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Original Article

Ambulatory nocturnal oximetry and sleep questionnaire-based findings in 38 patients with end-stage renal disease

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Abstract

Background. Patients with end-stage renal diseases (ESRD) have an increased risk of sleep-disordered breathing. With regard to this disorder, controversy persists about prevalence, cost-effective assessment and socio-economical relevance.

Methods. Therefore, we performed, for the first time, overnight ambulatory oximetry in combination with a sleep questionnaire in 38 unselected patients with ESRD and 37 healthy controls. An oxygen desaturation index (ODI) >15, defined as >15 falls in oxygen saturation of $\geqslant 4\%$ per h, was observed more frequently in ESRD patients than in healthy controls (47 *vs* 3%, $P<0.001$).

Results. In general, the results derived from the assessment of the Epworth Sleepiness Scale (ESS) as well as those from the visual analogue scale (VAS) did not reflect the ODI values of the respective patient population. Interestingly, 88% of ESRD patients with the questionnaire finding 'excessively loud snoring' had an ODI of >15 as compared with 13% without this complaint ($P<0.05$). Furthermore, 77% of ESRD patients with a systolic blood pressure >140 mmHg and a body mass index (BMI) >25, had an ODI of >15. The percentage of ESRD patients with a professional activity was higher in the absence of sleep-disordered breathing (63 *vs.* 21%, $P<0.05$).

Conclusion. 'Excessively loud snoring' and a BMI >25 combined with hypertension are risk factors for sleep-disordered breathing in ESRD patients. Nocturnal oxygen desaturations are assessed efficiently by ambulatory oximetry and correlate with relevant biological and socio-economical parameters in ESRD patients.

Key words: end-stage renal disease; haemodialysis; oximetry; peritoneal dialysis; sleep apnoea

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Introduction

The prevalence of obstructive sleep apnoea (OSA) in the general middle-aged population of the US is 2–4% [1]. Repetitive apnoeas and hypopnoeas during sleep are associated with significant morbidity and mortality [2,3]. Deaths are attributed mainly to hypertension and cardiovascular disease [2,4,5]. From the literature, there is some evidence that the prevalence of sleep apnoea is higher in end-stage renal disease (ESRD) patients compared with the normal population [6–15]. Although not proven, the high prevalence of coronary heart disease, stroke and congestive heart failure in ESRD patients could be partially related to a high prevalence of OSA in this patient group [16].

OSA may be an important contributor to the high incidence of hypertension in ESRD patients [16,17] and even to the progression of kidney failure [18–20]. Effective treatment of OSA (including nasal continuous positive airway pressure) shows beneficial effects in ESRD patients [11,12] and may reduce elevated blood pressure [21–23] and thereby cardiovascular disease and mortality. Therefore, timely assessment of patients with kidney disease is essential. Since polysomnography is time and labour intensive, it is important to test ambulatory methods to detect sleep-disordered breathing in patients with ESRD. The main objective of the present study was to analyse ambulatory nocturnal oximetry and a sleep questionnaire that included the Epworth Sleepiness Scale (ESS) [24] and visual analogue scale (VAS) [25] as screening methods in a population of ESRD patients undergoing chronic dialysis treatment.

Subjects and methods

Subjects

Thirty-eight patients with ESRD on chronic haemodialysis (HD) or continuous ambulatory peritoneal dialysis (CAPD) at our institution were enrolled in this prospective study. Patients were recruited simply on the basis of their willingness

to participate, and not because of the presence or absence or sleep problems. Patients were first recruited from the self-care HD unit and the CAPD unit and then from the full care HD unit. Within the time frame of the study (September 1996–September 1997), we investigated 18 out of a total of 24 CAPD patients (six refused to participate), 12 out of 16 patients performing self-care HD (four refusals) and the first eight HD patients who were willing to participate (10 were asked, two refused) out of the total of 72 patients of the full care HD unit. Seventeen of the CAPD patients performed 3–5 exchanges using 1.5–2.5 l bags during the day time. One patient was using a cycler system with seven exchanges of 1.5 l bags during the night. The HD patients underwent dialysis three times a week, using dialysate containing bicarbonate and a polysulfone hollow-fibre filter (HF80S or HF60S, Fresenius, Switzerland).

Thirty seven healthy subjects of comparable age were recruited for the study as controls. One additional male control subject was excluded because of treated hypertension. The clinical characteristics of patients and healthy subjects are summarized in Table 1.

