CASE REPORT
IN PSYCHIATRY

Quetiapine-related weight loss: Report of a rare adverse effect

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Abstract

Quetiapine is a second-generation antipsychotic that has been reported to be associated with moderate weight gain. Nevertheless, weight loss that is an infrequent adverse effect of quetiapine has been reported in a few cases of patients who were ab initio started on quetiapine or who gained weight during previous antipsychotic treatment but who lost weight when shifted to quetiapine. We report the case of a 28-year old quarry worker being treated for bipolar affective disorder. Due to unbearable muscle rigidity, she was switched from haloperidol to olanzapine. She gained about 26 kg over 12 months. Her repeated complaints about the weight gain and threats to stop all medications if nothing was done led to her being switched over to quetiapine. Within two months of this switch-over, she gained 1 kg before she gradually started losing weight and by the sixth month, she dropped from 85 kg to 67 kg despite eating well. Unsatisfied with the weight loss, she was switched to aripiprazole. Over few months, she gained up to 3 kg. She had remained mentally stable and functional, and also maintained roughly 70 kg over a year. Though weight gain could occur in virtually every antipsychotic, weight loss has been recorded in very few cases. The mechanism by which quetiapine causes weight loss is not certain. Some proposed mechanisms include paradoxical suppression of appetite, induction of deterioration in insulin resistance, induction of hypoglycaemia, as well as mere switching from a high-risk to a low-risk antipsychotic. Our patient had different experiences with three atypical antipsychotics: she gained excessive weight with olanzapine, lost significant weight with quetiapine, and maintained a normal weight with aripiprazole. Weight changes should be monitored on patients taking antipsychotics. Most of the time clinicians are concerned about weight gain but not weight loss. We recommend that clinicians should pay attention to weight loss as well.

KEY WORDS: Antipsychotics; quetiapine; switch-over; weight loss.

Riassunto

La quetiapina è un antipsicotico di seconda generazione che è stato associato ad un moderato aumento di peso. Tuttavia, la perdita di peso, che è un effetto negativo poco frequente della quetiapina, è stato riportato in alcuni pazienti trattati fin dall'inizio con la quetiapina o che avevano guadagnato peso durante precedenti terapie antipsicotiche perdendolo nel passaggio alla quetiapina. Noi riportiamo il caso di una donna di 28 anni, operaia nelle cave di marmo, trattata per un disturbo affettivo bipolare. A causa di un insopportabile rigidità muscolare, l'alloperidolo venne sostituito con l'olanzapina. Lei prese circa 26 Kg in 12 mesi. Le sue continue lamentele sull'aumento di peso e le minacce di non proseguire la terapia portarono allo switch terapeutico con la quetiapina. Nel giro di due mesi, la paziente guadagnò 1 Kg prima di perdere progressivamente peso, passando entro il sesto mese dall'inizio della terapia da 85 Kg a 67 Kg, nonostante conservasse un buon appetito. Non soddisfatta della perdita di peso, venne modificata la terapia alla paziente che iniziò ad assumere l'aripiprazolo. Nel giro di pochi mesi guadagnò 3 Kg. Ella rimase mentalmente stabile e funzionale e mantenne circa 70 Kg di peso per un anno. Sebbene l'aumento di peso possa verificarsi praticamente in tutti gli antipsicotici, la perdita di peso è stata registrata solo in pochi casi. Il meccanismo con cui la quetiapina causi la perdita di peso non è certo. Alcuni hanno ipotizzato meccanismi che includono la paradossale perdita di appetito, l'induzione dell'insulino- resistenza o di ipoglicemia, cosi come il semplice passaggio da antipsicotici ad alto rischio ad antipsicotici a basso rischio. La nostra paziente provò differenti esperienze con tre antipsicotici atipici: aumentò eccessivamente di peso con l'olanzapina, perse peso in modo significativo con la quetiapina e mantenne un peso normale con l'aripiprazolo. I cambiamenti di peso dovrebbero essere monitorati nei pazienti che assumono antipsicotici. La maggior parte delle volte i clinici sono preoccupati dell'aumento ma non della perdita di peso. Raccomandiamo che i clinici prestino attenzione anche alla perdita di peso.

