Our Experience with Antidepressant Treatment in the Obese and Type 2 Diabetics

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Received August 8, 2005, Accepted September 19, 2005

These results have been presented at the European Obesity Congress in Prague, May 2004 and at the Diabetology Days 2005 in Luhačovice.

Key words: Obesity antidepressants – Diabetes – Bupropion – Tianeptine – Orlistat – Sibutramine

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Abstract: We established depressive symptoms prevalence in 100 patients recommended to our obesity clinic and we started antidepressant treatment in 41 of them. It has been noted that administration of SSRI leads to weight reduction after 6 months, but is followed by a weight increase later. Our experience shows that 12 months long administration of bupropion and tianeptine leads to continuous weight loss. Antidepressant administration leads to an increase in pharmacotherapy adherence, which is significantly higher than in diet and psychotherapy alone. In diabetics, antidepressants reduce glucose levels, too. Their influence on weight and diabetes compensation is, however, smaller than in "classic" anti-obesity drugs, sibutramine and orlistat.

Introduction

Our department has had an Obesitology Unit for decades, since it was founded by Professor Jiří Šonka. Our patients suffer in higher proportion from depression, but we also meet patients who put on weight following psychiatric and antidepressant treatment. We already published some case studies of psychotic patients treated with anti-obesity drugs [1]. The increased prevalence of psychiatric diseases including depression and metabolic disorders like diabetes and obesity in general population means psychiatric treatment should take into account possible metabolic complications. Personal experience with such patients was exploited in an in-depth study of the area, resulting in two Czech publications [2, 3]. This article concentrates on our quantifiable experiences with antidepressant treatment in a defined set of patients.

The patients and methods

We retrospectively analysed 100 of patients consecutively treated at our Obesitology Unit. Upon registration, all patients underwent a detailed entrance examination, including screening of depressive symptoms: questions about the mood, morning "lows" and insomnia. We started antidepressant therapy after one ore more positive answer. We did not use any depression questionnaire. After the initial examination, antidepressant treatment was started in 41 patients. We also established the presence of diabetes, in history and by serum glucose. During the follow-up, we noted the weight changes, blood glucose at 6 and 12 months since the initial investigation and the length of treatment, or the drop-out rate. In obesity treatment, significant proportion of patients does not follow the recommendations and ceases to return for check-ups. Our results in depressive patients were compared with those only treated with diet and psychotherapy and patients with added anti-obesity drug. These drugs (orlistat and sibutramine) are indicated as a Type 2 diabetes treatment and therefore are partially paid by health insurance companies. Antidepressant treatment was of two kinds: SSRI type and antidepressants that according to published literature lead to weight reduction (bupropion, tianeptine) [3, 4, 5].

The results were evaluated by comparing the weight change in all four groups by analysis of variance, the comparison of glucose levels and weight change in diabetics and non-diabetics by non-paired t-test. Relative values were compared using t-test for relative proportion.

Results

Weight change was evaluated in four groups (Table 1): Patients treated with SSRI, patients treated with bupropion or tianeptine, patients treated with orlistat or sibutramine, and finally patients treated with diet and psychotherapy only. Comparing these groups, there is a significant difference in weight change after 6 months already, where antidepressant treatment is more effective than diet and psychotherapy only, and only marginally less effective than targeted anti-obesity treatment. After 12 months, the group treated with SSRI type antidepressants shows an increase in weight, while the other antidepressants allow for continuing weight loss. In the diet and psychotherapy group, we experienced high drop-out, after 12 months more than 2–3 of patients. Treatment with antidepressants leads to higher adherence, but not as high as in anti-obesity treatment.

Diabetes was present with the same frequency in groups with depressive symptoms and without (18 out of 41 and 27 out of 59 respectively, $p=0.46$). Diabetics showed the same weight loss after 6 and 12 months (4.9 and 3.7 kg) as nondiabetics (5.2 and 3.5kg – $p=0.38$ a $p=0.40$). The adherence to treatments was again comparable in diabetics and nondiabetics.

The reduction in glucose levels in diabetics with depressive symptoms was statistically significant (9.8 to 7.9 mmol/l after 12 months, $p=0.002$,), but only half as great as in diabetics treated with anti-obesity drugs (11.8 to 7.3 mmol/l after 12 months, $p=0.001$), reflecting the prescription limitation – the BMI in the depressive diabetics was lower.

