nausea, vomiting, headache, diarrhoea, increased appetite, and sexual dysfunction.
Conclusion: The study findings suggest that PTX may be effective and safe as an adjuvant antidepressant agent in patients with MDD, demonstrating a significant reduction in HAM-D scores. The results of this study need to be interpreted with caution considering several limitations.