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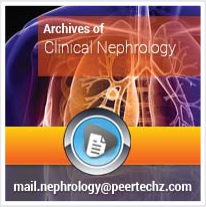

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Observational Study

The occurrence and influencing factors of fatigue and sleep disturbance in maintenance hemodialysis patients

Dong Kaixuan[1]*, Chen Xi[1], Zhou Rong[1] and Yu Xiaoyong[2]

[1]First Clinical Medical College, Shaanxi University of Traditional Chinese Medicine, Xianyang, Shaanxi 712046, China

[2]Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an, Shaanxi 710003, China

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***Corresponding author:** Dong Kaixuan, First Clinical Medical College, Shaanxi University of Traditional Chinese Medicine, Xianyang, Shaanxi 712046, China, Tel:15829943798; E-mail: 447546345@qq.com

ORCID: https://orcid.org/0000-0003-0600-2827

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Abstract

Objective: To investigate the occurrence and influencing factors of fatigue and sleep disturbance in Maintenance Hemodialysis (MHD) patients.

Methods: A total of 170 patients with end-stage renal disease who underwent MHD treatment in the hemodialysis room of Shaanxi Provincial Hospital of Traditional Chinese Medicine from October 2021 to March 2022 were selected as the research subjects. The basic information and laboratory indicators of the patients were collected by cross-sectional survey. The survey methods were evaluated by the revised Piper Fatigue Scale and the Pittsburgh Sleep Quality Rating Scale and the incidence and influencing factors of fatigue and sleep disturbance in MHD patients were analyzed.

Results: Fatigue occurred in 135 cases, the incidence rate was 79.41%; sleep disturbance occurred in 124 cases and the incidence rate was 72.94%. After one-way analysis of variance, factors such as exercise, Albumin (ALB, serum Creatinine(CRE), Phosphorus(P) and Hemoglobin(HGB) in MHD patients can affect fatigue; while age, gender, exercise, primary disease, dialysis frequency, Phosphorus(P), Hemoglobin(HGB) and high-sensitivity C-Reactive Protein (hs-CRP) factors can affect sleep. A multiple linear regression model was constructed for the factors affecting fatigue ($F = 81.110$, $p < 0.001$), and it showed that 70.3% of fatigue (adjusted $R2 = 0.703$) was related to albumin (ALB), serum creatinine(CRE), and hemoglobin(HGB) (all $p < 0.05$); A multiple linear regression model was constructed based on the factors of 58% ($F = 26.933$, $p < 0.001$), which showed that 58% of sleep disorders (adjusted $R2 = 0.580$) were significantly related to age, gender, exercise or not, phosphorus(P), high-sensitivity C-reactive protein(hs-CRP) (all $p < 0.05$) related. Pearson correlation analysis was used to analyze sleep disturbance and fatigue in MHD patients and the results showed that there was a positive correlation between the two ($r = 0.478$, $p < 0.001$).

Conclusion: The proportion of fatigue and sleep disturbance in MHD patients is relatively high, mainly mild to moderate and the two influence each other. Exercise intervention and nutritional support can effectively improve the occurrence of fatigue and sleep disturbance in MHD patients.

Hemodialysis (HD) is the most common treatment for patients with end-stage renal disease and about 89.4% of end-stage renal disease (ESRD) patients in China choose HD for treatment [1]. However, although maintenance hemodialysis treatment can prolong the life of ESRD patients, the vast majority of patients will have physical and psychological problems, which will reduce their quality of life of patients. A large number of studies have shown that fatigue and sleep disorders are common in maintenance hemodialysis patients and are also the main causes of anxiety and depression, decreased quality of daily life and death in MHD patients [2-4]. Based on this, this study provides a further theoretical basis for improving the quality of life of MHD patients by analyzing the occurrence and influencing factors of fatigue and sleep disturbance in MHD patients.

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Materials and methods

General information

A total of 170 patients with end-stage renal disease who underwent MHD treatment in the hemodialysis room of Shaanxi Provincial Hospital of Traditional Chinese Medicine from November 2021 to April 2022 were selected as the research subjects. A cross-sectional survey was conducted to collect patients' basic information and laboratory indicators. The revised Piper Fatigue Scale and Pittsburgh Sleep Quality Scale were evaluated by questionnaire. Figure 1 for the flow chart.

Inclusion and exclusion criteria

Inclusion criteria: (1) The selected patients were all patients with end-stage renal disease who were treated with hemodialysis; (2) The patients knew and agreed to participate in this study; (3) All the information of the patients was complete; (4) Dialysis age ≥ 3 months, the frequency of dialysis is 2 to 3 times/week and each dialysis is 4 hours; (5) Age 18 to 85 years old.

