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TITLE: Fragmented sleep – an unrevealed problem in peritoneal dialysis patients

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Title: Fragmented sleep – an unrevealed problem in peritoneal dialysis patients

ABSTRACT

Objective: The aim of this study was to describe the sleep-wake cycle, sleep quality, fatigue and HRQoL measured with questionnaires, actigraphy and sleep a diary during a one-week period in patients with peritoneal dialysis treatment at home. Further, to explore differences compared to patients with coronary artery disease (CAD) and individuals from the general population.

Material and Methods: In this study one week, actigraphy registration, four questionnaires (Uppsala Sleep Inventory, SF-36, FACIT-fatigue, International Restless Legs Study Groups' form) and a sleep diary were used.

Results: In total data from 68 participants and 470 nights were collected. PD-patients (n=28) had more fragmented sleep ($p<0.001$) and worse sleep efficiency (SE) ($p<0.0001$) compared to the CAD (n=22) and the population (n=18) groups. Pruritus (57%), restless legs (46%) and fatigue (89%) were prevalent in PD-patients. Pruritus correlated to fragmented sleep ($r=-0.45$, $p=0.01$) and SE ($r=-0.49$, $p=0.01$). In HRQoL, the physical component score was decreased in the PD and angina groups ($p<0.01$) compared to the population group.

Conclusions: To our knowledge this study is the first to demonstrate that PD-patients have a deteriorated sleep with serious fragmentation measured with a one-week actigraphy registration. Further, PD-patients exhibit worse sleep quality compared to CAD patients and individuals in the population. More evaluation of sleep in clinical practice is highly recommended since PD-patients are vulnerable individuals with extended self-care responsibilities and at risk for co-morbidity secondary to insufficient. Future research on whether PD-patient' sleep problems and fatigue can be improved by an individual non-pharmacological intervention programme is required.

Keywords: actigraphy, health related quality of life, insomnia, peritoneal dialysis, sleep disturbance, coronary artery disease, fatigue, pruritus, restless legs

INTRODUCTION

Despite the facts that sleep problems is a prevalent issue in peritoneal dialysis patients there is a lack of research that objectively evaluates the sleep wake-cycle. In a systematic review study including 61 studies evaluating the prevalence of uremic symptoms of end stage renal disease (ESRD) the weighted mean prevalence of fatigue and/or tiredness and sleepiness was high; 71% and 44%, respectively [1]. Difficulties to initiate and maintain sleep and waking too early i.e. insomnia vary from 45-71% in home dialysis patients [2]. Potential sleep disturbing factors are pruritus and restless legs syndrome (RLS) with a prevalence of 55% and 30%, respectively [1]. In addition, high rates (57%) of sleep apnoea in PD-patients have been reported [3]. Decreased sleep quality changes both metabolic [4] and immunological [5, 6] functions. This should be considered since the two most common causes of mortality in dialysis are cardiovascular diseases and infections [7].

Disturbed sleep also affects Health related Quality of Life (HRQoL) [8] cognitive functions [9] and daytime impairments which are important functions for PD-patients with extended self-care responsibilities for their treatment at home. Disrupted sleep further increases negative mood characteristics [10]. Sleep problems might be underestimated due to accumulation of a symptom burden with overlapping and co-existing disease related symptoms.

Koch et. al. [11] studied sleep-wake parameters for a consecutive seven-day period using questionnaires, actigraphy (a device that objectively estimates sleep and activity), sleep log and melatonin rhythm in different dialysis groups including six PD-patients who demonstrated impaired sleep efficiency and increased wake-time compared to normal values. Further more detailed evaluations of the sleep-wake cycle and sleep behaviours in larger groups of PD-patients are needed as well as investigations into whether

PD-patients at home differ compared to other patients with chronic illness and individuals in the general population.

The aim of this study was to describe the sleep-wake cycle, sleep quality, fatigue and health related quality of life measured with questionnaires, actigraphy and a sleep diary during a one-week period in patients with peritoneal dialysis treatment at home. Further, to explore differences compared to patients with coronary artery disease (CAD) and individuals from the general population.

MATERIAL AND METHODS

In this descriptive, comparative study patients with PD treatment at home were recruited from two university, two county council and two general hospitals in Sweden. PD-patients were matched for age, gender and month of data collection with two comparison groups.

Identical inclusion criteria for PD- and CAD-patients were: living at home, over 18 years of age, ability to read and understand the Swedish language, free from malignancy, persistent sequelae from stroke or any other disorder of importance, no known addiction to alcohol and/or to drug abuse and no current treatment for a mental disorder. Additional criteria for the PD-patients were: ongoing PD treatment more than three months and matching criteria to the comparison groups i.e. age, gender and month for data collection.

