

Japanese Study on Antipsychotic Polypharmacy Shows that Converting to Monotherapy is Feasible

The following is an extract from:

Suzuki T, Uchida H, Tanaka KF et al: Revising polypharmacy to a single antipsychotic regimen for patients with chronic schizophrenia. *International Journal of Neuropsychopharmacology* 2004; 7:133-142.

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Bottom Line:

- This study found that many instances of antipsychotic polypharmacy may be unnecessary.
- The majority of patients on antipsychotic polypharmacy can be successfully transitioned to monotherapy in both the inpatient (62.9%) and outpatient (85%) settings.

In a naturalistic, prospective study of 44 patients with chronic schizophrenia, researchers found that those on antipsychotic polypharmacy could be successfully cross-tapered to monotherapy without deterioration in functioning. Researchers found that in the outpatient setting 55% of study subjects remained stable and 30% improved when switched to monotherapy. In the inpatient setting 48% remained stable and 14.8% improved when switched to monotherapy. Lead authors Takefumi Suzuki and Hiroyuki Uchida conclude that many cases of antipsychotic polypharmacy are avoidable, which is in agreement with current clinical practice guidelines recommending monotherapy.^{1,2,3,4,5}

Study Background

Antipsychotic polypharmacy is a relatively common practice in the clinical setting, but has little research evidence supporting it. This study assesses the impact of discontinuing one of the antipsychotics in a polypharmacy regimen. The purpose of this study was to critically evaluate the usefulness of antipsychotic polypharmacy.

Study Details

Study subjects had an ICD-10 diagnosis of schizophrenia, were followed at the same psychiatric hospital, and had been on the same psychotropic regimen for at least six months. Exclusion criteria included: active somatic complications, mental retardation interfering with the ability to give consent, a history of substance abuse, neurological disorders, significant head injury and overt fluctuations of symptoms. For each subject, the primary antipsychotic in the polypharmacy

¹ APA (2004). Practice guideline for the treatment of patients with schizophrenia, second edition. *American Journal of Psychiatry* 161 (Suppl 2), 1-56.

² Expert Consensus Guidelines Series (ECGS) (1999). Treatment of schizophrenia. *Journal of Clinical Psychiatry* 60 (Suppl. 11), 3-80.

³ Lehman AF, Steinwachs DM, the coinvestigators of the PORT project (1998). Translating research into practice: the schizophrenia patient outcomes research team (PORT) treatment recommendations. *Schizophrenia Bulletin* 24, 1-10.

⁴ Miller AL, Chiles JA, Chiles JK, et al (1999). The Texas medication algorithm project (TMAP) schizophrenia algorithms. *Journal of Clinical Psychiatry* 60, 649-657.

⁵ Taylor D, McConnel D, McConnel H, et al (2001). The South London and Maudsley NHS Trust 2001 Prescribing Guidelines (6th edition) (pp.3-48). London: Martin Dunitz.

regimen was determined. The antipsychotic with the higher chlorpromazine dose equivalent (CPZ) was classified as the primary antipsychotic. Total daily antipsychotic CPZ equivalent dosage was maintained by increasing the dose of the primary antipsychotic and decreasing the dose of other antipsychotics. A reduction in the total CPZ equivalent dose was permitted as clinically indicated. Other medications, including psychotropics other than antipsychotics, were kept constant. Participants were evaluated at entry, weekly, and at the end of 24 weeks using the Global Assessment of Functioning (GAF), and the Clinical Global Impression (CGI), a combination of Severity of Illness (SOI) and Global Impression (GI, based on social functioning and adverse effects of the medications).

Results and Limitations

The study followed 44 patients, of whom 33 were male and 27 were inpatients. At baseline, mean GAF was 35.5 (on a scale of 31-40, indicating major impairment in several areas); mean SOI was 4.7 (with a maximum score of 5, indicating severe illness); and mean duration of illness was 24 years, indicating sustained illness. Almost all patients had been treated with combinations of high- and low-potency agents. Overall, switching resulted in the majority (54.5%, n=24) remaining stable, or improving (22.7%, n=10), while 22.7% (n=10) worsened. Among outpatients, 55% (n=11) remained stable and 30% (n=11) improved. Among inpatients, 48% (n=13) remained stable and 14.8% (n=4) improved. Overall GAF score remained unchanged at 35.5, and a GI of 4.05 was essentially stable. Among those who remained stable or improved, the number of antipsychotics decreased significantly (from 3.0 to 1.4, $p<0.0001$), tapering off over an average of 4.8 weeks. Medication dosage significantly decreased from 1171 mg to 952 mg ($p<0.0001$). Those who deteriorated did so an average of 10.3 weeks after the initiation of switching. Those who deteriorated were over-represented among inpatients (8 of 27 inpatients deteriorated compared to 2 of 20 outpatients), had a longer history of lifetime admission ($p<0.01$), and initially lower GAF scores ($p<0.05$).

The primary limitation was that risperidone was the only atypical on the market in Japan at the time of the study (1999). This meant that the present study mainly investigated polypharmacy of typical antipsychotics.

Clinical Implications

The authors emphasize that monotherapy was attainable even for the difficult to treat patients in this study (as indicated by low initial GAF scores and high average daily medication dosages in the study population). The authors conclude, "At least some instances of antipsychotic polypharmacy are unnecessary for patients with chronic schizophrenia. It should not be overused and should be the exception, to be used when other therapeutic approaches have failed."

No conflicts of interest were reported for this study.