Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis.

Relapse prevention with antipsychotic drugs compared with placebo in patients with schizophrenia has not been sufficiently addressed by previous systematic reviews. We aimed to assess the association between such drugs and various outcomes in patients with schizophrenia to resolve controversial issues. We searched the Cochrane Schizophrenia Group’s specialised register for reports published before Nov 11, 2008; and PubMed, Embase, and ClinicalTrials.gov for those before June 8, 2011. We also contacted pharmaceutical companies and searched the reference lists of included studies and previous reviews. Randomised trials of patients with schizophrenia continued on or withdrawn from any antipsychotic drug regimen after stabilisation were eligible. Our primary outcome was relapse between 7 and 12 months. We also examined safety and various functional outcomes. We used the random effects model and verified results for the primary outcome with a fixed effects model. Heterogeneity was investigated with subgroup and meta-regression analyses. We identified 116 suitable reports from 65 trials, with data for 6493 patients. Antipsychotic drugs significantly reduced relapse rates at 1 year (drugs 27% vs placebo 64%; risk ratio [RR] 0.40, 95% CI 0.33-0.49; number needed to treat to benefit [NNTB] 3, 95% CI 2-3). Fewer patients given antipsychotic drugs than placebo were...
readmitted (10% vs 26%; RR 0.38, 95% CI 0.27-0.55; NNTB 5, 4-9), but less than a third of relapsed patients had to be admitted. Limited evidence suggested better quality of life (standardised mean difference -0.62, 95% CI -1.15 to -0.09) and fewer aggressive acts (2% vs 12%; RR 0.27, 95% CI 0.15-0.52; NNTB 11, 6-100) with antipsychotic drugs than with placebo. Employment data were scarce and too few deaths were reported to allow significant differences to be identified. More patients given antipsychotic drugs than placebo gained weight (10% vs 6%; RR 2.07, 95% CI 2.31-3.25), had movement disorders (16% vs 9%; 1.55, 1.25-1.93), and experienced sedation (13% vs 9%; 1.50, 1.22-1.84). Substantial heterogeneity in size of effect was recorded. In subgroup analyses, number of episodes, whether patients were in remission, abrupt or gradual withdrawal of treatment, length of stability before trial entry, first-generation or second-generation drugs, and allocation concealment method did not significantly affect relapse risk. Depot preparations reduced relapse (RR 0.31, 95% CI 0.21-0.41) more than did oral drugs (0.46, 0.37-0.57; p=0.03); depot haloperidol (RR 0.14, 95% CI 0.04-0.55) and fluphenazine (0.23, 0.14-0.39) had the greatest effects. The effects of antipsychotic drugs were greater in two unblinded trials (0.26, 0.17-0.39) than in most blinded studies (0.42, 0.35-0.51; p=0.03). In a meta-regression, the difference between drug and placebo decreased with study length. Maintenance treatment with antipsychotic drugs benefits patients with schizophrenia. The advantages of these drugs must be weighed against their side-effects. Future studies should focus on outcomes of social participation and clarify the long-term morbidity and mortality of these drugs. German Ministry of Education and Research.