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Quality of sleep in renal transplant recipients and patients on hemodialysis

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ABSTRACT

Background: Sleep disorders are very common in patients with chronic kidney disease and they may not always subside after kidney transplantation.
Aim and methods: The aim of this cross-sectional study was to evaluate the self-reported quality of sleep, insomnia problems in particular, and examine the factors that disturb sleep of kidney transplant recipients (KTx: $n = 152$) in comparison to age- and sex-matched patients on dialysis (HD: $n = 67$) and participants with normal renal function (NOR: $n = 49$), through the administration of the Athens Insomnia Scale (AIS) at least six months after transplantation. Clinical and laboratory data, as well as health-related quality of life, depression, anxiety, post-traumatic stress symptoms, and the presence of restless legs syndrome (RLS) and pruritus were investigated in relation to sleep problems.
Results: The highest mean AIS score was observed in the transplant patients (KTx: 4.6 ± 13.3 vs. HD: 3.8 ± 8.1 vs. NOR: 2.4 ± 10.2); both KTx and HD patients had a lower quality of sleep compared to participants with normal renal function. Multiple linear regression analysis showed that the determinants of the total AIS score were the frequency of post-traumatic stress symptoms, depression, RLS, diastolic blood pressure, and pain (all $p < 0.0001$).
Conclusion: Although amelioration of renal function post-transplantation improves several aspects of quality of life, it does not seem to have a beneficial effect on self-reported sleep.

1. Introduction

Kidney transplantation is the preferred renal replacement therapy for the majority of patients with end-stage renal disease (ESRD) as it offers longer survival, and alleviation of many symptoms and complications related to uremia [1].

Sleep disorders are very common in patients with chronic kidney disease (CKD). They have gained attention due to serious health consequences (cardiovascular events, disturbances in immune function, increased mortality, and increased use of health care services) and diminished quality of life [2]. Although renal transplantation offers partial restoration of kidney function and clinical improvement in sleep-related disorders (i.e., sleep apnea/hypopnea [3] and restless legs syndrome [4]), sleep problems may persist. Several biological, psychological and social factors are considered to be responsible for the low quality of sleep in transplant recipients, such as comorbid conditions, immunosuppressive medication, depression, anxiety and stress [5]. In general, quality of sleep is believed to improve after successful renal transplantation; thus, it is reported to be better compared to that of patients on maintenance hemodialysis but still worse than that in the general population [5–8].

Sleep disorders are associated with poor health-related quality of life (HRQoL) in patients on dialysis, as well as in renal transplant recipients [9–12]. Improvement of sleep influences positively the quality of life, despite the fact that many factors may still be present and continue to act as promoters for sleep disorders [5,7].

The aim of the present study was to evaluate self-reported sleep problems and possible contributing factors in renal transplant recipients. To this end, we investigated several parameters considered to be potentially related to sleep disturbances, i.e., clinical and laboratory data, symptoms of anxiety and depression, and health-related quality of life. We also examined post-traumatic stress disorder (PTSD) symptoms, a factor rarely addressed by the existing literature on renal transplant patients [13].

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2. Materials and methods

One hundred seventy-five kidney transplant recipients (KTx), 74 patients on maintenance hemodialysis surveyed during their hemodialysis session (HD), and 70 subjects, with normal and stable renal function for at least 4 months before enrollment (NOR), who served as age- and sex-matched controls were approached. Of these, 18 kidney transplant recipients, 3 hemodialysis patients, and 21 subjects with normal renal function declined to participate in the study. Subsequently, 5 kidney transplant recipients (3 patients whose immunosuppressive medication was out of the therapeutic targets and 2 patients who reported fever during the last 24 h) and 4 hemodialysis patients (one patient with atrial fibrillation and 3 who had fever during the dialysis session) were excluded from participating in the study. Thus, in this cross-sectional study, sleep problems were assessed in 152 renal transplanted out-patients attending the Renal Transplantation Department of Laiko Hospital, Athens, Greece, during their periodic follow-up between 2009 and 2011, 67 hemodialysis patients, and 49 control subjects. Eligible patients were 18–75 years old individuals who had undergone renal transplantation for at least six months, had stable graft function for the last 4 months before enrollment, and the received doses of immunosuppressive medication were within the therapeutic targets. Patients with malignancy or any active recent disease (e.g. infection, severe cardiovascular disease, major psychiatric disorder, actively treated sleep apnea), as ascertained by medical records and confirmed by interview and physical examination, were excluded from the study. Patients with hypertension, diabetes, cardiovascular disease on stable condition, and a history of minor psychiatric disorders without psychotic symptoms, i.e., anxiety and depression, were included in the study. Also, renal function in the transplant group and normal controls had to be stable for at least four months before enrollment.

Socio-demographic information, anthropometric information, medical history (primary kidney disease, co-morbidities, type of donor, time on dialysis, duration of transplantation, etc.), medications and laboratory data were retrieved from the patient personal hospital file. Presence or absence of pruritus was also assessed. Blood pressure measurements in the transplant recipients were recorded during their visit to the outpatient clinic and in the dialysis patients at the end of their HD session.

