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Are changes in the pharmacokinetic (PK) and pharmacodynamic (PD) properties of antipsychotics able to improve efficacy and safety?

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Although atypical antipsychotics have provided clinical advantages over conventional medications, data from trials such as CATIE [1] have highlighted that there is still a need for improved medications to support continued adherence and optimal clinical outcomes. In particular, it would be of benefit to minimize side effects such as extrapyramidal symptoms (EPS) and weight gain. One approach to optimize antipsychotic activity is to modulate the pharmacokinetic profile and thus deliver improved pharmacodynamic effects. Oral formulations of antipsychotics are generally characterized by a relatively rapid rise and fall in plasma concentrations with levels above and below threshold levels being associated with an increased risk of side effects and reduced antipsychotic efficacy, respectively [2]. Achieving steady plasma levels at which the drug achieves maximum symptom control but below levels at which adverse events occur therefore remains the ideal profile. For atypical antipsychotics, efficacy begins at approximately 60% occupancy of the D2 receptor, and occupancy above 80% can lead to EPS [2-4]. Approaches to reduce the peak-to-trough fluctuations compared with immediate-release oral agents include the use of long-acting injectable agents which have smoother plasma concentration-time profiles [2,5]. For those patients who prefer oral agents, alongside the choice of agents such as olanzapine, quetiapine, ziprasidone and risperidone, there is the option of using paliperidone ER which uses oral osmotic pump (OROS) extended-release technology [6]. This provides a continual release of medication leading to minimal peaks and troughs in plasma concentrations over a 24-hour period. A sustained release formulation of quetiapine is also currently being assessed in clinical trials [7].

References

1. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK: **Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia.** *N Engl J Med* 2005, **353:**1209-1223.
2. Medori R, Mannaert E, Gründer G: **Plasma antipsychotic concentration and receptor occupany, with special focus on risperidone long-acting injectable.** *Eur Neuropsychopharmacol* 2006, **16:**233-240.
3. Kapur S, Zipursky R, Jones C, Remington G, Houle S: **Relationship between dopamine D(2) occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia.** *Am J Psychiatr* 2000, **157:**514-520.
4. Pani L, Pira L, Marchese G: **Antipsychotic efficacy: relationship to optimal D2-receptor occupancy.** *Eur Psychiatry* 2007, **22:**267-275.
5. Mamo D, *et al.*: **Neuropsychopharmacology.** 2004 in press.
6. Conley R, Gupta SK, Sathyan G: **Clinical spectrum of the osmotic-controlled release oral delivery system (OROS), an advanced oral delivery form.** *Curr Med Res Opin* 2006, **22:**1879-1892.
7. Kahn RS, Schulz SC, Palazov VD, Reyes EB, Brecher M, Svensson O, Andersson HM, Meulien D: **Study 132 Investigators. Efficacy and tolerability of once-daily extended release quetiapine fumarate in acute schizophrenia: a randomized, double-blind, placebo-controlled study.** *J Clin Psychiatry* 2007, **68:**832-842.