
Original article

Incidence and Characteristics of Restless Legs Syndrome in Hemodialysis Patients

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Abstract

Introduction. Restless legs syndrome is a serious problem in patients on hemodialysis. In our study we determine the prevalence and characteristics of this syndrome in hemodialysis patients.

Methods. The cross-section investigation involved patients treated by chronic hemodialysis. Demographic, anthropometric and clinical characteristics (body mass index, smoking, alcohol consumption, insomnia and residual diuresis, urea kinetic model, diabetes mellitus and cardiovascular disease) were recorded for each patient. Restless legs symptoms were determined according to criteria adopted by the International Restless Legs Syndrome Group. Patients were divided into groups with and without restless legs syndrome. Biochemical analyses were made at the start of dialysis in the middle of the week.

Results. Restless legs syndrome was found in 62% of the examined patients. The group with restless legs syndrome was older (63.5±10.6 vs. 53±13.2 years) than that without this syndrome (p=0.006). Statistically significant differences between the two groups of patients were also evident regarding the concentration of serum iron (p=0.018) and the degree of elimination of urea (p=0.03).

Conclusion. Patients who had restless legs syndrome were generally older, had lower concentrations of serum iron and lower adequacy of hemodialysis. The incidence of restless legs syndrome among our hemodialysis patients was 62%.

Key words: restless legs syndrome, hemodialysis, incidence

Introduction

The first modern medical description of restless legs syndrome was given by Ekbohm in 1943. Detailed diagnostic criteria were adopted by the International Restless Legs Syndrome Study Group (IRLSSG) in 1953. These criteria were revised recently by the international diagnostic workshop at the National Institute of Health in Washington. Epidemiological data generally estimated between 2 and 15%

prevalence of restless legs syndrome in the general population. It usually appears in mid-life (between 40 and 60 years of age), but can occur in younger populations [1]. Restless legs syndrome is a serious problem in hemodialysis patients. It is manifested by unpleasant leg movements, most commonly during rest or sleep, which lead to significant physical and emotional stress [2].

There is no specific diagnostic test for restless legs syndrome, but diagnosis is based on an assessment of the subjective symptoms of each patient and the clinical picture. Positive answers to four questions confirm the diagnosis of restless legs syndrome according to IRLSSG criteria:

1. Do you have an urge to move your legs due to an unpleasant feeling in them?
2. Does the urge to move your legs, or the unpleasant feelings in them, begin or get worse when you are at rest or not moving around frequently?
3. Is the urge to move your legs, or the unpleasant feelings in them, partly or completely relieved by movement (such as walking or stretching) for as long as the movement continues?
4. Is the urge to move your legs, or the unpleasant feelings in them, worse in the evening and at night, or does it only occur in the evening or at night [3]?

The aim of our study was to determine the prevalence and characteristics of restless legs syndrome in hemodialysis patients.

Patients and methods

The research was organized as a cross-section study of patients treated with chronic hemodialysis for at least 3 months at the Center for Hemodialysis of Kosovska Mitrovica Medical Center, Serbia. The investigation included 58 patients, 26(44.8%) men and 32(55.2%) women, of mean age 59±13.2 years. Their hemodialysis program was most often sessions three times a week for 3.5 to 4 hours, using commercially available dialyzers. The blood pump during dialysis ranged from 250-320 ml/min, while the dialysate flow was 500 ml/min.

The demographic structure and certain clinical features were recorded for all respondents, including smoking habits, alcohol consumption, the existence of sleep apnea, residual diuresis, iron and erythropoietin therapy, diabetes mellitus and cardiovascular disease. The elimination of urea (URR index) was calculated as a measure of adequacy of dialysis [4]. Residual renal function was defined as residual diuresis of at least 250 ml. Body Mass Index (BMI) was calculated as the ratio between the weight expressed in kilograms and the square of body height in m². Symptoms of restless legs were determined using the criteria adopted by the IRLSSG. The patients were then divided into a group with this syndrome and a group without it. Blood was taken in the middle of the week, at the beginning of hemodialysis for biochemical analyses (leukocyte and erythrocyte counts, hemoglobin, serum iron, urea, creatinine, total calcium, inorganic phosphorus and Ca x P product). A COULTER apparatus, using the flow cytometric method was used for hematological analysis, while the biochemical analyses were made spectrophotometrically on a Llab-600 apparatus. The protocol was approved by the Regional Ethics Committee and informed consent was obtained from all the patients according to the Helsinki declaration.

