The Levels of Depression and Somatization in Restless Legs Syndrome

Deniz Tuncel[1], Fatma Özlem Orhan[2], M. Fatih Karaaslan[2]

ÖZET:

Huzursuz bacak sendromunda depresyon ve anksiyete düzeyleri

Amaç: Huzursuz bacak sendromu (HBS) istirahat sırasında meydana gelen ve hareketle azalan, bacaklardaki hoşa gitmeyen duyumlarla karakterize, yaygın görülen fakat sıklıkla yanlış tanı konulan veya tanısı atlanılan bir nörolojik hareket bozukluğudur. HBS'nun, depresyon ve anksiyete ile ilişkili olduğu bildirilmiştir. HBS ve depresyonun birlikteliğinin nedeni henüz bilinmemektedir. Somatizasyon, fiziksel semptomlar şeklinde psikolojik endişenin yaşanması ve belirtilmesi olarak tanımlanır. HBS hastalarında somatik semptom puanları yüksek bulunmuştur. Bu çalışmanın amacı HBS'nun depresyon ve diğer psikolojik semptomlarla, özellikle de somatizasyon ile ilişkisini araştırmaktır.

Yöntem: Çalışma grubu, Uluslararası HBS Çalışma Grubunun (IRLSSG) tanı kriterlerini karşılayan 20 HBS hastası ve 20 sağlıklı kontrolden oluşuyordu. Katılımcılardan her biri depresyon ve diğer psikolojik semptomların araştırılması için Hamilton depresyon ölçeği (HAM-D), Hamilton anksiyete ölçeği (HAM-A) ve Belirti tarama listesi-90'ı (SCL-90R) içeren 3 ölçeği doldurdu. Sonuçlar deneyimli bir psikiyatrist tarafından değerlendirildi.

Bulgular: Yaş ortalaması 39,9 (min-mak: 21-65) olan 20 HBS hastası (16 kadın, 4 erkek) ve kontrol grubunda, yaş ortalaması 34,5 (min-mak: 20-52) benzer 20 sağlıklı birey (14 kadın, 6 erkek) vardı. Hamilton depresyon derecelendirme ölçeği ve Hamilton anksiyete ölçeği puanları, HBS hastalarında kontrol grubundakilerden anlamlı biçimde yüksekti, fakat SCL-90R'da yalnızca somatizasyon ve yemek /uyku bozukluğu puanları, HBS hastalarında kontrollerden yüksekti. İki grup arasında depresyon da dâhil olmak üzere diğer semptomlarda istatistiksel olarak anlamlı fark yoktu.

Sonuç: Biz HBS hastalarında SCL-90R puanlarına göre, somatizasyonun, depresyondan daha ön planda olan bir semptom olabileceğini düşünüyoruz. HBS hastalarında, somatik semptomlar dikkatlice değerlendirilmelidir. HBS hastalar depresyonun değerlendirildiği ölçeklerin yetersizliği nedeniyle, depresyon yanlış tanısı alabilirler. Gelecekteki çalışmalarda, depresyon ve HBS ilişkisini göstermek için psikomotor ve somatik parametreleri olmayan depresyon ölçekleri kullanılabilir.

Anahtar sözcükler: Huzursuz bacak sendromu, depresyon, somatizasyon, Hamilton depresyon derecelendirme ölçeği, belirti tarama listesi-90R

Klinik Psikofarmakoloji Bülteni 2009;19:143-147

ABSTRACT:

The levels of depression and somatization in restless legs syndrome

Objective: Restless legs syndrome (RLS) is a common but often misdiagnosed or underdiagnosed neurological movement disorder characterized by disagreeable sensations in the legs that occur at rest and are relieved by movement. RLS has been reported to be associated with depression and anxiety. The reason for the comorbidity of RLS and depression is not yet known. Somatization has been described as the experience and communication of psychological distress in the form of physical symptoms. Somatic symptoms scores in the RLS patients were found high. The purpose of this study was to investigate the relationship of RLS with depression and the other psychological symptoms, especially somatization.

