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Factors associated with overhydration in peritoneal dialysis patients

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ABSTRACT

Aim. Overhydration is a prevalent problem in peritoneal dialysis (PD) patients. The aim of the study was to evaluate the effect of several factors on the development of overhydration in PD patients.
Material and Methods. The study was performed on 74 PD patients, who were divided into two groups according to bioimpedance analysis hydration status (OH_{BIA}): Group A OH_{BIA} < 1.1 L (n = 40) and Group B OH_{BIA} ≥ 1.1 L (n = 34). The assessments of the adequacy of the dialysis dosage were based on the Kt/V ratio as well as weekly creatinine clearance. To evaluate the permeability of the peritoneal membrane a standard peritoneal equilibration test was used.
Results. A statistically significant difference between the groups was found in: the average age of patients (53 ± 18 vs. 62 ± 14 years; p < 0.03), the prevalence of diabetes (27.5% vs. 55.9%; p < 0.02) and residual diuresis (1.7 ± 0.8 vs 1.2 ± 0.9 L; p < 0.05). There was no statistically significant difference in gender distribution, although attention is paid to the greater participation of male in overhydrated group. The study found no statistically significant differences between PD vintage, type of PD, assessment of adequacy of PD and other parameters describing the PD method. Logistic regression model selected diabetes (p < 0.03) as a significant risk factor for the occurrence of hypervolemia.
Conclusions. Diabetes and older age are potential predisposing factors for the development of overhydration in PD patients. Overhydrated PD patients may have relatively high parameters regarding adequacy of dialysis therapy. Probably the most important protective factor in PD patients is residual diuresis.

Keywords: peritoneal dialysis, bioelectrical impedance analysis, state of hydration.

Introduction

Several years ago peritoneal dialysis (PD) was generally regarded as treatment, that could prevent the development of overhydration. However, recent studies have brought attention to the importance of overhydration also in PD patients [1]. Devolder et al. [2] compared hydration status of patients on hemodialysis and peritoneal dialysis, and showed that overhydration occurred more frequently in PD patients [2]. Similar results were obtained by van Biesen et al., who reported that overhydration in PD patients was more frequent than in patients on hemodialysis [3].

In PD patients, overhydration occurs mostly as a result of excessive sodium and fluid intake with insufficient elimination from the body [4, 5]. The problem of hypervolemia relates, in particular, to patients without

residual diuresis, in whom the dialysis method itself turns out to be insufficient in relation to fluid intake [5]. The study by Koning et al., showed a statistically significant correlation between the state of hydration and residual renal function [5]. Similarly, the EuroBCM study demonstrated the development of overhydration in patients with less residual diuresis [1]. The other potentially cause of overhydration in PD patients is loss of peritoneal ultrafiltration capacity [5]. Unfortunately, ultrafiltration and the efficacy of peritoneal dialysis gradually decrease during therapy. Impaired peritoneal ultrafiltration is a serious problem and important limitation of peritoneal dialysis [6]. However, there are probably more factors responsible for water excess in PD patients [4, 5].

Overhydration has numerous clinical consequences. Probably, even subclinical overhydration, which does not manifest with clinical symptoms, can result in numerous complications [1]. That is why it is important to objectively assess the hydration status, find factors responsible for overhydration and prevent hypervolemia.

Aim

The aim of our study was to evaluate association of selected factors with the hydration status of patients on peritoneal dialysis.

Material and Methods

This cross-sectional study was performed on 74 PD patients. The study protocol was approved by the institutional ethics committee (decisions No. 424/13). All patients were informed about the course of the study and gave written informed consent for participation in the study.

Inclusion criteria for the study were: age above 18 years, consent for participation in the study and a minimum 3-month period of treatment with peritoneal dialysis. Exclusion criteria were: presence of acute active inflammatory processes, and status after amputation of upper or lower limb or presence of a cardioverter-defibrillator (because of bioimpedance method used in the study).

