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Original paper

Obesity-related metabolic disturbances and quality of life in subjects diagnosed with schizophrenia treated with atypical neuroleptics

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Abstract

Introduction: Weight gain and related metabolic disturbances are frequent side effects observed during treatment with atypical neuroleptics, most commonly with olanzapine and quetiapine. Weight gain may also deteriorate the quality of life and cause treatment discontinuation. However, the use of these neuroleptics in orodispensible tablet (ODT) form was related to lower frequency of weight gain. Therefore, the aim of this study was to evaluate the incidence of weight gain and metabolic disturbances in patients with schizophrenia treated with classical tablet (SOT) and orodispensible (ODT) formulations of olanzapine and quetiapine, and analyze the relationship between the occurrence of these side effects and quality of life and patient attitude to the treatment depending on the therapy used.

Material and methods: A three-month questionnaire survey was performed by 400 psychiatrists from across Poland, during three consecutive outpatient visits. 4437 adult patients with schizophrenia treated with atypical neuroleptics for at least one month but not more than 12 months were enrolled.

Results: Weight gain was significantly more common among patients treated with olanzapine than those treated with quetiapine (54.7% vs. 20%, $p < 0.001$ and 34.7% vs. 28.6%, $p < 0.01$, on visits 1 and 3, respectively), and was less frequently observed in patients treated with ODT formulations. The prevalence of hypertension and type 2 diabetes on the treatment did not change significantly. Treatment with olanzapine regardless of the form used was associated with a better quality of life and a more positive attitude of the patient towards the treatment.

Conclusions: The risk of weight gain is greater during treatment with olanzapine than quetiapine. However, olanzapine use is associated with better quality of life and a more positive attitude of the patient towards the treatment. The use of neuroleptics in the ODT form may reduce the risk of weight gain but does not significantly affect the quality of life or the attitude of the patient towards the treatment.

Key words: obesity, schizophrenia, metabolic disturbances, atypical neuroleptics.

Introduction

Schizophrenia is a chronic disorder that significantly worsens the personal, professional and social life of patients [1]. Pharmacotherapy alleviates the symptoms of schizophrenia (abnormal things, perceiving, experiencing and mood), but its side effects may deteriorate quality of life, leading to discontinuation of treatment and relapse of the disease in about 50% of patients. It was observed that only 43% of patients with schizophrenia collaborate well in the therapeutic process [2], and as many as 40% of patients discontinue the pharmacotherapy within a year after the first hospitalization [3]. Subsequent relapses are a cause of increasing dysfunction, reduced periods of remission and longer duration of psychotic disorders [4].

Use of atypical neuroleptics (amisulpride, aripiprazole, quetiapine, clozapine, olanzapine, risperidone, paliperidone, sertindole, ziprasidone) as first-line drugs in the treat-

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ment of schizophrenia increased not only their tolerance (reduced incidence of extrapyramidal disturbances) but also the effectiveness of elimination of deficits as well as affective and cognitive symptoms of schizophrenia. It should be emphasized that atypical antipsychotics are a heterogeneous class of drugs, and may differ both in terms of elimination of symptoms of schizophrenia and the side effect profile [5].

One of the most common side effects of classical and atypical neuroleptics is weight gain caused by an increase in the feeling of hunger and consequently increased food intake [6]. It seems that particularly the use of olanzapine and quetiapine increases the risk of weight gain, which is directly proportional to serum concentration of the drug [7]. Weight gain was observed in more than half of the patients treated with olanzapine [8,9]. The excess of body fat, especially visceral, is the cause of systemic inflammation, hormonal dysfunction of adipose tissue and insulin resistance development, which increases the risk of type 2 diabetes and cardiovascular diseases. Epidemiological studies have shown that the life expectancy of patients suffering from schizophrenia is 15-25 years shorter than in the general population, which at least partially may be due to metabolic disorders induced by pharmacotherapy. It is suggested that the change from classical tablets (SOT) to an orodispensible (ODT) form reduces the risk of weight gain during treatment with olanzapine [10,11]. However, the results of recently published studies did not confirm this hypothesis [12]. On the other hand, Czekalla *et al.* [13] during treatment with ODT observed more adverse effects than during treatment with SOT (6.5% vs. 2.9%). It is hypothesized that this is caused by absorption differences.

It should be stressed that side effects of an atypical neuroleptic, including weight gain, may affect the quality of life of patients, and thus their attitude to treatment and consequently the continued use of the prescribed medication.

Therefore, the aim of this study was to evaluate the incidence of weight gain and metabolic disturbances in patients with schizophrenia treated with SOT and ODT formulations of olanzapine and quetiapine, and analyze the relationship between the occurrence of these side effects and quality of life and patient attitude to the treatment depending on the therapy used.

Material and methods

The observational survey was performed by 400 psychiatrists from across Poland. The study group consisted of 4437 patients (48.8% women) treated for schizophrenia with atypical neuroleptics for at least one month but not more than 12 months prior to enrollment.

Recruitment to the study was performed in May and June 2010. The initial and two follow-up study visits were carried out at up to 3-month intervals, depending on the individual patient's clinical needs. All visits were part of routine management.

During the visits, a survey and measurements of anthropometric parameters (body mass and waist circumference) and blood pressure were performed. Serum glucose and lipid levels were noted in the survey if they were done before the start or during the 3-month follow-up. In addition, quality of life and daily functioning were assessed on the basis of selected questions from the Quality and Satisfaction of Life Questionnaire (Q-LES-Q-SF) and patients' attitude to the treatment on the basis of the Drug Attitude Inventory (DAI).

