Original article / *Araştırma*

Metabolic parameters in patients with major depression treated with escitalopram

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ABSTRACT

Objective: *The aim of this study is to determine the change in metabolic parameters of patients with major depression treated with escitalopram.* ***Methods:*** *The height, body weight, waist circumference, blood pressure, lipid profile (total cholesterol, low density lipoprotein [LDL], high density lipoprotein [HDL], triglycerides [TG]), fasting blood glucose (FBG), thyroid stimulating hormone (TSH) and Hamilton Depression Scale (HamD) of 41 consecutively selected patients with major depression were measured before treatment and in the third month of treatment, for whom a decision to start treatment with escitalopram was decided. The relationship between treatment and changes in these metabolic parameters were evaluated at the end of this period.* ***Results:*** *The mean age of patients was 30.24±9.96 (18-62) years. Eleven (27%) patients were male and 30 (73%) were female. Twelve (29.3%) patients were treated with 10 mg/day escitalopram, and 29 patients (70.7%) 20 mg/day. Significant increases were detected in body weight, body mass index, waist circumference and systolic blood pressures of all patients from initiation of treatment to three months. A significant increase was found in the waist circumference of male patients (n=11) after three months of treatment. Body weight, body mass index, waist circumference, triglycerides, systolic blood pressure were found to be significantly increased after three months of treatment in female patients (n=30) who were treated with escitalopram. HamD scores were found to be significantly decreased after three months in patients treated with escitalopram.* ***Conclusion:*** *Escitalopram caused an increase in especially body weight and waist circumference in patients with major depression.* ***(Anatolian Journal of Psychiatry 2016; 17(6):482-488)***

Keywords: *major depression, metabolic syndrome, metabolic parameters, selective serotonin reuptake inhibitors, escitalopram*

Essitalopram ile tedavi edilen majör depresyon hastalarında metabolik parametreler

ÖZ

Amaç: *Bu çalışmanın amacı, essitalopram ile tedavi edilen majör depresyon hastalarında metabolik parametrelerin değişimini incelemektir.* ***Yöntem:*** *Essitalopram ile tedavisine karar verilmiş olan, ardışık olarak çalışmaya alınan 41 majör depresyon hastasında tedavi başlanmadan hemen önce ve tedavinin üçüncü ayında boy, vücut ağırlığı, bel çevresi, kan basıncı, lipit profili (total kolesterol, düşük yoğunluklu lipoprotein [LDL], yüksek yoğunluklu lipoprotein [HDL], trigliserit [TG]), açlık kan şekeri, tiroit uyarıcı hormon (TSH) ve Hamilton Depresyon Ölçeği (HamD) ölçümleri yapıldı. On iki hafta sonra tedavi ile metabolik parametreler arasındaki ilişki ve değişimler değerlendirildi.* ***Bulgular:***

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Hastaların ortalama yaşı 30.24±9.96 (18-62) idi. Hastaların 11'i (%27) erkek, 30'u (%73) kadındı. Hastalardan 12'si (%29.3) 10 mg/gün essitalopram ile, 29'u (%70.7) 20 mg/gün essitalopram ile tedavi edildi. On iki haftalık süreç sonunda beden ağırlığında, vücut kitle indeksinde, bel çevresinde ve sistolik kan basıncında anlamlı artış saptandı. Bu sürenin sonunda, erkek hastalarda (s=11) bel çevresinde anlamlı artış saptandı. Kadın hastalarda (s=30) ise vücut ağırlığında, vücut kitle indeksinde, bel çevresinde, trigliserit düzeylerinde ve sistolik kan basıncında anlamlı artış saptandı. Hastaların HamD puanlarında ise 12 haftanın sonunda anlamlı azalma saptandı. ***Sonuç:*** *Majör depresyon hastalarında essitalopram kullanımı özellikle beden ağrılığında ve bel çevresinde artışa neden olmuştur.* ***(Anadolu Psikiyatri Derg 2016; 17(6):482-488)***

Anahtar sözcükler: *Majör depresyon, metabolik sendrom, metabolik parametreler, seçici serotonin geri alım inhibitörleri, essitalopram*