Exclusion criteria: (1) Patients who cannot read, write and communicate normally; (2) Patients with serious diseases such as mental disorders, tumors, or cardiovascular and cerebrovascular systems; (3) Patients with serious complications within the past 1 month; (4) Patients who have taken psychotropic drugs or sedative drugs.

Research methods

Clinical data collection: (1) General information: including age, gender, educational level, exercise or not, dialysis age, ultrafiltration rate (UFR), blood pressure before dialysis, etc. Ultrafiltration rate (UFR) is the actual amount of dehydration per time (ml)/[dry body mass (kg) × time per dialysis (h)]. (2) Laboratory indicators: including hemoglobin (HGB), high-sensitivity C-reactive protein (hs-CRP), albumin (ALB), fasting blood glucose (GLU), serum creatinine (CRE), calcium (Ca), phosphorus (P), etc. The data of all laboratories are the results of the latest inspection in the month of the investigation.

Fatigue and sleep disorders scale survey: Through questionnaires, the revised Piper Fatigue Scale (RPFS) and Pittsburgh sleep quality index (PSQI) were used to evaluate the fatigue and sleep status of MHD patients. Among them, RPFS is used to assess fatigue, including 4 dimensions and 22 items, using a numerical scoring method of 0 to 10. The total score is the average score of the 22 items. 0 points mean no fatigue and 1 to 3 points indicate mild fatigue. Fatigue, 4-6 points indicate severe fatigue, 7-10 points indicate severe fatigue and Cronbach's α coefficient is above 0.9 [5]. PSQI was used to evaluate sleep quality in the last month, and the total score ranged from 0 to 21. The higher the score, the worse the sleep quality was. 0-5 points indicated good sleep quality, 6-10 points indicated good sleep quality, 11-15 points indicated poor sleep quality and 16-21 points indicated very poor sleep quality. Cronbach's α coefficient was above 0.8 [6].