In addition to the above data, the conducted survey (visit I) included patient demographics [age, gender, place of residence: urban/rural, marital status: single/married/widow/widower, domestic relations: living alone/with family, work activity: learning/working/unemployed/pensioner], clinical data [age of schizophrenia diagnosis, duration of treatment, currently used neuroleptics, their doses and duration of use, and form (ODT/SOT) and the regularity of use]. Questions included body mass and blood pressure before initiation of atypical neuroleptic use. Medical history on the occurrence of hypertension and diabetes as well as antihypertensive and hypoglycemic therapy before treatment with neuroleptic and after its administration was taken.

The survey performed on control visits included questions concerning the continuation of treatment with a neuroleptic and potential reasons for its discontinuation, current dose and form (ODT/SOT) of neuroleptic and an assessment of its regular use, and antihypertensive and antidiabetic therapy.

Data analysis

The required data were entered automatically with the proper form (Microsoft Office Access). The percentage of missing data was less than 3.0% and those entries were not removed from the analysis as they were missing at random.

Nutritional status was assessed on the basis of BMI according to WHO criteria [14]. Visceral obesity was diagnosed by measuring waist circumference according to the International Diabetes Federation (IDF) criteria for Caucasians in Europe (≥ 80 cm for women and ≥ 94 cm for men) [15].

The prevalence of diabetes and hypertension was estimated on the basis of medical history as well as laboratory data and blood pressure measurements, respectively.

Weight gain of 3 kg or more was considered as significant.

Statistical analysis

An analysis of the age structure, gender, place of residence, marital status, family relations and labor force

Table 1. Characteristics of the study group (n = 4437)

Age [years]	39.6 ± 1.4
Age groups [%]	
18-40 years	55.4
41-50 years	22.2
51-60 years	15.1
> 60 years	7.3
Gender: male/female [%]	51.2/48.8
Place of residence [%]	
Village	31.0
City	69.0
Marital status [%]	
Single	61.5
Married	33.3
Widow/widower	5.2
Home relations [%]	
Living alone	20.8
Living with family	79.2
Professional activity [%]	
Student	12.0
Employed	20.2
Unemployed	9.5
Pensioner	58.3
Age at diagnosis of schizophrenia [years]	26.9 ± 8.1
Percentage of patients diagnosed with schizophrenia at age [%]	
≤ 30 years	75.2
31-40 years	19.3
41-50 years	3.9
51-60 years	1.3
> 60 years	0.3
BMI before treatment with neuroleptic [kg/m²]	
< 25 [%]	45.5
25-29.9 [%]	44.8
≥ 30 [%]	9.7
BMI at time of enrollment [kg/m²]	
< 25 [%]	38.5
25-29.9 [%]	47.2
≥ 30 [%]	14.3
Waist circumference before treatment with neuroleptic [%]	
Women < 80 cm	51.0
Women ≥ 80 cm	49.0
Men < 94 cm	63.6
Men ≥ 94 cm	36.4
Waist circumference at time of enrollment [%]	
Women < 80 cm	48.1
Women ≥ 80 cm	51.9
Men < 94 cm	56.9
Men ≥ 94 cm	43.1
Blood pressure before treatment with neuroleptic [%]	
< 140/90	75.5
≥ 140/90	24.5
Blood pressure at time of enrollment [%]	
< 140/90	75.1
≥ 140/90	24.9
Hypertension before treatment with neuroleptic [%]	10.4
Treatment with hypotensive drug [%]	10.9
Diabetes before treatment with neuroleptic [%]	
Yes, only on diet	1.9
Yes, pharmacotherapy	1.6
Diabetes at time of enrollment [%]	
Yes, only on diet	1.5
Yes, pharmacotherapy	2.6
Laboratory tests performed before treatment [%]	37.7
Neuroleptic used [%]	
Risperidone	0.4
Olanzapine	97.0
Clozapine	0.2
Quetiapine	2.3
Ziprasidone	0.1
Mean duration of use (months)	
Risperidone	6.3 ± 3.2
Olanzapine	5.4 ± 3.5
Clozapine	10.0 ± 2.8
Quetiapine	6.0 ± 2.6
Ziprasidone	4.0 ± 1.4
Mean daily dose (mg)	
Risperidone	5.3 ± 2.3
Olanzapine	16 ± 10
Clozapine	450 ± 225
Quetiapine	525 ± 150
Ziprasidone	120 ± 0
Form of neuroleptic used [%]	
SOT	45.2
ODT	54.8
Regularly taken [%]	
Yes	95.8

Table 2. Association between changes of body mass, metabolic disturbances and used neuroleptic

	Visit I		Visit II		Visit III	
	Olanzapine (n = 4304)	Quetiapine (n = 102)	Olanzapine (n = 4282)	Quetiapine (n = 97)	Olanzapine (n = 4258)	Quetiapine (n = 93)
Changes of body mass [%]						
Decreased	9.5	20.0	20.0	14.3	20.6	9.5
Unchanged	35.8	60.0	46.8	52.4	44.7	61.9
Increased	54.7	20.0***	33.2###	33.3##	34.7	28.6++
Hypertensive medications [%]						
Yes	10.9	9.5	11.3	9.5	11.5	14.3++
Diabetes treatment [%]						
Yes, diet	1.6	0	2.1	0	2.3	0
Yes, pharmacotherapy	2.5	5.0	2.4	4.8	3.0	4.8

****p < 0.001 olanzapine vs. quetiapine, ##p < 0.01, ###p < 0.001 visit II vs. visit I, ++p < 0.01 visit III vs. visit II*

participation of the respondents was performed. We also analyzed the profile of used neuroleptics, their dose, form (ODT/SOT), the time of their application and regularity of use. In addition, the incidence of change in body mass and the occurrence of hypertension and diabetes were evaluated in relation to neuroleptics used and their formulation. Moreover, the association between quality of life or patients' attitude to the treatment and neuroleptics used and their formulations was evaluated.

