Pharmacological augmentation strategies for schizophrenia patients with insufficient response to clozapine: a quantitative literature review.

When schizophrenia patients have insufficient response to clozapine, pharmacological augmentation is often applied. This meta-analysis summarizes available evidence on efficacy of pharmacological augmentation of clozapine treatment in schizophrenia spectrum disorder. Only double-blind randomized controlled studies were included. Primary outcome measure was total symptom severity, and secondary outcome measures were subscores for positive and negative symptoms. Effect sizes were calculated from individual studies and combined to standardized mean differences (Hedges’s g). Twenty-nine studies reporting on 15 different augmentations were included. Significant better efficacy than placebo on total symptom severity was observed for lamotrigine, citalopram, sulpiride, and CX516 (a glutamatergic agonist). The positive effect of lamotrigine disappeared after outlier removal. The other positive findings were based on single studies. Significantly better efficacy on positive symptom severity was observed for topiramate and sulpiride. The effect of topiramate disappeared after outlier removal. Results for sulpiride were based on a single randomized controlled trial. Citalopram, sulpiride, and CX516 showed better efficacy for negative symptoms than placebo, all based on single studies. Evidence for efficacy of clozapine augmentation is currently scarce. Efficacy of
lamotrigine and topiramate were both dependent on single studies with deviating findings. The effect of citalopram, sulpiride, and CX516 were based on single studies. Thus, despite their popularity, pharmacological augmentations of clozapine are not (yet) demonstrated to be superior to placebo.