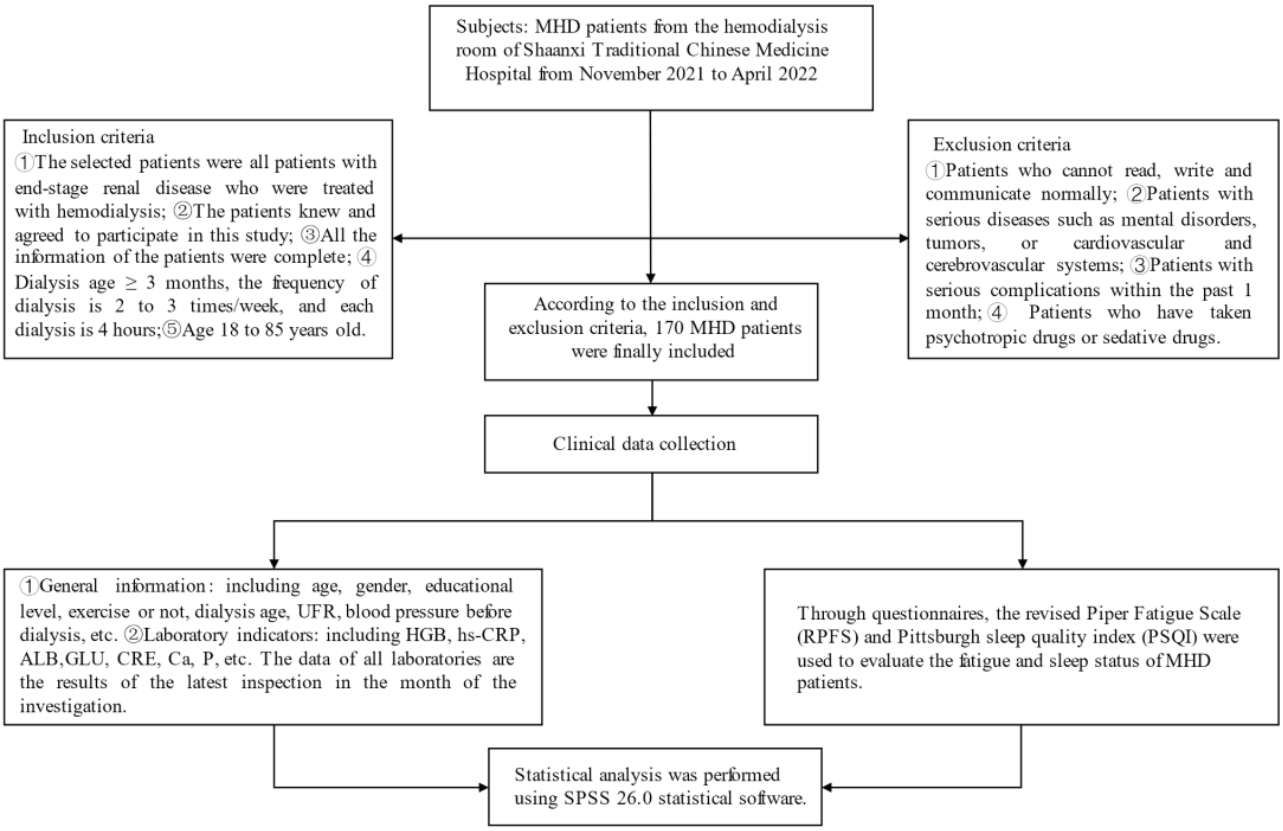

Figure 1: Remark: UFR(Ultrafiltration Rate) HGB(Hemoglobin),hs-CRP (High-Sensitivity C-Reactive Protein),ALB(Albumin),GLU(Blood Glucose),CRE(Serumcreatinine),Ca(Calcium),P(Phosphorus).

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Statistical analysis

Statistical analysis was performed using SPSS 26.0 statistical software. Measurement data were expressed as mean ± standard deviation and enumeration data were described by the number of cases and percentages. One-way ANOVA and multiple linear regression models were used to analyze the influencing factors of fatigue and sleep disturbance in MHD patients, and Pearson correlation analysis was used to analyze the correlation between fatigue and sleep disturbance. When $p < 0.05$, it was considered statistically significant.

Results

General situation

A total of 170 patients were included who had completed the study independently, including 114 males and 56 females, with an average age of 59.37 ± 12.84 years and an average dialysis age of 52.98 ± 43.81 months. Among the primary diseases of MHD patients, 77 cases (45.3%) of chronic glomerulonephritis and 69 cases (40.6%) of diabetic nephropathy were the main causes of end-stage renal disease, 14 cases (8.2%) of hypertensive renal damage were the other 10 cases (5.9%), including 4 cases of polycystic kidney disease, 2 cases of gout, 1 case of lupus nephritis, 1 case of Aristolochia nephropathy, 1 case of ANCA-associated vasculitis and 1 case of a solitary kidney. Table 1 for details.

The incidence of fatigue and sleep disorders in MHD patients

Fatigue occurred in 135 of 170 MHD patients, with an incidence of 79.41%. RPFS score greater than 0 was considered fatigue. The incidence of sleep disorders was 72.94% in 124 cases and PSQI scores greater than 5 were considered sleep disorders. According to descriptive statistics, the fatigue score of MHD patients was 3.65 ± 2.25 and the sleep score was 9.92 ± 4.89. In general, the proportion of fatigue and sleep disorders in MHD patients was high, and they were mainly mild to moderate.

Analysis of influencing factors

One-way analysis of variance showed that exercise, ALB, CRE, P, HGB and other factors could affect fatigue in MHD patients (Table 2). However, age, sex, exercise, primary disease, frequency of dialysis, P, HGB, hs-CRP and other factors can affect sleep (Table 3). On the basis of the above results, the multivariate linear regression model ($F = 81.110$, $p < 0.001$) was constructed for the factors affecting fatigue. The results showed that 70.3% of fatigue (corrected R2 = 0.703) was significantly associated with exercise or not, CRE, P (all P< 0.05) related to; Multivariate linear regression model ($F=26.933$, $p < 0.001$) showed that 58% of sleep disorders (corrected R2 = 0.580) were significantly associated with age, gender, exercise, P, hs-CRP (all P< (Table 4). Pearson correlation analysis was used to analyze the incidence of sleep disturbance and fatigue in MHD patients, and the results showed that there was a positive correlation between them ($r = 0.478$, $p < 0.001$).

Discussion

Fatigue, sleep disturbance, frailty, anxiety and depression belong to a group of symptoms, which can all lead to a decline in the function of important organs and a decline in the quality of daily life [7]. This study starts from two influencing factors, fatigue and sleep disturbance and believes that fatigue and sleep disturbance are the most common clinical symptoms of MHD patients, and they influence and promote each other, forming

Table 1: Primary diseases of MHD patients.