Statistical analysis was performed using STATISTICA software 10.0 (Cracow, Poland).

Qualitative data were presented as percentages, and quantitative data as mean and standard deviation. The separate subgroups were compared using the χ^2 test and χ^2 test for trend. The value $p < 0.05$ was considered as statistically significant.

Results

Study group characteristics

The characteristics of the study group are shown in Table 1. In 75.2% of respondents schizophrenia was diagnosed before the age of 30 years. 55.4% of respondents were persons aged 40 years or less. As many as 58.3% of respondents were pensioners. Only 33.3% of the study group had a partner. As many as 79.2% of the study population were living with their family.

The study design included patients treated with all atypical neuroleptics commercially available in Poland. 97.0% of the observed group were treated with olanzapine, 2.3% with quetiapine and only 0.7% with other atypical neuroleptics (risperidone, clozapine and ziprasidone). Both olanzapine and quetiapine were usually used in maximal doses of 20 mg and 600 mg respectively. The number of subjects limited the reasonable analysis to only two groups: patients treated with olanzapine and those treated with quetiapine. 45.2% of respondents used a SOT. 95.8% of patients reported regular use of neuroleptics.

Before starting treatment with a neuroleptic, overweight was diagnosed in 44.8% and obesity in 9.7% of study subjects, while visceral obesity was diagnosed in 49.0% of women and 36.4% of men. A significant increase in the prevalence of overweight and obesity was initially observed after the introduction of treatment with a neuroleptic (47.2% vs. 44.8%, $p < 0.05$, and 14.3% vs. 9.7%, $p < 0.001$). There was a parallel increase in the occurrence of visceral obesity among women (51.9% vs. 49%, $p < 0.05$) and among men (63.6% vs. 36.4%, $p < 0.001$).

Before starting treatment with a neuroleptic normal blood pressure (< 140/90) was observed in 75.5% of patients and after the start of treatment in 75.1%.

Diabetes before neuroleptic treatment was diagnosed in 3.5% of the study group, and during the follow-up its incidence insignificantly increased to 4.1%.

Plasma glucose and lipids before treatment with a neuroleptic were controlled in only 37.7% of the study group.

Changes in body mass and metabolic disturbances depending on the used neuroleptic

During the first visit of the survey, weight gain was observed significantly more frequently in patients treated with olanzapine than with quetiapine (54.7% vs. 20.0%, $p < 0.001$). However, on the second visit the percentage weight gain significantly decreased among subjects treated with olanzapine (54.7% vs. 33.2%, $p < 0.001$), but significantly increased among those treated with quetiapine (20.0% vs. 33.3, $p < 0.01$). On the third visit, the frequency of body mass gain stabilized among those treated with olanzapine (33.2% vs. 34.7%), and decreased among those treated with quetiapine (33.3% vs. 28.6%, $p < 0.01$) (Table 2).

Table 3. Association between changes of body mass, metabolic disturbances and the used form of neuroleptic

	Visit I		Visit II		Visit III	
	SOT (*n* = 4304)	**ODT (*n* = 102)**	**SOT (*n* = 4282)**	**ODT (*n* = 97)**	**SOT (*n* = 4258)**	**ODT (*n* = 93)**
Changes of body mass [%]						
Decreased	7.0	11.9	10.3	25.4	18.0	22.8
Unchanged	31.8	40.1	52.7	44.5	46.7	44.5
Increased	61.2	48.0**	37.0	30.1**	35.3	32.7*
Hypertensive medications [%]						
Yes	12.3	9.7	10.8	11.6	10.8	12.0
Diabetes treatment [%]						
Yes, on diet	1.7	1.4	0.3	3.0	0.3	3.0
Yes, on pharmacotherapy	1.7	3.2	1.2	3.2	1.3	3.2

**p < 0.05, **p < 0.01 SOT vs. ODT, ##p < 0.01, ###p < 0.001 visit II vs. visit I, ++p < 0.01 visit III vs. visit II*

Table 4. The quality of life in relations to the used neuroleptic

	Visit I		Visit II		Visit III	
	Olanzapine (*n* = 4304)	**Quetiapine (*n* = 102)**	**Olanzapine (*n* = 4282)**	**Quetiapine (*n* = 97)**	**Olanzapine (*n* = 4258)**	**Quetiapine (*n* = 93)**
Physical health [%]						
Very dissatisfied	2.2	0	1.7	0	1.7	0
Dissatisfied	17.0	19.1	10.2	14.3	8.0	0
Nor dissatisfied/nor satisfied	37.9	57.1	36.9	57.1	26.7	71.4
Satisfied	40.8	23.8	48.1##	28.6##	58.9++	28.6***
Very satisfied	2.1	0	3.1	0	4.7	0
Mood [%]						
Very dissatisfied	1.5	0	0.7	0	1.1	0
Dissatisfied	20.6	14.3	9.8	0	6.8	0
Nor dissatisfied/nor satisfied	39.4	47.6	38.1	57.1	25.4	42.9
Satisfied	37.0	38.1	48.7##	42.9#	62.8+++	57.1+++**
Very satisfied	1.5	0	2.7	0	3.9	0
Work [%]						
Very dissatisfied	1.2	0	2.7	0	2.4	0
Dissatisfied	20.4	6.2	6.6	6.2	7.0	0
Nor dissatisfied/nor satisfied	41.2	56.3	43.4	62.5	39.1	60.0
Satisfied	36.3	37.5	43.4##	31.3##	44.5	40.0++***
Very satisfied	0.9	0	3.9	0	7.0	0
Household activities [%]						
Very dissatisfied	1.7	0	0.6	0	0.9	0
Dissatisfied	18.3	14.3	10.4	0	40.8	47.6
Nor dissatisfied/nor satisfied	45.5	61.9	47.7	57.1	0	0
Satisfied	33.5	23.8	45.5##	42.9##	52.4++	52.4+++*
Very satisfied	1.0	0	2.8	0	5.9	0

Table 4. Cont.

