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Risk factors for erectile dysfunction in end-stage renal disease patients with short- or long-term hemodialysis therapy

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Abstract

Background: The influence of prolongation of hemodialysis (HD) period for erectile dysfunction (ED) has not been well evaluated. We evaluated the effects of various factors including hemodialysis duration for ED in hemodialysis patients.

Methods: One hundred seventy-eight HD patients including 50 patients who received HD more than 10 years were enrolled in this study. The questionnaire of the International Index of Erectile Function (IIEF)-5 in Japanese language was used for evaluation of ED status in this cohort. Various clinical factors of these patients were collected from review of medical records, and the relationship between these factors and ED status was also evaluated.

Results: The prevalence of diabetes ($p < 0.001$), obesity ($p = 0.011$), and hyperuricemia ($p = 0.010$) were significantly higher in patients with less than 10 years of HD (group 1) than those in patients with more than 10 years of HD periods (group 2). The mean score of IIEF-5 in group 2 was almost similar with that in group 1 ($p = 0.452$). Moderate to severe ED was also equivalent to that in group 1 ($p = 0.988$). More than 60 years old ($p < 0.001$) and absence of hyperuricemia ($p = 0.002$) appeared to be significant risk factors for moderate to severe ED in multivariate analysis.

Conclusions: Long periods of chronic hemodialysis therapy did not affect ED status, and absence of hyperuricemia was the risk factor for moderate to severe ED in HD patients.

Keywords: Erectile dysfunction, Hemodialysis, Renal failure, Hyperuricemia, IIEF-5

Background

Uremic condition is associated to various physical disorders which impair patient's quality of life. Erectile dysfunction (ED) is one of the common complications in male hemodialysis (HD) patients. Its prevalence is estimated to be approximately 20 to 80% in HD patients [1–6]. Various factors such as vascular dysfunction, neurogenic disturbance, adverse effect of medications, depression, hormonal abnormalities, anemia, secondary hyperparathyroidism, and zinc deficiency are related to ED in HD patients [3, 5–8]. Some of those risk factors for ED gradually progress with the extension of dialysis periods. However, whether long duration of HD is a significant risk factor of ED in HD patients is still controversial, because of the relatively short period of dialysis in those study cohorts and division of results. Moreover, the difference of clinical risk factor for ED between patients with short-term HD therapy and those with long-term therapy still remains uncertain. Hence, we evaluated the effects of various factors including HD duration for ED in HD patients.

Methods

From January to July 2011, male patients who were older than 20 years old and received chronic HD therapy at 13 facilities in Yamagata prefecture were recruited to the study. The study protocol was approved by the ethical committee of the Yamagata University Faculty of Medicine.

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The patients who received providing written informed consent and voluntarily completed the questionnaire of the International Index of Erectile Function (IIEF)-5 in Japanese language that consisted of 5 questions eliciting were enrolled in the study. An IIEF-5 score between 1 to 7 denotes a serious form of ED, 8 to 11 denotes moderate, 12 to 16 denotes moderate to mild, 17 to 21 denotes mild, and 22 to 25 denotes no ED. The information about past history of smoking, alcohol consumption, presence of sexual partner, and past history of treatment for ED were also obtained by the questionnaire.

Terms of patient's background including age, duration of HD therapy, primary disease, presence of comorbidities, and current medications were collected from review of medical records. Attending physician in each facility evaluated the presence of each comorbidity based on patient's clinical status, laboratory data, and medication profile. Patients were divided into two groups: patients with less than 10 years of HD periods were in group 1, and those with more than 10 years were in group 2.

Various parameters including patient's backgrounds and clinical features were compared between two groups. In order to evaluate differences between groups, Chi-square, Student's t test, Mann–Whitney U test, and Fisher's exact test were used as appropriate. Multivariate association between these factors and ED were measured with odds ratio (OR). Multivariable logistic regression analysis was used to examine the associations between predictor variables and ED. Significance of the individual regression estimates was tested by Wald statistics. The significance level was set at 0.05 for all tests. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [9]. More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.

Results

Two hundred of chronic HD male patients in 13 institutions participated in this study. Eight patients were excluded because they did not completed the EF domain from IIEF-5 in questionnaire, and 14 patients were also excluded because of their past history of medical treatment for ED. Thus, the sample was composed of 178 patients.