Methods

Nocturnal oximetry.

Ambulatory overnight pulse oximetry was performed in all patients and control subjects (Vitalog VX4 pulse oximeter, Respironics Inc., Murrysville, PA, USA). In the 20 HD patients, pulse oximetry was performed in the night immediately after a dialysis session; in eight of these patients, a further recording was accomplished during the following night preceding the next dialysis session. The pulse oximeter recorded arterial oxygen saturation (SpO_2) and movements of the sensor; artefacts were identified later and excluded by visual analysis on the computer screen. The oxygen desaturation index (ODI; defined as the number of falls of SpO_2 $\geqslant$4% per h of recording), the percentage of time spent at SpO_2 below 90% ($CT_{90\%}$), mean SpO_2 ($SpO_{2\ mean}$) and minimum SpO_2 ($SpO_{2\ min}$) were recorded.

Table 1. Characteristic features of ESRD patients and healthy controls, including oximetry findings, and scores of the Epworth Sleepiness Scale (ESS) and visual analogue scale (VAS)

	Healthy controls ($n=37$)	ESRD patients ($n=38$)
Clinical findings		
Age (years)	53±12.1	58±14.7
Female gender (%)	46	45
BMI (kg/m^2)	23±4.0	24±4.1
Systolic BP (mmHg)	126±7.1	141±29.0[b]
Diastolic BP (mmHg)	80±4.1	79±12.6
Coronary heart disease (n)	0	16
COPD (n)	0	7
Diabetes mellitus (n)	0	7
Arterial hypertension (n)	0	21
Oximetry and scores of ESS/VAS		
ODI >15 (%, n)	3 (1)	47 (18)[c]
ODI	6.7±3.4	17.3±12[b]
$CT_{90\%}$ (min)	11.8±23.5	37.5±64.7[a]
$SpO_{2\ mean}$ (%)	94.2±1.7	94.3±2.6
$SpO_{2\ min}$ (%)	81.0±5.7	75.5±9.3[a]
ESS	4.2±3.1	6.2±3.9[a]
VAS	0.19±0.14	0.49±0.30[b]

Values are mean±SD. [a]$P<0.05$; [b]$P<0.01$; [c]$P<0.01$ (*vs* healthy controls).
BMI, body mass index; BP, blood pressure; COPD, chronic obstructive pulmonary disease; ODI, oxygen desaturation index (falls in oxygen saturation $\geqslant$4% per h), $CT_{90\%}$, the percentage of time spent at SpO_2 below 90%; $SpO_{2\ mean}$, mean oxygen saturation; $SpO_{2\ min}$, minimum oxygen saturation; ESS, Epworth Sleepiness Scale; VAS, visual analogue scale (scores transformed by sigmoid regression).

Sleep questionnaire

The sleep questionnaire consisted of three parts: 36 questions designed by us, the ESS [24] and the single-item VAS [25]. Our questions focused on the sleep pattern types of sleep disturbances, and related symptoms such as 'snoring' and 'restless legs'. The majority of these questions required a 'yes' or 'no' type of answer; in addition, severity and frequency of positive responses were quantified. For instance, 'restless legs' was defined as a disorder characterized by disturbing sensations that cause an almost irresistible urge to move the legs [26,27]. The ESS, based on questions referring to situations of everyday life, was self-administered and is reproduced in Table 2. Subjects were asked to rate on a scale of 0–3 how likely they would be to doze off or fall asleep in eight situations. As a second method to assess daytime fatigue, a single-item VAS was used. The VAS consisted of a 10 cm long horizontal line, anchored by 'no tiredness at all' on the left side of the scale and by 'complete exhaustion' on the right side. Patients were asked to place a mark on the horizontal line that best described how tired they had been feeling over the past week. The intensity of the subject's fatigue was scored by measuring from the low end (left side) of the scale to the subject's mark in centimetres. The score was determined by dividing the measured distance

Table 2. The Epworth Sleepiness Scale[a]

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = would *never* doze
1 = *slight* chance of dozing
2 = *moderate* chance of dozing
3 = *high* chance of dozing

Situation	Chance of dozing
Sitting and reading	
Watching TV	
Sitting, inactive in a public place (e.g. a theatre or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	

[a]According to the study of Johns [24].

by 10 (range of the score: 0–1). A higher score indicated a greater level of fatigue.