Statistics

The data were analyzed statistically using the program In-stat (GraphPad Software Inc. San Diego, USA). To test hypotheses we used the χ^2 test and t-test. A value $p < 0.05$ was considered statistically significant.

Results

Based on the IRLSSG criteria we found that 38% of our patients had no symptoms of restless legs syndrome, while symptoms were identified in the remainder.

Lower serum iron concentrations were found in patients with restless legs syndrome compared with those without and the difference between the groups was statistically significant (8 ± 1.9 vs. 12 ± 6.9 mmol/l, $p = 0.018$). The degree of elimination of urea, as a parameter of dialysis adequacy, was significantly higher in patients without restless legs syndrome than in those patients with it (61.8 ± 7.1 vs. 55.9 ± 10.6 , $p = 0.03$). No statistically significant differences between the groups concerning the other laboratory parameters tested (Table 1).

Table 1. Biochemical characteristics of the patients examined

Parameters	With restless legs syndrome	Without restless legs syndrome	P
Leukocytes x 10 ⁹ /L	6.3 ± 2	5.2 ± 3.2	0.48
Erythrocytes x 10 ¹² /L	3.19 ± 0.66	3.1 ± 0.47	0.3
Hemoglobin g/L	97 ± 17	101 ± 30	0.35
Serum iron μmol/L	8 ± 1.9	12 ± 6.9	0.018*
Urea mmol/l	29.1 ± 7.0	29.3 ± 3.0	0.4
Creatinine μmol/L	776 ± 188	885 ± 259	0.39
URR index	55.9 ± 10.6	61.8 ± 7.1	0.03*
Ca mmol/l	2.09 ± 0.77	2.05 ± 0.16	0.16
P mmol/l	1.44 ± 0.28	1.57 ± 0.25	0.13
Ca x P	3.28 ± 1.3	3.7 ± 0.6	0.38

*Statistically significant difference

Table 2. Demographic and clinical characteristics of the patients

Parameters	With restless legs syndrome	Without restless legs syndrome	P
Gender (M/F)	16/20	10/12	0.9
Age (mean ± SD)	63.5 ± 10.6	53 ± 13.2	0.006*
Duration of dialysis [(mean ± SD) months]	15 ± 39.1	36 ± 39.9	0.29
Smoking (yes/no)	8/28	4/18	0.9
Insomnia (yes/no)	22/14	8/14	0.12
Alcohol consumption (yes/no)	4/32	2/20	0.8
Diabetes mellitus (yes/no)	14/22	2/20	0.17
Cardiovascular disease (yes/no)	24/12	14/8	0.8
ITM kg/m ² (mean ± SD)	22.9 ± 4.2	21.9 ± 4.2	0.42
Residual diuresis (yes/no)	22/14	12/10	0.8

*Statistically significant difference

The group of patients with restless legs syndrome was 63.5 ± 10.6 years old, while those without restless legs syndrome were younger (53 ± 13.2 years), the difference between the groups being statistically significant ($p = 0.006$). There were no other statistically significant differences between the groups regarding demographic, anthropometric and clinical parameters (Table 2).

Discussion

The frequency of restless legs syndrome in patients with end-stage renal disease is much higher than in the general population and varies from 17 to 62%. This syndrome is a significant cause of deterioration of quality of life in patients treated with chronic hemodialysis [5,6,7]. The symptoms can be confused with a condition called periodic limb movement disorder, myoclonus or night cramps. There are also mixed forms, because 80% of patients with restless legs syndrome have myoclonus and night cramps, while only about 30% of patients with nocturnal myoclonus have restless legs syndrome [8]. Most likely, this is one reason for the high incidence of restless legs syndrome, which was identified in 62% of our respondents.

