

REVERSAL OF WEIGHT GAIN WITH CONCURRENT NORMALIZATION OF FASTING GLUCOSE AND MARKED REDUCTION IN TRIGLYCERIDE AFTER CLOZAPINE DOSE-REDUCTION AND SIMPLIFICATION OF OTHER PSYCHOTROPICS IN CHRONIC SCHIZOPHRENIA: A CASE REPORT

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INTRODUCTION

Cardiovascular disease is the leading cause of death for patients with schizophrenia. One contributing factor is prevalent metabolic syndrome among these patients. Second-generation antipsychotics (SGAs), the current mainstream treatment in schizophrenia, are associated with weight gain, glucose intolerance and dyslipidemia (most notoriously clozapine and olanzapine) (Simon et al. 2009). Effective strategies to address these metabolic side effects are currently lacking.

Herein we present a case with schizophrenia for whom dose-reduction of clozapine and simplification of other psychotropics led to reversal of weight gain and concurrent normalization of fasting glucose and marked reduction in triglyceride.

CASE REPORT

A 50-year-old single male patient was admitted to the psychiatric acute ward for shouting and destructive behaviors under influences of auditory hallucinations and delusions of persecutory and grandiose themes. There were several hospitalizations in the recent one year due to refractory psychosis, and currently he took clozapine 725 mg/day, amisulpride 400 mg/day, haloperidol 17.5 mg/day, valproate 2000 mg/day with a serum level of 63 mcg/ml, and clonazepam 4 mg/day. He also took clonidine 0.15 mg/day and propranolol 40 mg/day for sialorrhea and akathisia respectively.

He had been treated under diagnosis of schizophrenia for 33 years with unrelenting course. He suffered from hallucinations, delusions and loosening of association on a continuous basis. He showed behavioral disturbances in acute phases, and led a loose life with poor self-hygiene at home in chronic phases. He had a height of 179 cm and maintained a weight of 85 kg throughout the illness. His medical history was unremarkable. There was no family history of diabetes mellitus, hyperlipidemia or hypertension. One year ago, clozapine was initiated for unremitting psychosis, with gradual dose-escalation and

subsequent combination with various psychotropics due to limited effect. At the same time, he had increased appetite and gradually gained weight.

On admission, he weighed 100 kg with a body mass index (BMI) of 31.2. He had fasting glucose of 126 mg/dL, triglyceride of 314 mg/dL and total cholesterol of 161 mg/dL. There was constant and profuse drooling by Drooling Frequency and Severity Scale (DFS) (Camp-Bruno et al. 1989), and prominent sedative effect. Considering the already complicated medication regimen with doubtful therapeutic effect, poor metabolic profile, and significant side effects hindering self-hygiene and psychosocial intervention for his behavioral disturbances, we adopted a strategy of minimizing current medication. Clozapine was tapered down to 400 mg/day, and haloperidol and clonazepam was tapered off gradually over 10 weeks. At the same time, amisulpride and valproate were titrated up to 800 mg/day and 2500 mg/day respectively, to address the fluctuation of his psychotic symptoms. At this dose, we were able to halve the dose of clonidine and propranolol. Otherwise, he was given regular inpatient treatment, without structured psychotherapy, exercise program or diet control.

As a result, he was less sedated, had occasional and mild drooling by DFS, and better self-hygiene. Besides, he controlled himself better under limitation-setting despite ongoing hallucinations and delusions. And unexpectedly, his weight decreased to 84 kg, with concurrent decreases of fasting glucose, triglyceride and total cholesterol to 91, 172 and 149 mg/dL respectively.

DISCUSSION

In this case, clozapine dose-reduction and simplification of other psychotropics led to reversal of weight gain associated with escalation of medication, with concurrent normalization of fasting glucose and marked reduction in triglyceride (Table 1). He also had better self-hygiene and behavior-control under decrease in side effects of sialorrhea and sedation.

Table 1. Changes in medication and metabolic profiles during hospitalization in our case

	At admission	At 10 weeks
Medication (mg/day)		
Clozapine	725	400
Amisulpride	400	800
Haloperidol	17.5	discontinued
Valproate	2000	2500
Clonidine	0.15	0.075
Clonazepam	4	discontinued
Propranolol	40	20
Metabolic profile		
Body weight (kg)	100	84
Body Mass Index	31.21	26.22
Fasting glucose (mg/dL)	126	91
Triglyceride (mg/dL)	314	172
Cholesterol (mg/dL)	161	149

Weight gain in patients receiving SGAs is well recognized and may be dose-dependent (Simon et al. 2009). Increased appetite is postulated to be the mechanism (Blouin et al. 2008). One pharmacological strategy for obese schizophrenia patients taking SGAs is switching to other medications of lower propensity for weight gain, such as ziprasidone, amisulpride, paliperidone, or aripiprazole (Brixner et al. 2006). One recent review showed that antipsychotic switching for schizophrenia patients with antipsychotic-induced weight or metabolic problems led to mean weight reduction of 1.94 kg and favorable fasting glucose and lipid profile within 26 weeks (Mukundan et al. 2010). In our case, increased appetite and weight gain paired with initiation and dose-escalation of clozapine. The case is unusual for losing 14 kg in only 10 weeks, under dose-reduction rather than switching of clozapine. This change of 14% bodyweight is clinically significant (Deberdt et al. 2005). There was also dramatic improvement of metabolic profiles, with 45.2%, 27.8% and 7.5% reduction in triglyceride, fasting glucose and total cholesterol respectively.

The weight and metabolic changes in our case may not be fully explained by dose-reduction of clozapine. Other factors should also be considered, such as the milieu effect of hospitalization, concurrent simplification of other psychotropics, and better self-regulation after medication adjustment. We tapered off haloperidol and clonazepam and halved the doses of propranolol and clonidine; all of these medications have been reported to be associated with weight gain (Blasi 2000, Martinez-Mir et al. 1993, Saddichha et al. 2008, Schlemmer et al. 1979).

Polypharmacy with different combinations of antipsychotics are well recognized in schizophrenia patients with profound side effects. Supporting evidence for this kind of use is lacking. Studies have shown that it's possible to simplify the regimen and decrease the dosage with better clinical outcome,

especially when the dosage is high (Tani et al. 2012). In our case, antipsychotics of equivalent chlorpromazine dose were decreased from 2725 mg daily to 1600 mg daily, a 41.3% reduction. We also tapered off the sedatives. Consequently, apart from more favorable metabolic profiles, he suffered from less side effects such as sialorrhea and sedation, which led to better functional outcome including self-hygiene and behavioral control.

There are some limitations in this case report. We have no access to the patient's records of previous use of psychotropic medication before the initiation of clozapine. His age should also be considered as a risk factor for developing metabolic disturbances. Furthermore, we do not follow this patient for longer time to see if the improvement of metabolic parameters is maintained on this dosages and drug regimens.

CONCLUSIONS

Metabolic syndrome is prevalent among schizophrenia patients under treatment of SGAs, and should be regularly monitored. Management may start from review and minimization of current medications, especially in treatment-refractory patients with irrational escalation to high doses of antipsychotics and polypharmacy. Apart from switching to antipsychotics of fewer propensities to cause weight gain and metabolic problems, simply dose-reduction may also have significantly positive metabolic impact. Simplification of medication in chronic schizophrenia patients may also have positive functional outcome due to decreased side effects such as sedation or cognitive impairment. Since medication is an important modifiable factor in the management of schizophrenia patients, cautious use with regular review is the best policy.

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