	Visit I		Visit II		Visit III	
	Olanzapine (*n* = 4304)	**Quetiapine (*n* = 102)**	**Olanzapine (*n* = 4282)**	**Quetiapine (*n* = 97)**	**Olanzapine (*n* = 4258)**	**Quetiapine (*n* = 93)**
Contact with friends [%]						
Very dissatisfied	2.6	0	0.8	0	1.1	0
Dissatisfied	27.2	14.3	14.6	9.5	9.1	0
Nor dissatisfied/nor satisfied	44.1	47.6	47.2	52.4	42.3	57.1
Satisfied	24.7	28.6	34.4$^{\#\#}$	33.3$^{\#}$	43.3^{++}	42.9^{+++*}
Very satisfied	1.4	9.5	3.0	4.8	4.2	0
Contact with family [%]						
Very dissatisfied	1.9	0	1.9	0	1.2	0
Dissatisfied	23.8	14.3	12.7	4.8	9.8	0
Nor dissatisfied/nor satisfied	37.7	61.9	31.8	81.0	28.9	57.1
Satisfied	34.6	23.8	49.3$^{\#\#\#}$	9.5$^{\#\#\#}$	54.2^{+}	38.1^{+++**}
Very satisfied	1.9	0	4.3	4.7	5.9	4.8
Free time activities [%]						
Very dissatisfied	2.1	0	0.8	0	0.6	0
Dissatisfied	22.6	14.3	11.0	0	7.9	0
Nor dissatisfied/nor satisfied	48.2	71.4	43.6	76.2	36.7	47.6
Satisfied	26.2	14.3	41.6$^{\#\#\#}$	23.8$^{\#\#\#}$	49.0^{++}	47.6^{+++}
Very satisfied	0.9	0	3.0	0	5.8	4.8
Ability to functioning in everyday life [%]						
Very dissatisfied	2.5	0	1.8	0	1.4	0
Dissatisfied	21.8	23.8	11.2	4.8	8.5	0
Nor dissatisfied/nor satisfied	43.0	52.4	40.6	71.4	31.8	61.9
Satisfied	32.0	23.8	43.1$^{\#\#\#}$	23.8	52.4^{++}	38.1^{+++***}
Very satisfied	0.7	0	3.3	0	5.9	0
Sexual life [%]						
Very dissatisfied	8.5	0	6.6	0	4.5	0
Dissatisfied	37.3	57.1	29.5	47.6	25.5	42.8
Nor dissatisfied/nor satisfied	42.2	23.8	42.8	42.9	41.6	42.9
Satisfied	11.6	19.1	19.0$^{\#\#}$	9.5$^{\#\#}$	26.3^{++}	14.3^{++***}
Very satisfied	0.4	0	2.1	0	2.1	0
Physical and mental health [%]						
Very dissatisfied	2.6	0	2.3	0	2.3	0
Dissatisfied	19.7	23.8	9.7	14.3	7.8	28.6
Nor dissatisfied/nor satisfied	46.2	52.4	42.2	66.7	32.7	47.6
Satisfied	30.3	23.8	42.7$^{\#\#}$	19.0	51.9^{++}	23.8^{+***}
Very satisfied	1.2	0	3.1	0	5.3	0

$^{*}p < 0.05$, $^{**}p < 0.01$, $p < 0.001$ olanzapine vs. quetiapine, $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ visit II vs. visit I, $^{+}p < 0.05$, $^{++}p < 0.01$, $^{+++}p < 0.001$ visit III vs. visit II