Method: The study population consisted of 20 patients who met the diagnostic criteria for International RLS Study Group (IRLSSG) RLS and 20 healthy control subjects. Patients with RLS were excluded if they had secondary forms of RLS. Each subject completed 3 questionnaires, which included the Hamilton Rating Scale for Depression (HAM-D), Hamilton Rating Scale for Anxiety (HAM-A) and Symptom Checklist-90 Revised (SCL-90R) for investigation of depression and other psychological symptoms. The results were evaluated by an experienced psychiatrist.

Results: There were 20 RLS patients (16 female, 4 male), with a mean age of 39.9 (min-max: 21-65) years, and 20 matched healthy subjects (14 female, 6 male) in the control group, with a mean age of 34.5 (min-max: 20-52) years. The Hamilton Rating Scale for Depression and Hamilton Rating Scale for Anxiety scores of RLS patients were statistically significantly higher than those in the control group, but in the symptom checklist-90R only somatization and eating/sleep disorder scores were higher in the RLS patients than those scores in the controls. There was no statistically significant difference between the two groups for the other symptoms including depression.

Conclusions: We demonstrated somatization to be a more predominant symptom than depression in RLS patients according to the SCL-90R scores. Patients with RLS should be carefully evaluated for somatic symptoms. RLS patients may be misdiagnosed as having depression because of the biases of questionnaires for evaluating depression. In future studies, the depression scales without psychomotor and somatic symptom parameters can be used to explore the relationship between depression and RLS.

Key words: Restless legs syndrome, depression, somatization, Hamilton Rating Scale for Depression, Symptom Checklist-90 Revised

Bulletin of Clinical Psychopharmacology 2009;19:143-147

Departments of [1] Neurology and [2] Psychiatry, Faculty of Medicine, University of Kahramanmaras Sutcu Imam, Kahramanmaras-Turkey

Yazışma Adresi / *Address reprint requests to:*
Deniz Tuncel, MD., Tip Fakultesi. Noroloji A.D., Kahramanmaras Sutcu Imam Universitesi, TR–46050, Kahramanmaras-Turkey

Telefon / *Phone*: +90-344-221-2337/245-360

Faks / *Fax*: +90-344-221-2371

Elektronik posta adresi / *E-mail address:*
tuncedeniz@yahoo.com

Kabul tarihi / *Date of acceptance:*
26 Ekim 2008 / October 26, 2008

INTRODUCTION

Restless legs syndrome (RLS) is a sensorymotor disorder characterized by an urge or need to move the limbs, usually associated with abnormal sensations in the legs described as creeping, crawling, tingling, or painful. These symptoms are worse at rest, are relieved by movement, and mainly occur in the evening and/or at night, resulting in RLS patients complaining of sleep disturbance, especially insomnia (1-3).

The pathophysiology of RLS is understood incompletely, but it probably results from derangements in dopamine and iron metabolism, and has a genetic component (4).

During the last few years, population- and clinic-based epidemiological studies have demonstrated that there are significantly higher rates of depressive and/or anxiety symptoms in RLS patients than in controls as assessed by the Hamilton Depression scale, the geriatric depression scale, the single question response: mood, the center for epidemiological studies depression scale, the Beck depression inventory, DSM-III criteria and etc (5-11). There is an overlap between the symptoms of depression and RLS; however, in clinical practice it is not difficult to make a differential diagnosis. The symptoms that could either be interpreted as symptoms of depression or as directly due to the sleep disorder include worry, restlessness, irritability, hopelessness, loss of appetite, suicidality, loss of interest, sleep disturbance, depressed mood, fatigue, and diminished concentration (5).