TAKE-HOME MESSAGE

Quetiapine, a second-generation antipsychotic associated with moderate weight gain, could also cause severe weight loss. Clinicians are reminded that while routinely enquiring about weight gain from patients on antipsychotics, they should also remember to enquire about weight loss which, though occurs rarely, could be severe especially with quetiapine medication.

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INTRODUCTION

The second-generation antipsychotic medications (aripiprazole, clozapine, olanzapine, quetiapine, risperidone, etc.) represent a new generation of therapies that have been reported to have greater efficacy, especially for negative symptoms, and fewer extrapyramidal side effects than first-generation antipsychotic drugs [1]. These new generation drugs have some benefits over their older counterparts but these benefits are not without a price. Weight gain has become a significant issue with the use of new generation antipsychotic medications [2–4], and it has been found to lead to noncompliance with medication regimens and medical complications including metabolic syndrome [5]. Quetiapine is a second-generation antipsychotic that blocks both dopamine and serotonin (5HT) receptors. Like most other second-generation antipsychotics, weight gain is a significant side effect associated with quetiapine use [2, 3, 6]. Nevertheless, weight loss is an infrequent adverse effect of quetiapine that has been reported in a few cases of patients who were *ab initio* started on quetiapine or who gained weight during previous antipsychotic treatment but who lost weight when shifted to quetiapine [7, 8].

CASE REPORT

Here we report a case of a gradual significant weight loss of up to 18 kilograms associated with the use of quetiapine. Our patient was a 28-year old married quarry worker whose first episode of mental illness occurred about 5 years before she presented at our department. She was referred by early 2015 from a private health facility to our psychiatric centre following her relocation of residence. She was being managed for bipolar affective disorder and her personal history revealed about four previous relapses, usually in manic phases. On referral, we continued her previous medications – oral haloperidol 5 mg bd and sodium valproate 200 mg bd. However, by mid-2015, she relapsed and was admitted for two weeks. Admission weight was 58 kg. On admission, she was given parenteral haloperidol, 5 mg and diazepam 10 mg, each 12 hourly for 72 hours. She became rigid the second day into admission and swore never to be placed on haloperidol of any form. She was, therefore, placed on oral olanzapine 10 mg nocte and sodium valproate 200 mg twice daily. Her weight at discharge was 60 kg and this rose to 84 kg in the next 11 months. She kept complaining about the weight gain and threatened to stop the medications if nothing was done about that. In July 2016, she was gradually switched over to quetiapine, 200 mg nocte with sodium valproate retained at the usual dose. She gained 1kg in about 2 months before she gradually started losing weight and by the sixth month, her weight dropped from 85 kg to 67 kg. She complained again that she did not like the way she had rapidly slimmed down despite that she was eating adequately. She was referred to two physicians – a gastroenterologist and an endocrionologist – who thoroughly reviewed and did not find anything to hold as the cause of the weight loss. A thorough metabolic work-up comprising investigations to rule out malignancy as well as laboratory tests like complete blood count, liver function test, serum electrolytes, urea, and creatinine, fasting blood sugar, as well as a brain and abdominal computed tomography scan were carried out but no positive finding suggesting the cause of the weight loss was found. Then, she was switched over from quetiapine to aripiprazole, 10 mg nocte. Within three months, she gained up to 3 kg, giving 70 kg – a weight she had maintained for over a year. She had remained mentally stable on her present daily doses of 10 mg and 400 mg, aripiprazole and sodium valproate, respectively. She was repeatedly screened for depression without any positive finding.