Complete medical history from each patient was collected. Clinical assessment of hydration status was based on the presence of dyspnoea, peripheral oedema, jugular vein distension and blood pressure measurement.

Hydration status was also assessed by bioimpedance spectroscopy (BIA) using the Body Composition Monitor (BCM) (Fresenius Medical Care, Germany). The measurements were performed under standardized conditions in the supine position after a 2-minute rest. The OH reference values range from -1.1 L to +1.1 L. The reference values were determined on the basis of bioimpedance studies conducted on a population of 1247 people of Caucasian race [7].

According to bioimpedance analysis hydration status (OH_{BIA}) patients were divided into 2 subgroups:

- Group A: $OH_{BIA} < 1.1$ L (n = 40)
- Group B: $OH_{BIA} \geq 1.1$ L (n = 34).

Peritoneal membrane function was measured with the peritoneal equilibration test (PET) during a 4-hour dwell using 2.27%-glucose dialysate [8]. The assessments of the adequacy of the dialysis dosage were made based on the size ratio Kt/V as well as weekly creatinine clearance [9, 10].

Statistical analyses were performed with STATISTICA 10.0 PL (StatSoft Polska, Kraków, Poland). Analyzed data were presented as means and standard deviations or percentage. All results were considered significant at $p < 0.05$. Normality of the distribution was tested with the Shapiro-Wilk test. The data with a normal distribution were analyzed with parametric methods (t-student test). The data that did not follow a Gaussian distribution were analyzed with the Mann-Whitney test. Categorical data were analyzed with the χ^2 test or the Fisher-Freeman-Halton test. The relationship between variables was analyzed with the Spearman's rank correlation coefficient and by multivariate linear regression.

Results

Characteristics of patients

The study group consisted of 40 females and 34 males. The age of patients ranged from 24 to 88 years. The mean age of the patients was 56.9 ± 16.6 years. Patients < 65 years made up 62.2% (n = 46). The causes of chronic kidney disease (CKD) were: diabetic kidney disease (n = 22; 29.7%), hypertensive nephrosclerosis (n = 17; 23.0%), chronic glomerulonephritis (n = 17; 23.0%), chronic tubulointerstitial nephritis (n = 6; 8.1%), other causes including polycystic kidney disease, status after nephrectomy and multiple myeloma (n = 12; 16.2%). Diabetes was present in 30 (40.5%) patients. The average dialysis vintage was 31.7 ± 22.2 months. In the study group: 58 (78.4%) participants were treated by continuous ambulatory peritoneal dialysis (CAPD) and 16 (21.6%) were using automated peritoneal dialysis (APD) cycler.

Characteristics of the subgroups were presented in **Table 1**. There was no statistical difference in gender distribution between the subgroups, although there was larger proportion of male in group B. A statistically significant difference was found regarding the mean age of patients ($p < 0.03$). In group A, patients' age ranged from 24 to 88 years. The mean age of the patients was 52.9 ± 17.7 years, wherein patients <65 years accounted for 72.5% (n = 28). In group B, patients' age ranged between 30 and 84 years. The mean age of the patients was 61.6 ± 14.2 years; and patients <65 years made up 50.0% (n = 17). A statistically significant difference was also demonstrated regarding the etiology of CKD ($p < 0.03$). In group A, the most common etiological factor of CKD was glomerulonephritis (n = 12; 30.0%) whereas in group B, the most common etiological factor was diabetic nephropathy (n = 16; 47.1%). The two groups also differed in terms of prevalence of diabetes, both type 1 and type 2 ($p < 0.02$). Diabetes was diagnosed in 27.5% (n = 11) of patients in group A and 55.9% (n = 19) of patients in group B. There was also statistically significant difference in residual diuresis between the two study groups ($p < 0.05$). In group A, almost all of the patients had adequate residual diuresis (n = 37; 92.5%).