The mechanism of interrelation between depression and RLS is not yet completely understood, and there are only a few studies that address this issue. Hypofunction of the dopaminergic system is thought to be involved both in the pathophysiology of depression and RLS (4,13). In a recent paper, Picchietti and Winkelmann presented a critical review of the literature on the association of RLS and depression. They suggested three causes for this association. First, RLS may cause depression. Second, depression may cause RLS. And finally, a third factor causes both RLS and depression. Another probability is that symptoms of one disorder are misdiagnosed as symptoms of the other disorder (5).

The few published studies on RLS patients have utilized scales that are specific to one or two psychiatric domains. We investigated depression and other psychological symptoms in 20 RLS patients and 20 healthy control subjects via the Hamilton Rating Scale for Depression (HAM-D), the Hamilton Rating Scale for Anxiety (HAM-A) and the Symptom Checklist-90R (SCL-90R), which is a validated clinical scale to screen for symptoms related to a spectrum of nine different psychological domains.

METHODS

Subjects

The study population consisted of 20 patients who met the diagnostic criteria for The International RLS Study Group (IRLSSG) RLS and 20 healthy control subjects, all matched for age and sex (14). The essential criteria for the syndrome are (1) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; (2) the urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying or sitting; (3) the urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues; and (4) the urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night. All four of these criteria must be met for RLS to be diagnosed. Patients experiencing sign of secondary RLS (e.g., endocrine, hematological, polyneuropathy, pregnancy and end-stage renal disease) were excluded. All subjects signed written informed consent after being provided standard information about the study. The study protocol was approved by the Ethics Committee of Kahramanmaras University Faculty of Medicine, Neurology Department.

Psychiatric evaluation

Each subject was interviewed to complete 3 questionnaires for the investigation of the psychiatric symptoms. These were the Hamilton Rating Scale for Depression (HAM-D) (15,16), the Hamilton Rating Scale for Anxiety (HAM-A) (17,18) and the Symptom Checklist-90 Revised (SCL-90R) (19,20). The SCL-90R is a well-established, self-report, clinical rating scale that assesses outpatient symptomatic psychological disturbance. It comprises the following 9 primary

symptom scales and one additional item: somatization, obsession–compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and the additional item of eating and sleep disorder scale. The results of these tests were evaluated by a qualified psychiatrist.

Data analysis

Statistical assessments were carried out with SPSS

0.570, p: 0.533).

The Hamilton Rating Scale for Depression and Hamilton Rating Scale for Anxiety scores of RLS patients (respectively; median: 16, 15) were significantly higher than that in the control group (Table 1).

The somatization and eating/sleep disorder scores in symptom checklist-90R were higher in the RLS patients as compared to controls. The other symptoms, including depression, were not significantly different between RLS patients and control groups (Table 2).

Table 1: The Hamilton Rating Scale for Depression and Hamilton Rating Scale for Anxiety scores of RLS patients and healthy controls.

	Patients (n=20) Median (min-max)	Controls (n=20) Median (min-max)	p
HAM-D	16 (3-30)	2 (0-9)	<0,001
HAM-A	15 (2-32)	2,5 (0-16)	<0,001

HAM-D: Hamilton Rating Scale for Depression, HAM-A: Hamilton Rating Scale for Anxiety

Table 2: The Symptom Checklist-90R (SCL-90R) scores of RLS patients and healthy controls.

	Patients Median (min-max)	Controls Median (min-max)	P
Somatization	1,3 (0,3-2,9)	0,6 (0-1,6)	0.001
Obsession–compulsion	0,8 (0,1-2)	1 (0,3-2,1)	0.242
Interpersonal sensitivity	0,4 (0-1,4)	0,9 (0,2-1,6)	<0.001
Depression	0,9 (0-2)	0,9 (0,3-1,5)	0.456
Anxiety	0,6 (0-2,2)	0,4 (0-1,1)	0.438
Hostility	0,3 (0-2,5)	0,7 (0,2-1,5)	0.068
Phobic anxiety	0 (0-0,7)	0,1 (0-1,6)	0.315
Paranoid ideation	1,2 (0-2,5)	0,8 (0,2-1,7)	<0.001
Psychoticism	0,1 (0-1,2)	0,4 (0,1-0,9)	0.012
Eating/sleep disorder	1,3 (0-2,1)	0,6 (0-1,6)	0.008
General Severity Index	0,7 (0,1-1,6)	0,7 (0-1,1)	0.055

