

WEIGHT LOSS DURING THERAPY WITH OLANZAPINE ORALLY DISINTEGRATING TABLETS: TWO CASE REPORTS

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SUMMARY

The aim of this article is to report weight loss in patients with schizophrenia after switching from olanzapine standard oral tablet (SOT) to olanzapine orally disintegrating tablets (ODT).

In the first case report, the patient was switched to olanzapine ODT in daily dosage of 20 mg, while in the second case report, the patient was switched to olanzapine ODT in daily dosage of 15 mg, and weight loss was similar (14 kg vs. 15 kg). Switching patients from olanzapine SOT to olanzapine ODT treatment resulted in significant weight loss that was maintained during 12 months in both case reports. Further controlled clinical investigations are necessary to evaluate change in weight during treatment with olanzapine ODT, and to improve our understanding of this change.

Key words: olanzapine – schizophrenia - weight loss - treatment

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INTRODUCTION

Several papers and communications have reported possible weight reduction or less weight gain when patients start or switch to orally disintegrating olanzapine, as contrasted with standard oral olanzapine tablets. The data are still preliminary and mechanisms of action are not well understood (Karagianis et al. 2008). Still, difference in absorption between olanzapine orally disintegrating tablets (ODT) and olanzapine standard oral tablets (SOT) is suggested to be important regarding this matter. Partial sublingual absorption occurring with orally disintegrating olanzapine may bypass gastrointestinal metabolism and hence lead to differences in metabolite versus parent compound ratios (Arranz et al. 2007).

The findings of an investigation that compared the changes in weight (kg) and body mass index (BMI) (kg/m²) in hospitalized adolescents between baseline and after 12 weeks of monotherapy with either olanzapine ODT, or olanzapine SOT, or risperidone suggested that adolescents gain less weight with OLZ ODT than OLZ SOT,

possibly because the former formulation shortens the time of interaction with digestive serotonin receptors mediating satiety (Crocq et al. 2007).

The aim of this article is to report weight loss in patients with schizophrenia after switching from olanzapine SOT to olanzapine ODT.

CASE REPORT 1

Patient Z-P (male, 56 years old), with diagnosis of schizophrenia, according to Diagnostic and statistical manual of mental disorders (DSM-IV-TR) (APA 2000), who was clinically stable on olanzapine SOT treatment was switched to olanzapine ODT. Prior to initiation of olanzapine ODT, the patient received olanzapine SOT in daily dosage of 20 mg during period of six months, and during this period gained 22 kg. The patient was not receiving any concomitant medication during the same period, and no other changes of therapy were made. Weight was measured before switching to olanzapine ODT, after 1, 2, 3, 6, and 12 months of therapy with olanzapine ODT. Baseline body weight was 105

kg. The observed weight loss on the following assessments was 8 kg after one month, 10 kg after two months, 12 kg after three months and 15 kg after six months. During the observed period the patient received olanzapine ODT in daily dosage of 20 mg and at 12 months recorded weight loss was 15 kg. Peak weight loss was observed at five months. The patient did not have any other changes regarding treatment, or generally in the behavior regarding health habits and life style.

CASE REPORT 2

Patient D-G (female, 38 years old), with diagnosis of schizophrenia, according to DSM-IV-TR (APA, 2000), who was clinically stable on olanzapine SOT treatment was switched to olanzapine ODT.

Prior to initiation of olanzapine ODT, the patient received olanzapine SOT in daily dosage of 15 mg during period of one year, and during this period gained 10 kg. The patient was taking zolpidem 10 mg in the evening during the same period. Weight was measured before switching to olanzapine ODT, after 1, 2, 3, 6, and 12 months of therapy with olanzapine ODT.

Baseline body weight was 78 kg. The observed weight loss on the following assessments was 6 kg after one month, 10 kg after two months, 11 kg after three months and 14 kg after six months.