Measurement of blood pressure

After resting for a minimum of 10 min in the supine position, systolic and diastolic blood pressure were measured at least twice with a standard sphygmomanometer. In HD patients, blood pressure was always measured prior to a haemodialysis session and, in CAPD patients during an exchange with an empty peritoneal cavity.

Laboratory analyses

Haemoglobin, urea, creatinine, glucose, sodium, potassium, albumin, bicarbonate and 24 h creatinine clearance were measured by standard methods prior to HD or at steady state during CAPD.

Statistics

The statistics software package SYSTAT was used for data analysis (SYSTAT 6.01, SSPS Inc., Evanston, USA). In the case of the VAS, the basic observations were proportions. Therefore, an angular transformation (sigmoid regression) of the VAS scores was performed for variance stabilization. Data were expressed as mean values $\pm$SD. Students' *t*-test, χ^2 test (2×2 tables), the Fisher exact test (two-tail) and analysis of variance ANOVA, including the Tukey *post-hoc* test, were applied as appropriate.

Results

We analysed 75 individuals, as summarized in Table 1. Age and sex distribution were very similar in ESRD patients ($n=38$) and healthy control subjects ($n=37$), as shown in Table 1. Within the group of ESRD patients, CAPD patients were older (64 ± 12 years *vs* 52 ± 15 years, $P<0.05$) and had a higher body mass index (BMI) (26 ± 4.1 *vs* 22 ± 3.3, $P<0.05$) compared with HD patients. Importantly, co-morbidity was otherwise similar in these two subgroups; it consisted mainly of coronary heart disease, arterial hypertension, diabetes mellitus and chronic obstructive pulmonary disease.

Nocturnal oximetry findings

In accordance with the statistical findings of Gyulay *et al.* [28], the limit was set at an ODI of 15 for distinction between patients with and without a relevant sleep-disordered breathing. ODI values were significantly higher in ESRD patients than in controls (Figure 1 and Table 1). An ODI >15 was found in 18 out of 38 (47%) ESRD patients (nine CAPD and nine HD patients; Table 3), while only one (3%) out of the 37 control subjects (Table 1) showed an ODI of >15 ($P<0.001$). The ODI in this control subject, a healthy 54-year-old smoker, was 17.

There was no significant difference between the 20 HD and the 18 CAPD patients with regard to ODI,

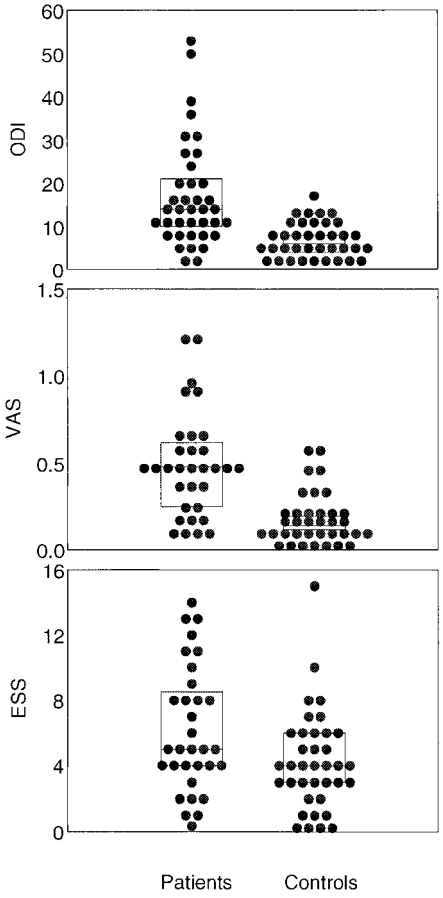

Fig. 1. Oxygen desaturation index (ODI) in 38 ESRD patients and 37 healthy subjects. Visual analogue scale (VAS) and Epworth sleepiness score (ESS) in 32 patients with end-stage renal disease (ESRD) and in 36 healthy subjects. Each point represents the result of one individual. Graphs show median values, 75th and 25th percentile values (upper and lower box margins, respectively).