11.0 packet program. All data were given as mean ± standard deviation (SD). Chi-square test was used to evaluate distribution of sex. The Mann-Whitney U test was used to compare the mean ranks because of the distribution between groups weren't equal. Statistical significance was determined as $p < 0.05$.

RESULTS

There were 20 RLS patients (16 female, 4 male), with a mean age of 39.9 (min-max: 21-65) years, and 20 matched healthy subjects (14 female, 6 male), in the control group, with a mean age of 34.5 (min-max: 20-52) years. Age and sex distributions of patients and control groups were determined to be similar (respectively: p:

DISCUSSION

In previous studies, it had been shown that RLS was associated with increased depression and anxiety scores and a reduced quality of life (5). Furthermore, EEG mappings have revealed findings characteristic of major depression (21). Our investigation showed that RLS patients were more anxious and depressed than the controls, according to the HAM-D and HAM-A scales. This result is similar to the previously reported population- and clinic-based studies on RLS using anxiety and depression scales (5,6). Although depression symptoms are reported to be common in studies of RLS patients, the relationship appears to be complex, with an overlap between RLS and depression-related symptoms

Klinik Psikofarmakoloji Bülteni, Cilt: 19, Sayı: 2, 2009 / *Bulletin of Clinical Psychopharmacology, Vol: 19, N.: 2, 2009* - www.psikofarmakoloji.org

145

confounding the issue. Sometimes, though, RLS patients may be misdiagnosed as having depression because of the biases of questionnaires for evaluating depression. Sevim and et al. evaluated psychiatric symptoms by HAM-D and HAM-A scales and used the International RLS Study Group Rating Scale (IRLSSGRS) to assess the severity of RLS. Their results showed that the RLS population had high scores for depression and anxiety and a clear relationship, indicating that the HAM-A and HAM-D scores were directly related to IRLSSG Rating Scale scores. They suggested that the HAM-D and HAM-A scales were not designed to measure the level of anxiety and depression among RLS patients, and items related to sleep were excluded before comparing the total scores of patients and controls (6).

We found that the HAM-D and HAM-A scores of RLS patients were significantly higher than those of the control group but depression scores from the SCL-90R were not higher in the RLS patients as compared to controls. This may be explained by the fact that many items of the Hamilton Depression Scale refer to psychomotor and somatic symptoms of depression, which casts doubt on the validity of the HAM-D scale scores in the presence of somatic comorbidity. Linden et al. investigated the validity of the HAM-D rating scale in cases where the patient is suffering from a depressive illness together with somatic illnesses and showed that multimorbidity interferes with the validity of the HAM-D rating scale (22). There were 8 items for which more than half of all positive scores, as rated by psychiatrists, were seen by the internists as being possibly related to somatic disorders. Furthermore, four of the 9 DSM-IV criteria for major depression can also be caused by RLS: 'insomnia or hypersomnia', 'fatigue /loss of energy', 'diminished concentration', and psychomotor retardation or agitation'. Only 5 of the 9 criteria are required to make a diagnosis of major depression. In this way, an individual with RLS might just have nearly enough of these symptoms to exceed the threshold for an abnormal score on a depression questionnaire, even in the absence of a real major depressive episode (5).

The SCL-90R is a self-report inventory designed to provide a reflection of the psychological symptom profile of a community of medical and psychiatric subjects. It measures the present psychological symptom status and is not a direct measure of personality (19). Published studies have demonstrated that SCL-90R were able to discriminate between patients with major and minor depression and the absence of mood disorders (23,24). However, in contrast to the above results, we did not find a statistically significant difference between the two groups in the depression and anxiety subscales of the SCL-90R. However, in the other subscales of SCL-90, including somatization and eating/ sleep disorder, the difference between the two groups were statistically significant.