Table 5. Quality of life in relation to the form of used neuroleptic

	Visit I		Visit II		Visit III	
	SOT (*n* = 4304)	**ODT (*n* = 102)**	**SOT (*n* = 4282)**	**ODT (*n* = 97)**	**SOT (*n* = 4258)**	**ODT (*n* = 93)**
Physical health [%]						
Very dissatisfied	1.7	2.4	2.1	1.4	1.3	1.8
Dissatisfied	16.4	17.4	9.0	10.9	7.8	7.8
Nor dissatisfied/nor satisfied	34.1	41.7	34.6	39.2	27.5	28.1
Satisfied	45.1	37.1	50.9$^{\#}$	45.7$^{\#}$	57.2^{+}	58.6^{+}
Very satisfied	2.7	1.4	3.4	2.8	6.2	3.7
Mood [%]						
Very dissatisfied	1.5	1.4	0.6	0.7	1.0	1.1
Dissatisfied	19.1	21.3	11.1	8.6	8.2	5.8
Nor dissatisfied/nor satisfied	35.0	43.1	33.9	40.9	24.8	26.3
Satisfied	42.4	33.2	51.9$^{\#\#}$	47.1$^{\#\#}$	62.1^{++}	63.1^{++}
Very satisfied	2.0	1.0	2.5	2.7	3.9	3.7
Work [%]						
Very dissatisfied	1.1	1.2	2.8	2.4	3.6	1.4
Dissatisfied	14.9	24.4	11.1	3.4	9.4	4.8
Nor dissatisfied/nor satisfied	50.9	33.1	48.6	41.6	42.1	38.6
Satisfied	32.0	40.7	35.4	47.8$^{\#}$	42.0^{+}	46.2**
Very satisfied	1.1	0.6	2.1	4.8	2.9	9.0
Household activities [%]						
Very dissatisfied	2.0	1.4	0.6	0.5	0	0
Dissatisfied	15.9	19.8	10.8	9.7	2.3	0.2
Nor dissatisfied/nor satisfied	45.1	46.6	40.4	41.1	41.8	40.3
Satisfied	35.5	31.6	45.7$^{\#\#}$	45.9$^{\#\#\#}$	52.0^{+}	52.8^{+**}
Very satisfied	1.5	0.6	2.5	2.8	3.9	6.7
Contact with friends [%]						
Very dissatisfied	3.2	2.0	0.9	0.7	2.6	0.2
Dissatisfied	25.7	27.7	16.7	13.2	11.4	7.4
Nor dissatisfied/nor satisfied	43.9	44.6	45.5	48.1	41.5	43.5
Satisfied	26.0	23.9	35.6$^{\#\#}$	33.9$^{\#\#}$	42.5^{+}	43.6^{++*}
Very satisfied	1.2	1.8	1.3	4.1	2.0	5.3
Contact with family [%]						
Very dissatisfied	1.7	2.0	2.5	1.4	2.3	0.5
Dissatisfied	22.5	24.3	13.6	11.8	10.8	8.9
Nor dissatisfied/nor satisfied	34.1	41.7	32.1	33.9	28.8	30.3
Satisfied	39.7	30.2	49.4$^{\#\#}$	47.6$^{\#\#\#}$	53.9	53.6^{+}
Very satisfied	2.0	1.8	2.4	5.3	4.2	6.7
Free time activities [%]						
Very dissatisfied	2.4	1.6	0.9	0.7	1.6	0
Dissatisfied	20.1	24.3	11.7	10.1	10.5	6.2
Nor dissatisfied/nor satisfied	48.3	49.4	45.4	43.6	37.3	36.6
Satisfied	28.7	23.5	41.1$^{\#\#}$	41.6$^{\#\#\#}$	47.7^{++}	49.9^{++***}
Very satisfied	0.5	1.2	0.9	4.0	2.9	7.3

Table 5. Cont.

	Visit I		Visit II		Visit III	
	SOT (n = 4304)	ODT (n = 102)	SOT (n = 4282)	ODT (n = 97)	SOT (n = 4258)	ODT (n = 93)
Ability to function in everyday life [%]						
Very dissatisfied	2.2	2.6	2.2	1.6	2.3	0.9
Dissatisfied	20.1	23.3	13.0	9.9	9.8	7.4
Nor dissatisfied/nor satisfied	40.2	45.5	41.5	40.9	34.3	32.3
Satisfied	36.3	28.3	41.8$^{\#}$	43.6$^{\#\#}$	50.0^{++}	53.5^{++***}
Very satisfied	1.2	0.2	1.5	4.0	3.6	6.9
Sexual life [%]						
Very dissatisfied	7.4	9.1	7.7	5.6	6.2	3.3
Dissatisfied	33.8	40.7	29.0	30.5	26.5	25.8
Nor dissatisfied/nor satisfied	46.3	38.3	45.7	41.5	45.8	39.6
Satisfied	12.0	11.5	17.6$^{\#}$	19.2$^{\#}$	21.5^{+}	28.1+***
Very satisfied	0.5	0.4	0	3.2	0	3.2
Physical and mental health [%]						
Very dissatisfied	2.4	2.6	3.1	1.8	3.3	1.6
Dissatisfied	19.4	19.8	12.0	8.5	11.4	6.5
Nor dissatisfied/nor satisfied	42.1	49.6	41.0	43.7	33.3	33.0
Satisfied	35.6	26.9	41.4$^{\#}$	42.7$^{\#\#\#}$	48.1^{+}	53.0^{+++**}
Very satisfied	1.5	1.1	2.5	3.3	3.9	5.9

$^{*}p < 0.05$, $^{**}p < 0.01$, $p < 0.001$ SOT vs. ODT, $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ visit II vs. visit I, $^{+}p < 0.05$, $^{++}p < 0.01$, $^{+++}p < 0.001$ visit III vs. visit II

During all visits weight gain was significantly more frequently observed among subjects treated with SOT than with ODT (61.2% vs. 48.0%, $p < 0.001$; 37.0% vs. 30.1%, $p < 0.01$; and 35.2% vs. 32.7%, $p < 0.05$, respectively) (Table 3).

During the observation the percentage of subjects on antihypertensive therapy did not change significantly among patients treated with olanzapine (10.9% vs. 11.5% vs. 11.3%), regardless of the used form of neuroleptic. However, on the second visit the percentage of subjects on antihypertensive therapy increased significantly among subjects using quetiapine (14.3% vs. 9.5%, $p < 0.01$) (Table 2).

The prevalence of diabetes remained unchanged during the observation period (Table 2), and was unaffected by the used form of neuroleptic (Table 3).

Association between quality of life and used neuroleptic and its form

In both groups treated with olanzapine and quetiapine there was a significant improvement of satisfaction with physical health, mood, work, household activity, contacts with friends and with family, spending free time and ability to function in everyday life. However, an improvement of satisfaction with sexual life as well as physical and mental life was found only in the group treated with olanzapine (Table 4).

