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Original article

Sleep complaints and restless legs syndrome in adult type 2 diabetics

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Abstract

Objective: To determine the prevalence and characteristics of sleep complaints and restless legs syndrome (RLS) in type 2 adult diabetics. To test the hypothesis that sleep complaints are more common among adult diabetics.

Background: Restless legs syndrome is a common disorder and is a cause of insomnia and daytime somnolence. An association between RLS and diabetes mellitus has been hypothesized but has not been established.

Methods: Consecutive type 2 diabetic patients and controls were subjected to sleep questionnaires, examinations for sensory neuropathy, and laboratory investigations.

Results: Diabetics had higher rates of insomnia (50 vs. 31%, $P = 0.04$) and used more hypnotics (25.9 vs. 6.0%, $P = 0.02$) than controls. The proportion of diabetics with elevated Epworth Sleepiness Scores ($\geq$12) was higher than controls (15.5 vs.2.1%, $P = 0.02$). The prevalence of RLS among diabetics was not significantly different than in controls (24.1 vs. 12.5%, $P = 0.1$). The prevalence of sensory polyneuropathy was similar in diabetics with and without RLS. Age, BMI, duration and level of diabetes control, hemoglobin, ferritin and creatinine levels did not predict the presence of RLS in diabetics.

Conclusions: Adult type 2 diabetics have higher rates of insomnia, excessive somnolence and hypnotic use than controls. There is no evidence that RLS is significantly more common in adult diabetics.

Keywords: Diabetes mellitus; Restless legs syndrome; Insomnia; Sleep; Somnolence

1. Introduction

Restless legs syndrome (RLS) is a disorder characterized by uncomfortable leg sensations usually occurring prior to sleep onset or during periods of inactivity and often described as 'crawling, creeping, or pulling' [1]. These sensations are commonly felt in the lower extremities and result in an irresistible urge to move limbs. Typically patients obtain relief by movement. Restless legs syndrome has recently been characterized by The International Restless Legs Syndrome Study Group (IRLSSG) as a clinical syndrome consisting of the following symptoms: (i) desire to move the limbs associated with paresthesias/dysesthesias; (ii) motor restlessness; (iii) exacerbation of symptoms with inactivity and relief by activity; (iv) worsening of symptoms at night [2].

This syndrome has been reported to be associated with uremia, pregnancy, polyneuropathy, rheumatoid

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arthritis, anemia, a variety of metabolic and endocrine disorders, including diabetes mellitus, hypothyroidism, B_{12} deficiency and medications [3–19]. Most of these associations, however, are based on case reports or case series and were reported prior to the recent IRLSSG description of the syndrome.

There is no conclusive evidence based on rigorous studies that an association between diabetes mellitus and RLS exists. Although RLS has been reported to be associated with polyneuropathy [7,12,14,18,19] and diabetes is a common cause of polyneuropathy, there is no data on the prevalence of RLS in patients with diabetic neuropathy. Although sleep complaints in diabetics are thought to be common [13,15] their prevalence and etiology in a consecutive sample of diabetic outpatients has not been reported.

We hypothesized that diabetics have worse sleep than controls. We wished to determine the nature and prevalence of sleep complaints and the prevalence of RLS in adult diabetic outpatients and a sex and age-matched control group.

2. Methods

2.1. Patient selection

Participation in the study was offered to 58 consecutive type 2 diabetic patients over the age of 18, and to 48 age and sex matched non-diabetic controls attending the St. Boniface General Hospital, Winnipeg, Manitoba, Canada outpatient endocrinology clinics. The control group consisted of patients attending the same clinics for follow-up of previously diagnosed and treated endocrine disorders and were free of current active disease. Pregnant and dialysis-dependent patients were excluded. Informed consent was obtained. The study protocol was approved by the University of Manitoba Committee on the use of Human Subjects in Research.

2.2. Protocol

Information pertaining to diabetes (duration and type of diabetes, presence of diabetic complications), past medical history and medication use was obtained from chart review and patient interview. The type of diabetes was confirmed by the endocrinology specialists participating in the study. Diabetic complications were sought by careful chart review and were noted if an objective documentation was found. Microvascular complications were thought to be present if (i) retinopathy was identified by detailed ophthalmologic examination or the patient underwent previous laser photocoagulation; (ii) nephropathy was identified (as indicated by the presence of microalbuminuria (over 30 mg/24 h), proteinuria or elevated creatinine); (iii) polyneuropathy identified by the presence of typical glove and stocking type sensory deficits. Macrovascular complications were thought to be present if an objective documentation of coronary artery disease (diagnostic cardiac exercise test, coronary angiography, documented myocardial infarction or coronary artery bypass surgery) or cerebral vascular disease (documented focal neurologic findings supported by appropriate imaging studies) was found.