Somatization is the tendency to express emotional problems in somatoform symptoms. Few studies have studied and revealed a correlation between somatization and RLS. Gillespie et al. suggested that sleep disturbance is one of the most important dimensions of somatoform disorders beside depression, somatic distress, and phobic anxiety (25,26). Ulferberg and et al. reported that RLS may be associated with several somatic and neuropsychiatric symptoms (25). Also, Aigner et al. showed that patients with somatoform pain disorder (SPD) should be carefully diagnosed for RLS and suggested that further studies are warranted to highlight the common pathophysiological background of SPD and RLS (27). Alternatively, individuals with major depression could be misdiagnosed in the epidemiological studies as having RLS, since elderly individuals with depression often somatize (28). Hornyak et al. showed that untreated RLS patients had slightly elevated Beck depression inventory scores especially the somatic items and sleep related symptoms (29). Our study showed that somatization is a more predominant symptom than depression in RLS patients according to SCL-90R scores.

The psychiatric illness comorbidity or a contributing cause of RLS is not known. However, the excessive antidepressant use in RLS patients, whether a correct diagnosis of depression was made or not, may aggravate RLS symptoms (2,30). In the evaluation of depression in RLS patients, specific features not directly related to RLS symptoms should be focused upon, including depressive mood, loss of interest, preoccupation with guilt, and suicidal ideation (5).

In conclusion, depression and anxiety disorders further complicate the clinical picture of RLS. Symptoms of depression and somatization can contribute to overdiagnosis or underdiagnosis of the condition. In this preliminary study, we demonstrated that somatization is a

more predominant symptom than depression in RLS patients. In future studies, the depression scales without

psychomotor and somatic symptom parameters should be used to study the relationship between depression and RLS.

References:

1. Ekbom KA. Restless legs syndrome. Neurology 1960;10:868-873.

2. Earley CJ. Clinical practice. Restless legs syndrome. N Engl J Med 2003; 22: 2103-2109.

3. Walters AS. The International Restless Legs Syndrome Study Group. Toward a better definition of the restless legs syndrome. Mov Disord 1995; 10: 634-642.

4. Barriere G, Cazalets JR, Bioulac B, Tison F, Ghorayeb I. The restless legs syndrome. Prog Neurobiol 2005; 77: 139-165.

5. Picchietti D, Winkelman JW. Restless legs syndrome, periodic limb movements in sleep, and depression. Sleep 2005; 28: 891-898.

6. Sevim S, Dogu O, Kaleagasi H, Aral M, Metin O, Camdeviren H. Correlation of anxiety and depression symptoms in patients with restless legs syndrome: a population based survey. J Neurol Neurosurg Psychiatry 2004; 75: 226-230.

7. Sukegawa T, Itoga M, Seno H et al. Sleep disturbance and depression in the elderly in Japan. Psychiatry Clin Neurosci 2003; 57: 265-270.

8. Ulfberg J, Nystrom B, Carter N, Edling C. Prevalence of restless legs syndrome among men aged 18 to 64 years: an association with somatic disease and neuropsychiatric symptoms. Mov Disord 2001; 16: 1159-1163.

9. Rothdach AJ, Trenkwalder C, Haberstock J, Keil U, Berger K. Prevalence and risk factors of RLS in an elderly population. Neurology 2000; 54:1064-1068.

10. Vandeputte M, de Weerd A. Sleep disorders and depressive feelings: a global survey with the Beck depression scale. Sleep Med 2003; 4: 343-345.

11. Mosko S, Zetin M, Glen S et al. Self-reported depressive symptomatology, mood rating, and treatment outcome in sleep disorders patients. J Clin Psychol 1989; 45: 51-60.