The total population of PD-patients was 115 individuals, md (Q₁-Q₃), 60 yrs (53-69 yrs), 69 men and 46 women, 62 yrs, (53-75 yrs) and 59 yrs, (51.5-65 yrs), respectively. Out of these, 48 patients met the inclusion criteria and were asked to participate. Thirteen were unwilling to participate and three did not answer. Thirty-two patients accepted participation. Of these four dropped out due to progress in the disease. Finally, 28 PD-patients were included (Table 1). Renal diagnoses were; glomerulonephritis, diabetic nephropathy, vasculitis, nephrosclerosis and polycystic kidney disease.

Table 1. Descriptions and comparison of group characteristics self-reported in Uppsala Sleep Inventory (USI) and biochemical parameters from patient records.

	PD-group n=28	CAD-group (A) n=22	Population group (B) n=18	P-value
	Md (Q ₁ -Q ₃)	Md (Q ₁ -Q ₃)	Md (Q ₁ -Q ₃)	
Age (year)	60 (54-67)	62 (58-70)	60 (55-64)	0.419
Body Mass Index	25 (20-28)	29 (23-30)**(PD,B)	25 (22-27)	0.004
Haemoglobine (g/L)	131 (116-137)	-	-	-
p-creatinine (µmol/L)	555 (436-732)	-	-	-
p-urea mmol/L	19 (16-22)	-	-	-
p-albumin (g/L)	34 (31-36)	-	-	-
Time in PD-treatment (months)	19 (5.5-19)	-	-	-
	n (%)	n (%)	n (%)	
Treatment modality ^a				
<i>CAPD</i>	21			
<i>APD</i>	9			
Gender				0.826
<i>male</i>	16 (57)	14 (64)	8 (44)	
<i>female</i>	12 (43)	8 (36)	10 (56)	
Working	9 (32)	12 (54)	9 (50)	0.082
Married	24 (86)	16 (73)	14 (78)	0.485
Daily nicotine use	10 (36)	5 (23)	3 (17)	0.501
Daily coffee drinker	25 (89)	20 (91)	18 (100)	0.430
Regular hypnotics use	13 (46)*(B)	5 (23)	2 (11)	0.058
Insomnia ^b	10 (34)	7 (32)	5 (29)	0.691
Snoring ^c	10 (36)	6 (22)	3 (17)	0.574
Apnoeas ^c	1 (4)	3 (14)	0 (0)	0.171

*p<0.016**p<0.01 versus coronary artery disease (CAD) patients (A) and general population (B).

^aContinuous Ambulatory Peritoneal Dialysis(CAPD), Automatic Peritoneal Dialysis (APD). Two patients had a combination of both treatment modalities.

^bAccording to definition (ICD-10) b self-assessment, Uppsala Sleep Inventory (USI) i.e. sleep latency >30 min, sleep duration <6h, total nocturnal awakenings >45 min or early morning awakenings combined with any daytime symptom.

^cBased on self-assessment, as confirmed by a bedmate (USI) on a 5-graded scale score; (1) never, (5) every night.

Comparison groups

As uraemia is a chronic disease like CAD which is also prevalent in the uraemic population a comparison with a group of chronic CAD patients was included. They were derived from a larger study (n=680) with a history of stable angina pectoris (Canadian Cardiovascular Society Class I-II), listed for percutaneous coronary intervention at a University Hospital in Sweden, two years ago. From that study 22 patients fitted the matching criteria of the PD-group. Of these 22, ten patients were treated by surgery, eight pharmacologically, three conservatively and one had missing data. The matching by month was performed as the daylight in northern Europe varies substantially during the year. Further, 18 general population individuals from the Swedish Government Person and Address Register Database [12], who were already matched controls to the CAD group also matched the PD-patients.

Procedures

A list of PD-patients who met the inclusion criteria was obtained from the clinic. Patients were consecutively contacted by post providing information about the study. Thereafter, patients who agreed to participate were sent four questionnaires, an actigraph and a sleep diary by post.

Measurements

Actigraphy

For seven days all participants wore an actigraph (Actiwatch-L®, Cambridge Neurotechnology Ltd), applied at the non-dominating wrist like a wristwatch. The actigraph measures the sleep-wake cycle, activity and indirect sleep. The device is an accelerometer and records limb movements. Periods of movement are scored as wakefulness and inactivity as

Table 2. Description of actigraphy variables measured in the three groups.

