

CATIE Shows Olanzapine and Quetiapine Have Greatest Impact on Nonfasting Triglycerides

The following is an extract of:

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Bottom Line:

- This study provides further confirmation of the differential effects of atypical antipsychotics on cardiometabolic risk.
- Olanzapine (Zyprexa) and quetiapine (Seroquel) were associated with increases in nonfasting triglycerides.
- Ziprasidone (Geodon) was neutral, showing no increases in nonfasting triglycerides.
- Risperidone (Risperdal) and perphenazine (Trilafon) showed decreases in nonfasting triglycerides.
- Quetiapine (Seroquel) carries a greater cardiometabolic risk than risperidone (Risperdal).

This study presents the first data looking at the differential impact of atypical antipsychotics on nonfasting serum triglycerides (TGs). Olanzapine and quetiapine were associated with the greatest increases in nonfasting TGs. The result for quetiapine agrees with several recent studies suggesting that quetiapine carries a greater cardiometabolic risk than risperidone, formerly grouped with quetiapine in regards to adverse lipid events in a 2004 American Diabetes Association/American Psychiatric Association consensus statement.

Study Background

The Clinical Antipsychotics Trial of Intervention Effectiveness (CATIE) Phase 1 is the largest randomized, double-blind non-industry sponsored antipsychotic study undertaken, and was conducted between January 2001 and December 2004 at 57 US treatment sites. In CATIE Phase 1, outpatients with schizophrenia were assigned to one of four antipsychotics: olanzapine, perphenazine, quetiapine or risperidone. Participants were followed for 18 months or until treatment discontinuation. CATIE Phase 1 showed a differential impact of antipsychotics on fasting and random serum TGs. Other studies have shown an association between worsening lipid profiles and treatment with olanzapine¹ and quetiapine.^{2,3,4,5} Fasting TGs have

¹ Meyer JM, Koro CE. The effects of antipsychotic therapy on serum lipids: a comprehensive review. *Schizophrenia Research* 70:1-17,2004.

² Correll CU: Balancing efficacy and patient safety in treatment with antipsychotics. *CNS Spectrums* 12:12-20, 2007.

³ Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *New England Journal of Medicine* 353:1209-1223,2005.

⁴ McEvoy JP, Lieberman JA, Perkins DO, et al. Efficacy and tolerability of olanzapine, quetiapine, and risperidone in the treatment of early psychosis: a randomized, double-blind 52-week comparison. *American Journal of Psychiatry* 164:1050-1060,2007.

been associated with increased cardiovascular risk.⁶ However, most people are in a nonfasting state most of the day. Moreover, recent studies have shown robust associations between nonfasting TGs and CV risk.^{7,8,9,10} Clinicians still await consensus recommendations regarding whether nonfasting TGs will replace, or be used in addition to, fasting TGs in assessing CV risk.

Study Details

Participants in the CATIE study who were nonfasting, defined as having eaten less than 8 hours before blood draw, were assessed at baseline and at 3 month follow-up. Change in nonfasting triglycerides were compared between antipsychotic groups using various statistical methods in order to assess age, gender, race/ethnicity, smoking status, baseline antipsychotic medication, and baseline fasting TGs. Treatment group comparisons were adjusted for factors found to be statistically significant. Thirty-seven subjects were randomized to the same medication that they had been taking at baseline, which may have underestimated change in TGs at three months. Consequently, a second analysis was undertaken which excluded these nonswitchers.

Results and Limitations

Increases in nonfasting TGs were found for those randomized to quetiapine (adjusted mean +54.7 mg/dl) and olanzapine (adjusted mean +23.4 mg/dl). Ziprasidone was neutral (adjusted mean +0.0 mg/dl). Decreases were found in those treated with risperidone (adjusted mean 18.4 mg/dl) and perphenazine (adjusted mean -1.3 mg/dl). Adjusting for baseline nonfasting TG values showed overall significant treatment differences ($p=0.009$). The second analysis excluding nonswitchers showed that adjusted changes from baseline were highest for olanzapine (+61.5) and quetiapine (+59.8). Decreases were found for risperidone (-13.1), perphenazine (-2.4) and ziprasidone (-1.8). Overall treatment differences were significant at $p=0.001$.

The study was limited by small sample size which precluded stratification by time since last meal, age, gender, or race.

Clinical Implications

The authors note that the result for quetiapine “suggests that quetiapine has a lipid profile distinct from risperidone... in a manner not appreciated several years ago, when the American

⁵ Meyer JM, Davis VG, Goff DC, et al. Change in metabolic syndrome parameters with antipsychotic treatment in the CATIE Schizophrenia Trial: prospective data from phase 1. *Schizophrenia Research* 101:273-286,2008.

⁶ Jeppesen J, Hein HO, Suadicani P, et al. Triglyceride concentration and ischemic heart disease: an eight-year follow-up in the Copenhagen Male Study. *Circulation* 97:1029-1036,1998.

⁷ Bansal S, Buring JE, Rifai N, et al. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *Journal of the American Medical Association* 298:309-316, 2007.

⁸ Nordestgaard BG, Benn M, Schnohr P, et al. Nonfasting triglycerides and risk in myocardial infarction, ischemic heart disease, and death in men and women. *Journal of the American Medical Association* 298:299-308,2007.

⁹ Nordestgaard BG, Benn M, Schnohr P, et al. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *Journal of the American Medical Association* 208:299-308, 2007.

¹⁰ Bansal S, Buring JE, Rifai N, et al. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *Journal of the American Medical Association* 298:309-316, 2007.

Diabetes Association/American Psychiatric Association consensus paper on antipsychotic metabolic effects found these agents comparable on the basis of available data.”¹¹ The authors conclude that this study provides further confirmation of the differential effects of atypical antipsychotics on metabolic profiles, especially for quetiapine, and points to the need for routine monitoring of these parameters in patients treated with atypical antipsychotics.

Potential conflicts of interest were reported for Drs Meyer, Davis, McEvoy, Goff, Nasrallah, Swartz, Stroup, and Lieberman, who report having received research support/funding and/or compensation from various pharmaceutical companies.

¹¹ American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Journal of Clinical Psychiatry* 65:267-272,2004.