Antipsychotic Augmentation vs Monotherapy in Schizophrenia

By Brian Miller, MD, PhD, MPH
Inadequate response to antipsychotic treatment in schizophrenia is common.¹
Strategies for antipsychotic non-responders:

- Wait for delayed response
- Dose adjustment
- Antipsychotic switching
- Clozapine
- Antipsychotic polypharmacy
Antipsychotic polypharmacy is common despite:

- Lack of strong evidence for efficacy
- Being considered a last-stage option after clozapine failure
- Concerns about cost, adherence, and adverse effects
Galling and colleagues\textsuperscript{2} conducted a meta-analysis comparing the efficacy and adverse effects of antipsychotic augmentation versus monotherapy.
Study Methods

- Systematic search of MEDLINE, PsycINFO, and 2 Chinese databases.

- Included randomized controlled trials (RCTs of at least 20 adults with schizophrenia or schizoaffective disorder) of antipsychotic augmentation with a different antipsychotic versus either augmentation with placebo or continuation of antipsychotic monotherapy.
Methods (2)

Primary outcomes
- Total symptom reduction
- Study-defined treatment response

Secondary outcomes
- Discontinuation
- Reduction in symptom domains (e.g., positive symptoms, negative symptoms, depression)
- Reduction in global illness severity
- Improvement in functioning
- Frequency and severity of adverse effects
Group differences for continuous outcomes were analyzed as the pooled standardized mean difference in change from baseline to endpoint.

Dichotomous data were analyzed as the pooled risk ratio.

Subgroup analyses were performed for double-blind and “high-quality” studies (those using an intent-to-treat/last-observation-carried-forward design).
Study Results

31 studies were included in the meta-analysis.

22 studies, comprising 1342 patients, were analyzed regarding efficacy (primary outcome).
Antipsychotic augmentation was not superior to monotherapy for total symptom reduction in either double-blind or high-quality studies.

Similarly, there was no significant difference between augmentation and monotherapy for treatment response rates in double-blind and high-quality studies.

The pattern of the results was unchanged in augmentation studies of clozapine.
Results (3)

All-cause and intolerability-related discontinuation did not differ between antipsychotic augmentation and monotherapy.

Augmentation of D2 antagonists with a partial D2 agonist, but not another D2 antagonist, was associated with significant reduction in negative symptoms with a small-to-medium effect size.
Results (4)

Antipsychotic augmentation and monotherapy did not differ regarding depressive symptoms.

Few differences in adverse effects were observed:

- D2 antagonist augmentation was associated with less insomnia but greater prolactin elevation
- Aripiprazole augmentation was associated with reduced prolactin levels and body weight
Discussion

• This is the first meta-analysis of RCTs focusing exclusively on augmentation strategies versus continued treatment with antipsychotic monotherapy, regardless of the baseline antipsychotic.

• There was no evidence for symptom improvement or treatment response with augmentation of either clozapine or non-clozapine antipsychotics.
Discussion (2)

- Outside of greater prolactin elevation, the authors did not find evidence that antipsychotic polypharmacy carries a greater risk of adverse effects.

- The authors emphasize that findings should be interpreted with some caution given the relatively small number of double-blind studies, and heterogeneity of the included studies.
The Bottom Line

Findings suggest that the common practice of antipsychotic augmentation in schizophrenia lacks double-blind/high-quality evidence for efficacy, except for negative symptom reduction with partial D2 agonist augmentation.
REFERENCES


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