Majority of Study Participants Can Successfully Switch to Antipsychotic Monotherapy and Show Improved BMI

The following is an extract of:

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Corresponding author: Susan M. Essock

Bottom Line:

- In this RCT adult outpatients with schizophrenia, persistent psychopathology and currently on 2 antipsychotics were randomly assigned to "stay" on polypharmacy or "switch" to monotherapy.
- At 6 months, 69% of the "switch" group had successfully switched to monotherapy.
- Symptom control did not differ between the two groups.
- BMI decreased by -0.5 points in the "switch" group; BMI increased by +0.28 points in the "stay" group. This net difference of 0.8 points corresponds to a net of 5 pounds for a 5-foot,7-inch, 203-pound individual (mean baseline height and weight of the study participants).

Study Background

Antipsychotic polypharmacy (APP) is a prevalent practice despite concerns about its risks and costs, as well as the absence of clear evidence supporting the practice. Randomized clinical trials (RCTs) to date have looked only at APP combinations using clozapine and another agent, and the results of these studies have been mixed. Research suggests that less complicated medication regimens are associated with better adherence, fewer side effects, lower costs and lower mortality. Switching to monotherapy may be accompanied by worsening of symptoms, yet only a limited number of studies have directly compared outcomes when switching from APP to monotherapy. The present study is an RCT comparing the risks and benefits of staying on APP vs. switching to monotherapy.

Study Details

Fifteen sites in NIMH's Schizophrenia Trials Network and five sites in Connecticut's public mental health system participated between December 2004 and March 2008. Inclusion criteria were: age ≥18 years; diagnosis of schizophrenia or schizoaffective disorder; currently on 2 antipsychotics (determined by blood screen); persistent psychopathology or significant side effects; willingness to change medication; continued access to medication without financial impediment; and at least one clinic visit every 3 months for the last 6 months. Exclusion criteria were: severe symptoms or side effects requiring immediate change of medication; recent exacerbation of psychiatric symptoms requiring significant intervention; residence in a skilled nursing facility; pending criminal charges; currently pregnant or breast feeding; currently on ≥3 antipsychotics daily; quetiapine dose <100 mg (if quetiapine was one of the two medications prescribed).

Participants were randomly assigned to stay on APP or switch to monotherapy ("stay" vs. "switch" groups). Switches were required to be completed within thirty days. In the "switch" group, the decision regarding which antipsychotic to discontinue was left to the participant and

the prescriber. Assigned medication regimens were required to be continued for six months unless contraindicated, with dosage adjustments left to providers' clinical judgments. Adjunctive psychotropics other than antipsychotics were allowed. Six months of naturalistic follow up occurred after study end.

The primary outcome measure was time to all-cause medication discontinuation. Secondary outcomes relied on blinded raters and included measures of psychiatric symptoms, medication side effects and medical and psychiatric hospitalizations.

Results and Limitations

Of 127 participants entering randomization, 114 began treatment ("stay" group: n=56; "switch" group: n=58). Eight (14%) of the "stay" group discontinued assigned treatment. Participants in both groups received comparable doses of antipsychotics at baseline. Between group differences in race and gender were noncontributory results in the statistical analysis. Eighteen (31%) of the "switch" group discontinued assigned treatment, the majority of whom (n=12) returned to their original APP regimen. The "switch" group had a shorter time to all-cause treatment discontinuation than did the "stay" group. The two groups did not differ significantly regarding psychiatric symptoms, sexual side effects, new onset movement disorders, time to first psychiatric hospitalization or total hospitalizations (psychiatric or medical). BMI decreased by 0.5 points in the monotherapy group, a significant finding compared to the APP group for whom it increased by +0.28 points (p=0.05).

Limitations: the open-label nature of this trial may have introduced bias since those in the "switch" group may have attributed changes in symptoms to the change in medication. Thus, the "switch" group may have been more likely to discontinue treatment sooner than those in the "stay" group, who may have attributed changes in symptoms to normal variations in illness.

Clinical Implications

This is the first published study of an RCT that compared outcomes for participants with schizophrenia or schizoaffective disorder on APP vs. monotherapy. The results indicate that a majority of participants (69%) can successfully switch to monotherapy. Most of the "switch" group who discontinued treatment went back to their original APP regimen. The results provide further support for guidelines calling for trials of monotherapy in consumers currently receiving APP. Returning to APP should remain an option after an adequate trial of monotherapy has proved unsuccessful. This study provides evidence that switching to monotherapy is not accompanied by worsening of symptom control or increased hospitalizations, and has benefits, including improved body mass that may be expected to lead to accompanying metabolic effects associated with weight loss.

Drs Schooler, Stroup, and McEvoy report receiving research support or consulting fees from various pharmaceutical companies.