Olanzapine associated heart block in weight-restored anorexia nervosa

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Anorexia nervosa is a serious psychiatric disorder but the search for disease-modifying biological agents have yielded few options. This case describes the efficacious use of olanzapine off-label in weight restoration in an adolescent. However, occurrence of first-degree heart block during treatment flags up a need for cardiac monitoring with such treatment across this age group.

Eating disorders include several debilitating conditions, defined by maladaptive eating patterns and pervasive difficulties with body image. Anorexia nervosa (AN) is a serious psychiatric disorder with lifetime prevalence estimated at 0.9%. For individuals 15-24 years old, prevalence rates are closer to 0.5%.[1,2] Since the 1980s, there has been growing awareness of the level of biopsychosocial impairment resulting from AN, especially in the child and adolescent population. To date, few treatments have been shown to be efficacious in adolescents, eg family based therapy, and overall treatment success rates are limited.[2]

The search for a curative or disease-modifying biological agent for AN has yielded few options, with variable degrees of evidence. Weight restoration is one of the primary aims of a treatment. Therefore, developing pharmacological agents that support dietary rehabilitation and weight restoration has been a focus for researchers. Atypical antipsychotics are thought to modify both low weight and cognitive symptoms.[1] A small randomised controlled trial by Bissada *et al*[1] showed olanzapine to be not only more effective in weight restoration compared with placebo ($p<0.001$), but also did so at a faster rate. Additionally, olanzapine impacted cognitive symptoms, with a greater reduction in obsessive scores on the Yale-Brown Obsessive Compulsive Scale compared with placebo ($p<0.02$). Although atypical antipsychotics are not officially approved in any country for adolescents with AN, they have regularly been employed off-label or to treat comorbidity.[3] Despite the mixed results in the degree and significance of benefits for eating disorder symptoms, olanzapine remains a reasonable treatment choice for the more serious and treatment resistant cases of AN. Since most side effects are studied in the adults, careful consideration should be given for its use in children and adolescents.

Presentation

Our case is of a 16 year-old girl, admitted for weight restoration to a psychiatric inpatient unit with a body mass index (BMI) of 17.6kg per m^2. During admission, olanzapine was initiated to facilitate this goal and also to decrease cognitive rigidity and obsessionality regarding over-exercising. Overall, the patient tolerated monotherapy on olanzapine up to 7.5mg daily and achieved adequate weight restoration to calculated ideal body weight for age and height. The patient had no previous trials of any psychopharmacological agent and had neither psychiatric nor medical co-morbidity. She had neither family nor past history of cardiac morbidity. A physical examination and echocardiography revealed normal cardiac structure and function during the admission.

Olanzapine was initiated at the smallest available dose of 2.5mg daily and increased by the same increment over one month. The patient tolerated olanzapine throughout, with no reported side effects. Gradual improvement with above average weight restoration (0.5-1kg/week), reduction in obsessive exercising and increased tolerance of mealtimes was achieved during hospitalisation. These gains were especially evident following weight restoration at Week 4 of treatment at a dose of 7.5mg daily with a BMI of 18.7kg per m^2. The patient was deemed vitally stable throughout treatment, without orthostatic blood pressure or heart rate change abnormalities.

All re-feeding protocols recommend monitoring of cardiac status using electrocardiograms at baseline and at regular intervals thereafter. With the addition of antipsychotic treatment, this became mandatory. Therefore, a brief period of nightly heart rate

monitoring was initiated. Routine biochemistry and haematological investigations completed throughout re-feeding were insignificant.

Electrocardiogram at baseline immediately prior to treatment with olanzapine showed sinus rhythm, with a heart rate of 55 beats per minute, PR interval of 166 milliseconds and a corrected QT (QTc) interval of 383-420 milliseconds. However, a week later the PR interval increased to 176 milliseconds while on olanzapine. In spite of weight restoration at Week 4 of treatment PR interval continued to increase to reach a maximum of 264 milliseconds; diagnostic of first-degree atrioventricular (AV) block. Since the patient was completely asymptomatic from a cardiac standpoint, and had shown a positive therapeutic response with weight restoration, the dose of olanzapine was cautiously maintained at 7.5mg, with a plan to closely monitor any rhythm abnormalities. Repeat ECGs over the next 10 days showed persistent first-degree AV block, with PR interval ranging 190-252 milliseconds. No other arrhythmias were documented and QTc remained within normal limits. Due to the persisting first-degree AV block, the treating physician discontinued olanzapine. The patient had a BMI of 19.89kg per m^2 at the time of discontinuation. The PR interval gradually normalised over the following four weeks to 174 milliseconds with stable weight within range of ideal body weight for height and age maintained. Olanzapine was used for a total duration of six weeks. The patient was weight restored for the last two weeks of her treatment with olanzapine, which coincided with the most significant PR interval quoted.

Discussion

Prolongation of PR interval is not listed as a side effect of olanzapine. However, first-degree AV block and prolongation of PR and QTc intervals have been reported in adult patients with schizophrenia treated with olanzapine.[4] In our search, we came across one case of PR prolongation in an adolescent – a 12-year-old boy prescribed olanzapine for aggressive behaviour. Although this case suggested causality, the presence of other psychotropic medications, including lithium, were confounding factors.[5] Furthermore, investigation with electrocardiogram for the quoted case was prompted by an episode of chest pain. This feature was not seen in our patient, who remained asymptomatic of subjective cardiac symptoms. While no major cardiac rhythm abnormalities have been so far reported with the use of olanzapine, it seems reasonable at the present time to monitor cardiac conduction across the age range, with a focus on serial estimation of PR and QTc intervals using routine electrocardiograms throughout treatment with olanzapine, especially in cases of co-morbid malnutrition.

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Declaration of interests

No conflicts of interest were declared.

References:

1. Bissada H, Tasca GA, Barber AM, *et al.* Olanzapine in the treatment of low body weight and obsessive thinking in women with anorexia nervosa: a randomized, double-blind, placebo-controlled trial. *Am J Psychiatry* 2008;165:1281–8.
2. Brown TA, Keel PK. Current and emerging directions in the treatment of eating disorders. *Subst Abuse* 2012;6:33–71.
3. Balestreiri M, Oriani MG, Simoncini A, *et al.* Psychotropic drug treatment in anorexia nervosa. Search for differences in efficacy / tolerability between adolescent and mixed-age population. *Eur Eat Disord Rev* 2013;3:361–73.
4. Suzuki Y, Sugai T, Ono S, *et al.* Changes in PR and QTc intervals after switching from olanzapine to risperidone in patients with stable schizophrenia. *Psychiatry Clin Neurosci* 2014;68:353–6.
5. Rajput MI, Singh T, Rais T. Olanzapine and prolonged PR interval. *Psychiatry* (Edgmont) 2006;3(3):9.