

Consensus development conference on anti-psychotic drugs and obesity: the available evidence does not support the conclusion that certain anti-psychotics drugs are associated with a higher risk of diabetes

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Dear Editor,

We commend the opinion paper in Diabetes Care for focussing our attention on the physical health of people with schizophrenia and serious mental illnesses and on the need for glucose monitoring (1). There is little consensus about the risk of diabetes in people with schizophrenia and the role of atypical anti-psychotic drugs (2-4) and recently I was a member of a group of international psychiatrists and diabetologists who reviewed the evidence surrounding this issue (proceedings to be published in the British Journal of Psychiatry). I was therefore interested to see that the conclusions published in Diabetes Care differed in some respects from our deliberations and those of the US Food and Drug Administration. The FDA wrote in September 2003 to manufacturers of all atypical anti-psychotic drugs to ask that their respective labels be changed to recommend regular glucose testing for all schizophrenia patients at risk of diabetes. The FDA went on to explain that, "Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical anti-psychotics are not available."

The Diabetes Care opinion paper suggests that the risk of hyperglycemia for some "atypicals", such as clozapine and olanzapine, is greater than for others (1). It is unclear how this opinion was reached as, although a bibliography was given, the paper was unreferenced. One may speculate that the weighting given to the 35 retrospective studies was greater than for the prospective trials (4); the placebo-controlled studies (5-7) and the longest prospective study able to assess

glucose over 1 year comparing clozapine and chlorpromazine are not mentioned in the bibliography (8).

None of the retrospective studies can state how many patients given each drug received blood tests. This is a crucial confounder as patients receiving typical anti-psychotics have less blood monitoring than those receiving “atypicals” (9). Any study that introduces glucose screening will undoubtedly find new previously undiagnosed diabetes, because of the high prevalence of undiagnosed type 2 diabetes.

I am unaware of any prospective trial showing any difference between “atypicals” in terms of emergent glucose abnormalities. The best trial data comparing aripiprazole with olanzapine over 6 months found that emergent glucose abnormalities was identical (4.7% vs 4.5%) (5,7). The use of placebo cohorts is critical in understanding what part of the risk of glucose abnormalities is attributable to drugs. There are two such data sets and the incidence of diabetes in the placebo cohorts does not differ from that in the active drug group (5,6).

Interestingly, during the RCTs, weight gain was not associated with the development of diabetes and incidence of diabetes did not differ between the various “atypicals” despite differing propensity for weight gain. Linking short-term weight gain to the risk of diabetes ignores the many other genetic and environmental reasons why people with schizophrenia develop diabetes (10,11).

Anti-psychotic medication is essential for people with schizophrenia and effectiveness should be the most important consideration when selecting

treatment. The FDA was nearer to the mark in its judgement and to choose an anti-psychotic drug on the basis of its potential to worsen glycemia is failing to understand the available data.

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