During the observed period the patient received olanzapine ODT in daily dosage of 15 mg during 12 months. At 12 months recorded weight loss was 14 kg. Peak weight loss was observed at five months.

The patient started working two weeks after baseline. The patient did not have any other changes regarding treatment, or generally in the behavior regarding health habits and life style.

DISCUSSION

Here we reported weight decrease after switching from olanzapine SOT to olanzapine ODT what can have significant implication for the patients.

In the first case report, the patient was switched to olanzapine ODT in daily dosage of 20

mg, while in the second case report, the patient was switched to olanzapine ODT in daily dosage of 15 mg, and weight loss was similar (14 kg vs. 15 kg). In the second case report, the patient started working two weeks after baseline. The patients did not have any other changes regarding treatment, or generally in their behavior regarding health habits and life style. Obesity related weight gain is one of the criteria for metabolic syndrome, a risk factor for the development of cardiovascular disease and diabetes mellitus type 2. Anti-psychotic-induced weight affects 80% of individuals being treated with antipsychotic drugs (Alvarez-Jiménez et al. 2008). In short-term studies, a definite rank order of weight-gain potential among atypical antipsychotics has been demonstrated: clozapine is related to the highest risk of weight gain, followed in decreasing order of magnitude by olanzapine, quetiapine, risperidone, amisulpride, aripiprazole and ziprasidone. However, in long-term studies, except for clozapine at one end of the scale and ziprasidone at the other, the differences in weight-gain liability showed by the other atypical antipsychotics became less intense (Gentile 2006).

In the study whose objective was to investigate the long-term weight loss outcomes during usual clinical practice after switching from SOT to olanzapine ODT, the results showed that patients incurred an average weight loss of 2.7 +/- 0.7 kg ($p = 0.001$) after switching patients from olanzapine SOT to olanzapine ODT at 12 months. Peak weight loss was observed at 6 months; however, significant weight loss was achieved as early as 3 months. Patients treated with higher doses of olanzapine ($>$ or $=$ 20 mg) incurred a greater weight loss of their body weight, compared to those treated with lower doses ($<$ 20 mg). Authors concluded that the study demonstrated that, in usual clinical practice, switching patients from olanzapine SOT to olanzapine ODT treatment resulted in significant weight loss that was maintained over 12 months (Chawla & Luxton-Andrew 2008).

The difference in absorption between olanzapine ODT (partial bypassing of gastrointestinal metabolism leading to differences in metabolite versus parent compound ratios) and

olanzapine SOT is probably important regarding weight loss, as suggested in an earlier article (Arranz et al. 2007).

So far, results of investigations showed variation of the degree of weight gain within drug classes (Arranz et al. 2007, Üçok & Gaebel 2008). A post-hoc analysis of the data from a randomized clinical trial involving prescription of antipsychotic treatment to never treated first-onset psychotic patients was used to compare the weight change after 6-week olanzapine treatment (standard tablets vs. orally disintegrating formulation). After 6-week treatment with olanzapine, a significant higher increase in weight was noted in those patients on standard tablets as compared to those on orally disintegrating olanzapine. Body mass index (BMI) increase was also significantly higher in the olanzapine tablet group (Arranz et al. 2007).

Also, differences in provocation of other side effects have been noticed between different antipsychotics. Probably, different antipsychotics provoke hyperglycemia in different and multiple ways. That may be the explanation of their different potency to provoke diabetes mellitus (Filaković et al. 2005).

Authors have searched for other articles on this subject in PubMed and found that, so far, only two papers, including this one, presented results of investigations on the subject of weight loss after switching from olanzapine SOT to olanzapine ODT. For this reason it is very difficult to make some clear conclusions; further controlled clinical investigations are required for evaluation, better understanding and explanation of this change.

CONCLUSION

Treatment with olanzapine ODT is better choice than with olanzapine SOT regarding obesity related to weight gain, according to our case reports. Further controlled clinical investigations

are necessary to evaluate change in weight during treatment with olanzapine ODT, and to improve our understanding of this change.

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