Item		Number	Percent %	Item	Min	Max	mean ± SD
Gender	Male	114	67.1	Age	20	85	59.37 ± 12.84
	Female	56	32.9	Dialysis age (months)	4	220	52.98 ± 43.81
Level of education	Primary school	16	9.4	Ultrafiltration rate	1.6	20.9	11.56 ± 3.67
	Junior high school	55	32.4	Pre-dialysis systolic blood pressure	90	188	143.53 ± 17.06
	High school	52	30.6	Diastolic blood pressure before dialysis	49	120	78.26 ± 11.26
	college	34	20.0	ALB	29.9	53.1	38.49 ± 3.59
	Bachelor's degree or above	13	7.6	GLU	3.46	26.75	6.53 ± 3.35
Movement or not	Y	54	31.8	CRE	519.1	1494.7	1050.6 ± 245.29
	N	116	68.2	Ca	1.16	2.85	2.23 ± 0.23
Dialysis frequency	2 times per week	56	32.9	P	0.73	3.57	2.06 ± 0.68
	2.5 times per week	92	54.1	HGB	63	168	106.24 ± 18.67
	3 times per week	22	12.9	hs-CRP	0.11	30.81	5.37 ± 5.20
The primary disease	CGN	77	45.3	Sleep score	0	20	9.92 ± 4.89
	DN	69	40.6	Fatigue rating	0	8.91	3.65 ± 2.25
	Hypertensive nephropathy	14	8.2				
	other	10	5.9				

Remark: CGN(chronic glomerulonephritis),DN(diabetic nephropathy),ALB(albumin),GLU(blood glucose),CRE(serum creatinine),Ca(calcium),P(phosphorus),HGB(hemoglobin),hs-CRP (high-sensitivity C-reactive protein) .

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Table 2: Univariate analysis of fatigue in MHD patients.

Item	F-value	*p*-value	Item	F-value	*p*-value
age	1.104	0.327	Ultrafiltration rate	0.438	0.989
gender	0.708	0.401	ALB (g/L)	2.088	0.001
Movement or not	7.018	0.009	GLU (mmol/L)	1.114	0.373
Level of education	1.633	0.168	CRE (umol/L)	6.718	0.020
The primary disease	1.321	0.269	Ca (mmol/L)	0.892	0.695
Dialysis age (months)	1.066	0.386	P (mmol/L)	1.616	0.038
Dialysis frequency	1.033	0.358	HGB (g/L)	1.917	0.002
Pre-dialysis systolic blood pressure (mmHg)	0.982	0.508	hs-CRP(mg/L)	1.538	0.203
Diastolic blood pressure before dialysis (mmHg)	1.008	0.467			

Table 3: Univariate analysis of influencing sleep disorders in MHD patients.

Item	F-value	*p*-value	Item	F-value	*p*-value
age	1.824	0.004	Ultrafiltration rate	0.807	0.739
gender	8.965	0.003	ALB (g/L)	1.612	0.016
Movement or not	11.489	0.001	GLU (mmol/L)	1.050	0.453
Level of education	1.920	0.109	CRE (umol/L)	1.752	0.278
The primary disease	6.183	0.001	Ca (mmol/L)	0.992	0.511
Dialysis age (months)	1.118	0.307	P (mmol/L)	1.813	0.014
Dialysis frequency	6.103	0.003	HGB (g/L)	1.623	0.014
Pre-dialysis systolic blood pressure (mmHg)	1.130	0.301	hs-CRP(mg/L)	3.916	0.005
Diastolic blood pressure before dialysis (mmHg)	0.933	0.578			

Table 4: Multiple linear regression analysis affecting fatigue and sleep disturbance in MHD patients.

Fatigue model	*T*-value	Sig	Sleep model	*T*-value	Sig
Movement or not	-0.541	0.004	gender	-2.293	0.023
ALB	-3.531	0.589	age	4.574	0.000
CRE	8.542	0.001	Movement or not	-2.043	0.043
P	1.829	0.000	Dialysis frequency	0.186	0.853
HGB	-2.330	0.069	The primary disease	1.270	0.206
			P	5.957	0.000
			HGB	-1.570	0.118
			hs-CRP	4.336	0.000
			ALB	-0.258	0.797