A control group of sex and age matched non-diabetic patients was chosen from the same outpatient adult endocrinology clinic. Diabetics and controls were subjected to a detailed personal interview by one of the investigators. This consisted of questions, which focused on presence, frequency and characteristics of sleep-related complaints: insomnia, sleep disordered breathing (snoring and witnessed apneas) and restless legs syndrome. Insomnia was defined as difficulty with sleep onset or maintenance occurring at least three times per week. Subjects were asked to identify the most likely factors contributing to sleep complaints. Epworth Sleepiness Score was obtained from the diabetics and controls.

All subjects were subsequently examined by one of the investigators for presence of peripheral polyneuropathy in the lower extremities using Semmes–Wienstein filaments and 128 Hz vibration tuning forks. Polyneuropathy was defined as an abnormality on at least one of these tests and existence of symptoms of paresthesias in characteristic glove and stocking distribution. A blood sample was obtained and analyzed for complete blood count, glycosylated hemoglobin (A_{1c}), electrolytes, urea, creatinine, serum iron, ferritin, folate and vitamin B_{12} levels.

3. Statistical methods

Baseline characteristics of the diabetics and controls were compared using unpaired one-tailed t-

tests and Chi-square analysis. The prevalence of RLS and sleep problems was determined in diabetic patients and compared to the control group using Chi-square analysis. The single-tailed test was used because we predicted a priori the direction of findings. Logistic regression was performed to determine which of the following factors predicted presence of RLS among diabetics: age, body mass index (BMI), duration of diabetes, Hgb A_{1c}, Hgb, creatinine and ferritin levels. A p value of 0.05 or less was considered statistically significant.

4. Results

Baseline characteristics of the diabetics and controls are presented in Table 1. The diabetics and the controls were similar with regards to age, sex distribution, and laboratory results but the diabetic group was more obese. The diabetic group had a high prevalence of microvascular (58.6%) and macrovascular (24.1%) complications. The average duration of diabetes in this group was 10 years.

Sleep complaints were common among adult type 2 diabetics. Higher rates of insomnia (50 vs. 31.3%, $P = 0.04$) were found among diabetics than controls. Difficulty with sleep maintenance was reported by 40% of diabetic insomniac patients, and 42.9% reported a combination of sleep onset and maintenance difficulties. Sleep onset insomnia was less frequent, accounting for 17.1% of complaints among diabetics with insomnia. Nocturia and musculoskeletal (MSK) discomfort were commonly identified by the diabetics suffering from insomnia as contributing to or causing sleep disturbance and were more frequent than in controls (nocturia, 41.4 vs. 18.8%, $P = 0.01$); (MSK discomfort, 29.3 vs. 12.5%, $P = 0.03$). The prevalence of night-time restlessness (27.6 vs. 14.6%, $P = 0.1$) was not significantly higher in the diabetic group.

Over 55% of diabetics complained of daytime sleepiness. An Epworth Sleepiness Score (ESS) ≥ 12 was thought to be indicative of significant somnolence. Similar cut-off values for excessive somnolence were used in other studies [20]. The diabetic group had a larger proportion of patients with ESS over 12 (15.5 vs. 2.1%, $P = 0.02$) (Table 2). Approximately half of the diabetics reported habitual snoring. Frequency of self-reported nocturnal apneas was not increased in the diabetic group (10.3 vs. 16.7%, $P = 0.17$).

The use of hypnotics in diabetics was significantly higher than in non-diabetics (26 vs. 6%, $P = 0.02$). Frequent daytime naps were reported by 25.9% of diabetics and 16.7% of controls ($P = 0.19$).

Restless legs syndrome was common in both groups affecting over 24% of diabetic patients and 12.5% of the non-diabetic controls. The difference between the two groups was not statistically significant using the one-tailed *t*-test ($P = 0.1$).