At the end of the study the percentage of subjects very satisfied and satisfied with physical health and mood was significant higher among patients treated with olanzapine than those treated with quetiapine (63.6% vs. 28.6%, $p < 0.001$ and 66.7% vs. 57.1%, $p < 0.01$, respectively). Moreover, the percentage of subjects very satisfied and satisfied with work and household activity was significantly higher among patients treated with olanzapine than those treated with quetiapine (51.5% vs. 46%, $p < 0.01$ and 58.3% vs. 52.4%, $p < 0.05$, respectively). Furthermore, the percentage of subjects very satisfied and satisfied with contacts with friends and with family was significantly higher among patients treated with olanzapine than those treated with quetiapine (47.5% vs. 42.9%, $p < 0.05$ and 60.1% vs. 42.9%, $p < 0.01$, respectively). There were no differences in the percentage of subjects very satisfied and satisfied with spending free time between those treated with olanzapine and those treated with quetiapine (54.8% vs. 52.4%). In addition, the percentage of subjects very satisfied and satisfied with ability to function in everyday life, sex life as well as physical and mental life was significant higher among patients treated with olanzapine than those treated with quetiapine (58.3% vs. 38.1%, $p < 0.001$; 28.4% vs. 14.3%, $p < 0.001$ and 57.2% vs. 23.8%, $p < 0.001$, respectively) (Table 4).

Table 6. Attitude of the patient to the drug in relation to the used neuroleptic

	Visit I		Visit II		Visit III	
	Olanzapine (n = 4304)	Quetiapine (n = 102)	Olanzapine (n = 4282)	Quetiapine (n = 97)	Olanzapine (n = 4258)	Quetiapine (n = 93)
Good effects of the drug outweigh the bad effects [%]						
True	86.6	52.4***	90.7#	61.9##***	94.3+	66.7***
I feel strange when I take the drug [%]						
True	22.9	61.9***	20.2#	47.6###***	18.2+	38.1++***
I take the medication voluntarily [%]						
True	85.8	95.2**	88.9#	100.0#***	91.5+	95.2+*
The drug makes me feel more relaxed [%]						
True	65.1	52.4**	74.5##	52.4***	80.6+	61.9+***
The drug causes fatigue and heaviness [%]						
True	40.1	61.9***	35.2#	61.9***	28.4+	47.6++***
I take the medication only when I'm sick [%]						
True	36.8	57.1**	34.1	47.6##**	31.8+	42.9+**
I feel more normal when I use the drug [%]						
True	74.3	52.4***	82.3#	52.4***	85.9	52.4***
It is unnatural when the drug controls my mind and body [%]						
True	43.9	71.4***	39.1	57.1##***	36.6	61.9***
Thanks to the drug I can think more clearly [%]						
True	77.6	52.4***	85.1#	57.1#***	89.2	61.9***
By taking the medication I can prevent the disease [%]						
True	85.0	52.4***	90.9#	90.5###	94.3	100.0++*

**p < 0.05, **p < 0.01, p < 0.001 olanzapine vs. quetiapine, #p < 0.05, ##p < 0.01, ###p < 0.001 visit II vs. visit I, +p < 0.05, ++p < 0.01, +++p < 0.001 visit III vs. visit II*

In both groups treated with SOT and ODT a significant improvement of satisfaction with physical health, mood, work, household activity, contacts with friends and with family, spending free time and ability to function in everyday life, sexual life as well as physical and mental life occurred (Table 5).

The percentage of subjects very satisfied and satisfied with physical health and mood at the end of the study did not differ between those treated with SOT and those treated with ODT (63.4% vs. 62.3% and 66.0% vs. 66.8%, respectively). The percentage of subjects very satisfied and satisfied with work and household activity was significantly higher among those treated with ODT than those treated with SOT (55.2% vs. 44.9, $p < 0.01$ and 62.5% vs. 55.9%, $p < 0.01$, respectively). Furthermore, the percentage of subjects very satisfied and satisfied with contacts with friends was significantly higher among those treated with ODT than those treated with SOT (48.9% vs. 44.5%, $p < 0.05$). However, the percentage of subjects very satisfied and satisfied with contacts with family did not differ between those treated with ODT than those treated with SOT (60.3% vs. 58.1%). Finally, the percentage of subjects very satisfied and satisfied with spending free time, ability to function in everyday life, sex life as well as physical and mental life was significant higher among those treated with ODT than those treated with SOT (57.2% vs. 50.6%, $p < 0.001$; 60.4% vs. 53.6%, $p < 0.001$ and 31.3% vs. 21.5%, $p < 0.001$ and 58.9% vs. 52.0%, $p < 0.01$, respectively) (Table 5).

Attitude of study subjects to the treatment and used neuroleptic and its form

During successive visits, the percentage of subjects who supposed that the good effects of the drug outweighed the bad effects significantly increased in both groups, and was significantly higher among those treated with olanzapine than those treated with quetiapine (Table 6).

Also the percentage of subjects who state that they feel strange when taking the drugs during successive evaluations decreased in both groups, but was significantly lower among those treated with olanzapine than those treated with quetiapine (Table 6).