Sleep problems pertaining to insomnia were investigated through the 8-item self-assessment Athens Insomnia Scale (AIS); a score ≥ 6 on this scale indicates the presence of insomnia [14,15]. The Johns Hopkins RLS Severity Scale (JHRLSS) was used for screening the presence of restless legs syndrome (RLS) (the fourth optional rating which provides an indication of its severity was omitted) [16,17]. Health-related quality of life was evaluated using the validated Greek version of the Short-Form Health Survey (SF-36). The eight subscales of this instrument measure different aspects of well-being and higher scores indicate a better health status [18]. The validated Greek version of the Hospital Anxiety and Depression Scale (HADS) was used for the assessment of depression and anxiety; scores ≥ 9 indicate the presence of clinically significant symptoms of depression and anxiety [19]. The self-rated Davidson Trauma Scale (DTS) was used to assess the severity and frequency of post-traumatic stress disorder (PTSD) symptoms; higher scores indicate greater severity and frequency of symptoms after a traumatic experience [20].

Laboratory data [Ht, Hb, WBC, PLT, CRP, glucose, urea, creatinine, proteins, albumin, Na, K, Ca, P, Fe, ferritin, transferrin saturation percentage (TSAT), PTH, 25(OH) D3, and HbcA1c] were collected from the patients' medical records. Additional information on the dialysis and the transplant group was recorded. More specifically, for the dialysis patients primary kidney disease, comorbidities, time on dialysis, shift (morning, afternoon, evening), vintage (hemodialysis HD, on-line hemodiafiltration pre- or post-, on-line HDF), duration of session, and efficacy of the method (spKt/V) were assessed. For the transplant counterparts primary kidney disease, comorbidities, previous method of renal replacement therapy (hemodialysis, peritoneal dialysis, PD) and time spent on it, time on transplantation, origin of the graft (deceased, living donor), rank of transplantation (first, second), and stage of chronic kidney disease (it was estimated using the Modification of Diet in Renal Disease equation, MDRD) were included in the collected data [21]. The study was carried out in accordance with the Declaration of Helsinki and informed consent was obtained from all participants.

2.1. Statistical analysis

Continuous variables are presented with mean and standard deviations. The Kruskal-Wallis test was used for comparisons among the three study groups, and the Wilcoxon-Mann-Whitney test was used for comparisons between two groups.

Univariate analyses among dependent and independent variables were applied, separately for each group (renal transplant recipients, hemodialysis patients and subjects with normal renal function) before running stepwise regression analysis. Four different stepwise regression analyses were run. One separate model for each group in which all variables were entered in the model and one regression analysis combining the three groups using only the common variables and with a dummy variable indicating normal subjects/patients with CKD (HD and KTx). The most significant variables were kept in a model.

Stepwise multiple linear regression analysis was performed to predict the effect of the study parameters (shown in Table 1) along with the study groups as dummy variables on the participants' AIS score. The Kolmogorov-Smirnov test was applied to check if the assumptions of linear regression were satisfied (sig. 0.051). All p values reported are two-tailed; statistical significance was set at 0.05. Analyses were conducted using the SPSS statistical software version 19.0 (IBM Corporation, Armonk, New York).

3. Results

One hundred and fifty-two transplant patients, 67 patients on maintenance hemodialysis and 49 subjects with normal renal function fully completed the study questionnaires. The three study groups were age- and sex-matched (mean age ± SD: kidney transplant recipients, KTx = 49.2 ± 14.0; hemodialysis patients, HD = 51.4 ± 14.3; subjects with normal renal function, NOR = 49.1 ± 15.8 years; sex: KTx = M: 51%, F: 49%, HD = M: 54%, F: 46%, NOR = M: 49%, F: 51%). Patients whose primary kidney disease was unknown constituted the largest diagnostic group for both renal transplant patients (32%) and patients on hemodialysis (39%). The second more common diagnostic group was glomerulonephritis for both patient groups (KTx: 27%, HD: 21%). In the transplant group 56% underwent deceased and 44% living donor transplantation. The mean time elapsed since the transplantation was 88.2 ± 115.2 months, while the mean time on dialysis was 48.3 ± 4.2 months for HD and 48.3 ± 37.8 months for KTx.

Immunosuppressant regimen was as follows: corticosteroids 76.3%, mycophenolate 77.6%, tacrolimus 55.3%, cyclosporine 25%, TOR inhibitors 17.1%, azathioprine 4.6%, and leflunamide 1.6%. Renal transplant recipients were treated either with a double (25%) or with a triple regimen (75%) of immunosuppressant agents. Antidepressant agents were used by 14.9% of the dialysis population and 2.6% of transplant patients. Although sleeping pills were taken by 7.2% of KTx and 29.9% of HD patients it did not have a significant effect on the presence/absence of insomnia.

Restless legs syndrome (RLS) was present in 62% of the dialysis patients and 14% of the renal transplant recipients. Patients on dialysis had significantly lower mean values of Ht, Hb, Ca, and iron, in comparison to renal transplant recipients (Table 2). Also, significantly higher mean values of PTH and P were noted in the HD group compared to those observed in the KTx group (Table 2). These parameters might have played a role in the higher prevalence of RLS in the dialysis group. Uremic pruritus was observed in 37% of HD and 11% of KTx patients. The prevalence of comorbid conditions such as hypertension,