Diabetic patients with and without RLS were similar with regards to age, sex distribution, duration of diabetes, level of diabetic control and biochemical indices (Table 3). ESS scores were significantly higher in the diabetics with RLS than in non-RLS diabetics (8.2 vs. 4.8, $P = 0.02$). Epworth scores

Table 1
Characteristics of Type 2 diabetics and control subjects[a]

	Controls ($n = 48$)	Type 2 diabetics ($n = 58$)	P value
Age (years)	53.1 (15.2)	57.2 (14.5)	0.16
Males (%)	56	50	0.66
BMI	27.4 (4.7)	30.1 (7.3)	0.03
Hgb (g/l)	135 (11.3)	136 (14.7)	0.82
Creatinine (μmol/l)	74.0 (25.7)	79.3 (30.1)	0.47
Urea (mmol/l)	5.7 (1.8)	6.3 (2.7)	0.31
Folate (nmol/l)	29.4 (17.5)	25.7 (12.7)	0.27
VitaminB_{12} (pmol/l)	315.0 (119.5)	352.2 (231.2)	0.36
Ferritin (μg/l)	107 (95.0)	154.7 (178.6)	0.14

[a] Values presented are mean (standard deviations). BMI - body mass index; Hgb - hemoglobin.

Table 2
Sleep complaints of type 2 diabetics and controls

	Controls ($n = 48$)	Type 2 diabetics ($n = 58$)	P value
RLS (%)	12.5	24.1	0.10
Insomnia (%)	31.3	50	0.04
EDS (%)	37.5	55	0.15
ESS[a]	5.1 (3.8)	5.6 (4.6)	0.27
ESS > 12 (%)	2.1	15.5	0.02
Hypnotic use (%)[b]	6.0	25.9	0.02
Daytime naps (%)	16.7	25.9	0.19
Witnessed apneas (%)	16.7	10.34	0.17
Snoring (%)	64.6	53.4	0.17

[a] Epworth Sleepiness Score – mean (standard deviation).
[b] Hypnotic use – percentage of subjects using medication to induce or promote sleep. % - percent of subjects.

were also higher in controls with RLS than in non-RLS controls, although this difference did not achieve statistical significance (7.0 vs.4.8, $P = 0.21$).

A high prevalence rate of insomnia was also found in the diabetics with RLS (Table 3), but this rate was not significantly higher than in diabetics without RLS. The prevalence rates of sensory polyneuropathy were similar in diabetics with and without RLS syndrome (43 vs. 34%, $P = 0.78$).

Regression analysis revealed that none of the following factors were associated with RLS among diabetics: age, BMI, duration of diabetes, creatinine, ferritin level, Hgb and Hgb A_{1c}.

5. Discussion

This study examined the prevalence and characteristics of sleep complaints and prevalence of restless legs syndrome in a population of adult type 2 diabetic outpatients attending endocrinology clinics.

We found that sleep complaints were common in the diabetics. High rates of insomnia and daytime somnolence were reported. This is consistent with previous reports. A large Finnish study assessed the quality of life in 1804 adult diabetics and included sleep-related questions. Almost half reported early awakening, 28% had difficulty with sleep onset,

Table 3
Characteristics and sleep complaints of the diabetic group with and without restless legs syndrome[a]

	Diabetics with RLS ($n = 14$)	Diabetics without RLS ($n = 44$)	P value
Age (years)	58.1 (15.3)	56.9 (14.4)	0.66
Males (%)	57	48	0.76
BMI	33.1 (8.2)	29.2 (6.8)	0.08
Duration (years)	9.7 (7.7)	10.1(8.1)	0.60
Insomnia (%)	72	43	0.13
EDS (%)*	72	50	0.27
ESS**	8.2 (6.5)	4.8 (3.7)	0.02
Neuropathy (%)	43	34	0.78
Hgb (g/l)	137 (19)	136 (14)	0.80
Creatinine (μmol/l)	83 (30)	78 (30)	0.60
Ferritin (μg/l)	188 (151)	144 (187)	0.24
$HgbA_{1c}$ (%)	7.6 (1.3)	7.7 (1.8)	0.88

[a] Values presented are mean (standard deviations). *EDS - excessive daytime somnolence; **ESS - Epworth Sleepiness Score; % - percent of subjects; Hgb - hemoglobin; $HgbA_{1c}$ - glycosylated hemoglobin. Duration - years with diabetes.

while 32% were taking hypnotics [15]. In another study elderly Swedish patients with diabetes were more likely to complain of hypersomnolence [13]. These reports, primarily based on mail-in questionnaires, did not attempt to characterize sleep complaints further or to determine their severity. In our group of diabetic subjects we found that sleep maintenance complaints were common and accounted for a large proportion of sleep disruption in this group of patients. Sleep onset insomnia was less common. Nocturia and musculoskeletal complaints were identified by patients as the most common reasons for insomnia and were significantly more frequent than in the control group.

