Antipsychotic Polypharmacy, Part 2: Tips on Use and Misuse

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**Issue:** Antipsychotic polypharmacy is common in clinical practice, but has not been adequately studied.

Presented here is a visual lesson to accompany last month’s Brainstorms feature: “Antipsychotic Polypharmacy, Part 1: Therapeutic Option or Dirty Little Secret?” (1999;60:425–426)

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**Figure 1. First-Line Antipsychotic Use**

When switching from one atypical antipsychotic to another, it is frequently prudent to “cross-titrate,” i.e., build down the dose of the first drug while building up the dose of the other. This leads to transient administration of 2 drugs, but is justified in order to reduce side effects and the risk of rebound symptoms and to accelerate the administration of the second drug.

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**Figure 2. Getting Trapped in Cross-Titration**

When switching from one atypical antipsychotic to another, the patient may improve in the middle of cross-titration. The polypharmacy that results if cross-titration is stopped and the patient continues both drugs indefinitely is not currently justified.
**Figure 3. Time Course of Full Antipsychotic Effects: Who Gets the Credit?**

The time course of full clinical effects of an atypical antipsychotic can take up to 9 months. If drugs are changed every 2 months, their effects may be cumulative over time. Thus, the patient may apparently “respond” optimally to the third drug, but it is really the cumulative effects of all 3 drugs with the last one getting the credit. Thus, sequential trials of antipsychotics longer than 2 months may be justified, especially before resorting to polypharmacy.

**Figure 4. Use of Conventional Antipsychotics to “Lead In” or “Top Up” Atypical Antipsychotics**

One of the most important and justified uses of antipsychotic polypharmacy is to “lead in” to treatment with a conventional antipsychotic when an unmedicated patient is acutely psychotic, combative, or out of control. Such patients may also require periodic “top-up” for bouts of aggressiveness, allowing more rapid and robust relief of symptoms than an additional dose of the maintenance

**Figure 5. When All Else Fails**

If all of the atypical antipsychotics show insufficient efficacy, it may be necessary to use high doses. This is quite costly, and can lead to the loss of the “atypical” therapeutic advantages of such drugs. Another option is to give a second antipsychotic from the conventional class to augment an inadequately efficacious atypical antipsychotic.