In most cases, the cause of restless legs syndrome is unknown, he may have a genetic component, specific gene variants have been associated with restless legs syndrome, also, low levels of iron in the brain may be responsible for restless legs syndrome. Restless legs syndrome also appears to be related to the chronic diseases such as kidney failure, diabetes, and peripheral neuropathy, although researchers do not yet know if these factors actually cause restless legs syndrome. Serum iron concentrations in our patients with symptoms of restless legs were significantly lower than in those without the syndrome. However, recent studies were unable to establish positive correlations with this disorder, which was found to be an independent factor reducing the quality of life and mortality among dialysis patients. Significant associations with habitual use of coffee and cigarette smoking were revealed. Moreover, restless legs syndrome is more common in women and in patients with diabetes mellitus [6,7]. Among our respondents, electrolyte imbalance would be a significant parameter for the occurrence of restless legs syndrome. The increased mortality of patients with this syndrome is most likely connected with reduced quality of dialysis, which was lower in our patients who had manifest symptoms of restless legs. Although electrophysiological studies have shown no correlation between restless legs syndrome and chronic kidney disorders, at least for some patients losing senso-motor activity may be an interesting theoretical possibility [6]. Our patients were not examined neurologically, so we had no opportunity to interpret this aspect.

Treatment of restless legs syndrome is extremely complex. Moving may provide temporary relief. Lifestyle changes and activities that may reduce symptoms, include decreased use of caffeine, alcohol, and tobacco, supplements in iron, folate, and magnesium, a regular sleep pattern, moderate exercise, and massaging the legs. Medications are usually helpful (dopaminergic agents, benzo-

diazepines, opioids, anticonvulsants) but no single medication effectively manages restless syndrome [7].

In the general population restless legs syndrome is associated with diabetes mellitus but in patients with chronic renal failure there was no relevant connection of restless legs syndrome with comorbid diseases or etiologic categories of kidney weakness [6]. We found diabetic nephropathy as an etiological category of renal failure in almost one quarter of the patients in the group with symptoms of restless legs, and two thirds of them had cardiovascular disease. However, probably due to the small sample size, this did not reach statistical significance. Nevertheless, it can be assumed that the presence of cardiovascular disease together with hemodynamic changes can lead to damage to the peripheral microcirculation resulting in restless legs syndrome.

Restless legs syndrome has serious consequences, as in some cases significant mental problems, chronic insomnia and daytime sleepiness arise. In addition, in severe forms, daily activities may cease or be seriously compromised, leading to social isolation, decline in mood, anxiety and depression [2,9,10]. Given the large number of drugs employed in the therapy of hemodialysis patients one cannot safely ignore the positive selection of patients with restless legs syndrome, because of therapeutic polypragmasy. In our study, two thirds of the patients with restless legs syndrome had insomnia and preserved diuresis but there was no significant difference between the groups in relation to sleep disturbance and residual renal function. In other studies contradictory positions have been taken regarding known risk factors for the occurrence of restless legs syndrome in hemodialysis patients. These paradoxical interpretations of the pathophysiology of restless legs syndrome is partly due to different methodological approaches to the problem. Combinations of similar phenomena (night myoclonus, muscle cramps) add to difficulties in determining the incidence and prevalence of restless legs syndrome, the pathophysiological mechanisms of origin, symptomatology, and their different correlative relationships. Despite the clear IRLSSG criteria, complete confusion about the definition of this syndrome is not surprising. In this regard, certain cardiovascular diseases are common among subpopulations of hemodialysis patients with restless legs syndrome [7]. Of course, in further investigations it must be noted that the "specific" subpopulation of dialysis patients with restless legs syndrome, has less efficient dialysis, is longer on hemodialysis, has more smokers, and is dominated by older people. The high incidence of restless legs syndrome appears to be a consequence of reduced dialysis adequacy and that leads to reduced quality of life for patients on hemodialysis. Therefore imperative to improve the quality of hemodialysis depuration.

Conclusion

The incidence of restless legs syndrome in our population of patients was 62%. Patients who have restless legs syndrome were generally older, had lower concentrations of serum iron and lower adequacy of hemodialysis.

Conflict of interest statement. None declared.

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