Actigraphy		
<i>Variables</i>	<i>Description</i>	<i>Scale</i>
Sleep variables	Bedtime, sleep latency, wake time during night, number of wake bouts, sleep duration and nap time.	-
Movement and Fragmentation index	This index is an indicator for disrupted sleep i.e. percentage of minutes moving + percentage of immobility.	>50 = poor sleep, <20 = good sleep.
Sleep efficiency	Ratio of actual sleep time divided by time in bed expressed in per cent.	<85% = poor sleep.
Interdaily stability	Quantifies the degree of similarity concerning the activity between individual days.	Range; 0-1. Values of 0,6 = normal.
Interdaily variability	Quantifies the fragmentation of periods of rest/sleep and activity/wakefulness. A higher value is similar to more fragmented rhythm.	Range; 0-2, <1= typical value
The amplitude of the rhythm (AMP)	Differences between the average activity of the five least (night) and the ten most (day) active hours, are sensitive to the overall activity.	-
Relative amplitude	Ratio of AMP and average activity of the five least and the ten most active hours gives a correction for the sensitivity.	Range 0-1, values close to 1= more active rhythm.

sleep. With advanced algorithms a number of variables are obtained [13] (Table 2). Data were processed in the software package *Actiwatch Sleep Analysis 2001*, version 1.9 [14].

Questionnaires

The PD-patients were sent four questionnaires and a sleep diary. Two of the questionnaires and the sleep diary had also been completed by the comparison groups.

Simultaneously with wearing the actigraph a study specific sleep diary was completed day by day. In the morning; bedtime, sleep latency, nocturnal awakenings and sleep duration and in the evening; final morning awakenings, naps and daytime symptoms.

Habitual sleep during the last four weeks was assessed by the Uppsala Sleep Inventory (USI) [15] in a modified form [16] measuring sleep variables; bedtime, sleep latency, nocturnal awakenings, morning awakening, sleep duration, assumed sleep duration, numbers and duration of naps. Items about sleep, pruritus, RLS and daytime functioning were answered in a 5-point scale scored from “never” (1) to “very often” (5). Further, snoring and apnoeic behaviour, as confirmed by a bedmate were scored in the same way. USI has earlier been validated in a Swedish population [17]. In this study the definition of insomnia corresponds to ICD-10, sleep duration <6h, sleep latency >30 min, five or more nocturnal awakenings or a nocturnal wake time >45 min combined with one or more daytime symptoms. If these persist for three weeks or more, the patients are diagnosed with insomnia [18].

HRQoL was assessed with a generic instrument, Short form-36 (SF-36), where the questions relate to the last four weeks [19]. This is the most widely used questionnaire for the evaluation of health outcome assessing eight health domains; physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social function, role limitations due to emotional problems and mental health. Each domain scores

0-100, where a higher score indicates better HRQoL [20]. The eight domains are dichotomized in two principal dimensions; physical (PSC) and mental (MSC) component summary. SF-36 has a good reliability and validity [19, 21] with a Cronbach-alpha between 0.79 and 0.91 [19] and was in this study 0.75 in both PSC and MSC. The above questionnaires and the sleep diary were completed by the three groups.

Questionnaires completed by the PD-group only

The International Restless Legs Study Groups' validated questionnaire (IRLS) evaluates the severity of RLS symptoms. It is a ten item, five-point scale scored from "none" (0) to "very severe" (4) symptoms, total range; 0-40. The index scoring is divided as: negligibly (0-10), moderate (11-20), severe (21-30) and very severe (31-40) [22]. Cronbach-alpha for IRLS has been reported to 0.93-0.95 [22] and was in this study 0.95.

Degree of fatigue was measured by the Functional Assessment of Chronic Illness Therapy (FACIT-) fatigue scale [23]. The scale is a 13-item, five-point scale score from "not at all" (0) to "very much" (4), total range; 0-52. Cut-off score for fatigue is 43 or below [23]. The scale essentially assesses activity i.e. functional fatigue. Cronbach-alpha for FACIT-fatigue scale has been reported to 0.94 [23] and was in this study 0.87. Diagnoses and biochemical parameters were collected from patients' records at the time of actigraphy registration for each patient.

This study was approved by the Regional Ethical Review Board in Linköping. Principles according to the Helsinki declaration (WMA 2004) have been followed. Written informed consent was obtained from all participants.

Statistical analyses

Description of data was given by frequencies, percentage, median (md) and inter-quartile range (Q₁-Q₃). Non-parametric statistics were used when data were assessed on interval or nominal level and not normally distributed. Analysis of variance between the three groups was performed with Kruskal-Wallis and for comparison between two groups the Mann-Whitney *U*- test was used. Dichotomous variables were analysed using the Chi-square test. Actigraphy and sleep diaries variables were averaged over the seven days of recording. Wilcoxon's signed rank test between groups was used when appropriate. Spearman's rank order correlations coefficient (*r*) was used to explore associations between variables. The internal consistency was calculated with Cronbach's alpha, at the three index scales; SF-36, IRLS, FACIT-fatigue. Internal drop outs occurred in four items (two patients) in the FACIT-fatigue scale and were replaced by a patient-specific mean value. Adjustment for multiple comparisons with Bonferroni post hoc analysis [24] was performed and a two-tail *p*-value of < 0.016 was considered as statistically significant, otherwise a *p*-value of < 0.05 was accepted. SPSS software package 18.0 for Windows was used for all analysis.

