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RESEARCH ARTICLE

The relationship between microvascular complications and depression in patients with type 2 diabetes mellitus who use insulin

İnsülin kullanan tip 2 diabetes mellitus hastalarında mikrovasküler komplikasyonlar ile depresyonun ilişkisi

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ABSTRACT

Objective: This study aimed to assess the relationship between Type 2 Diabetes Mellitus (DM) and its complications with the severity of depression.

Methods: Eighty diabetics under the age of 65 using insulin were enrolled and clinical and biochemical data were recorded. The severity of neuropathy was determined by the "United Kingdom neuropathy screening score" (UKNS) whereas the severity of depression was determined by the "Beck depression scale" (BDS). Nephropathy and retinopathy were assessed by the microalbumin-creatinine ratio in spot urine samples and by detailed examination of the retina with an ophthalmoscope, respectively.

Results: There were more patients who has high neuropathy severity in the group with the highest Beck depression scale score ($p<0.001$). In the correlation analyses, positive correlation was found between the severity of depression determined by the BDS and UKNS ($r=0.231$, $p=0.039$). No relationship was found between nephropathy, retinopathy and severity of depression.

Conclusion: There was significant relationship between the severity of neuropathy and that of depression. Hence, cases with a diagnosis of Type 2 DM require screening in terms of neuropathy and the presence of depression. Appropriate approach towards such conditions associated with each other may be crucial in the context of increasing the quality of life. *J Clin Exp Invest 2013; 4 (1): 34-39*

Key words: Type 2 Diabetes Mellitus; neuropathy, nephropathy; retinopathy; depression

ÖZET

Amaç: Bu çalışmada kronik bir hastalık olan Tip 2 Diabetes Mellitus (DM) ve komplikasyonlarının depresyon şiddeti ile ilişkisi değerlendirilmesi amaçlandı.

Yöntemler: Çalışmaya 65 yaşından küçük, insülin kullanmakta olan 80 Tip 2 DM hastası alınarak klinik ve biyokimyasal verileri kaydedildi. Nöropati şiddeti "United Kingdom nöropati tarama skoru" (UKNS) ile, depresyon şiddeti ise "Beck Depresyon Envanteri" (BDE) ile belirlendi. Nefropati spot idrar örneğinde mikroalbumin-kreatinin oranı ile, retinopati ise göz dibi muayenesi ile değerlendirildi.

Bulgular: Beck depresyon şiddeti yüksek olan hasta grubu içindeki nöropati şiddeti yüksek olan hasta sayısı daha fazlaydı ($p<0,001$). Korelasyon analizinde BDE şiddeti ile UKNS arasında pozitif korelasyon saptandı ($r=0,231$, $p=0,039$). Nefropati ve retinopati ile depresyon şiddeti arasında bir ilişki bulunmadı.

Sonuç: Çalışmamızda nöropati şiddeti ile depresyon şiddeti arasında anlamlı bir ilişki vardı. Bu nedenle Tip 2 DM tanısı olan olgular nöropati ve depresyon varlığı açısından taranmalıdır. Eşlik eden bu durumlara yönelik uygun yaklaşımlar hayat kalitesini arttırmak açısından önemli olabilir.

Anahtar kelimeler: Tip 2 Diabetes Mellitus, nöropati, nefropati, retinopati, depresyon

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INTRODUCTION

Type 2 Diabetes Mellitus (DM) is a chronic and progressive disease during which microvascular complications such as nephropathy, neuropathy and retinopathy may develop.[1,2] As is the case in other chronic diseases, the frequency of anxiety and depression increases in Type 2 DM.[3,4]

Depression, first in line among diseases most frequently associated with Type 2 DM, has been reported to disrupt the glycemic control, and recovery from hyperglycemia, improvement in depression symptoms.[5-7] The presence of depression is thought to complicate the glycemic control by disrupting the harmony between diet, exercise and therapy.[8] Besides studies suggesting a correlation between the level of HbA1c, a good marker of glycemic control, and depressive symptoms, there are some which point to the contrary.[9]

In our study, we investigated the impact of diabetic microvascular complications on the frequency and severity of depression in Type 2 DM cases.

METHODS

Cases under the age of 65 admitted to our Endocrinology clinic, which had been using insulin for the past 6 months and/or more, were enrolled in this study. The study was approved by Harran University ethics committee. After informing patients about the study, their verbal and written consents were collected. Patients who had been diagnosed with depression or those who received anti-depressant therapy within the past 6 months were excluded from the study. For the determination of diabetic nephropathy, the spot urine albumin-creatinine ratio was measured in the first morning urine. Cases with a serum creatinine level of >1.4 mg/dl were excluded from the study. Detailed examination of the retina with an ophthalmoscope was performed for the determination of diabetic retinopathy. The presence and severity of diabetic neuropathy was defined by the “United Kingdom neuropathy screening score” (UKNS) as normal, mild, moderate and severe. The severity of the depression symptoms was assessed by the “Beck depression scale” (BDS). Patients were divided into four groups according to the severity of their depression determined by the Beck depression scale (total score=63 points), and hence group 1, 2, 3 and 4 were defined as minimal (0-9 points), mild (10-16 points), moderate (17-29 points) and severe (30-63 points), respectively.

Statistical analysis

SPSS version 15.0 (Windows, Chicago, IL, USA) was used for statistical analyses. Results were given as average ± standard deviation (SD). Categorical variants were compared via the Chi-squared test whereas the continuous variants were compared via the unpaired Student’s t or Mann-Whitney U tests according to their compatibility with normal distribution. One-way ANOVA was used for the comparison between parametric data between three or more groups, and the Turkey test was used as the post hoc test. In the comparison between three or more groups, Kruskal-Wallis variation analysis was used along with the Mann-Whitney U test for sub group comparisons of the obtained results. Spearman correlation test was used in correlation analysis. $p<0.05$ was considered to be statistically significant.

RESULTS

An overall number of 80 Type 2 DM patients were included in the study. The groups were found to be biochemically similar (Table 1 and Table 2). Depression severity determined by the BDS showed significant increase going from group 1 to group 4 ($p<0.001$ between all groups). Furthermore, as going from group 1 to group 4 according to the UKNS, there was an increase in the ratio of patients with moderate neuropathy (8.3% for group 2, 26% for group 3, 8.3% for group 4) or in the ratio of patients with severe neuropathy (4.2% for group 2 and 33.3% for group 4) ($p<0.001$). In the Spearman correlation analysis, there was a positive correlation between the severity of the depression determined by the BDS and triglyceride (TG) ($r=0.235$, $p=0.036$) and the UKNS ($r=0.231$, $p=0.039$) (Figure 1, Figure 2). No correlation was found between the presence of retinopathy and nephropathy and the severity of the depression (Table 3).

Table 1. A comparison of clinical data between groups (*p<0.001 between all groups).

	Group 1 (n=14)	Group 2 (n=24)	Group 3 (n=30)	Group 4 (n=12)
Age (years)	48.3±14.0	51.3±10.0	51.2±8.1	48.3±10.4
BMI (kg/m^2)	28.9±4.8	28.6±3.9	30.1±4.9	31.5±10.6
BECK*	8.0±0.7	12.0±1.9	23.9±3.7	33.2±3.8
Gender (M/F)	7/7	9/15	8/22	2/10
History of smoking (Yes/No)	7/7	6/18	8/22	3/9
History of drinking (Yes/No)	0/14	0/24	0/30	0/12
Marital status				
Married	13	23	30	11
Single	1	0	0	0
Divorced/Widower	0	1	0	1
Retinopathy (Yes/No)	3/11	6/18	8/22	5/7
History of depression (Yes/No)	4/10	2/22	7/23	5/7
Neuropathy (Yes/No)	4/10	3/21	9/21	5/7
UKNS*				
None	10	21	21	7
Mild	4	0	1	0
Moderate	0	2	8	1
Severe	0	1	0	4

UKNS: United Kingdom neuropathy screening score
UKNS: United Kingdom neuropathy screening score, BMI: Body mass index

Table 2. A comparison of biochemical data between groups* (*p>0.05 for all data).

	Group 1 (n=14)	Group 2 (n=24)	Group 3 (n=30)	Group 4 (n=12)
Glucose (mg/dl)	347.2±119.9	284.6±129.2	294.4±116.3	276.3±113.7
Creatinin (mg/dl)	1.0±0.3	0.9±0.3	0.8±0.3	0.8±0.3
TCHOL (mg/dl)	173.6±40.0	182.1±59.6	213.0±74.6	189.9±44.6
LDL-C (mg/dl)	98.8±33.6	97.7±32.5	110.9±34.7	103.3±37.9
HDL-C (mg/dl)	35.8±9.6	37.2±3.0	35.5±8.0	34.1±13.5
TG (mg/dl)	217.0±207.3	259.3±157.1	276.0±169.4	271.3±94.1
Albumin (g/dl)	3.5±0.7	3.5±0.9	3.6±0.6	3.4±0.8
HbA1c (%)	10.8±3.0	10.4±2.3	11.1±1.4	11.5±2.7
ACR (µg/mg)	268.8±365.7	149.6±246.0	198.0±289.0	149.2±337.8

HbA1c: Glucosilated hemoglobin, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, ACR: Urine albumin-creatinin ratio, TG: Triglyceride, TCHOL: Total cholesterol

Table 3. A correlation between the Beck depression severity and clinical and biochemical data

	r	p
Age (years)	0.010	0.933
BMI (kg/m^2)	0.92	0.419
Fasting Glucose (mg/dl)	-0.185	0.101
TCHOL (mg/dl)	0.174	0.122
LDL-C (mg/dl)	0.124	0.292
HDL-C (mg/dl)	0.012	0.918
TG (mg/dl)	0.235	0.036
HbA1c (%)	0.121	0.287
ACR (µg/mg)	-0.049	0.664
UKNS	0.231	0.039

HbA1c: Glucosilated hemoglobin, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, ACR: Urine albumin-creatinin ratio, TG: Triglyceride, TCHOL: Total cholesterol, UKNS: United Kingdom neuropathy screening score, BMI: Body mass index

DISCUSSION

Chronic diseases generally lead to anxiety and depression due to the fear of the future, of organ loss and of death. The symptoms of the chronic and progressive disease Type 2 DM frequently yield depression because of emerging organ function loss and complications, disrupted quality of life and secondary biological changes to brain disease.[10] The frequency of life-long depression in diabetic cases has raised two fold in comparison with the healthy control group.[8] Moreover, depression is associated with behavior such as the habit of smoking, and weight gain rooting from lack of physical activity and inappropriate food intake, hence, may cause obesity and impaired glucose tolerance followed by organ defects.[8,11]

It is well known that the frequency of depression increases in cases with diabetes-related complications.[12] In our study, the severity of depression symptoms and that of neuropathy were rising proportionally whereas no evidence was found to the significant correlation between depression severity and the presence of retinopathy and nephropathy. The relationship between diabetic neuropathy and the presence of depression has been shown in a number of studies.[13-16] However, the number of studies investigating the relationship between depression symptoms and neuropathy is limited. Even though several systems were used in the assessment of depression severity until today, the UKNS was reported to be a realistic, objective and accurate scoring system for the assessment of diabetic peripheral neuropathy.[17] Therefore, the use of UKNS in our study seems like quite a valid assessment method, and accordingly, there is a significant relationship between the UKNS. This finding supports the previous study results obtained by other scoring systems used for the determination of neuropathy severity and pointing out proportional increase in depression severity linked to neuropathy severity.[18,19]

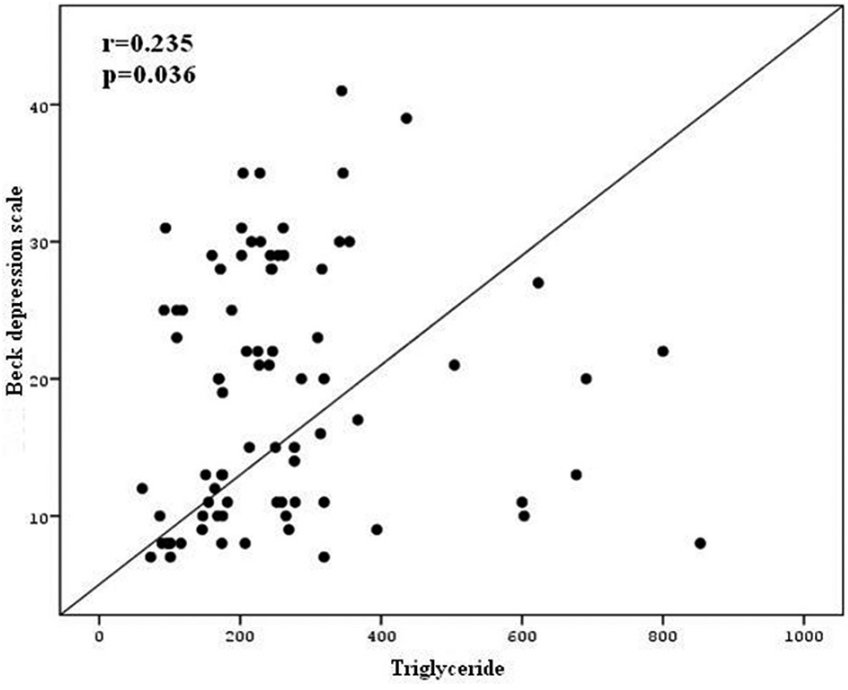

Figure 1. A correlation between the Beck depression severity and the level of triglyceride.

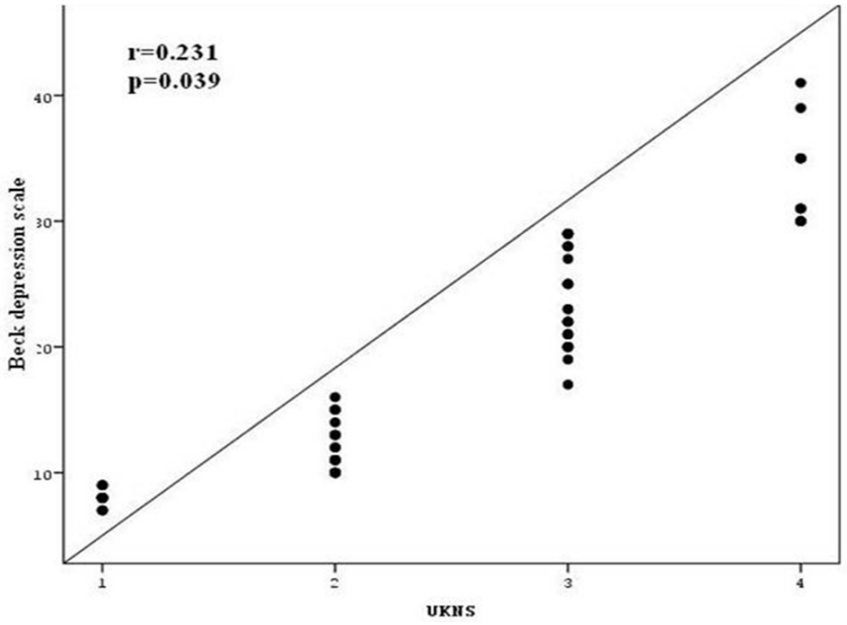

Figure 2. A correlation between the Beck depression severity and the UKNS.

We were not able to detect evident relationship between depression severity and TG. Lipid parameters, especially the relationship between low density lipoprotein cholesterol (LDL-C) and depression, were investigated in various patient groups, however, conflicting results were obtained.[20-22] Heckbert et al. did not able to find any correlation between depression and LDL-C; whereas, Gary et al. neither found any correlation between depression and LDL-C however defined significant relationship between depression and TG.[23,24] In another study, TG was found to be higher in patients with associated cardiac disease among Type 2 cases with major depression.[25] As we did not perform sub group analyses in terms of cardiac diseases on our study patients, it does not seem possible to comment on such a correlation. On the other hand, one study showed that increase in TG levels leads to neuropathy independent of age, duration of disease and glycemic control.[26] In the light of the current data, even if TG levels were not found to be so high, this increase may augment the severity of diabetic neuropathy, and this may be clinically vital for the approach towards neuropathy.

Though the impact of dyslipidemia on the severity of neuropathy has been evaluated in various studies, the mechanism of action of dyslipidemia-dependent neuropathy is not yet clarified. As is well known, oxidative stress increases with Type 2 DM, and this leads to oxidation of various vital molecules containing lipids.[27] It is advocated that the severity of diabetic neuropathy is related to these oxidized lipids.[28]

In conclusion, severity of depression increases along with that of neuropathy in diabetic patients. There is a relationship between TG levels and depression in diabetic patients. Due to these facts, the presence of neuropathy and depression might be investigated in diabetic patients especially with other micro vascular complications. The presentation of appropriate approach towards these associated conditions may have a positive effect on the patients' quality of life. It is also possible that treatment of hyperlipidemia cause decrease in the severity of neuropathy and hence contribute to the treatment of depression.

REFERENCES

1. Schellhase KG, Koepsell TD, Weiss NS. Glycemic control and the risk of multiple microvascular diabetic complications. Fam Med 2005;37:125-130.
2. Ma J, Yang W, Fang N, et al. The association between intensive glycemic control and vascular complications in type 2 diabetes mellitus: a meta-analysis. Nutr Metab Cardiovasc Dis 2009;19:596-603.
3. Carney C. Diabetes mellitus and major depressive disorder: an overview of prevalence, complications, and treatment. Depress Anxiety 1998;7:149–157.
4. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care 2001;24:1069-1078
5. Lustman PJ, Griffith LS, Freedland KE, et al. Cognitive behavior therapy for depression in type 2 diabetes: a randomized controlled trial. Ann Intern Med 1998;129:613-621.