INTRODUCTION

Alterations in body weight are often observed during treatment of psychiatric diseases, causing non-compliance and relapse.[1,2] Depression is a frequent mental disorder in which selective serotonin reuptake inhibitors (SSRI) are drug of choice. Reader et al. had detected an increase in waist circumference and body weights of patients using paroxetine and no change in metabolic parameters with citalopram. But an increase in waist circumference and hypercholesterolemia were detected in patients taking fluoxetine, fluvoxamine and sertraline.[4] Serretti et al. also found that paroxetine causes weight gain.[5] Ye et al. had found a decrease in body weights, fasting glucose levels and triglyceride levels in patients with type 2 diabetes using fluoxetine.[6] Citalopram had caused an increase in triglyceride levels in a study by Beyazyuz et al. on patients with generalized anxiety disorder. Escitalopram, on the other hand, had caused a decrease in waist circumference while increasing triglyceride levels.[7] A significant effect of escitalopram on metabolic syndrome was not detected in a study by Peh et al.[8]

Deteriorating metabolic parameters was found to lead a decrease in antidepressant response, eventually causing worsening in depression.[9] Investigation of probable metabolic effects of SSRIs in patients with major depression will provide information in the follow-up of these patients. Selection of escitalopram, which has the weakest interactions with other receptors among SSRIs, conducting a prospective investigation in patients with major depression who has no DSM-IV axis I comorbidity and inclusion of thyroid enzyme measures are distinctive aspects of this study. Escitalopram is unique among SSRIs that it selectively inhibits reuptake of serotonin and it does not have any significant interactions with other monoamines.[3] For this reason, escitalopram was selected as an SSRI in the present study.

The aim of this study is to determine the changes in metabolic parameters such as lipid profile, fasting glucose level, blood pressure, and waist circumference in patients with major depression, treated with escitalopram.

METHODS

Participants

Forty-one major depression patients who were between the ages of 18-65 years, decided to start treatment with escitalopram, compliant with the initially planned treatment for at least three months, obtained written informed consent for participating in the study, and whose index major depression episode started within the last six months are included.

Presence of a medical disease (cardiovascular illness, diabetes, hyperlipidemia, thyroid disease, etc.), lifetime diagnosis of eating disorder, history of any psychotropic medication, metabolic drug, or a hormone preparation use, non-compliance with the escitalopram treatment, discontinuing the antidepressant medication, addition of another psychotropic agent during follow-up, history of a lifelong diagnosis of any Axis-I mental disease according to DSM-IV, except major depression and specific phobia were set as exclusion criteria.

Eleven patients were excluded from the study because of some reasons such as adverse effects, existing metabolic issues or discontinuing the antidepressant medication.

Procedure and measures

The height, body weight, waist circumference, blood pressure, lipid profile (total cholesterol, low density lipoprotein [LDL], high density lipoprotein [HDL], triglycerides [TG]), fasting blood glucose (FBG), thyroid stimulating hormone (TSH) and Hamilton Depression Scale (HamD) of 41 patients with major depression were measured before starting treatment and in the 3rd month, for whom a decision to start treatment with escitalopram was decided. Body weights and

and body mass indices of the patients were measured before the treatment. The response to treatment was determined with Hamilton Depression Scale (HamD). The relationship between treatment and the change in metabolic parameters were examined at the end of the treatment period. Axis I diagnosis were examined with DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) Structured Clinical Interview for DSM Diagnosis for Axis I Disorders (SCID-I). Approval from the Ethics Committee and written informed consents of the patients were obtained in order to conduct this study. The patients were consecutively included in this study. Bakirkoy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery Ethics Committee permission was acquired before the study.

Sociodemographic and Clinical Characteristics Data Form: This is a form containing questions on sociodemographic and clinical characteristics that were developed by the investigators taking into account the features of this study. The items in this form were age, gender, smoking and alcohol consumption, beginning of major depression, duration of depression, and history of drug use.