Table 3. Findings in ESRD-patients with an oxygen desaturation index (ODI) of >15 and those without sleep-disordered breathing (ODI <15)

	ESRD patients with ODI >15 ($n=18$)	ESRD patients with ODI <15 ($n=20$)
Age (years)	61 ± 12.0	55 ± 16.5
Female gender (%)	39	50
HD/CAPD patients (*n*)	9/9	11/9
Patients with residual CCI (%, *n*)	39 (7)	30 (6)
BMI (kg/m^2)	25.7 ± 3.6	22.5 ± 4.0[a]
Systolic BP (mmHg)	150 ± 26.7	133 ± 29.1
Diastolic BP (mmHg)	80 ± 12.6	79 ± 12.9
ODI	26.1 ± 12.0	9.5 ± 4.0[b]
ESS	6.7 ± 3.9	5.7 ± 3.8
VAS	0.44 ± 0.27	0.53 ± 0.32

Values are mean $\pm$SD. [a]$P<0.05$; [b]$P<0.001$ (*vs* ESRD-patients with ODI >15).
CCI, creatinine clearance; BMI, body mass index; BP, blood pressure; ODI, oxygen desaturation index (falls in oxygen saturation $\geq 4\%$ per h); ESS, Epworth Sleepiness Scale; VAS, visual analogue scale (scores transformed by sigmoid regression).

mean SpO_2 ($SpO_{2\ mean}$), percentage of time at SpO_2 below 90% ($CT_{90\%}$), minimum oxygen saturation ($SpO_{2\ min}$) or with regard to any questionnaire finding (data not shown).

Importantly, we did not find a statistically significant correlation between pH (patients were not acidotic) or bicarbonate (before and after dialysis) and oxymetric findings in the 20 HD patients. In eight HD patients, the oximetry was performed on two consecutive nights to compare the night prior to haemodialysis with the night thereafter. The mean ODI values from the first to the second night were not significantly different (16.8 ± 9.5 *vs* 11.9 ± 8.5); four patients showed a slight improvement, two subjects an impairment and two individuals no change in nocturnal oxygen saturation.

The 16 CAPD patients with nocturnal dialysate in their peritoneal cavity displayed an ODI of 15.7 ± 2.2. In this patient group, we did not find a correlation between any oxymetric findings and the amount of nocturnal dialysate (1.5–2.5 l). Furthermore, there was also no correlation between ODI and the amount of dialysate fluid corrected by BMI, body weight or body surface, respectively (data not shown). The ODI in the CAPD patient without nocturnal intrabdominal dialysate was 8, and the remaining patient using a cycler system during the night had an ODI of 24.

Since we did not observe any significant differences between CAPD and HD patients in terms of nocturnal oximetry and in co-morbidity (with the exception of age and BMI), these subjects were considered as a single group in the following analyses, hereafter named ESRD patients.

The ODI values were similar in the 13 ESRD patients with residual renal function (mean creatinine clearance, 5.6 ± 2.3 ml/min) and the 25 anuric ESRD patients (18.1 ± 13.6 *vs* 15.8 ± 8.7). Furthermore, there was no statistical correlation between the ODI and laboratory findings, including haemoglobin, urea, creatinine, sodium, potassium, glucose, albumin and bicarbonate.

ESRD patients with an ODI of >15 had a higher BMI, but not a significantly higher blood pressure than the individuals with an ODI <15, as summarized in Table 3. In ESRD patients with both hypertension and BMI >25, an ODI of >15 was found in 77% of the patients ($n=13$), a percentage much higher than that of 44% in hypertensive but not overweight patients ($n=9$) and that of 25% in normotensive patients ($n=16$). Interestingly, none of the normotensive ESRD patients were overweight (BMI $\leqslant 25$).

Regression analysis showed that the BMI correlated with the ODI ($r=0.54$, $P=0.001$), but not significantly with blood pressure ($r=0.30$, $P=0.08$) or age ($r=0.26$, $P=0.12$). Moreover, stepwise multiple linear regression between ODI and age, blood pressure and BMI revealed that blood pressure was dependent on the BMI; a significant correlation was found between blood pressure and BMI ($r=0.48$, $P=0.003$).

Sleep questionnaire-based findings

Compared with control subjects, ESRD patients complained more frequently about symptoms of 'restless legs' (54% *vs* 16%, $P<0.01$) but not about other factors included in the questionnaire such as 'nocturnal awakening', 'snoring' or 'excessively loud snoring' (data not shown). The symptoms 'restless legs' and 'nocturnal awakening' were slightly, but not significantly, more frequent in the 18 ESRD patients with an ODI of >15 than in the 20 ESRD patients with an ODI of <15, i.e. 50% *vs* 35% and 50% *vs* 40%, respectively.