We found no statistically significant differences between dialysis vintage, type of peritoneal dialysis, parameters of adequacy of peritoneal dialysis or other features describing the method of dialysis (**Table 2**). Whereas higher mean D/P creatinine values by PET were observed in patients in group B, the difference was not statistically significant.

Hydration status

In the whole study group, one or more clinical features of overhydration were found in 19 (25.7%) patients, while bioelectrical impedance criteria for overhydration were met by a 34 (46.0%) of the patients. Frequency of clinical symptoms of overhydration differed significantly ($p < 0.001$) between the two subgroups. Peripheral edema occurred in 7.5% (n = 3) of patients in group A and in 47.1% (n = 16) of patients in group B. Detailed results obtained with the BIA method in both subgroups were shown in **Table 3**.

Table 1. Characteristics of subgroups

	Group A	Group B	P value
Number of Patients	40	34	NS
Gender	25 (62.5%) women; 15 (37.5%) men	15 (44.1%) women; 19 (55.9%) men	NS
Age (years)	52.9 ± 17.7	61.6 ± 14.2	< 0.03
Etiology of CKD	6 (15.0%) diabetes 10 (25.0%) hypertension 12 (30.0%) glomerulonephritis 12 (30.0%) other	16 (47.1%) diabetes 7 (20.6%) hypertension 5(14.7%)glomerulonephritis 6 (17.7%) other	< 0.03
Presence of Diabetes	11 (27.5%)	19 (55.9%)	< 0.02
Diuresis (mL/day)	1662.5 ± 846.3	1224.2 ± 927.5	< 0.05

Values are expressed by mean and standard deviations

Table 2. Characteristics of dialysis methods

	Group A	Group B	P value
Duration of dialysis therapy (mc)	31.1 ± 23.1	32.3 ± 21.6	NS
Type of peritoneal dialysis	9 (22.5%) APD; 31 (77.5%) CAPD	7 (20.6%) APD; 27 (79.4%) CAPD	NS
Glucose Load (g/week)	979.5 ± 283.9	930.3 ± 283.8	NS
patients using or amino acids	8 (20.0%)	4 (11.8%)	NS
D/P creatinine in PET	0.62 ± 0.09	0.66 ± 0.11	NS
Types of peritoneal transport	1 (2.5%) H 14 (35.0%) HA 21 (52.5%) LA 4 (10.0%) L	2 (5.9%) H 16 (47.1%) HA 12 (35.3%) LA 3 (8.8%) L	NS
Kt/V (l/week/1.73 m^2)	2.91 ± 0.89	2.74 ± 0.87	NS
Creatinine clearance (l/week/1.73 m^2)	99.3 ± 35.6	100.4 ± 39.2	NS
Ultrafiltration(ml/day)	1133.3 ± 503.8	1266.7 ± 614.8	NS
GFR (ml/min/1.73 m^2)	6.6 ± 4.8	7.0 ± 5.2	NS

Values are expressed by mean and standard deviations

Table 3. Indices of hydration status obtained by the bioelectrical impedance method

	Group A	Group B	P value
OH_{BIA} (ml)	227.0 ± 2030.8	3544.1 ± 2095.0	< 0.001
OH_{BIA} (%)	0.1 ± 3.0	5.0 ± 3.0	< 0.001
TBW (L)	33.6 ± 6.6	36.5 ± 7.2	NS
ECW (L)	15.0 ± 2.3	19.0 ± 3.9	< 0.001
ICW (L)	18.6 ± 5.2	17.5 ± 3.7	NS

Values are expressed by mean and standard deviations.
Abbreviations: OH_{BIA}, overhydration according to bioelectrical impedance analysis; TBW, total body water; ECW, extracellular water; ICW, intracellular water; all according to according to bioelectrical impedance analysis.