Structured Clinical Interview for DSM Diagnosis for DSM-IV Axis I Disorders (SCID-I): This semi-structured tool was developed by First et al. according to DSM-IV diagnostic criteria, in order to investigate the presence of a first axis diagnosis. It was translated to Turkish by Corapcioglu et al. and its validity and reliability for Turkish was shown before.[10,11]

Hamilton Depression Rating Scale (HamD): This scale was developed by Max Hamilton in order to evaluate the severity of depression in patients with a diagnosis of depression. It was developed by Hamilton with 17 items. Validity and reliability of the Turkish version was shown by the study of Akdemir et al.[12]

Evaluation of Metabolic Syndrome Criteria: Waist circumferences, body weights and heights of the patients in the study group were measured, their body mass indexes (BMI: weight[kg]/height[m^2]) were calculated and blood pressures were measured. The waist circumferences were measured when the waist area was uncovered, while the patient stood and freely breathed, at the level of umbilicus and upper limit of the iliac crest, without any pressure applied to change the result. Blood pressure measurement was done while the patient was seated, after at least five minutes of rest.

The laboratory data of the patients were obtained in the morning, after an overnight fasting. The FBG, HDL and TG values that are used in the diagnosis of metabolic syndrome were obtained from these investigations. The blood samples were examined at the same laboratory.

Statistical analysis

In the statistical evaluation of the data of this investigation, Shapiro-Wilk normal distribution test was used to determine if the data showed a normal or non-normal distribution. Dependent inter-group patient data (baseline and third month) were compared with Wilcoxon signed-rank test for data not showing a normal distribution and paired two group t test for data with a normal distribution. The relationship between the patient data was determined with Pearson correlation test for data showing a normal distribution and with Spearman correlation test for data not showing a normal distribution.

The height, body weight, waist circumference, blood pressure, lipid profile (LDL, HDL, TG), FBG, TSH, and HamD of 41 consecutively selected patients with major depression were measured before treatment and in the third month of treatment, for whom a decision to start treatment with escitalopram was decided. The relationship between treatment and changes in these metabolic parameters were evaluated at the end of this period.

RESULTS

The mean age of patients was 30.24±9.96 (18-62) years. Eleven (27%) patients were male and 30 (73%) were female. Twelve (29.3%) patients were treated with 10 mg/day escitalopram, and 29 patients (70.7%) 20 mg/day. Significant increases were detected in body weight ($p<0.001$), body mass index ($p<0.001$), waist circumference ($p<0.001$), and systolic blood pressures ($p=0.009$) of all patients from initiation of treatment to three months. A significant increase was found in the waist circumference of male patients after three months of treatment ($p<0.05$). Body weight ($p<0.01$), BMI ($p<0.01$), waist circumference ($p<0.001$), triglycerides ($p<0.05$), systolic blood pressure ($p<0.05$) were found to be significantly increased after three months of treatment in female patients (n=30) who were treated with escitalopram. HamD scores were found to be significantly decreased after three months in patients treated with escitalopram ($p<0.001$).

Sociodemographic and clinical characteristics; when the mean escitalopram doses that the patients used during the three months are examined, it is seen that 12 (29.3%) took 10 mg/day, and 29 (70.7%) took 20 mg/day. The mean age of the patients was 30.24±9.96 (18-62). Eleven patients (27%) were male and 30 (73%) were female. The mean age of female patients was 29.13±9.94 and the mean age of male patients was 33.27±9.82, and the difference is not statistically significant (z=1.38, p>0.05). Fourteen (34.1%) patients were smokers while 27 (65.9%) were non-smokers. Thirteen (%31.7) patients were social alcohol drinkers. 28 (68.3%) did not use alcohol. Twelve (29%) patients had a past history of major depression episode.

The effects of escitalopram treatment for three months on the metabolic parameters of all patients (n=41): Significant increases were detected in body weight (p<0.001), BMI (p<0.001), waist circumference (p<0.001), and SBP (p=0.009) values from baseline to the third month. A significant decrease was detected in the comparison of baseline and third month HamD scores (p<0.001) (Table 1).

