Evaluation of the metabolic safety of aripiprazole

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Background: Metabolic abnormalities have consistently been identified as a part of schizophrenic illness. With the introduction of second generation antipsychotics and their possible association with metabolic abnormalities, the interest in this topic has been renewed. Many studies have since then provided convincing evidence for a high risk of diabetes and other glucose abnormalities, the metabolic syndrome, lipid abnormalities, increased cardiovascular risk factors and mortality due to elevated cardiovascular risk in patients with schizophrenia. These metabolic abnormalities are of major clinical concern, not only because of their direct, somatic effects on morbidity and mortality, but also because of their association with psychiatric outcome, such as a higher prevalence of psychotic and depressive symptoms, a lower functional outcome, a worse perceived physical health and lower adherence to medication. The reasons that underlie the high prevalence of these metabolic abnormalities are much debated, especially when considering the possible role of secondgeneration, 'atypical' antipsychotics in the occurrence of these abnormalities. Clinical trial data, evaluating patients with fasting blood samples, suggest a metabolic safe profile for aripiprazole.

Method: A large scale metabolic study is ongoing at our University hospital in Belgium. The metabolic safety of aripiprazole was evaluated in a prospective naturalistic study. All patients started on aripiprazole underwent an extensive metabolic evaluation, including an oral glucose tolerance test (OGTT), at baseline, at 6 weeks and at 3 months follow-up. 30 schizophrenic patients were included in the study. 5 patients met criteria for diabetes on their previous antipsychotic treatment at the moment of switch to aripiprazole.

Results: At 3 months follow-up there was a significant reduction in weight and waist circumference. There was a significant reduction in fasting glucose, fasting insulin, insulin resistance and serum lipids (cholesterol, triglycerides, LDH and non-HDL cholesterol). There was also a significant reduction of prolactin. All cases of recent onset diabetes were reversible at 3 months follow-up. Four patients had normal glucose values fasting and at 120 min in the OGTT. One patient had impaired glucose tolerance at endpoint. There were no new cases of emergent glucose abnormalities during treatment with ariprazole. There was a significant reduction in the prevalence of ATP-III metabolic syndrome comparing baseline with endpoint ($p = 0.0011$).

Conclusion: The importance of actively screening for metabolic abnormalities needs to be stressed and, by consequence, the widespread use of adequate screening guidelines is crucial. In choosing between antipsychotic agents the risk-benefit evaluation taking metabolic side-effects is important. This evaluation should also take the existing metabolic risk-factors of the individual patient into account. Our prospective data confirm the metabolic safety of aripiprazole, both on glucose homeostasis and lipids. Our results support the reversibility of recent onset diabetes on antipsychotic medication, if detected early and when switch is done to a safer metabolic antipsychotic.