a vicious circle. About 42% to 89% of patients undergoing hemodialysis suffer from fatigue [8], while the incidence of fatigue in patients undergoing hemodialysis in China is between 60% and 97% [9]. About 50% - 80% of patients undergoing hemodialysis or peritoneal dialysis have sleep disorders [10]. Gao Menglin et al. reported that the incidence of sleep disorders in maintenance hemodialysis was 61.7% [11]. Studies have shown that age, education level, exercise, uremia, anemia, hypoproteinemia, malnutrition, sleep disorders and negative psychological problems can lead to fatigue in patients with MHD. Sleep disorders are also closely related to factors such as urea nitrogen, serum creatinine, blood pressure, blood glucose, anemia, age, pain, pruritus, inflammatory reaction, fatigue, anxiety and depression [12-14]. This is basically consistent with our results. The incidence of fatigue (79.41%) and sleep disorders (72.94%) in MHD patients is high and the influencing factors are complex, and they are closely related to each other, but they are mainly mild to moderate. The influencing factors of fatigue in MHD patients include exercise or not, ALB, CRE, P, HGB, etc. and exercise or not, CRE, and P are independent risk factors for fatigue. Factors affecting sleep include age, gender, exercise or not, primary disease, dialysis frequency, P, HGB, hs-CRP and age, gender, exercise or not, P, hs-CRP are independent risk factors for sleep disorders. However, we considered inconsistencies that may have resulted from differences in patients' basic characteristics or because of their own subjective perceptions of fatigue and sleep.

Of course, our study also has some limitations. First of all, this study is a cross-sectional study with small sample size and limited observation indexes. Secondly, this study used scale measurement to evaluate the fatigue and sleep of patients and the assessment tool was relatively simple. Finally, we only evaluated the influencing factors of fatigue and sleep in MHD patients. In the future, we expect to conduct more comprehensive large-sample, multicenter prospective studies including anxiety, depression and other factors that can affect patients' quality of life.

In addition, because MHD patients sleep more during the day when receiving dialysis treatment, the change of circadian rhythm is also an important factor leading to sleep disorders [15]. And we found that low levels of plasma creatine concentrations were strongly associated with fatigue. Creatine is a natural nitrogenous organic acid, which can be consumed from fresh meat or fish through diet and can also be converted to Guanidinyl Acetate by Glycinamidine Transferase (AGAT), which is subsequently converted by Guanidinyl Acetate N-Methyltransferase (GAMT) to synthesize endogenous creatine, which is mainly present in skeletal muscle. AGAT is mainly expressed in the kidney. When renal function is impaired, AGAT activity decreases, resulting in reduced endogenous creatine synthesis. Hemodialysis in patients with the end-stage renal disease also leads to lower creatine concentrations in the blood. Hypoproteinemia and gender are also important factors affecting creatine concentration [16]. There was also a strong association between higher plasma Fibroblast Growth Factor 21(FGF21) levels and fatigue. FGF21 is an endocrine factor that maintains protein intake and metabolic homeostasis. Studies have found that a low protein diet leads to an increase in plasma FGF21 level and the plasma FGF21 level is positively correlated with age, serum creatinine, urea nitrogen and cystatin C [17].

Exercise intervention is a non-drug-assisted therapy recommended by current guidelines mainly for fatigue and sleep disorders in MHD patients. Multiple systematic reviews have confirmed that exercise therapy can effectively alleviate fatigue and sleep disorders in MHD patients. In patients with end-stage renal disease, the loss of systemic protein and energy stores due to dietary restriction, inflammation, insulin

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resistance, metabolic acidosis, reduced physical activity and depression leads to Protein-Energy Expenditure (PEW), which can be manifested as muscle atrophy, sarcopenia, malnutrition, weakness, fatigue, or cachexia. Exercise can also effectively improve protein consumption and thus improve fatigue and sleep disorders in MHD patients [18-21]. It is worth noting that there are certain risks in exercise intervention, so it is necessary to take full account of the patient's physical function and proceed step by step according to one's ability [22]. In addition, eating a sufficient amount of high-quality protein every day can also reduce fatigue. Studies have proved that dietary nutrition plays an important role in sleep health, and the use of dietary management to improve sleep is a feasible, convenient and cheap strategy [23]. The level of fatigue and the degree of sleep disorders in MHD patients is negatively correlated with the degree of family care. We can reduce the level of fatigue and sleep disorders in patients by improving the degree of family care [24,25]. Poor economic status and living alone also become risk factors for fatigue and sleep disturbance in MHD patients, while no complications are protective factors for fatigue and sleep disturbance in MHD patients [26].

In conclusion, MHD patients have a high incidence of fatigue and sleep disorders. We should take timely and effective measures to prevent and reduce the occurrence of fatigue and sleep disorders, and improve their quality of life and survival rate.

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