RESULTS

Sleep-wake cycle

In total data from 68 participants and 470 nights were collected by actigraphy and sleep diaries. The PD-patients had significantly more disrupted sleep, explored by the movement and fragmentation index (MFI) (Table 3). In contrast to the comparison groups, none of the PD-patients had MFI below 20 but 11 (39.3%) had above 50, which indicates seriously disrupted sleep (Figure 1). The nocturnal sleep duration did not differ between the groups (Table 3). However, nocturnal awakening time in PD-patients was 30 minutes longer than in the CAD-group and 36 minutes longer than in the population group (*p*<0.001) (Table 3)

Table 3. Group comparison of sleep variables assessed by actigraphy and sleep diary during one week and the questionnaire Uppsala Sleep Inventory (USI) covering habitual sleep over 4 weeks.

<i>Sleep variables</i>	PD-group n=28 Md (Q ₁ -Q ₃)	CAD group (A) n=22 Md (Q ₁ -Q ₃)	Population group (B) n=18 Md (Q ₁ -Q ₃)	P-value (Kruskal-Wallis)
Sleep quality (score) 1=bad, 5=very good	3 (2-4)**(A)	2 (1-3)	2 (1-4)	0.006
Sleep latency (min)				
Actigraphy	30 (22-59)***(B)	24 (10-41)	13 (7-26)	0.002
Sleep diary	28 (16-75)	16 (12-34)	18 (9-34)	0.1
USI	25 (6-60)**(A)	10 (1-20)	10 (3-23)	0.007
Sleep duration (hour.minutes)				
Actigraphy	6.42 (5.58-7.17)	6.50 (6.05-7.37)	6.43 (6.30-7.12)	0.903
Sleep diary	7.06 (5.54-8.00)	6.55 (6.03-7.25)	6.17 (5.50-7.05)	0.132
USI	7.00 (5.00-8.00)	7.00 (4.42-8.00)	7.00 (5.06-7.00)	0.951
Go to bed (time)				
Actigraphy	22:41 (21:41-23:04)	22:55 (22:33-23:20)	23:03 (22:41-23:19)	0.079
Sleep diary	22:23 (21:29-22:55)	22:27 (22:00-22:56)	22:35 (22:27-23:03)	0.278
USI	22:00 (21:00-23:00)**(B)	22:00 (21:42-22:30)*(B)	23:00 (22:00-23:00)	0.009
Wake time during night (min)				
Actigraphy	94 (70-122)**(A)***(B)	64 (41-91)	58 (47-73)	0.001
Sleep diary	20 (8-52)	24 (10-37)	21 (12-43)	0.973
USI ^a	4 (2-5)	3 (1-4)	4 (1-6)	0.056
Wake bouts (freq)				
Actigraphy	32 (27-36)**(A)	26 (19-34)	24 (20-31)	0.051
USI	2 (1-3)**(B)	3 (1-4)*(B)	2 (0-2)	0.015
Nap time (min)				
Actigraphy	59 (39-92) ** (B)	48 (30-57)	32 (14-47)	0.009
USI	45 (10-60)	45 (11-60)	30 (11-60)	0.463
Fragmentation index ^b				
Actigraphy	49 (41-64) ***(A)***(B)	35 (25-42)	34 (26-37)	0.0001
Sleep efficiency ^c (%)				
Actigraphy	71 (68-80)**(A)***(B)	78 (75-85)	83 (82-87)	<0.0001
Sleep Sufficient Index ^d (%)				
USI	80 (72-94)*(A)	93 (83-100)	93 (86-100)	0.027

*(<0.016), ** (<0.01), *** (<0.001) versus coronary artery disease (CAD) patients (A) and general population (B). Mann-Whitney *U* test adjusted with Bonferroni.

^a Score; <5 min (1), 5-15 min (2), 15-30 min (3), 30-60 min (4), 1-2 h (5), 2-3 h (6), >3 h (7).

^b Fragmentation index (i.e. movement and fragmentation index) indicates restless and fragmented sleep; summary of percentage of minutes moving and percentage of immobility, bad sleep (>50) and very good sleep (<20).

^c Sleep efficiency; ratio of sleep duration and time in bed in per cent, below 85% indicates insufficient sleep efficiency.

