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Case Report Open Access

Low-Dose, Off-Label Quetiapine Use, Metabolic Syndrome and Impaired Fasting Glucose in an Elderly Man: A Case Report

Margaret K. Hahn[1,2*], **Sylvia Gomes**[1] **and Gary J. Remington**[1,2]

[1]*Center for Addiction and Mental Health, 250 College Street, Toronto, Ontario, Canada*

[2]*Department of Psychiatry, University of Toronto, 1 King's College Circle, Toronto, Ontario, Canada*

[*]**Corresponding author:** Margaret K. Hahn, Center for Addiction and Mental Health 250 College Street, Toronto, Ontario, Canada M5T 1R8, Tel: 416535-8501; Fax: 416979-4292; E-mail: maggie.hahn@utoronto.ca

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Abstract

'Atypical' antipsychotics (AAPs), which have been associated with serious metabolic side effects, are increasingly being used for off-label indications other than psychosis, with little guidance available in this context as to risk of side effects, or monitoring.

Here we report on a case of emergent metabolic syndrome, in association with low-dose quetiapine used for insomnia in an elderly gentleman, which reversed following quetiapine discontinuation.

Case Report

Mr. S was a non-smoking, 71-year-old Caucasian male with a longstanding history of recurrent major depressive disorder, and posttraumatic stress disorder. He was hospitalized for recurrence of a depressive episode, associated with initial insomnia, but no reported changes in appetite or objective changes in weight. His medications at the time included: Phenelzine 45 mg, gabapentin 1800mg, Clonazepam 1 mg, Nabilone 2 mg, Bisoprolol 7.5 mg, Diclofenac 60 mg QID, Rosuvastatin 10 mg OD, and had remained unchanged for the 2 preceding years. His metabolic profile was largely unremarkable, with a weight of 74.5 kg (BMI of 25.1 kg/m^2), waist circumference of 95cm, fasting glucose 5.2 mmol/L, fasting insulin 37 pmol/L, total cholesterol 3.7 mmol/L, HDL 1.34 mmol/L, LDL 1.64 mmol/L, and triglycerides 1.58 mmol/L. Repeated blood pressure (BP) measures were within normal limits (<130/80). A review of his family history indicated that his father suffered from hypertension, and had a stroke in his 70ies. There was no other family history of cardiovascular illness, or related risk factors. Quetiapine was initiated and titrated to a dose of 300 mg, but due to postural hypotension, decreased to 50mg within 4 weeks of initiation, a dose that appeared to help with the reported insomnia.

Mr. S was referred to our Metabolic Clinic due to concerns of weight gain, 3.5 months after initiation of the quetiapine (50 mg), during which time his other medications had remained unchanged. With no reported associated lifestyle changes, there was a 10 kg increase in weight (BMI of 27), an increase in waist circumference to 114 cm. Fasting glucose increased to 6.1 mmol/L (repeated on 2 separate measurements), and fasting insulin rose to 74 pmol/L. The lipid profile indicated a decrease in HDL to 0.99mmol/L, and an increase in triglycerides to 1.94 mmol/L. Repeated BP measures suggested hypertension (>140/80). As such, Mr. S met full criteria for the metabolic syndrome, according to the National Cholesterol Education Program (NCEP) criteria [1]. Given the deterioration in metabolic profile, quetiapine was tapered and discontinued over the next month. Clonazepam was increased to 6mg to help with the sleep disturbance.

When the patient returned for follow-up 4 months following quetiapine discontinuation, other than an increase in phenelzine to 60 mg, no medication changes had occurred. By self-report, his activity levels decreased due to an exacerbation of fibromyalgia. His weight decreased to 74.5 kg, waist circumference to 98 cm, and aside from triglycerides remaining marginally elevated (1.87 mmol/L), all other metabolic parameters, including BP returned to normal.

Discussion

Despite a growing body of literature around metabolic abnormalities associated with AAP use, there remains a paucity of data regarding the relationship between dosing and metabolic side effects. This issue may be particularly relevant in the context of growing off-label use of these agents for conditions other than psychosis, where doses tend to be lower than those used for approved indications such as schizophrenia or bipolar disorder [2], with little to no guidance existing as to risk, or metabolic monitoring. Further, how age may factor into metabolic risk remains an interesting question, with some suggestion that geriatric patients as a group may be less prone to antipsychotic-induced weight gain [3-5].

Quetiapine, due to sedative and anxiolytic properties, has gained widespread off-label use for insomnia, headaches, and agitation in delirium or dementia [6]. Two recent studies in non-elderly populations examined use of quetiapine at doses below 200mg for insomnia, reporting a significant weight gain [7,8]. In a recent review, no association was found between quetiapine dosing and weight gain [9], supporting the notion that metabolic deterioration could occur at a lower end of dosing. This is in agreement with our report of emergence of metabolic syndrome (5/5 criteria), in association with quetiapine 50 mg, with reversal of the noted abnormalities four months after quetiapine discontinuation. To support causality, the Naranjo criteria would suggest a probable adverse drug reaction [10]. It is also noteworthy that this occurred in an elderly gentleman who

might be considered at reduced risk for antipsychotic-induced metabolic side effects compared to younger individuals. Moreover, a lack of family history of type 2 diabetes (which can have strong genetic determinants) [11], supports the inherent risk of antipsychotic drugs to induce changes in glucose metabolism.

Taken together these data suggest that clinicians should not assume that the improved tolerability of AAPs compared to their conventional counterparts, in combination with the lower doses often associated with off-label use, translates to absence of serious side effects. Future studies examining the relationship between dose, age and adverse side effects are required. In the meantime, physicians should at minimum employ metabolic screening according to current guidelines [12], regardless of indication, patient age, or prescribed antipsychotic dose.

Disclosures

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