Discussion

Doctors still tend to look at psychiatric and somatic disorders separately. But it has been long ago noted that depression can be manifested by somatic symptoms, or that some somatic disorders can be connected with psychiatric ones.

Table 1 – Weight reduction and drop out of patients during one year of therapy

Type of therapy	Weight loss 6 month	12 months	drop-out of patients
SSRI inhibitors	−5.2 kg	+ 0.4 kg	15.1%
Other antidepressant	−4.9 kg	−8.2	11.1%
Antiobesity medication	−6.9 kg	−10.2	6.6%
Diet and psychotherapy only	−3.3 kg	−4.8 kg	68.9%
p	0.02	< 0.001	

Obesity, Type 2 diabetes and metabolic syndrome are all disorders with some characteristics of somatic and psychiatric disease. Obese patients often cannot critically reflect on their disorder and behave illogically. They cannot actively participate in their treatment and the treatment regime fails. Typically, patients put on weight at the time of personal, family or work crisis. Obesity cannot be successfully treated without psychotherapeutic support.

Metabolic syndrome and its components can to a large degree be caused by administration of some drugs used in psychiatry [3, 6, 7, 8]. Insulin resistance is present in the brain [9, 10], as modelled by the NIRKO (neuron insulin receptor knockout) mice [11]. Treatment of psychiatric disorders can contribute to manifestation of diabetes [12].

Depression is commonly present in obese and diabetic patients. Its prevalence is variable; according to some analyses can be as high as several tens of per cent [13, 14]. For instance Rakovac [15] observed depression in 31% of Type 2 diabetics. In our obese diabetics its prevalence was even higher. We speculate that there is an endogenous connection rather than reactive depression to serious disease. Importantly, two factors of obesity and diabetes are combined here.

Antidepressants vary in their effect on weight. Table 2 rounds up the results of numerous works [according to 3].

Our results confirm short term weight loss after SSRI followed by weight increase, as for instance summarized by Fava and O'Kane [5, 16]. Weight reduction is according to numerous works ideal after bupropion, tianeptine, selective MAO inhibitors or hypericum [17, 18].

Recently, numerous patients with bipolar disorder are treated with the combination of atypical neuroleptic, antiepileptic and antidepressant. This combination can lead to the manifestation of diabetes due to the inclusion of the atypical neuroleptic [6].

Targeted anti-obesity treatment (orlistat, sibutramine) in diabetics [11] is understandably more effective than antidepressant treatment. But antidepressant treatment also leads to reduction in glucose levels [14], as confirmed by our results.

Obesity and psychiatric patients have in common their low adherence to treatment regimes. Psychiatric patients often cease taking their medication

Table 2 – Semi-quantitative increase in weight after antidepressants

4	Lithium, mirtazapine, paroxetine
3	Tricyclic antidepressants
2	SSRI inhibitors long term, nonselective MAO inhibitors
0–1	SSRI inhibitors short term, selective MAO inhibitors
0	bupropion, tianeptine, nefazodon, hypericum

4 – maximun increase, 0 – no increase

because of the weight increase [19]. Obese patients have primarily low adherence to treatment. Therefore it seems to be desirable to exploit the synergy and to treat obesity complicated by depressive symptoms with antidepressants with positive influence on weight loss.

Conclusion

Large number of "non-metabolic" drugs nowadays has metabolic effects. They influence weight, levels of lipids and glucose. These effects have complex origin not only in the drug itself, but also in the interaction of the drug with genetic disposition and behavioural changes. These drugs are often used in psychiatry, for instance antidepressants, antiepileptics, but similar effect is also present in immunosuppressants.

Depression is a frequent disorder and therefore according to our results all pharmacologically treated patients should have their weight and glucose level followed, and drugs with positive influence on weight and diabetes compensation should be used, for instance tianeptine, bupropion or selective MAO inhibitors, in short term use SSRI type antidepressants. In situation where depression is accompanied by excessive weight loss, mirtazapine and paroxetine should be used.

Our results can therefore be concluded:

1. Antidepressant administration in obese diabetics with depressive symptoms leads to better adherence to anti-obesity treatment and to results in weight loss similar to non-diabetics with depressive symptoms.
2. When treating depressive symptoms in obese, antidepressants with positive influence on weight loss should be used.
3. Adherence to drug treatment and antidiabetic effect is greater in anti-obesity drugs than in antidepressants.

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