Factors associated with overhydration

We analyzed the associations of OH_{BIA} with age, gender, co-existence of diabetes and residual urine volume. Overhydrated patients were significantly older ($p < 0.04$) and older age was associated with more frequent diagnosis of diabetes ($p < 0.001$). There was no statistically significant difference in the assessment of hydration status, age, residual diuresis or presence of diabetes between the genders. Fluid overload ($OH_{BIA} \geq 1.1$ liters), was more common among patients with diabetes ($p < 0.05$). The risk of fluid overload in patients with diabetes was more than three times higher than that of those without diabetes while presence of diabetes did not associate with volume of residual urine. Using a logistic regression model diabetes ($p < 0.03$) was found as significant risk factor for overhydration.

Discussion

The results of the current study indicate that subclinical signs of overhydration, that can be detected by bioimpedance analysis, are very common in peritoneal dialysis patients. Overhydration in that group of patients were associated with older age, diabetes and low residual renal function.

The results of our study are consistent with previous studies, showing a high prevalence of fluid overload in PD patients, ranging from 22% to 72% in different studies [1, 2, 11, 12]. Devolder et al. [2] reported that more than 22% of PD patients showed clinical features of overhydration. In the study of European Body Composition Monitoring (EuroBCM) [1] overhydration in BIA was present in more than 53% of the patients. Furthermore, in the study by Kwan et al. [12] comprising of 122 asymptomatic PD patients, showed that in BIA overhydration was present in over 72% of patients. Also Juan-Garcia et al. [11] pointed out that the BIA method allows for identification of fluid excess in a greater number of patients than clinical evaluation. In addition, Duman et al. [13] in their work showed that the BIA better correlated with results of echocardiography than result obtained by clinical evaluation. Thus, it seems that due to the prevalent of subclinical state of overhydration in PD patients, the BIA is a better criterion for assessing fluid status than clinical evaluation in that group of patients.

In our study attention was drawn to the larger percentage of male in the group of overhydrated patients, which - although the difference was not statistically significant - may suggest that male gender is a predisposing factor for the development of overhydration. Many authors draw attention to the male gender as a risk factor for development of overhydration in patients on PD. Van Biesen et al. in their work showed a statistically significant relationship between gender and the state of hydration, indicating that male gender is a risk factor for the development of overhydration [1]. Similar results were presented by Kwan et al. [12], stating that fluid overload assessed by bioelectrical impedance, was more frequent among men. Furthermore, Tang et al. [14] found that male gender was associated with a higher incidence of fluid overload in both clinical assessment and examination by bioelectrical impedance.

Our study demonstrated a statistically significant difference regarding the mean age of patients in both groups, which may indicate age as one of the factors predisposing to overhydration. The results of our study are consistent with the literature. In the EuroBCM study [1] it was shown that there was a relationship between hydration status and age of the patients. Similarly, Demirci et al. [15] in their work pointed out, that overhydrated patients were characterized by older age. Also, the study by Guo et al. [16] demonstrated a statistically significant correlation between age and the state of hydration.

Our study also highlights differences in the pathogenesis of chronic kidney disease in both groups. In the overhydrated patients, diabetic nephropathy was the most common diagnosis, whereas other causes of chronic kidney disease were more frequent in patients with normal hydration status. Differences also included the frequency of co-existence of diabetes as an addi-

tional diagnosis in both groups. This may indicate diabetes as one of the risk factors for overhydration. Our results confirm those previously obtained by the others [1, 17, 18]. The EuroBCM study demonstrated a relationship between the prevalence of diabetes and overhydration in PD patients [1]. The same relationship was found in a study conducted in a group of patients on hemodialysis therapy [19]. Moreover, the relationship has also been shown in another study, involving pre-dialysis patients [18]. The study by Hung et al. [18] included 338 patients diagnosed with chronic kidney disease in stages 3 to 5. When overhydration was assessed by BIA, it was found that over 50% of patients were overhydrated and a statistically significant correlation between the presence of diabetes and the state of hydration was found [18]. This may indicate diabetes as an additional risk factor for the development of overhydration also in earlier stages of chronic kidney disease and regardless of the type of renal replacement therapy [18]. Although the exact mechanisms for the development of these complications in diabetes are not known.