Effects of escitalopram treatment for three months in female patients (n=30): body weight (p<0.01), BMI (p<0.01), waist circumference (p<0.001), TG (p<0.05), SBP (p<0.05) values at the third month were found to be significantly increased in female patients, in comparison to

Table 1. The effects of escitalopram use for three months in all patients (n=41)

	Baseline	Third month	p	t	z	w
Body weight (kg)	60.6±10.3	61.8±10.6	<0.001***	3.83		
BMI[+]	21.5±2.9	21.9±3.2	<0.001***	3.70		
Waist circumference (cm)[++]	68 (64.5-77)	69 (64-78)	<0.001***		-3.94	347.0
HDL[++]	49 (36-61)	49 (38-59)	0.540		0.61	95.0
LDL[++]	118.2±36.31	15.0±35.7	0.140	1.51		
Cholesterol[++]	185.0±40.71	81.4±34.9	0.227	1.23		
TG[++]	74 (62-118.5)	84 (67-128)	0.064		1.85	-287.0
TSH[++]	1.4 (0.89-2.23)	1.5 (0.91-2.24)	0.907		0.12	19.0
SBP++	110 (100-120)	110 (110-120)	0.009**		2.60	-156.0
DBP++	70 (70-80)	70 (70-80)	0.739		0.28	-7.0
HDS++	50 (47-56)	34 (31-37.5)	<0.001***		-5.59	61.0
FBG	84 (80.5-93)	86 (81.5-91.5)	0.886		0.14	23.0

*** p<0.01, *** p<0.001, [+] Mean±Standard Deviation, [++] Median (%25-%75) = Median (%25 quartile value-%75 quartile value), SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, BMI=Body Mass İndex, HDS=Hamilton Depression Scale, Paired two group t test and Wilcoxon signed-rank tests were used.*

Table 2. Effects of escitalopram for three months in female patients *(n=30)*

	Baseline	Third month	p	t	z	w
Body weight (kg)	56.5±6.6	57.8±7.5	<0.005**	3.32		
BMI[+]	20.9±2.7	21.3±3.2	<0.005**	3.20		
Waist circumference (cm)[++]	66.6±5.2	67.3±5.8	<0.001***	3.72		
HDL[++]	53 (42.8-63)	53.5 (47.8-60.2)	0.876		0.16	6.0
LDL[++]	117.2±36.3	115.8±34.5	0.498	0.69		
Cholesterol[++]	187.2±41.2	186.5±33.5	0.834	0.21		
TG[++]	73.5 (57.8-116.8)	86 (69-125.8)	<0.02*		2.49	-243.0
TSH[++]	1.6 (0.9-2.5)	1.6 (0.9-2.3)	0.537		20.62	61.0
SBP[++]	110 (107.5-112.5)	110 (110-120)	<0.05*		2.00	-77.0
DBP[++]	70 (70-80)	70 (70-80)	1		0	-1
HDS[++]	50.5 (48-56)	34 (31-39.3)	<0.001***		-5.12	465.0
FBG	85 (79.8-97)	84 (80.8-91.3)	0.585		0.55	54.0

* p<0.05, ** p<0.005, *** p<0.001, [+] Mean±Standard Deviation, [++] Median (%25 quartile value-%75 quartile value), SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, BMI=Body Mass İndex, HDS=Hamilton Depression Scale, Paired two group t test and Wilcoxon signed-rank tests were used.*

the baseline values. When HamD baseline and third month scores were compared, a significant decrease was detected (p<0.001) (Table 2).

Effects of escitalopram for three months in male patients (n=11): baseline waist circumference was found to be significantly increased after treatment with escitalopram for three months (p<0.05). HamD scores showed a significant decrease after treatment with escitalopram for three months (p<0.001) (Table 3).

In conclusion, escitalopram caused an increase in especially body weight and waist circumference in patients with major depression.

Table 3. Effects of escitalopram for three months in male patients (n=11)

	Baseline	Third month	p	t	z	w
Body weight (kg)	71.7±10.4	72.9±10.2	0.10	1.82		
BMI^{+}	23.4±2.9	23.8±2.7	0.103	1.80		
Waist circumference (cm)$^{++}$	84.6±10.6	85.5±10.4	<0.02*	3.11		
HDL^{++}	38.2±6.6	37.0±7.7	0.374	0.93		
LDL^{++}	120.8±38.0	112.8±40.8	0.176	1.46		
Cholesterol^{++}	178.5±40.5	167.4±36.7	0.081	1.94		
TG^{++}	96.3±34.9	93.5±35.4	0.316	1.06		
TSH^{++}	1.3 (0.9-1.4)	1.4 (1.1-1.5)	0.278		1.08	-26.00
SBP^{++}	120 (100-120)	120 (110-120)	0.120		1.56	-15.00
DBP^{++}	80 (70-80)	80 (70-80)	0.773		0.29	-2.00
HDS^{++}	48.9±14.0	29.8±14.0	<0.001**	5.76		
FBG	86.2±7.8	88.5±7.2	0.346	0.99		