Patient's background was shown in Table 1. The number of patients whose duration of chronic HD was shorter than 10 years (group 1) was 128, and that of the others who received chronic HD more than 10 years (group 2) was 50. Mean duration of HD was 4.5 ± 2.5 years in group 1 and 17.3 ± 5.4 years in group 2 ($p < 0.001$). Body mass index (BMI) was significantly lower in group 2 ($p = 0.011$). The most frequent primary disease of end-stage renal

disease was diabetes mellitus (DM) nephropathy in group 1, while that in group 2 was chronic glomerular nephritis (CGN) ($p = 0.016$). The prevalence of DM was also higher in group 1 ($p < 0.001$). Group 1 had a high frequency of hyperuricemia ($p = 0.010$) and a lower frequency of liver dysfunction ($p = 0.031$). The prevalence of other comorbidities was not significantly different between the 2 groups. Chronic kidney disease mineral and bone disorder (CKD-MBD) status including serum calcium (Ca), phosphate (P), and intact parathyroid hormone (iPTH) levels was also compared between 104 of 128 patients and 41 of 50 patients whose data of these parameters could be collected from medical records. Serum Ca (9.0 ± 0.8 mg/dL and 9.1 ± 0.8 mg/dL; $p = 0.366$), P (5.7 ± 1.7 mg/dL and 5.4 ± 1.6 mg/dL; $p = 0.477$), and iPTH (154.1 ± 124.5 pg/mL and 147.3 ± 125.7 pg/mL; $p = 0.645$) were not significantly different between the 2 groups.

IIEF-5 scores and grade of ED assessed by IIEF-5 in each group were shown in Table 2. The mean score of IIEF-5 in group 2 was almost similar with that in group 1 ($p = 0.452$). The rate of each ED grade assessed by IIEF-5 score in group 2 was also comparable to that of group 1 ($p = 0.959$). Moderate to severe ED on the basis of IIEF-5 score in group 2 was 66%, which was almost equivalent to 68% in group 1 ($p = 0.849$).

On univariate analysis, associated risk factors for moderate to severe ED on the basis of IIEF-5 score were age older than 60 years ($p < 0.001$) and absence of hyperuricemia ($p = 0.008$) (Table 3). HD duration more than 10 years was demonstrated not to be the significant risk factor for moderate to severe ED ($p = 0.779$). We also evaluated the relationship between ED and these risk factors in multivariate analysis. While HD duration also did not have significant correlation with moderate to severe ED in this analysis, age more than 60 years old ($p < 0.001$) and absence of hyperuricemia ($p = 0.005$) appeared to be important correlate of moderate to severe ED.

Discussion

As a result of improvement in HD therapy and small number of kidney transplantation due to extreme shortage of kidney donation in Japan, the number of both end-stage renal disease (ESRD) patients with long-term chronic HD therapy and patients who receive short period of chronic HD but have various comorbidities are gradually increasing [10]. Several cross-sectional studies revealed that ED is a very common disease in ESRD patients; however, the influence of long-term chronic HD for ED was not well evaluated. In this study, the frequency of ED was almost equivalent between short-term HD patients and long-term patients, and hyperuricemia was demonstrated to be an independent risk factor in not only all patients but also long-term hemodialysis patients.

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Table 1 Patient demographics

			All patients	Duration of HD <10 years patients	Duration of HD ≥10 years patients	p values
			n = 178	(Group 1; n = 128)	(Group 2; n = 50)	
Age	mean ± SD	(years)	59.2 ± 10.7	60.0 ± 10.5	57.4 ± 11.0	0.19
Duration of dialysis	mean ± SD	(years)	8.1 ± 6.8	4.5 ± 2.5	17.3 ± 5.4	<0.001
Body mass index	mean ± SD	(kg/m/m)	23.5 ± 8.4	24.3 ± 8.7	21.2 ± 7.1	0.01
Primary renal diseases						0.02
Diabetes mellitus	n	(%)	54 (30)	49 (38)	5 (10)	
Chronic glomerular nephritis	n	(%)	64 (36)	34 (27)	30 (60)	
Hypertensive nephrosclerosis	n	(%)	13 (7)	12 (9)	1 (2)	
Others	n	(%)	47 (26)	33 (26)	14 (28)	
Comorbidities						
Hypertension	n	(%)	156 (88)	115 (90)	41 (82)	0.19
Diabetes mellitus	n	(%)	48 (27)	45 (35)	3 (6)	<0.001
Hyperlipidemia	n	(%)	25 (14)	20 (16)	5 (10)	0.47
Hyperuricemia	n	(%)	42 (25)	37 (29)	5 (10)	0.010
Cardiovascular disease	n	(%)	36 (20)	30 (23)	6 (12)	0.100
Cerebrovascular disease	n	(%)	13 (7)	8 (6)	5 (10)	0.52
Liver dysfunction	n	(%)	10 (6)	4 (3)	6 (12)	0.03
Depression	n	(%)	2 (1)	2 (2)	0 (0)	1
Smoking						0.699
Former smoker	n	(%)	90 (51)	62 (48)	28 (56)	
Current smoker	n	(%)	41 (23)	31 (24)	10 (20)	
Alcohol consumption						0.39
Social drinker	n	(%)	70 (39)	47 (37)	23 (46)	
Daily drinker	n	(%)	20 (11)	14 (11)	6 (12)	
Presence of sexual partner	n	(%)	131 (74)	100 (78)	31 (62)	0.08