During successive visits, the percentage of subjects reporting voluntary use of drugs was lower among those treated with olanzapine than those treated with quetiapine. The increase in the percentage of subjects

Table 7. Attitude of the patient to the drug in relation to the used form of neuroleptic

	Visit I		Visit II		Visit III	
	SOT (*n* = 4304)	ODT (*n* = 102)	SOT (*n* = 4282)	ODT (*n* = 97)	SOT (*n* = 4258)	ODT (*n* = 93)
Good effects of the drug outweigh the bad effects [%]						
True	84.8	86.8	88.0$^{\#}$	91.4$^{\#}$	92.2^{+}	94.4^{+}
I feel strange when I take the drug [%]						
True	23.8	24.1	18.8$^{\#}$	22.1	18.0	19.6^{+}
I take the medication voluntarily [%]						
True	90.2	82.8*	92.9	87.1$^{\#*}$	94.1^{+}	89.8^{+*}
The drug makes me feel more relaxed [%]						
True	66.4	63.4*	73.5$^{\#\#}$	74.2$^{\#\#}$	76.8	81.3^{++*}
The drug causes fatigue and heaviness [%]						
True	42.4	39.3	36.1$^{\#}$	35.7$^{\#}$	30.4^{+}	28.2^{+}
I take the medication only when I'm sick [%]						
True	33.1	40.5	28.7	37.5	24.2	35.6
I feel more normal when I use the drugs [%]						
True	76.7	71.1	83.0$^{\#}$	80.8$^{\#}$	85.0	84.4^{+}
It is unnatural when the drug controls my mind and body [%]						
True	45.1	44.4	34.6$^{\#\#}$	42.3*	34.8	38.1^{+*}
Thanks to the drug I can think more clearly [%]						
True	79.2	75.3	85.2$^{\#}$	84.1$^{\#}$	88.2	88.7^{+}
By taking the medication I can prevent the disease [%]						
True	88.7	82.6	92.9$^{\#}$	89.8$^{\#}$	94.4	94.2^{+}

$^{*}p < 0.05$ SOT vs. ODT, $^{\#}p < 0.05$; $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ visit II vs. visit I, $^{+}p < 0.05$, $^{++}p < 0.01$, $^{+++}p < 0.001$ visit III vs. visit II

who voluntarily used drugs during the follow-up increased among those treated with olanzapine only (Table 6).

The feeling of relaxation during the use of drug was more frequently reported by subjects treated with olanzapine than those treated with quetiapine on all visits. In addition, during the follow-up the percentage of subjects feeling relaxation increased significantly in the group treated with olanzapine only (Table 6).

On all visits the feeling of fatigue and heaviness during the use of the drug was less frequently reported by those treated with olanzapine than those treated with quetiapine. The percentage of subjects expressing this opinion decreased significantly at the end of the study in both groups (Table 6).

At the beginning of the study, subjects treated with olanzapine less frequently than those treated with quetiapine reported that they used the drug when they fell ill. The proportion of people expressing this opinion significantly decreased during the observation in both groups (Table 6).

Feeling more normal during the use of drugs was more frequently expressed by subjects treated with olanzapine than those treated with quetiapine, and increased with time of treatment with olanzapine, only (Table 6).

Patients treated with olanzapine significantly less frequently than those taking quetiapine believed that the control of their mind and body by drugs is unnatural. Moreover, during follow-up a decrease in the percentage of subjects expressing this opinion was found among subjects treated with olanzapine, only (Table 6).

Furthermore, patients treated with olanzapine significantly more often than those taking quetiapine stated that thanks to the drug they can think more clearly. The percentage of subjects expressing this opinion significantly increased with time of follow-up in both groups (Table 6).

At the end of the study the proportion of patients who reported that they take drugs to prevent the disease relapse was greater than at the beginning, and among treated with olanzapine than those treated with quetiapine (Table 6).

During the successive visits the percentage of subjects who believe that the good effects of the drug outweigh the bad effects and were feeling relaxed was lower among those treated with SOT than among those treated with

ODT. The percentages increased significantly during the follow-up in both groups (Table 7).

The percentage of subjects who report that they feel strange when taking medication was comparable in those treated with SOT and those treated with ODT, and decreased with time of observation in both groups (Table 7).

There were more subjects reporting voluntary drug use among those treated with SOT than those treated with ODT. During follow-up an increase in the percentage of subjects using the drug voluntarily was found among those treated with ODT, only (Table 7).

Patients treated with SOT less frequently than those treated with ODT reporting taking the drug when feeling ill. During follow-up the percentage of subjects expressing this opinion decreased significantly in both groups (Table 7).

At the end of the study there were no differences in the percentage of subjects who feel more normal during drug use between those treated with SOT and those treated with ODT. In addition, during the follow-up the percentage of subjects expressing this opinion increased significantly in both groups. The percentage of subjects stating that control of their mind and body by drugs is unnatural was significantly lower among those treated with SOT than those treated with ODT. During the follow-up the percentage of subjects expressing this opinion decreased significantly among those treated with ODT, only (Table 7).

Finally, there was no difference between the groups in the percentage of subjects stating that thanks to the drug they can think more clearly and that by using the drugs they can prevent the disease (Table 7).

Discussion

The prevalence of obesity in the study group before inclusion of the neuroleptic was lower than in the general adult Polish population (9.7% vs. 20.4%) [14]. While, the percentage of subjects diagnosed with visceral obesity among both women and men was higher than among the general Polish population (49.0% vs. 40.4% and 36.4% vs. 28.3%, respectively) [16]. However, it should be noted that the main cause of these differences is the use of more restrictive diagnostic criteria than in the WOBASZ study (IDF 2005 vs. NCEP-ATP III in 2001) and does not warrant the finding that visceral obesity in people with schizophrenia is more common than in the general population [16].

