

Weight Gain Associated with Long Term Quetiapine Treatment Has No Clear Dose Relationship

The following is an extract of:

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Bottom Line:

- Long term follow-up of weight changes observed in the Astrazeneca clinical trials program after 12, 26, 52 and 104 weeks of quetiapine exposure.
- Quetiapine was associated with significant weight gain ($\geq 7\%$ increase over baseline body weight, as defined by the FDA). 18% of individuals on quetiapine monotherapy had significant weight gain at 12 weeks.
- 39% had significant weight gain at 52 weeks.
- 48% had significant weight gain at 104 weeks.
- There was no clear relationship between dose and weight gain.

Astrazeneca examined the data from their clinical trials program from July 1993-May 1999, and reported weight change for participants treated with quetiapine at 12, 52, and 104 weeks. This study is one of the largest to look at the association between quetiapine treatment and long term weight gain.

Study Background

Among consumers with schizophrenia, weight gain has multiple repercussions, including effects on quality of life, physical health, and treatment adherence. Second generation antipsychotics (SGAs) have been shown to carry variable risk profiles that contribute to increased cardiometabolic risk. While long-term weight gain has been widely recognized to be associated with olanzapine and clozapine, the picture is less clear for quetiapine.

Study Details

This study is a retrospective analysis of information in the Astrazeneca Quetiapine Clinical Trials Safety Database from July 1993 to May 1999, which evaluated the relationship between long term quetiapine treatment and weight gain. Participants had a DSM-IV diagnosis of schizophrenia and were being treated with quetiapine. The primary outcomes were weight change at weeks 12, 52 and 104. Before study entry concomitant medication was stopped, with the exception of concomitant antipsychotics in some open-label extension phases. The FDA definition of clinically significant weight gain ($\geq 7\%$ of baseline body weight) was used. Mean weight change was stratified by baseline BMI and modal daily dose of quetiapine. Weight changes over time were assessed in longitudinal cohorts consisting of patients at 12, 26 and 52 weeks; or 12, 52 and 104 weeks.

Results and Limitations

A total of 378 participants had weight data available at 12 weeks, of whom 340 were on quetiapine monotherapy. Mean weight gain was 1.46 kg (95% CI 0.98-1.95; median 1.15 kg) for all subjects, and 1.48 kg (95% CI 0.98-1.99; median 1.36) for those on monotherapy. Those who were overweight or obese at baseline had no significant weight gain. There was no relationship between quetiapine dose and weight change in the all patients group or those on

monotherapy. Clinically significant weight gain was found in 17.46% (n=66) of all patients and 17.94% (n=61) of patients on monotherapy.

In total, 352 participants had weight data available at 52 weeks, of whom 297 were on quetiapine monotherapy. Mean weight gain was 3.19 kg (95% CI 2.27-4.11; median 2.5 kg) for all patients, and 3.59 kg (95% CI 2.57-4.61; median 3.0 kg) for those on monotherapy. Those with lower BMIs at baseline gained the most weight. Dosage stratification revealed mean weight gains of: 1.54 kg (median 0.95 kg) for <200 mg/day dosages; 4.08 kg (median 3.40) for 200-399 mg/day; 1.89 kg (median 2.00) for 400-599 mg/day; and 3.57 kg (median 3.34) for >600 mg/day. Clinically significant weight gain was found in 37.22% (n=131) of all patients and 38.72% (n=115) of those on monotherapy.

A total of 166 participants had weight data available at 104 weeks, of whom 143 were on quetiapine monotherapy. Mean weight gain was 5.16 kg (95% CI 3.62-6.70; median 4.10 kg) for all patients, and 5.59 kg (95% CI 3.98-7.20; median 4.5 kg) for those on monotherapy. The data on weight gain and baseline BMI was variable. There was no consistent relationship between quetiapine dose and mean weight change in either patient group. Clinically significant weight gain was found in 45.18% (n=75) of all patients and 47.55% (n=68) of those on monotherapy. For two cohorts of participants whose weight data was available at three time points (12, 26 and 52 weeks for one cohort, n=97; and 12, 52, and 104 weeks for the second cohort, n=50), the authors report that most weight gain occurred in the first 12 weeks of treatment. However methods and results were not clearly described for this aspect of the study.

The authors note the following limitations: small sample size at the 104 week time point; retrospective analysis and lack of control group. In addition, individuals with larger amounts of weight gain may have preferentially dropped out of the study.

Clinical Implications

This study provides important information about the long term effects of quetiapine exposure on weight gain. After 2 years on quetiapine, nearly half of exposed individuals have significant weight gain (as defined by FDA, $\geq 7\%$ increase of baseline body weight). Contrary to results from other studies suggesting that weight gain associated with olanzapine or clozapine is dose dependent, results from the current study indicate that weight gain with quetiapine may not be associated with dosage. The authors stress the importance of careful risk-benefit analysis in choosing SGA treatment, especially given the potential for increased morbidity and reduced treatment adherence associated with weight gain.

Disclosure: Drs Brecher, Leong, Stening, Osterling-Koskinen and Jones work for Astrazeneca.