DISCUSSION

Quetiapine is an atypical antipsychotic of the dibenzothiazepine derivate with N-desalkyl quetiapine as the active metabolite. In human serum, quetiapine and its active metabolite have greater affinity at serotonin ($5HT_2$) and dopamine $D_1$and D_2 receptors [6]. They also have high affinity at histamine and adrenergic

Alpha 1 receptors, and moderate affinity to Alpha 2 adrenergic and serotonin $5HT_{1A}$ receptors. The indications of quetiapine include the treatment of schizophrenia, bipolar disorders, and other mood spectrum disorders. Antipsychotic agents differ in their potential to cause weight gain. Studies have proven that clozapine and olanzapine cause most weight gain and have the greatest maximal weight gain liability [9–11]. Many studies have also reported quetiapine therapy to be associated with moderate weight gain [3, 6, 12–14] and ziprasidone to have the least risk [15]. Grahovac and colleagues [6] reported a case of a 33-year old female being treated for schizoaffective disorder who gained as much as 19 kg within two months of quetiapine medication. Weight gain usually results from increased appetite - a common side-effect of many atypical antipsychotic drugs - and subsequent excessive food consumption.

Though weight gain is seen in virtually every antipsychotic, weight loss has been recorded in only few of them, especially quetiapine [16]. The mechanism by which quetiapine causes weight loss is not very certain. Some mechanisms have been proposed such as paradoxical suppression of appetite, induction of deterioration in insulin resistance [17], induction of hypoglycaemia [18, 19], and so on. Switching from a high-risk antipsychotic to a low-risk antipsychotic is known to usually mitigate or reverse weight gain [20]. Yoshino and colleagues reported a case of a 19-year young female who lost weight while being managed for schizophrenia with quetiapine. The weight loss was attributed to deterioration in insulin resistance induced by quetiapine [17]. In a 10-week open-label study to investigate the strategy of switching patients who had gained excessive weight on olanzapine to quetiapine, it was reported that the 12 participants who had gained over 20% weight and had body mass index of over 25 m^2/kg each on olanzapine had a mean weight loss of 2.25 kg within 10 weeks of being switched to quetiapine [21]. The authors were of the view that switching patients to quetiapine would be a viable strategy for managing olanzapine-induced weight gain.

Our patient gained as much as 26 kg over a year while on olanzapine. When she was switched to quetiapine her weight increased slightly by 1 kg in 2 months before she started slimming down to the extent of losing up to 18 kg in six months despite that her appetite remained good. The source of the weight loss could not be detected following thorough evaluations. On replacement of quetiapine with aripiprazole, she started regaining weight and within 3 months, regained about 3 kg. The pattern of weight increase shortly after the commencement of quetiapine before a gradual decline is similar to that reported by Khawaja and his team [8]. They reported the case of a 68-year old Caucasian male who gained five pounds in 24 months while he was taking olanzapine but for the unbearable sedative effect, he was changed to quetiapine during which he had his weight increased from 138 pounds (on olanzapine) to 140 pounds. After taking quetiapine for five months, the patient started to experience a significant reduction in his appetite and subsequently stopped eating entirely on the grounds that he was not hungry at all, and he began to lose weight, losing up to 21 pounds within four months [8]. In our own patient, however, there was no associated loss of appetite or failure to eat. Our patient could not be maintained on haloperidol as well as olanzapine (an atypical antipsychotic). Also, while on quetiapine, she developed a worrisome weight loss that led to a thorough metabolic work-up whose results were unremarkable. These were similar with the case reported by Demily and colleagues [22]. Their patient was a 37-year-old man with a 22q11.2 deletion syndrome, who developed schizophrenia when he was 20 years old but failed to derive benefits from treatments by atypical antipsychotics and haloperidol and when he was switched-over to quetiapine, he lost a terrible weight (-17,6 Ib) within 3 months. We were convinced that quetiapine was the cause of the weight loss. To the best of our knowledge, this is the first report of quetiapine-induced weight loss in sub-Saharan Africa.

CONCLUSION

This case illustrates the importance of monitoring weight changes among patients who are taking second-generation antipsychotic medications. Most of the time clinicians are concerned about weight gain but not weight loss. With the newer medications, which might be weight neutral, clinicians should pay attention to weight loss as well.

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