Snoring prevalence was high in ESRD patients regardless whether the ODI was above or below 15, i.e. as 94 or 76%, respectively. On the contrary, 'excessively loud snoring' was reported more frequently in patients with an ODI of >15 than in patients with an ODI of <15 (42% *vs* 6%, $P<0.05$). Moreover, patients with the symptom 'excessively loud snoring' showed an ODI of >15 in the oximetry markedly more frequently than patients without this symptom (88% *vs* 38%, $P<0.05$). The questionnaire findings on 'general sleeping problems', 'early awakening in the morning' as well as sleep duration were not different in the two patient groups separated by the ODI value of 15.

With regard to ESS and VAS, only the results from 32 ESRD patients and 36 healthy subjects could be analysed, due to incomplete answers from seven individuals. Both VAS and ESS were significantly higher in ESRD patients compared with the control subjects, as shown in Figure 1 and Table 1. The results from the ESS as well as the score derived from the VAS were similar in HD *vs* CAPD patients (ESS, 5.3 ± 2.4 *vs* 7.2 ± 4.9; VAS; 0.43 ± 0.31 *vs* 0.57 ± 0.27). These results were similar irrespective of ODI being <15 or >15. Furthermore, the scores from both the ESS and VAS did not correlate with ODI values or any other measured parameter of oximetry.

Interestingly, according to the sleep questionnaire, ESRD patients with an ODI of <15 more frequently had a professional activity as compared with ESRD patients with an ODI of >15 (63% *vs* 21%; $P<0.05$), as shown in Figure 2.

Discussion

We investigated a group of ESRD patients with nocturnal home oximetry for the presence of sleep-

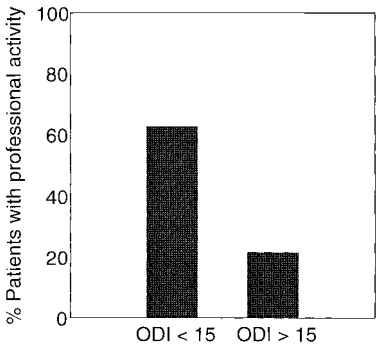

Fig. 2. Professional activity in ESRD patients according to oxygen desaturation index (ODI). Black bars represent the percentage of patients with a professional activity.

disordered breathing. The advantages of this screening method compared with polysomnography are the ease of applicability, the lower financial burden and the possibility of performing the investigation on an outpatient basis. The usefulness of nocturnal pulse oximetry in establishing the diagnosis of sleep apnoea in patients who are suspected of having this disease was shown in several studies [28–31]. Gyulay *et al.* [28] demonstrated that in a population with a high risk of sleep apnoea, the specificity of this test is high. The positive predictive value of oximetry amounted to 83% if the pre-test probability of sleep apnoea was 30%, and >90% if the pre-test probability was at least 50% [28]. We omitted polysomnography in our investigations—although it represents the gold-standard for definition of the mechanism of sleep apnoea—for the following reasons: first, polysomnography in our institution is very expensive. Second, we studied a high-risk patient population who are most likely to result in a high specificity and a good predictive value of oximetry as stated above [28]. Third, the aim of the present study was to use oximetry together with a questionnaire for screening purposes and not to define the mechanisms of hypoxaemia. Our study design with nocturnal home oximetry is in line with the recent investigation of Zoccali *et al.* where oximetry without polysomnography was utilized for studying overnight oxygen saturation in dialysis patients [5].

From previous reports, there is evidence that the prevalence of sleep apnoea is unusually high in ESRD patients [6–15], as shown in Table 4. However, the authors of these 10 studies either analysed only small [6,8,9,11,14,15] and mostly symptomatic subgroups [7,9,11,12], did not fully report patient selection criteria [6,8,10,14] or no sleep questionnaire was administered [6–12,15]. In none of the studies was a healthy control group included. In eight studies, sleep apnoea was diagnosed exclusively by polysomnography [6–12,14]. In the study by Hallett *et al.* [13], only some of the HD and CAPD patients and in the study by Rodriguez *et al.* [15] only CAPD patients were monitored by overnight oximetry, using the same ODI cut-off value of 15 for definition of sleep apnoea. In addition to these reports, sleep complaints were analysed by a sleep questionnaire in two larger patient series, but no quantification of sleep-disordered breathing was provided by polysomnography or nocturnal oximetry [32,33]. Our study represents the first investigation of unselected ESRD patients and healthy control subjects all analysed by nocturnal home oximetry combined with a sleep questionnaire. In accordance with the literature, the present investigation confirms the high prevalence of sleep-disordered breathing in ESRD patients whether on chronic HD or on CAPD.