Another factor, which seems to have an impact on the development of overhydration in PD patients is residual diuresis. In the EuroBCM study [1] it was shown that there is a tendency for development of overhydration in patients with reduced residual diuresis. Similarly, in the study by Konings et al. [5] a statistically significant relationship between the state of hydration and the residual kidney function was found. It appears that in the case of PD patients, residual diuresis plays a critical role in the state of hydration of an individual. However, the results of several studies suggest that the benefits of preservation of residual renal function in PD surpass the regulation of hydration alone [20].

The average time on dialysis therapy in the study group was 31.7 ± 22.2 months and did not differ significantly between the subgroups. The results of our study are consistent with those obtained in the EuroBCM study [1], in which the average duration of dialysis was approximately 33 months and comparable in the overhydrated and normovolemic groups. However, it seems that when observed for a longer period of time, the dialysis vintage may play an integrative role in the development of overhydration, due to ultrafiltration failure in patients on prolonged PD therapy, as pointed out by Matsuda et al. [21].

Our study also draws attention to the lack of differences between groups in terms of the method of PD (CAPD vs. APD). Similar findings can be found in literature. Cnossen et al. for example compared the state of hydration in groups of patients treated with CAPD and APD systems and found no statistically significant difference between the groups [22]. Similarly, in earlier study by Davenport et al., the authors did not demonstrate any significant relationship between the state of hydration and the type of PD [23]. Thus, it seems that both of these methods are equally effective in regulating the body's hydration status.

There was also no significant difference in the adequacy of PD. Moreover, it was observed that in overhydrated patients the parameters for adequate dialysis therapy were relatively high. The results of our study are consistent with the results obtained by Van Biesen et al. [1]. In addition, in a study by Asqhar et al. [24], composed of 68 stable patients on PD, the authors showed no differences in Kt/V and the average weekly creatinine clearance in overhydrated patients and those with a normal hydration state. This may indicate that patients on PD who are overhydrated can have relatively satisfactory parameters of adequate PD.

Higher mean values of D/P creatinine in PET in overhydrated patients were observed, although it did not reach statistical significance. However, a statistically significant correlation was found between the values of D/P creatinine in PET and the relative and absolute state of hydration in BIA. The results of our study are probably due to the relatively short period of dialysis therapy in our group of patients. Perhaps with a longer period of observation differences between the groups would be more pronounced, because time of PD seems to be the deciding factor affecting the type of peritoneal transport. Our results are only partially in line with those obtained in the EuroBCM study [1] in which the authors demonstrated a relationship between the state of hydration and type of peritoneal transport, as well as a tendency for development of overhydration in the group with fast peritoneal transport. However, in the study by Konings et al. [5], the results were dependent on the duration of the test, which seems to confirm the effect of time- dependency in this regard. The results from the initial time point in the cross-sectional study showed no statistically significant correlation between the state of hydration and the results of PET, whereas the long-term follow-up showed a statistically significant correlation between the values of D/P creatinine and the state of hydration when assessed by bioelectrical impedance [5].

Conclusions

Overhydration in bioimpedance analysis was present in 46% of PD patients, despite absence of clinical markers of fluid overload in over half of these patients,

suggesting that the bioelectrical impedance method may be a more sensitive method. Older age and diabetes appeared as potential predisposing factors for the development of overhydration. In contrast, residual diuresis in patients on PD plays an important protective role against the development of overhydration. Interestingly, it seems that the parameters of peritoneal dialysis are less critical for the regulation of hydration status in these patients. The PD patients who are significantly overhydrated (OH_{BIA} > 1.1 L) may have relatively high parameters regarding adequacy of dialysis therapy.

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Conflict of interest statement
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