12. Dailly E, Chenu F, Renard CE et al. Dopamine, depression and antidepressants. Fundam Clin Pharmacol 2004; 18: 601-607.

13. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med 2003; 4: 101-19.

14. Williams BW. A structured interview guide for Hamilton Depression Rating Scale. Arch Gen Psychiatr 1978; 45: 742-747.

15. Akdemir A, Orsel S, Dag I, Türkcapar H, İscan N, Ozbay H. Hamilton depresyon derecelendirme ölçeği (HDDÖ)'nin geçerliği, güvenirliği ve klinikte kullanım. Psikiyatri Psikoloji Psikofarmakoloji Dergisi 1996; 4: 251-259.

16. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959; 32: 50-55.

17. Yazıcı MK, Demir B, Tanrıverdi N, Karaağaoğlu E, Yolaç P. Hamilton Anxiety Rating Scale: Interrater Reliabilty and Validity Study. Turk Psikiyatri Derg 1998; 9: 114-117.

18. Derogatis LR. SCL-90: Administration, scoring and procedure manual-1 for the revised version. Baltimore, MD: John Hopkins Univ., School of Medicine, Clinical Psychometrics Unit. 1977.

19. Dag I. Belirti Tarama Listesi (SCL-90R)'nin üniversite öğrencileri için güvenirliği ve geçerliği. Turk Psikiyatri Derg 1991; 2: 5-12.

20. Saletu M, Anderer P, Saletu B, et al. EEG-mapping in patients with restless legs syndrome as compared with normal controls. Psychiatry Red. 2002; 115: 49-61.

21. Linden M, Borchelt M, Barnow S, Geiselmann B. The impact of somatic morbidity on the Hamilton Depression Rating Scale in the very old. Acta Psychiatr Scand 1995; 92: 150-154.

22. Gillespie NA, Zhu G, Heath AC, Hickie IB, Martin NG. The genetic aetiology of somatic distress. Psychol Med 2000; 30:1051-61.

23. Rosenberg R, Bech P, Mellergard M, Ottosson JO. Secondary depression in panic disorder: an indicator of severity with a weak effect on outcome in alprazolam and imipramine treatment. Acta Psychiatr Scand Suppl 1991;365:39-45.

24. Vollrath M, Koch R, Angst J. The Zurich Study. IX. Panic disorder and sporadic panic: symptoms, diagnosis, prevalence, and overlap with depression. Eur Arch Psychiatry Neurol Sci 1990;239: 221-230.

25. Ulfberg J, Nyström B, Carter N, Edling C. Prevalence of restless legs syndrome among men aged 18 to 64 years: an association with somatic disease and neuropsychiatric symptoms. Mov Disord 2001; 16: 1159-1163.

26. Sayar K, Ak I. The predictors of somatization: A review. Bull Cli Psychopharmacol 2001;11:266-271.

27. Aigner M, Prause W, Freidl M et al. High prevalence of restless legs syndrome in somatoform pain disorder. Eur Arch Psychiatry Clin Neurosci 2007; 257: 54-57.

28. Gallo JJ, Rabins PV. Depression without sadness: alternative presentations of depression in late life. Am Fam Physician 1999; 60: 820-826.

29. Hornyak M, Kopasz M, Psych. MA, Berger M, Riemann D, Voderholzer U. Impact of sleep-related complaints on depressive symptoms in patients with restless legs syndrome. J Clin Psychiatry 2005; 66: 1139-1145.

30. Nader P, Coralie L, Baleydier B, Andrei C, Susanne M, Damsa C. Restless legs syndrome induced by citalopram: a psychiatric emergency? Gen Hosp Psychiatry 2007; 29: 72-74.

Klinik Psikofarmakoloji Bülteni, Cilt: 19, Sayı: 2, 2009 / Bulletin of Clinical Psychopharmacology, Vol: 19, N.: 2, 2009 - www.psikofarmakoloji.org

147