The results of our study confirm previously published observations that treatment with olanzapine and quetiapine is associated with development of overweight and obesity [7], and visceral fat distribution, especially among men. However, this did not result in a significant increase the prevalence of hypertension and type 2 diabetes in the study population. It should be emphasized that while the blood pressure measurements were performed on all the visits, the serum glucose concentrations was determined in less than 38% of respondents. Therefore, there is a high probability of underestimating the newly occurring type 2 diabetes, and the present results do not allow one to draw any conclusion concerning the risk of type 2 diabetes development in patients with weight gain on treatment with atypical neuroleptics. In addition, the short 3-month period of observation in many cases was too short for the development of this late complication of obesity.

In accordance with the results of previous studies, after initiation of treatment with olanzapine weight gain was observed in over 50% of patients [8,9]. This percentage was higher than among those treated with quetiapine; however, during the 3-month follow-up weight gain also occurred in over 1/3 of those treated with this drug. Thus, the results of the present study confirm previous observations showing that treatment with olanzapine and quetiapine is associated with a high risk for weight gain [7]. It should also be noted that the tendency to weight gain during treatment with olanzapine decreased with the duration of therapy.

Neuroleptic in ODT form at baseline was used in 54.8% of the study population. According to the results of some previous studies [10,11], but in contrast to a recently published study [12], the use of neuroleptics in the ODT form was associated with a lower risk of weight gain than SOT. However, there was no association between the form used and the incidence of hypertension and type 2 diabetes. The strength of this finding is limited by the low rate of blood sampling (38.0%), precluding drawing a strong conclusion about the impact of the neuroleptics on the incidence of type 2 diabetes. Therefore, the effect of different forms of neuroleptics on the risk of developing metabolic disorders requires further study.

Olanzapine treatment was associated with a better quality of life (QoL) in terms of physical health, mood, work, functioning in terms of household, contacts with friends and family, ability to function in everyday life, sex life, and the cumulative assessment of physical and mental health than treatment with quetiapine. In contrast, administration of quetiapine was only associated with the better spending of free time aspect of QoL.

It should be emphasized that, regardless of the type of neuroleptic, the QoL improved with time of their use, in terms of physical health, mood, performance in terms of household tasks, contacts with family, free time activities, and ability to function in everyday life. However, QoL related to work and contacts with friends or sexual life, and the cumulative assessment of physical and mental health, improved in the group treated with olanzapine, only. These results may suggest that treatment with olanzapine is associated with better QoL for patients with

schizophrenia. These results are consistent with a previous study [17] but opposite to another one, in which treatment with quetiapine significantly improved QoL [18]. It should be noted that the negative effect of neuroleptics on QoL is reflected apparently at the duration of treatment.

Better QoL in terms of physical health, mood, work, household functioning, contacts with friends and family, spending free time, everyday life, sex life, and overall assessment of physical and mental health was observed in those treated with SOT than those treated with ODT. However, it should be noted that regardless of the used form of the drug, improvement of QoL in all aspects during follow-up was observed. This is in contrast to previously published studies that either showed no difference in the impact of the neuroleptic form on QoL [12] or significantly better quality of life during treatment with ODT [19]. These differences may be the effect of higher incidence of adverse effects during treatment with ODT than SOT [13]. However, this aspect has not been evaluated in the study.

A positive attitude to the therapy used in both those treated with olanzapine and with quetiapine increased with time during the follow-up. Treatment with olanzapine more frequently was associated with a positive assessment in terms of perceiving the benefits of treatment, feeling relaxed after treatment, less frequently feeling fatigue and heaviness, more frequent use of the drug, not only in the sense of the disease, more common sense of normalcy during the treatment, rarer unnatural feeling of mind and body control by the drug, frequent sense of mental clarity and frequent use of the drug to prevent the disease. In contrast, treatment with quetiapine less frequently was associated with negative effects on well-being and more frequent use of the drug voluntarily. Thus, it seems that the patients' attitude to the treatment was better among subjects treated with olanzapine than with quetiapine despite a more negative impact on body mass. So far, a more positive attitude of patients to treatment with olanzapine has been demonstrated only in comparison with risperidone and haloperidol [20].

The use of ODT more frequently was associated with a positive patient attitude in terms of perceiving the benefits with treatment and less frequently feeling fatigue and heaviness. We did not observe an effect of the used form of therapy on the perception of well-being. While, treatment with SOT frequently was associated with the voluntary use of the drug, feeling relaxed during treatment, frequent use of drugs not only in the sense of the situation of the disease, a sense of normalcy, rarer unnatural feeling of mind and body control by drugs, frequent feeling of normality, and the use of the drug to prevent the disease. During the follow-up, regardless of the form of neuroleptics used, there was an increase in the percentage of subjects who saw the benefits of treatment, felt relaxed during treatment, had a sense of normality, a feeling of normality and used drugs to prevent the disease and felt decreased negative effects on well-being, felt tired and heaviness and using drugs only sense of the situation of the disease, and experienced unnatural control of the mind and body by drugs. On the other hand, the percentage of subjects voluntarily taking medication increased significantly during the follow-up in the group treated with ODT, only. Thus, similar to the results the atypical neuroleptic form used had no significant effect on the patients' attitude towards the treatment [12,21]. It should also be noted that a positive attitude to treatment increased during the follow-up, regardless of the form of atypical neuroleptics used.

The main limitations of the study were the short period of observation and rare serum glucose determination. In addition, the comparison of olanzapine and quetiapine is flawed due to the size of group treated with quetiapine.

Conclusions

The risk of weight gain is greater during treatment with olanzapine than with quetiapine. Olanzapine use is associated with a better quality of life and more positive attitude of patients towards the treatment. The use of neuroleptics in the ODT form may reduce the risk of weight gain but does not significantly affect the quality of life or patient attitude towards the treatment.

Disclosure

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