PHARMACOLOGIC COTREATMENT in Patients With Schizophrenia

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Which psychotropic combinations unlock the door to successful treatment?
Combination Treatment in Schizophrenia

• Many patients with schizophrenia have residual symptoms despite ongoing antipsychotic treatment
• Adding medications to antipsychotics is a common treatment strategy in schizophrenia, but no combination is approved for this indication
Combination Treatment in Schizophrenia (2)

- Many (generally small) randomized controlled trials (RCTs) have studied pharmacologic combination strategies in schizophrenia.
- Meta-analyses of these strategies have led to evidence-based recommendations; however, these approaches have not been quantitatively compared with antipsychotic monotherapy.
- Moreover, the quality of these meta-analyses (and their individual studies) have not been examined.
• Correll and colleagues[1] performed a **systematic review** of meta-analyses of pharmacologic combination strategies in schizophrenia to facilitate decision-making
• They searched PubMed and PsycINFO from inception until May 2016
• Meta-analyses of RCTs that reported effect sizes for pharmacologic agents plus antipsychotics versus antipsychotic monotherapy in schizophrenia were included
• The primary outcome measure was change in total psychopathology rating scale scores
• Key secondary outcomes were positive and negative symptom subscale scores, and the recommendation for or against combination treatment
• Data for combination strategies involving clozapine were analyzed separately
Study Methods (3)

• Methodological quality of included meta-analyses was assessed using A Measurement Tool to Assess Systematic Reviews (AMSTAR)
• Study authors developed additional items to assess content quality of these meta-analyses
• The authors conducted random-effects meta-analyses of effect sizes for combination treatments versus monotherapy
• They also performed meta-regression analyses of study quality scores and sample size on associations with psychopathology
Study Results

- Twenty-nine meta-analyses were included, representing 381 meta-analyzed trials and 19,321 patients, and 42 different psychotropic cotreatment strategies.
- The individual meta-analyses included a mean of 8 studies and a mean of 50 subjects per study.
- Subjects had a mean age of 38 and illness duration of 13 years, and 65% were male.
Study Results (2)

- Fourteen of 32 agents combined with antipsychotics were significantly superior to controls for total psychopathology, generally with medium to large effect sizes (compared with 6 of 25 agents for positive symptoms, 12 of 26 for negative symptoms, and 0 of 5 for studies with clozapine).
- Twenty augmentation strategies were at least partially recommended by authors, including 12 for which there were not significantly different effects between combination treatments and controls.
Of 37 comparisons, 33 (89%) had good study quality (AMSTAR scores of > 7) and 18 (49%) had the maximum AMSTAR score of 11. However, evidence for most combination treatments was exposed to potential inconsistencies, including small cumulative sample size, between-study heterogeneity, and potential publication bias. Effect sizes for total psychopathology were positively correlated with author recommendations and negatively correlated with study quality.
Discussion

• Fourteen of 37 pharmacologic combination strategies outperformed controls for reducing total psychopathology.
• However, effect sizes were inversely correlated with meta-analytic study quality, reducing confidence in recommendations.
• The authors called for higher-quality trials and patient-based meta-analyses to determine if certain subpopulations might benefit from specific combination treatments
• No single combination treatment strategy can be recommended for patients with schizophrenia based on the current literature
REFERENCE: