

Relationship between Opium Abuse and Severity of Depression in Type 2 Diabetic Patients

Sepehrmanesh Zahra¹, Sarmast Hossein², Kord Valeshabad Ali^{3,4}

¹Department of Psychiatry, Kashan University of Medical Sciences, Kashan,

²Emergency Center, Kashan University of Medical Sciences, Kashan,

³Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran,

⁴National Elites Foundation, Tehran, Iran

Background: Opium use in diabetic populations is associated with major depressive disorder (MDD). This study was designed to investigate the relationship between opium use and severity of depression in Iranian diabetic patients.

Methods: In this case-control study, 642 type 2 diabetic patients were recruited from those presenting at two outpatient clinics at the Akhavan Hospital in Kashan, Iran; of them, 600 diabetic patients were included in the study and divided into two groups: opium-abusers (150 patients) and non-opium-abusers (450 patients). Clinical and demographic information was obtained through a detailed questionnaire. Depression symptomatology and severity were assessed with the Beck Depression Inventory (BDI), and a corresponding diagnosis was made based on the Diagnostic and Statistical Manual of Mental Disorders-IV, Text Revision, 2000 (DSM-IV TR) criteria.

Results: The mean depression score was higher in the opium abuse group than in the non-abuser group (29.27 ± 1.44 vs. 18.29 ± 1.31 , $P < 0.001$). In general, a significant association was found between opium abuse and depression among patients (odds ratio [OR], 4.54; 95% confidence interval [CI], 2.87 to 7.44; $P = 0.001$). No significant relationship was found between dysthymia and opium abuse (OR, 0.68; 95% CI, 0.18 to 1.192; $P = 0.155$), while MDD was significantly higher in the opium abuser group (OR, 7.32; 95% CI, 5.20 to 12.01; $P < 0.001$).

Conclusion: Depression is more frequent in opium-dependent diabetic patients, and its severity is also greater. Given these findings, opium-dependent diabetic patients should be advised about the increased risks of depression and related comorbidities.

Keywords: Depression; Diabetes mellitus; Opium

INTRODUCTION

Diabetes mellitus is a chronic disease that can have many complications, such as retinopathy, neuropathy, and nephropathy; it affects patients' quality of life, and it is often associated with depression [1-3]. Dietary restrictions, constant dependence on medicine, short- and long-term side effects, and the cost-burden of the disease may help to explain the high prevalence of depression among these patients [4].

Opium has traditionally been consumed in Iran as a treat-

ment for pain, diarrhea, insomnia, and premature ejaculation. It is also used for enjoyment and elimination of tension [5,6]. Some Iranian patients consume opium for their diabetes, although the reasons and prevalence are not clear. The pain reduction effects of opium and a lack of adequate knowledge may explain their opium usage to some extent, but research is needed to gain a better understanding. However, it is known that opium abuse among diabetics is associated with an increased risk of severe depression [7]. Overall, about 90% of opioid-dependent patients are recognized to have a psychiatric disorder,

Corresponding author: Sarmast Hossein
Emergency Center, Kashan University of Medical Sciences, Kashan, Iran
E-mail: beheena2002@yahoo.com
Received: Jan. 8, 2011; Accepted: Sep. 8, 2011

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

which most typically include depression [8], antisocial character, anxiety [9], and memory and psychosomatic disorders [10,11].

Depression is one of the most common psychiatric disorders [12]. Initial presenting symptoms tend to include an increasingly reduced sense of self-efficacy, reduced self-care behaviors, mood swings, and in some cases increased suicidal ideation [9,13]. These symptoms, although significant in and of themselves, can also exacerbate problems for patients with diabetes [3], such as poor medical adherence, functional impairment, and high health care costs (up to 86% in primary care) [14].

Although opium abuse is known to have negative effects on diabetic patients [7], few studies have specifically assessed the impact of opium abuse on depression in this population. Therefore, the current study is designed to investigate the association between opium abuse and severity of depression in Iranian diabetic patients.

METHODS

In this prospective case-control study, we recruited 642 type 2 diabetic patients presenting at two outpatient clinics of the Akhavan Hospital in Kashan, Iran: 173 with a diagnosis of opium abuse (cases) and 469 without this diagnosis (controls). We obtained clinical and demographic information about all participants through a detailed questionnaire. Opium use status was ascertained by self report; however, because of variation in opium quality and difficulty in uniform measurement across all study patients, the quantity of opium intake was not estimated. However, all opium abusers reported having regularly used opium for at least 12 months prior to admission (as indicated by the question, "Has the client continued to use opium despite recurrent problems aggravated by the substance use within the last 12-month period?") [15]. Data on the frequency and duration of opium intake was missing or incomplete in some cases.

Depressive symptomatology and severity were assessed through administration of the Beck Depression Inventory (BDI) [16], and patients scoring over 16 were considered to be depressed. A corresponding diagnosis was made based on the Diagnostic and Statistical Manual of Mental Disorders-IV, Text Revision, 2000 (DSM-IV TR) criteria [17]. To distinguish opium-induced major depressive disorder (MDD) from independent MDD, patients with a history of depression before beginning opium

use, such as those who had used antidepressants or been hospitalized due to depression, were excluded. Patients were considered to have hypertension if they were currently using anti-hypertensive medications or if they had blood pressure readings above 140/90 mm Hg on two different occasions. Hypercholesterolemia was defined as having one or more serum cholesterol level readings above 6.2 mmol/L (240 mg/dL) [18]. Blood glucose control was assessed by measuring HbA1c levels, and values above 7% were considered uncontrolled [19]. The study protocol was approved by the ethics committee of Kashan University of Medical Sciences (Kashan, Iran). Informed consent was obtained from the patients before enrollment.

Statistical analysis

In a case-control study, cases and controls ideally match on all characteristics except the variable of interest. In order to consider the confounding effects of unmatched characteristics, we treated them as covariates in a multiple logistic regression analysis. Variables with *P* values less than 0.2 for differences between the two groups were considered to be covariates: these included age, marital status, literacy, hypertension, and hyperlipidemia. Results were reported as mean \pm standard deviation for quantitative variables and percentages for categorical variables. The groups were compared using the Student's *t*-test for continuous variables and the chi-square test (or Fisher's exact test as appropriate) for categorical variables. Odds ratios (OR) and 95% confidence intervals (CI) for OR were calculated. To decrease the effects of probable confounders, adjusted ORs were estimated when appropriate. Results for which *P* values were 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the 642 Iranian subjects with type 2 diabetes who satisfied the inclusion criteria, 600 (150 opium-abusers and 450 non-opium-abusers) patients were selected for analysis in this study. Their demographic and clinical characteristics are summarized in Table 1.

Depression and MDD were found to be more prevalent among opium-abusing diabetic patients than in non-abusers, and the mean depression score was higher in the opium abuse group. In contrast, dysthymia was diagnosed in 6.7% of abus-

Table 1. Demographic and clinical data of diabetic patients with and without opium dependence

Characteristic	Opium-abuser (n=150)	Non-opium-abuser (n=450)	P value
Male gender	32.0	35.6	0.425
Age, yr	45.1±4.6	44.3±5.1	0.089
Married	74.0	59.8	0.001
Literacy	84.0	70.0	0.008
Family history of depression	51.3	55.1	0.419
Hypertension	51.3	44.0	0.12
Hyperlipidemia	70.7	60.2	0.021
Diabetes duration, yr	8.2±1.1	8.3±2.3	0.608
Controlled diabetes	47.3	48.9	0.734

Data are presented as percent or mean ± standard deviation. $P < 0.05$ significant.

ers and 10.9% of non-abusers. Table 2 shows the prevalence of the different types of depression detected in the two groups.

In general, depression was found to be over four times more likely among opium abusers than non-abusers (OR, 4.54; 95% CI, 2.87 to 7.44; $P = 0.001$). No significant relationship was found between dysthymia and opium abuse (OR, 0.68; 95% CI, 0.18 to 1.192; $P = 0.155$). However, MDD was over seven times as likely in the opium abuse group (OR, 7.32; 95% CI, 5.20 to 12.01; $P < 0.001$).

DISCUSSION

Depression is frequently comorbid in type 2 diabetic patients, with a prevalence of unipolar depression of about 10.9% and that of significant depressive symptoms of about 32.9% [20]. However, depression is under-recognized, and it is estimated to be untreated in approximately two-thirds of depressed diabetic patients. This is unfortunate, since the course of depression tends to be chronic and severe in patients with diabetes [21].

The association between diabetes and depression seems to be interactional, with some studies indicating that diabetes increases the incidence of depression [1-3], and others reporting that depressed adults have an increased risk of developing type 2 diabetes [22-24]. The latter might be explained by an increased likelihood for depressed adults to have a sedentary lifestyle, obesity, and smoking [21]. Conversely, Golden et al. [25] described a reduced risk of depression in patients with

Table 2. Prevalence of different types of depression seen in the two groups

Variable	Opium-addicted (n=31)	Non-opium-addicted (n=165)	P value
Depression symptoms	80.6	47.3	0.001
MDD	74.3	36.1	<0.001
Dysthymia	6.7	10.9	0.15
Depression score	29.27±1.44	18.29±1.31	<0.001

Data are presented as percent or mean ± standard deviation. MDD, major depressive disorder.

impaired fasting glucose levels and untreated type 2 diabetes. In addition, depression has been seen as a predictive factor for the severity and number of diabetic complications in some studies [26,27], while others have not found any such associations [28].

A surprising report states that up to 17.9% of Iranians have used opium at least once, and 8.8% are regular users [29]. Opium contains as much as 12% morphine and is the crudest and least potent form of opiate. Opium abuse has propagated among youth and in various nations for reasons such as ample accessibility and affordability of the drug, unemployment, and mental health problems.

From a physiopathological point of view, opiates act at the basomedial hypothalamus to inhibit the release of gonadotropin releasing factor and thus decrease the circulating concentrations of luteizing hormone and follicular-stimulating hormone. As a result of these decreased pituitary hormone concentrations, the testosterone plasma level declines [30]. McIntyre et al. [31] found that depressed men had lower mean bioavailable and total testosterone levels; likewise, several lines of evidence suggest that testosterone might be effective for the treatment of depression [32,33].

In several studies, it was established that opiate addicts were significantly more depressed than normal controls [8] and even slightly more depressed than psychiatric patients [34]. The reason why opium abuse appears to worsen depression severity in diabetic patients has not been clarified. Although opium use was once recommended as a treatment for diabetes mellitus [35], studies have demonstrated that opium addiction adversely affects some serum factors in diabetic patients by increasing serum glucose, decreasing high density lipoprotein cholesterol, and thus adding to metabolic derangements [36]. Further, serum glucose elevation in diabetics appears to be

correlated with MDD [3].

Association between opium and depression or diabetes and depression has been discussed in several studies, and recent studies have found a significant association between opium abuse and depression in diabetic patients [7]. The current study also found this association to be significant, with 74.3% of opium abusing diabetic patients diagnosed with MDD, compared to 36.1% of non-abusing diabetic patients. In contrast, Shiri et al. [7] detected MDD in only 22.8% of diabetic men which was 1.7 times more than non-abuser diabetics. The reason for this considerable difference in results is not clear, but study design differences and confounders are likely contributors. In another study, Khamseh et al. [1] reported a 71.8% prevalence of MDD in all diabetic patients (abuser or non-abuser), just slightly less than the 74.3% in our study's abuser group. Their study included both type 1 and type 2 diabetic patients, while only type 2 diabetics were enrolled in our study. This appears to highlight the direct impact of opium consumption on diabetics' depressive symptoms compared to the effects of diabetes alone.

There is a fallacy among Iranian people that opium has favorable effects on diabetes mellitus. A previous study that addressed this possibility found that opium temporarily decreased blood glucose, but it had no distinct, long-lasting effects on blood glucose, as determined by HbA1c measurements [37]. Cerebral vascular involvement [38], vascular impairment following retinopathy, multiple hospital admissions, and sexual dysfunction seem to be worsened with comorbid depression among diabetic patients [39]. This may be related to the negative effects of psychiatric disorders on blood glucose control, which implies the importance of treatment for comorbid depression [40].

In the present study, opium use was ascertained by self report, and the quality of the opium intake was not quantified. It is possible that varying quality and frequency of opium use among abusing patients affected study outcomes. Additionally, while one of the exclusion criteria was a documented history of depression before beginning opium use, it is difficult to distinguish opium-induced major MDD from independent MDD, and there may have been pre-existing MDD that was not diagnosed. Group differences were adjusted for unmatched variables, but there are many possible confounders which were not measured or presented in this study. These include other aspects of physical health, mental health, and social support which might have modified the observed association between opium addiction and depression. Similarly, other possible con-

founders, such as thyroid function and folate levels, which may impact depression, were not matched between the groups. Findings could also have been enhanced by adding another control group consisting of non-diabetic opium abusers to assess the direct effects of opium abuse on depression.

We found that depression is both more frequent and more severe in diabetic patients who regularly use opium than in those who do not. Thus, our results suggest that opium-dependent diabetic patients should be advised about the associated increased risks of depression and related comorbidities. Further research is indicated to assess whether consultation about opium abuse in diabetic patients with depression can reduce the severity of depressive symptoms.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Siamak Mehdizadeh Seraj for language revision of the manuscript.

REFERENCES

1. Khamseh ME, Baradaran HR, Rajabali H. Depression and diabetes in Iranian patients: a comparative study. *Int J Psychiatry Med* 2007;37:81-6.
2. Nau DP, Aikens JE, Pacholski AM. Effects of gender and depression on oral medication adherence in persons with type 2 diabetes mellitus. *Gend Med* 2007;4:205-13.
3. Larijani B, Khoram Shahi Baiat M, Khalili Gorgani M, Bandarian F, Akhondzadeh S, Sadjadi SA. Association between depression and diabetes. *German J Psychiatry* 2004;7:62-5.
4. Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. *Harrison's principal of internal medicine*. 15th ed. New York: McGraw-Hill; 2001.
5. Ahmadi J, Sharifi M, Mohagheghzadeh S, Dehbozorgi GR, Farrashbandi H, Moosavinasab M, Firoozabadi A, Pridmore S, Evren C, Busch S, Farash S. Pattern of cocaine and heroin abuse in a sample of Iranian population. *German J Psychiatry* 2005; 8:1-4.
6. Ahmadi J, Maharlooy N, Alishahi M. Substance abuse: prevalence in a sample of nursing students. *J Clin Nurs* 2004;13:60-4.

