Antipsychotic polypharmacy

Polypharmacy can be a confusing term in the selection of antipsychotic treatment options. Here it is defined as using two antipsychotics simultaneously, either as atypical-atypical antipsychotic polypharmacy, atypical-conventional polypharmacy or as conventional-conventional polypharmacy. Also, polypharmacy as used here does ***not*** include antipsychotic augmentation strategies, which add a psychotropic drug other than antipsychotics to an antipsychotic (such as the addition of a mood stabilizer or antidepressant to an antipsychotic).

Recommendations for antipsychotic polypharmacy differ depending upon whether the use is short term or long term, and whether the patient is hospitalized and out of control, or in outpatient treatment and relatively stable.

Short term polypharmacy during the switching from one antipsychotic to another is justified during the crossover phase in order to transition a patient smoothly between drugs. Abrupt discontinuation of an antipsychotic can lead to the worsening of psychotic symptoms, so a transition period of several days to 3 weeks or so is generally recommended. Abrupt discontinuation could also lead to "tolerance problems such as those observed when stopping an anticholinergic." In hospital settings , short term polypharmacy, such as the "topping up" of an atypical antipsychotic with a conventional antipsychotic for several days to hasten onset of antipsychotic actions and potentially reduce hospital stays may also be justified in patients with severe symptoms or who are not responding rapidly to an atypical antipsychotic alone. Sedative antipsychotics are often associated at an initial phase of treatment in very acute patients and withdrawn later. This is especially true in the short term for the use of intramuscular administration of conventional or atypical antipsychotics in emergency settings.

Long term antipsychotic polypharmacy in outpatient settings is far more problematic. No compelling studies support the rationale or have generated evidence to support this practice, although some clinicians elect this option in up to half of patients. Combining two conventional antipsychotics has perhaps the least rationale and combining two atypical antipsychotics has the greatest cost. All polypharmacy options can be a form of high dosing that leads to increased side effects, and in the case of atypical antipsychotics, reduces or eliminates the atypical's potential advantages such as cognitive enhancement and a lower incidence of motor side effects.

The best evidence base may exist for the case of combining another antipsychotic to patients who do not even have a robust response to clozapine. Other options with significantly greater base of evidence, better rationale and lower cost should generally be considered prior to combining two antipsychotics, especially two atypical antipsychotics for long term outpatient treatment, including augmentation with divalproex or other mood stabilizers, and reconsideration of longer term treatments with each atypical antipsychotic as a monotherapy.

References

Chong MY. Tan CH. Fujii S. Yang SY. Ungvari GS. Si T. Chung EK. Sim K. Tsang HY. Shinfuku N. Antipsychotic drug prescription for schizophrenia in East Asia: rationale for change. Psychiatry & Clinical Neurosciences. 58(1):61-7, 2004

McCue RE. Waheed R. Urcuyo L. Polypharmacy in patients with schizophrenia. Journal of Clinical Psychiatry. 64(9):984-9, 2003

Stahl SM and GradyMM. Current Medicinal Chemistry, 2004, *11*, 313-327.