** p<0.02, ** p<0.001, $^{+}$ Mean±Standard Deviation, $^{++}$ Median (%25 quartile value-%75 quartile value), SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, BMI=Body Mass İndex, HDS=Hamilton Depression Scale, Paired two group t test and Wilcoxon signed-rank tests were used.*

DISCUSSION

All major depression patients included in this study were treated with escitalopram (n=41). Twelve patients used escitalopram at a mean dose of 10 mg/day, and 29 patients used escitalopram at a mean dose of 20 mg/day. Body weight, BMI, waist circumference, HDL, LDL, cholesterol, TG, TSH, SBP, DBP and FBG values at baseline and at the third month were compared. Significant increases were found in body weight (p<0.001), BMI (p<0.001), waist circumference (p<0.001), SBP (p=0.009) values after treatment of three months. There is a study with a large sample size suggesting that antidepressants may increase the risk of type 2 diabetes in the general population.[13] Antidepressants were reported to be associated with an increase again in body weight in patients that had lost weight in a diabetes prevention program.[14] Paroxetine among SSRIs was found to be associated with the highest increase in body weight in a meta-analysis.[5] The weight increasing effects of other antidepressants are dependent on duration of use and individual differences of patients.[5] Association of SSRIs with cardiovascular diseases was not detected in a prospective cohort study including 14784 adults.[15] Unlike other SSRIs, escitalopram specifically inhibits serotonin re-uptake and it does not show a significant interaction with other monoamines.[3] Citalopram had caused an increase in TG in the study by Beyazyüz et al. in patients with generalized anxiety disorder.[7] Escitalopram on the other hand, caused an increase in TG and a decrease in waist circumference. Increases in waist circumference and body weight were found in patients taking paroxetine in the study by Reader et al.[4] Significant changes in metabolic syndrome criteria were not observed in patients using citalopram. Absence of a significant effect of escitalopram use on metabolic syndrome was found in the study by Peh et al.[8] Escitalopram had caused a mild increase (a mean 0.14 kg) in body weight in patients with depression after three months in the study by Uher.[16] In view of the findings of our study, metabolic parameters and especially body weight should be carefully monitored in patients with depression when treatment with escitalopram is initiated.

Metabolic parameters in patients taking escitalopram and gender: a significant increase in waist circumferences (p<0.05) was found in

male patients (n=11) from baseline to the third month in this study.

Significant increases in body weight (p<0.01), BMI (p<0.01), waist circumference (p<0.001), TG (p<0.05), SBP (p<0.05) values after treatment with escitalopram for three months were found in female patients (n=30). Women with symptoms of depression in adulthood were reported to be more inclined to gain weight in comparison to males.[17] Both obesity and depression may show an association of causality in women.[18] In the present study, severity of depression decreased while waist circumference increased in both sexes. This increase in both genders shows the importance of monitoring this parameter. Although the significant increases in BMI, waist circumference, TG, SBP values along with the increase in body weight in female patients may suggest the presence of a higher risk in women in terms of metabolic effects of the escitalopram, but these results should be reproduced in larger patient groups.

The most important limitation of this study is the larger number of female patients in comparison with males and the short follow-up duration. Weight gain gradually increases after the first year of treatment with SSRIs.[1] The strengths of this study include its longitudinal design, inclusion of patients only with a diagnosis of major depression, and exclusion of first axis diagnosis other than specific phobia and major depression.

In conclusion, treatment with escitalopram was shown to cause especially an increase in body weight and waist circumference in patients who were diagnosed to have major depression. The importance of monitoring metabolic parameters is highlighted again in this study. Longer prospective studies will provide more information in this respect.

Authors' contributions: *O.O.D.: Patient interviews, applying scales, writing manuscript; N.F.: Finding topic, planning; E.S.: Statistical analyses; N.K.: Literature research, revision on manuscript; A.Y.: Literature research, planning; M.C.İ.: Revision on manuscript, literature research.*

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