^d Sleep Sufficient Index; ratio of sleep duration and self-estimated need for sleep in percent, below 80% indicates insufficient sleep efficiency.

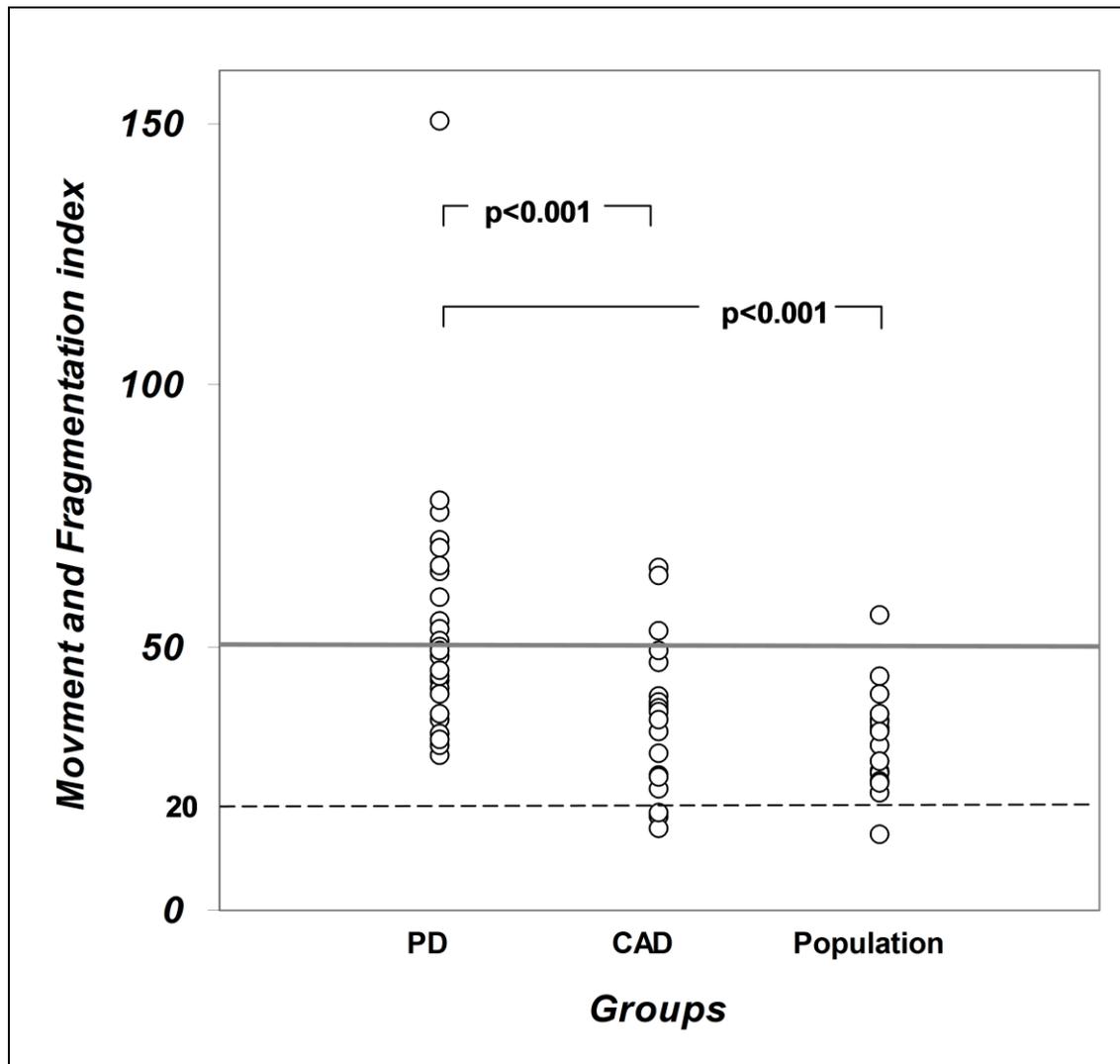


Figure 1: Illustration of the distribution of fragmented sleep in the three groups. Above 50 indicates very disrupted sleep and below 20 means well consolidated sleep.

measured by actigraphy. Interdaily variability and –stability were within the normal range, which indicates stable sleep-wake cycles (Table 4).

Quality of sleep and sleep disturbing factors

PD-patients had 7% lower sleep efficiency than the CAD-group and 12% lower than the population group ($p < 0.001$) (Table 3). One third ($n=10$) of the PD-patients could be categorised as insomniacs (Table 1). PD-patients classified as insomniacs had significantly decreased sleep quality, md (Q_1 - Q_3) 2 score (1.25-3.0 score) compared to non-insomniacs 3

score (2.0-4.0 score), ($p<0.05$). Further, on the dichotomized question “Do you get too little sleep?” 61% (n=17) of PD-patients gave an affirmative answer compared to 23% (n=5) in the CAD group ($p<0.05$) and 50% (n=9) in the population group (not significant). All 22 insomniacs in the three groups were in agreement to the specific question ($p<0.05$).