7. Shiri R, Hassani KF, Ansari M. Association between opium abuse and comorbidity in diabetic men. *Am J Addict* 2006;15:468-72.
8. Gharagozlou H, Behin MT. Frequency of psychiatric symptoms among 150 opium addicts in Shiraz, Iran. *Int J Addict* 1979;14:1145-9.
9. Kaplan H, Sadock B. Kaplan and Sadock's synopsis of psychiatry. 9th ed. Baltimore: Lippincott Williams & Wilkins; 2002.
10. Ahmadi J, Toobaee S, Kharras M, Radmehr M. Psychiatric disorders in opioid dependants. *Int J Soc Psychiatry* 2003;49:185-91.
11. Pavarin RM. Substance use and related problems: a study on the abuse of recreational and not recreational drugs in Northern Italy. *Ann Ist Super Sanita* 2006;42:477-84.
12. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med* 2000;160:3278-85.
13. Kivela SL, Pahlkala K. Clinician-rated symptoms and signs of depression in aged Finns. *Int J Soc Psychiatry* 1988;34:274-84.
14. Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Depressive symptoms and occurrence of type 2 diabetes among Japanese men. *Diabetes Care* 1999;22:1071-6.
15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561-71.
17. Othmer E, Othmer SC. The clinical interview using DSM-IV-TR. Fundamentals. 1st ed. Vol. 1. Washington, DC: American Psychiatric Publishing; 2002.
18. The Expert Panel. Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *Arch Intern Med* 1988;148:36-69.
19. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care* 2003;26 Suppl 1: S33-50.
20. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2006;23:1165-73.
21. Katon WJ. The comorbidity of diabetes mellitus and depression. *Am J Med* 2008; 121(11 Suppl 2):S8-15.
22. Williams MM, Clouse RE, Lustman PJ. Treating depression to prevent diabetes and its complications: understanding depression as a medical risk factor. *Clin Diabetes* 2006;24:79-86.
23. Musselman DL, Betan E, Larsen H, Phillips LS. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. *Biol Psychiatry* 2003;54:317-29.
24. Knol MJ, Twisk JW, Beekman AT, Heine RJ, Snoek FJ, Pouwer F. Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. *Diabetologia* 2006;49:837-45.
25. Golden SH, Lazo M, Carnethon M, Bertoni AG, Schreiner PJ, Diez Roux AV, Lee HB, Lyketsos C. Examining a bidirectional association between depressive symptoms and diabetes. *JAMA* 2008;299:2751-9.
26. Harris MD. Psychosocial aspects of diabetes with an emphasis on depression. *Curr Diab Rep* 2003;3:49-55.
27. Ludman EJ, Katon W, Russo J, Von Korff M, Simon G, Ciechanowski P, Lin E, Bush T, Walker E, Young B. Depression and diabetes symptom burden. *Gen Hosp Psychiatry* 2004;26:430-6.
28. Bryan CJ, Songer TJ, Brooks MM, Thase ME, Gaynes BN, Klinkman M, Rush AJ, Trivedi MH, Fava M, Wisniewski SR. A comparison of baseline sociodemographic and clinical characteristics between major depressive disorder patients with and without diabetes: a STAR*D report. *J Affect Disord* 2008; 108:113-20.
29. Ahmadi J, Pridmore S, Alimi A, Cheraghi A, Arad A, Parsaeyan H, Mohagheghzadeh MS, Kianpour M. Epidemiology of opium use in the general population. *Am J Drug Alcohol Abuse* 2007;33:483-91.
30. Goodman LS, Gilman A. The pharmacological basis of therapeutics. 7th ed. New York: McGraw Hill; 1985.
31. McIntyre RS, Mancini D, Eisfeld BS, Soczynska JK, Grupp L, Konarski JZ, Kennedy SH. Calculated bioavailable testosterone levels and depression in middle-aged men. *Psychoneuroendocrinology* 2006;31:1029-35.
32. Kanayama G, Amiaz R, Seidman S, Pope HG Jr. Testosterone supplementation for depressed men: current research and suggested treatment guidelines. *Exp Clin Psychopharmacol* 2007; 15:529-38.
33. Kumano H. Hormone replacement up-to-date. The effects of androgen replacement therapy on brain function. *Clin Calcium* 2007;17:1378-83.
34. Blatt SJ, Rounsaville B, Eyre SL, Wilber C. The psychodynamics of opiate addiction. *J Nerv Ment Dis* 1984;172:342-52.
35. Elson DF, Meredith M. Therapy for type 2 diabetes mellitus. *WMJ* 1998;97:49-54.

36. Karam GA, Reisi M, Kaseb AA, Khaksari M, Mohammadi A, Mahmoodi M. Effects of opium addiction on some serum factors in addicts with non-insulin-dependent diabetes mellitus. *Addict Biol* 2004;9:53-8.
37. Azod L, Rashidi M, Afkhami-Ardekani M, Kiani G, Khoshkam F. Effect of opium addiction on diabetes. *Am J Drug Alcohol Abuse* 2008;34:383-8.
38. D'Mello DA, Rooker GM. Refractory depression, cardiovascular risk factors, and leukoariosis. *J Clin Psychiatry* 1997;58:274.
39. Lishman WA. *Organic psychiatry: the psychological consequences of cerebral disorder*. 3rd ed. London: Blackwell Science; 1998.
40. Lustman PJ, Clouse RE, Griffith LS, Carney RM, Freedland KE. Screening for depression in diabetes using the Beck Depression Inventory. *Psychosom Med* 1997;59:24-31.