6. Mazze RS, Lucido D, Shamoon H. Psychological and social correlates of glycemic control. Diabetes Care 1984;7:360-366.
7. Testa MA, Simonson DC. Health economic benefits and quality of life during improved glycemic control in patients with type 2 diabetes mellitus. JAMA 1998;280:1490-1496.
8. Lin EH, Katon W, Von Korff M, et al. Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care 2004;27:2154–2160.
9. Georgiades A, Zucker N, Friedman KE, et al. Changes in depressive symptoms and glycemic control in diabetes mellitus. Psychosom Med 2007;69:235-241.
10. Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biol Psychiatry 2003;54:216-226.
11. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care 2008;31:2383-2390.
12. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. Psychosomatic Med 2001;63:619-630.
13. Turkington RW. Depression masquerading as diabetic neuropathy. JAMA 1980;243:1147-1150.
14. Moreira RO, Amâncio AP, Brum HR, et al. Depressive symptoms and quality of life in type 2 diabetic patients with diabetic distal polyneuropathy. Arq Bras Endocrinol Metabol 2009;53:1103-1111.
15. Vileikyte L, Leventhal H, Gonzalez JS, et al. Diabetic peripheral neuropathy and depressive symptoms: the association revisited. Diabetes Care 2005;28:2378-2383.
16. Takahashi Y, Hirata Y. A follow-up study of painful diabetic neuropathy: physical and psychological aspects. Tohoku J Exp Med 1983;141:463-471.
17. Oguejiofor OC, Oli JM, Ajaero CN, et al. Are the symptoms of diabetic peripheral neuropathy in Nigerian patients objective? An evaluation using the United Kingdom Screening Test (UKST) and Bio-Thesiometry. Niger J Clin Pract 2009;12:113-119.
18. Gore M, Brandenburg NA, Dukes E, et al. Pain severity in diabetic peripheral neuropathy is associated with patient functioning, symptom levels of anxiety and depression, and sleep. J Pain Symptom Manage 2005;30:374-385.
19. Moreira RO, Papelbaum M, Fontenelle LF, et al. Comorbidity of psychiatric disorders and symmetric distal polyneuropathy among type II diabetic outpatients. Braz J Med Biol Res 2007;40:269-275.
20. Lehto SM, Hintikka J, Niskanen L, et al. Low HDL cholesterol associates with major depression in a sample with a 7-year history of depressive symptoms. Prog Neuropsychopharmacol Biol Psychiatry 2008;32:1557-1561.
21. Lehto SM, Ruusunen A, Niskanen L, et al. Elevated depressive symptoms and compositional changes in LDL particles in middle-aged men. Eur J Epidemiol 2010;25:403-409.
22. Tyrovolas S, Lionis C, Zeimbekis A, et al. Increased body mass and depressive symptomatology are associated with hypercholesterolemia, among elderly individuals; results from the MEDIS study. Lipids Health Dis 2009; 8:10-11.
23. Heckbert SR, Rutter CM, Oliver M, et al. Depression in relation to long-term control of glycemia, blood pressure, and lipids in patients with diabetes. J Gen Intern Med 2010;25:524-529.
24. Gary TL, Crum RM, Cooper-Patrick L, et al. Depressive symptoms and metabolic control in African-Americans with type 2 diabetes. Diabetes Care 2000;23:23-29.
25. Katon WJ, Lin EH, Russo J, et al. Cardiac risk factors in patients with diabetes mellitus and major depression. J Gen Intern Med 2004;19:1192-1199.
26. Wiggin TD, Sullivan KA, Pop-Busui R, et al. Elevated triglycerides correlate with progression of diabetic neuropathy. Diabetes 2009;58:1634-1640.
27. Vincent AM, Edwards JL, Sadidi M, et al. The antioxidant response as a drug target in diabetic neuropathy. Curr Drug Targets 2008;9:94-100.
28. Vincent AM, Hinder LM, Pop-Busui R, et al. Hyperlipidemia: A new therapeutic target for diabetic neuropathy. J of Periph Nerv Syst 2009;14:257-267.