Hypersomnolence was more common in the diabetics than in the controls. In approximately 26% of the diabetics daytime somnolence was of high enough severity to prompt introduction of regularly scheduled naps. Since our study was not designed to differentiate between different causes of daytime somnolence, the reasons for this finding are not clear. Various factors such as use of sedatives and sleep disordered breathing and RLS may be contributing. In our study approximately half of the patients with elevated Epworth scores were prescribed sedatives. The use of hypnotics may, therefore, explain elevated ESS scores in this group. It has been suggested that uncontrolled diabetes may be a cause of daytime somnolence although exact mechanisms are not clear [17]. Our diabetic patients were regularly attending specialty clinics and had good control of blood glucose. We cannot therefore attribute their hypersomnolence to poor control of the diabetes. Although the prevalence of snoring and witnessed apneas was similar in both diabetics and controls we cannot exclude the possibility that the prevalence of sleep-disordered breathing was higher among the diabetics.

We found that symptoms of RLS were common in the diabetic group, although not significantly higher than in the control group. In our group of diabetics, 24% of patients satisfied the criteria for RLS as described by The International Restless Legs Syndrome Study Group [2]. Few studies have addressed the question of an association between diabetes mellitus and RLS. Our center recently reported in an epidemiologic study that patients referred to a sleep disorders center with RLS were not more likely to have been previously diagnosed with diabetes than matched controls [21]. Machtey reported an increased prevalence of diabetes mellitus in a group of rheumatology patients with RLS [10]; Banerji et al reported symptoms of RLS in 17% of diabetics [16]. A questionnaire study of US Veterans, however, reported no significant increase in RLS among diabetic patients [11]. The difference in prevalence rates reported by these studies likely reflects the differences in diagnostic criteria and populations investigated.

In our study there was no association between RLS and diabetes. Both disorders are common in general population and may co-exist, especially in older adults. Since our diabetics were four years older than controls it is possible that age differences contributed to the observed difference in rates of RLS. Our study was not prospective and we could not determine the duration of RLS symptoms in our subjects. It is therefore unknown if RLS preceded or followed the development of diabetes. If an association between RLS and DM exists, it is not strong and an epidemiological study involving a larger sample may be necessary to detect its presence. Such a prospective study of RLS in a large consecutive sample of diabetic patients has not been performed.

Even though our controls were not recruited from the general population the prevalence rate of RLS among our controls was similar to that previously reported for the general population in Canada, emphasizing that RLS is a common condition. A large questionnaire study performed in Canada estimated that RLS affects 10–15% of general population [22]. Our study differs from that and other reports in that we utilized a questionnaire based on the 1995 International RLS Study Group Criteria and we examined consecutive diabetic patients. We also evaluated patients with RLS for sleep complaints and elicited symptoms of EDS and polyneuropathy. Laboratory investigations were performed to rule out disorders associated with RLS and to eliminate confounding factors.

We found high rates of EDS and insomnia in the diabetic RLS group. This is not unexpected, as this syndrome is a known cause of insomnia and daytime sleepiness. Diabetic insomniacs had a significantly increased rate of RLS – 33% of diabetics patients with insomnia met the criteria for RLS while only 13% of control patients with insomnia had RLS.

This finding suggests that RLS may account for a higher percentage of insomnia among the diabetics that in the control population.

Diabetics with RLS were similar in age, sex distribution and biochemical indices to diabetics without RLS. None of the RLS patients reported the use of phenothiazines and only one was prescribed tricyclics. The prevalence of clinically detectable polyneuropathy was similar in two groups. Our study suggests that RLS occurs in diabetic patients irrespective of medication use, renal insufficiency, iron deficiency anemia or neuropathy. Neither the duration of diabetes nor level of control (as determined by Hgb A_{1c} levels) were significant predictors of RLS in a regression analysis. A large number of statistical comparisons used in this study may have affected the validity of the results.

6. Conclusions

Sleep complaints are common among adult type 2 diabetics. These complaints prompt patients to obtain pharmacological therapy and consequently the use of hypnotics is high in this group of patients. Insomnia, which in this group of subjects is commonly related to difficulty with sleep maintenance, is common and is associated with nocturia and musculoskeletal discomfort. Symptoms of RLS in diabetics could not be attributed to medication use, uremia, iron deficiency or polyneuropathy. Restless legs syndrome is a common cause of insomnia in this group of patients, as it is in the general population. Since it represents a treatable cause of insomnia, it is reasonable to inquire about symptoms of RLS among diabetics with insomnia. Daytime hypersomnolence is a frequent complaint and may be related to the high prevalence of hypnotic use in these patients.

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