The results of our study revealed that the values derived from the ESS and VAS do not correlate with nocturnal oxygen desaturation in a population of ESRD patients. None of the sleep questionnaire-based findings, with the exception of 'excessively loud snoring', were helpful for the assessment of sleep-disordered breathing. A very large proportion of ESRD patients with 'excessively loud snoring' had significant nocturnal oxygen desaturation, whereas only a few without this complaint had a desaturation. Therefore, 'excessively loud snoring' is a risk factor for sleep-disordered breathing in ESRD patients, an observation made previously for other patient populations.

In line with previous reports [34,35], we showed that overweight and hypertension are associated findings not only in the general population but also in a population of ESRD patients. Furthermore, we were able to demonstrate that obesity is associated with an impressively high incidence of sleep-disordered breathing especially in hypertensive ESRD patients. This is particularly important in the light of the presumed link of hypertension to sleep-disordered breathing [2,16,17,36–38]. The impact of obesity on ODI in ESRD patients is reminiscent of the relationship between hypothyroidism and sleep-disordered breathing. The incidence of sleep-disordered breathing is also increased in these patients, but is related mainly to obesity and male gender rather than to hypothyroidism *per se* [39].

The effect of the type of dialysis on nocturnal oxygen desaturation remains a controversial issue. In accordance with the literature [10,13], no difference in sleep-

Table 4. Previous reports of sleep apnoea in ESRD patients

Author, year	Patients on		Symptomatic patients (*n*)	Asymptomatic patients (*n*)	Symptoms not stated (*n*)	Patients (%) with sleep apnoea
	CAPD	HD				
Millmann, 1985 [6]	–	8	8	–	–	6[a] (75%)
Kimmel, 1989 [7]	–	26	22	4	–	16[a] (62%)
Mendelson, 1990 [8]	–	11	–	–	11	6[a] (55%)
Wadhwa, 1991 [9]	11	–	11	–	–	6[a] (55%)
Wadhwa, 1992 [10]	15	15	–	–	30	17[a] (57%)
Pressmann, 1993 [11]	1	6	7	–	–	7[a] (100%)
Stepanski, 1995 [12]	18	–	18	–	–	11[a] (61%)
Hallett, 1995 [13]	16	20	–	–	36	27[b] (75%)
Guillaume, 1995 [14]	–	10	–	–	10	6[a] (60%)
Rodriguez, 1995 [15]	18	–	–	–	18	6[c] (33%)

[a]Diagnosed by polysomnography; [b]diagnosed by polysomnography ($n=15$) and by oximetry ($n=21$); [c]diagnosed by oximetry.

disordered breathing was found, between ESRD patients treated by HD and peritoneal dialysis. Interestingly, we found no correlation between the amount of nocturnal peritoneal dialysate and oxygen desaturation in CAPD patients. However, Wadhwa *et al.* [9] observed a positive correlation between the amount of dialysate drained in the morning and the degree of minimum oxygen saturation in six CAPD patients suffering from sleep apnoea. Therefore, an increase in sleep-disordered breathing due to the nocturnal fluid load may be important in a subgroup of patients on CAPD, and further studies are indicated to define that population exactly.

Haemodialysis patients are dialysed three times a week. Thus, the question arises of whether nocturnal hypoxaemia is a function of the time of haemodialysis treatment in relation to the night of the oximetry. This question was addressed previously by Mendelson *et al.* [8] in 11 subjects. Overall, these authors found that conventional haemodialysis treatment did not significantly modulate the severity of sleep apnoea. In our patient group consisting of eight individuals, we also did not observe any consistent changes in oximetry as a function of time when haemodialysis treatment was performed. It would certainly require a large study to resolve this issue conclusively.

A practically relevant finding of our study is that ESRD patients with sleep-disordered breathing less frequently have a professional activity compared with those without significant nocturnal oxygen desaturation. This underlines the importance of accurate assessment and treatment of sleep-disordered breathing in ESRD patients and implies its great socio-economical importance.

Conclusions

The symptom of 'excessively loud snoring' and a BMI >25, especially in combination with hypertension, are important risk factors and should alert the physician to investigate breathing during sleep in ESRD patients. Nocturnal home oximetry represents a simple and inexpensive tool for the detection of sleep disorders in these subjects. The ESS and the VAS provide no additional help in the assessment of sleep-disordered breathing in patients suffering from ESRD.

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