In PD-patients pruritus was a common sleep disturbing factor at sleep onset. Sixteen patients (57%) had moderate to very severe pruritus at sleep onset and a correlation to MFI ($r=-0.42$, $p=0.034$) was found. Nocturnal pruritus also correlated to MFI ($r=-0.49$, $p<0.01$), sleep efficiency ($r=-0.49$, $p<0.01$), bodily pain ($r=-0.39$, $p<0.05$) and general health ($r=-0.42$, $p<0.05$). RLS was reported by 13 patients (46%) as being moderate to very severe problems. Correlations to sleep quality (USI) ($r=-0.39$, $p<0.05$), sleep efficiency (actigraphy) ($r=-0.54$, $p<0.01$), role physical ($r=-0.39$, $p<0.05$), vitality ($r=-0.36$, $p<0.05$) were found. Further, sleep duration ($r=-0.40$, $p<0.05$) and sleep latency measured by actigraphy ($r=-0.40$, $p<0.05$) and sleep diary ($r=0.45$, $p<0.05$) were associated to RLS.

Daytime symptoms and health related quality of life

Sleepiness and physical tiredness were the most prevalent daytime symptoms in all three groups (Table 4). The prevalence of fatigue was high in PD-patients, 25 (89%) scored below the cut off (43) and fatigue-score was correlated to MFI ($r=-0.43$, $p<0.05$). PD- and CAD-patients reported worse physical function in SF-36 compared to the population (Table 5). The PD-patients also reported worse general health.

No differences concerning the sleep variables were found between patients on automatic PD (APD) and manual PD (CAPD). Influence of the seasonal variation of light was not detected on any of the variables (data not shown).

Table 4. Group comparison of circadian rhythm assessed by actigraphy during one week and daytime symptoms assessed by Uppsala Sleep Inventory (USI) questionnaire referring to the last four weeks.

	PD-group n=28		CAD-group n=22 (A)		Population group n=18 (B)		P-value
	Md (Q ₁ -Q ₃)	Severe Problems Freq (%) ^e	Md (Q ₁ -Q ₃)	Severe Problems Freq (%) ^e	Md (Q ₁ -Q ₃)	Severe Problems Freq (%) ^e	(Kruskal-Wallis)
<i>Daily activity (Actigraphy)</i>							
Interdaily stability ^a	0.58 (0.45-0.64)	-	0.54 (0.47-0.63)	-	0.57 (0.46-0.64)	-	0.957
Interdaily variability ^b	0.83 (0.70-1.01)	-	0.82 (0.69-0.95)	-	0.82 (0.69-1.07)	-	0.815
Amplitude ^c	13387 (8743-19396)*(B)	-	15672 (12361-21401)	-	21288 (14391-26448)	-	0.04
Relative amplitude ^d	0.84 (0.76-0.87)**(B)	-	0.88 (0.85-0.90)	-	0.90 (0.85-0.93)	-	0.002
<i>Daytime symptoms (USI)</i>							
Score;(1) no problem- (5) very big problems							
No refreshing sleep	3 (2-4)	18 (62)	2 (2-3)	10 (44)	3 (1-3)	9 (56)	0.315
Sleepiness	3 (2-4)	21 (72)	3 (2-4)	14 (61)	3 (1-3)	9 (56)	0.617
Physical tiredness	3 (2-4)	22 (76)	3 (2-4)	13 (56)	2 (1-4)	6 (38)	0.235
Mental tiredness	2 (2-2)	7 (24)	2 (2-3)	8 (35)	2 (1-3)	5 (31)	0.854
Exhaustion	2 (1-2)	7 (24)	2 (1-3)	8 (35)	2 (1-3)	6 (38)	0.662

*(<0.016), ** (<0.01), *** (<0.001) PD-group versus coronary artery disease (CAD)-group (A) and population group (B). Mann-Whitney *U* test adjusted with Bonferroni.

^a quantifies the resemblance between the activity pattern on individual days, ranges from 0 (low) to 1 (high), 0.6 is typical.

^b quantifies the fragmentation of sleep and activity, ranges from 0 (low) to 2 (high), below 1 is typical.

^c Amplitude of the rhythm i.e. difference of average activity and the five least and the ten most active hours.

^d Range from low (0) to high (1) activity. Ratio of the rhythm amplitude and the sum of average activity counts of the five least and the ten most active hours.