SD standard deviation, *HD* hemodialysis

Various physiological changes including secondary hyperparathyroidism and arteriosclerosis due to prolonged chronic hemodialysis are well-known to be getting worsen progressively [11]. ED status in ESRD patients with long-term chronic HD was predicted to be progressed; however, long-term chronic HD did not appear to deteriorate ED status under adjustment of various factors. This is a cross-sectional study based on questionnaire and we could not include various clinical factors such as high-intact parathyroid hormone level, zinc deficiency, evaluation of malnutrition status, and degree of arteriosclerosis. Among these parameters, degree of arteriosclerosis might not be advanced in ESRD patients with long-term HD as strong as we suspected

Table 2 IIEF-5 score and ED status in HD patients

			All patients	HD duration <10 years patients	HD duration ≥10 years patients	p values
			n = 178	(Group 1; n = 128)	(Group 2; n = 50)	
IIEF-5 score	mean ± SD		8.9 ± 7.1	8.8 ± 7.2	9.2 ± 6.8	0.45
Grade of ED (IIEF-5 scores)						0.96
No ED (22–25)	n	(%)	17 (10)	13 (10)	4 (8)	
Mild (17–21)	n	(%)	16 (9)	11 (9)	5 (10)	
Mild to moderate (12–16)	n	(%)	23 (13)	16 (13)	7 (14)	
Moderate (8–11)	n	(%)	29 (16)	20 (16)	9 (18)	
Severe (1–7)	n	(%)	91 (51)	67 (52)	24 (48)	

IIEF-5 International Index of Erectile Function-5, *ED* erectile dysfunction, *SD* standard deviation, *HD* hemodialysis

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Table 3 Odds ratio of ED in HD patients for variables included in univariate analysis and multivariate analysis

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Age ≥60 years	3.110	1.680–5.740	<0.001	3.610	1.890–6.880	<0.001
HD duration ≥10 years	0.910	0.473–1.750	0.779			
BMI ≥25	0.736	0.394–1.38	0.337			
Hypertension	0.761	0.361–1.600	0.472			
Diabetes mellitus	1.830	0.928–3.600	0.081			
Hyperlipidemia	1.220	0.523–2.870	0.642			
Hyperuricemia	0.372	0.180–0.768	0.008	0.303	0.139–0.656	0.002
Cardiovascular disease	1.400	0.668–2.930	0.373			
Cerebrovascular disease	1.540	0.484–4.910	0.463			
Liver dysfunction	0.606	0.165–2.230	0.451			
Smoking	0.803	0.563–1.140	0.225			
Alcohol consumption	0.714	0.460–1.110	0.132			
Presence of sexual partner	0.504	0.250–1.010	0.055			
Ca >10 mg/dL	0.437	0.125–1.520	0.193			
P >6 mg/dL	0.969	0.475–1.980	0.930			
iPTH >250 pg/mL	1.450	0.623–3.400	0.387			

HD hemodialysis, *BMI* body mass index, *ED* erectile dysfunction, *Ca* calcium, *P* phosphate, *iPTH* intact parathyroid hormone

because the number of past history of CVD in patients with long-term HD was not larger than those in patient with short-term HD even though they had long duration of chronic kidney disease. Prospective cohort study which assess progression of ED status according to prolongation of hemodialysis period and include various clinical factors which are mentioned above might be more eligible to assess whether long-term HD affect ED severity or not.

Hyperuricemia was well-known as a risk factor for various vascular complications such as stroke, coronary disease, heart failure, and chronic kidney disease [12–15]. ED is closely associated with endothelial dysfunction and CVD, and the relationship between coronary artery disease and high uric acid level was reported [16]. On the other hand, inverse correlation between uric acid levels and all causes and CVD mortality in HD population was reported in contrast to the association of hyperuricemia and CVD risk in general population [17]. While the possibilities of surrogate for a better nutritional status and antioxidative properties of uric acid were pointed out, the potential mechanisms of this association in HD patients still remain uncertain[17, 18]. This cardioprotective mechanism of hyperuricemia in HD population might contribute to lower frequency of ED.

There are various considerations in this study that limit our findings. First, this is a relatively small sample size cross-sectional study. Second, we enrolled only patients who accepted our proposal and filled out the questionnaire so that we could not reflect information on patients who refused to participate or excluded from the study cohort. Third, IIEF-5 based on self-reporting was the only tool to evaluate ED in this study, and no other physical and diagnostic tests which evaluated not only ED status but also pathogenesis factors. Last, we could not assess influence of variables which have been reported to be linked to ED, such as autonomic neuropathy, residual renal function, hormonal status, anemia, secondary hyperparathyroidism, zinc deficiency, and so on. Prospective large cohort study including various clinical factors as mentioned above will be needed to address this subject.

Conclusions

In conclusion, longer periods of chronic HD therapy did not affect ED status, and there is reverse correlation between hyperuricemia and ED status of ESRD patients with either short or long periods of chronic HD. Further evaluation for the reason why hyperuricemia improve ED status in HD patients is needed.

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