^e Reporting severe to very severe problems (score 4-5)

Table 5. Group comparison of Health Related Quality of life (HRQoL), assessed by SF-36.

<i>Variable</i>	PD-group (n=28) Md (Q ₁ -Q ₃)	CAD-group (A) (n=18 ^a) Md (Q ₁ -Q ₃)	Population group (B) (n=13 ^b) Md (Q ₁ -Q ₃)	p-value (Kruskal-Wallis)
Physical functioning	70 (54-85)***(B)	70 (43-90)**(B)	88 (80-100)	0.003
Role physical	29 (0-100)	75 (0-100)	100 (60-100)	0.051
Bodily pain	61 (39-88)	51 (39-84)	63 (44-96)	0.663
General health	40 (29-48)**(A)***(B)	60 (39-74)	75 (52-96)	<0.001
Vitality	50 (29-65)	58 (49-76)	70 (36-85)	0.134
Social functioning	75 (50-100)	88 (50-100)	100 (53-100)	0.182
Role emotional	100 (33-100)	100 (58-100)	100 (67-100)	0.827
Mental health	84 (63-92)	84 (67-92)	82 (68-92)	0.995
Physical component summary	37 (25-44)***(B)	41 (27-49)*(B)	51 (39-57)	0.002
Mental component summary	49 (41-56)	55 (44-58)	52 (39-58)	0.610

*(<0.016), ** (<0.01), *** (<0.001) PD-group versus coronary artery disease (CAD)-group (A) and population group (B). Mann-Whitney *U* test adjusted with Bonferroni.

^{a,b} Four participants in the CAD-group and five in the population group did not complete the questionnaire.

DISCUSSION

To our knowledge this is the first study describing a one-week sleep-wake cycle and demonstrating that fragmented sleep is a reality for PD-patients. Compared with the CAD and the population groups the PD-patients had more deteriorated sleep.

The fragmented sleep can explain that PD-patients had significantly lower sleep quality, compared to the comparison groups, as fragmented sleep reduces the restorative deep sleep [25]. In addition, PD-patients seem to have an increased need for recovery which was reflected by the Sleep Sufficient Index which was lower than in the comparison groups. Although an optimized treatment regime, a uraemic state still persists contributing to more tiredness [1] and an increased need for recovery, i.e. sleep [26]. About one-third of all participants from all three groups fulfilled the insomnia criteria which can be one explanation to the fragmented sleep. Insomnia has been described as a prevalent problem in dialysis populations [16, 27] earlier. Although the proportion of insomniacs was similar in all three groups, only the PD-patients had significantly higher fragmentation and decreased sleep quality. There might, however, possibly be other explanations for the fragmentation of sleep.

In this study 46% of the PD-patients reported RLS, another potential sleep disturber and prevalent in ESRD [1] and PD [16] patients. The high prevalence may explain the inability to consolidate sleep [16, 27] causing fragmented sleep or insomnia depending on when the symptoms peak: at the sleep onset or during the night. In this study no significant association between RLS and fragmented sleep was found, although such an association has been described previously [28]. RLS in our study was correlated to decreased sleep quality. Unruh and co-workers (2004) showed that RLS in dialysis patients was associated with decreased physical function, decreased well-being and even an increased risk for mortality [29]. Another prevalent source for sleep disruption is pruritus, which in our study was reported by 57% of the PD patients. Pruritus has earlier been reported to vary between 40-

55% in uremic populations [1, 16, 30] and one study supports a relationship between pruritus and mortality, in haemodialysis patients, attributed to poor sleep [30]. This study bears no evidence that disturbed sleep is related to APD treatment. Previous studies have shown only tendencies and no significant instances of APD treatment causing a more disturbed sleep. Contrary, our research group previously found that APD-patients reported significantly better sleep quality than CAPD-patients ($p=0.03$) [16].

Only one PD-patient (4%) reported apnoeic behaviour, but this sleep behaviour is difficult to self-report. Evidence has been presented for a tenfold higher prevalence of sleep apnoea (57%) in uraemic patients [3] than in people with normal renal function (2-4%) [25]. Obese people suffer more from sleep apnoea. Although the CAD-patients in our study had significantly higher BMI than the PD-and the population group ($p=0.004$) no significant differences were found in the self-reported sleep apnoea. However, this is difficult to evaluate since only 4 out of 68 patients reported sleep apnoea in this study. One possible explanation could be that an increased intra-abdominal pressure from the dialysis solution can affect the breathing in PD-patients. In haemodialysis water overload can cause oedema and obstruction in the airways. Furthermore, a central destabilization of respiratory control and acidosis can be another explanation [31]. Sleep fragmentation caused by sleep apnoea is an alarming problem in peritoneal dialysis patients leading to nocturnal hypoxemia which is a serious risk for fatal cardiovascular incidences [32, 33]. The discrepancy between self-assessed and actigraphy-registered wake bouts in this study can be explained by the fact that actigraphy-registered fragmentation is mostly unconscious awakenings i.e. micro arousals, with an increased EEG frequency [34] and decreased slow-wave sleep and sleep quality. It is essential to keep in mind that apnoea, RLS and pruritus can induce fragmented sleep or insomnia, either separately or in combination. Therefore evaluation of symptoms is essential because the clinical picture is so complex.

This study showed a correlation between fragmented sleep and fatigue which is new knowledge concerning PD-patients. Poor sleep has also been shown to have a substantial impact on fatigue for patients with primary Sjögrens´ s syndrome and rheumatoid arthritis [35]. The prevalence of fatigue among the PD-patients in this study was extremely high, but consistent with previous studies, 55-88% [16, 36]. Despite the fact that the PD-patients in this study had more fragmented sleep, longer sleep latency onset and worse sleep efficiency, than the comparison groups, they did not report more daytime symptoms related to poor sleep. In healthy subjects daytime symptoms have been reported after only one night with fragmented sleep [37]. Our findings can partly be explained by the fact that symptoms of fatigue are, both by patients and healthcare personnel, considered to be a part of the disease [26, 38] and therefore are easily overlooked. Nevertheless, in this study and in a previous study by our research group [16] napping was a frequently used behaviour (74%) and presumably a way to manage daytime sleepiness attributed to the fragmented sleep. Extended naps, with a duration of more than 30 minutes, can mean an awakening from slow-wave sleep which is characterized by confusion, grogginess and decreased performance i.e. sleep inertia [39]. Symptoms of sleep inertia can be misinterpreted as fatigue and vice versa as fatigue is characterized as diminished energy and mental capacity and an increased need for rest [40]. Healthcare personnel may be able to help patients to address their symptoms and to keep structured daily routines to promote good sleep behaviours. Sleep scheduling interventions reducing nap frequency and nap time [41] are one way of management. However, sleep apnoea and insomnia are not the only factors affecting daytime function, other co-existing problems such as depression also have to be considered [42].

The overall activity, measured by actigraphy, was significantly lower in the PD-group compared to the comparison groups. The decreased activity in PD-patients was also reflected in SF-36 where PD- and CAD- patients reported decreased physical functioning. In

addition for the PD- patients the high prevalence of fatigue for the PD- patients can partly be addressed to decreased physical function when the FACIT-fatigue scale essentially assesses functional fatigue. Interestingly, decreased physical functioning has showed an association to a high prevalence of RLS previously [29].

The strength of our study is that data from more than a total of 400 days were collected in an everyday context with a device for repeated measurements which does not affect habitual life or routines. Further, data were collected through a combination of questionnaires and a sleep diary where several parameters showed similar results. Another strength in the study is the combined evaluation of RLS by both a questionnaire and actigraphy which has been described as a valid and reliable method [28] since RLS is closely related to sleep disorders. Finally the reliability calculated FACIT-fatigue and SF-36 were satisfactory.

This study also had some limitations: First, a small sample size and the findings must be generalized carefully. However, the PD-group represents approximately 4% of the total PD population in Sweden and had a gender distribution similar to the national sample. Second, actigraphy measures sleep/wake periods indirectly when activity indicates wakefulness. This can implicate that actigraphy underestimates sleep latency when a motionless period precedes sleep or overestimates daytime sleep when the patient is resting. Nevertheless, sleep fragmentation assessed by actigraphy has shown high sensitivity (89%) and specificity (95%) for diagnosing sleep apnoea [43, 44]. Actigraphy has also measure acceptable accuracy to polysomnographical variables; number of nocturnal awakenings, waking after sleep onset, total sleep time and sleep efficiency in insomnia patients [45]. Finally, we did not reach the same number of participants in the three groups, partly due to the three matching variables and in particular the month for data collection. Therefore, between groups statistics was chosen. Another comparison group could have been patients

with chronic kidney disease not yet on dialysis, in order to study how dialysis per se might cause sleep disturbances.

Conclusion

To our knowledge this study is the first to demonstrate that PD-patients have a deteriorated sleep with serious fragmentation measured by one-week actigraphy registration. Further, PD-patients exhibit worse sleep quality compared to CAD patients and individuals in the population. More evaluation of sleep in clinical practice is highly recommended since PD-patients are vulnerable individuals with extended self-care responsibilities and at risk for comorbidity secondary to insufficient. Future research to investigate whether PD-patients sleep problems and fatigue can be improved by an individual non-pharmacological intervention programme is required.

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