Overhydration, A New Risk Factor for Peritonitis in Peritoneal Dialysis

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Introduction. Overhydration (OH) remains a recurrent problem in peritoneal dialysis (PD), with deleterious effect in outcomes. Recent evidence suggests a direct relation between OH and increased peritonitis risk. The mechanisms of this connection are not well defined, but gut wall edema and malnutrition are probably involved.
Methods. Our aim was to assess OH as a risk factor for peritonitis in patients on PD. Retrospective study was done in a PD program with a bio impedance analysis. The investigator reviewed patient charts and documents. The Fresenius® Body Composition Monitor was used to obtain hydration parameters. OH was considered when Overhydration/Extracellular Water (OH/ECW) parameter was over 15% of the dry weight. The diagnosis of peritonitis was made according to the International Society of Peritoneal Dialysis guidelines. Associations between peritonitis rate and the collected variables were assessed using Chi-square test and Pearson's correlation.
Results. An association between OH and the risk of peritonitis was established.
Conclusion. OH is prevalent in our patients undergoing PD and it is a modifiable risk factor for peritonitis. The bio impedance analysis is economical and should be used in association with a physical exam and treatment results to achieve the normo-hydrated status in those patients.

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INTRODUCTION

Overhydration (OH) and protein energy malnutrition are prevalent among dialysis' patients.[1,2] Clinicians assess the volume status by evaluating parameters such as edema, weight gain and blood pressure (BP).[2] In dialysis, these traditional methods are not consistent for the determination of volume status.[3] Fluid overload, measured by body composition monitor (BCM), is associated with increased mortality in dialysis patients and it is an independent predictor of mortality.[4,5] OH is usual among peritoneal dialysis (PD) patients, with the prevalence ranging from 56.5 to 73.1%.[6] It is considered a contributor to mortality and technique failure among PD patients.[5] OH is associated with complications such as hypertension, heart failure, increased cardiovascular events, arterial stiffness, peritonitis, inflammation, malnutrition, and loss of residual renal function.[2,7] It remains unclear whether OH is an independent predictor of the clinical outcomes of PD or if it just reflects underlying comorbidities such as hypertension and cardiac dysfunction.[6] The same amount of OH can be of different clinical relevance depending on the size of the patient thus, studies using BCM have normalized the OH

value to Overhydration / Extra-Cellular Water (OH/ECW) and/or Extra-Cellular Water / Total Body Weight (ECW/TBW).[9] Those measures might be independent predictors for all-cause mortality and technique failure among PD patients.[6] Some studies identified OH/ECW as an independent risk factor for all-cause mortality, but they use different cutoffs, OH/ECW > 10% and OH/ECW > 15%.[8,9] In our work we decided to use the higher cutoff OH/ECW > 15%.

Regular monitoring of body composition using BCM facilitate the maintenance of euvolemia, thereby avoiding both volume overload and hypovolemia.[2]

Until now only retrospective observational studies were made, however, there is evidence to support the thesis that an optimization of fluid overload and the correction of OH will improve patient outcomes. Peritonitis related to PD is a common complication and it is associated with significant morbidity and mortality.[10,11] Peritonitis is also associated with significant costs to the Health Service: hospitalization, catheter loss, technique failure, and patient death. Recurrent peritonitis is one of the leading causes of patient transfer to hemodialysis.[10]

Rates of PD-associated peritonitis have decreased substantially over the years through improvements in equipment, techniques and prophylactic measures.[12]

The PD catheter is the source of infection for the vast majority of PD-related cases of peritonitis.[12] Exit-site and tunnel infections may also lead to peritonitis, while less commonly the abdomen itself may be the source. Abdominal infectious processes (diverticulitis, appendicitis, cholecystitis, or others) may be the source, as well as intra-abdominal surgery, colonoscopy, hysteroscopy and transmigration of bowel flora from constipation. When an intra-abdominal source is identified, the infecting organisms are usually Gram-negative enteric bacteria, streptococci and anaerobic bacteria. However, bacteremia from another source may also seed the peritoneum.[12,13] Potentially modifiable risks of peritonitis are malnutrition, obesity and smoking.[13]

The underlying mechanism that associates inflammation to fluid overload in PD patients remains unclear Still, Niebauer *et al.* have shown that endotoxin concentrations and proinflammatory cytokines are elevated in patients with heart failure who have peripheral edema.[14] Similarly, Hassan *et al.* demonstrated that endotoxemia is common among chronic kidney disease (CKD) patients, and the degree of endotoxemia is linked to the severity of kidney failure and volume overload. In their work, CKD patients had elevated endotoxin levels compared to the controls.[15]

Similar to patients CKD, patients with congestive heart failure had increased proinflammatory cytokines, which was possibly owed to gut translocation of bacterial products in the context of bowel edema.[14–16] Given the high prevalence of cardiovascular disease in dialysis patients, it is rational to deduce that a comparable phenomenon occurs in PD patients. Alternatively, it is hypothesized that systemic inflammation alters peritoneal transport status, which in turn leads to less effective ultrafiltration and fluid overload.[3]

Hypoalbuminemia, present in the inflammatory state, is an important determinant of the hydration status in PD patients.[17] It reduces plasma oncotic pressure and may lead to fluid accumulation in the extracellular space.[3]

From the literature review it can be concluded that the relationship between hydration parameters and PD-related peritonitis has been poorly investigated and is therefore meritorious of further research.

The purpose of this study is to investigate whether hydration status evaluated by BCM was associated with the incidence of peritonitis in PD patients.

MATERIALS AND METHODS

We did a retrospective study of prevalent patients from the PD program in Centro Hospitalar do Médio Tejo, EPE unit between January 2015 and December 2016.

The investigator reviewed patient charts and documents. Data collected comprised demographic information, hydration status, comorbidities, PD modality, PD solutions, Charlson Comorbidity Index (CCI), serum albumin and peritonitis episodes.

The *Fresenius® Body Composition Monitor (BCM)* ((Fresenius Medical Care, Bad Homberg, Germany) was used to obtain hydration parameters. The BCM employs bio impedance spectroscopy techniques. It measures at 50 frequencies over a range from 5 to 1000 kHz to determine the electrical resistances of the total body water (TBW) and the extracellular water (ECW).

Data was transferred via *Patient Card* for further analysis with the *Fluid Management Tool (FMT)*.

The FMT displays the development of the three primary compartments adipose tissue mass (ATM), lean tissue mass (LTM) and overhydration (OH) over time.

BCM use these estimates to calculate TBW volumes and their intracellular (ICW) and extracellular (ECW) fractions. These calculations can be used to detect and quantify OH.

Overhydration was considered when Overhydration/Extracellular Water (OH/ECW) parameter was over 15% the dry weight. BCM measurements were performed routinely during clinical appointments (monthly or bi-monthly).

The diagnosis of peritonitis was made according to the International Society of Peritoneal Dialysis (ISPD) guidelines.

The hydration status and other factors were compared between patients with and without peritonitis.

Statistical analysis was performed using SPSS version 23 for Mac OS X. Continuous variables were presented as mean and standard deviation, or median and interquartile range (IQR) for variables with skewed distributions and other nominal variables were presented as number (frequency) and percentage.

We used the Chi-square test and Pearson's correlation to analyze associations between peritonitis rate and the collected variables. Underlying assumptions were met, unless otherwise indicated. A *P* value of < .05 was considered statistically significant.

RESULTS

Thirty-five patients undergoing PD with a mean age of 53.46 ± 11.83 years were analyzed. The mean length of time on PD was 12.49 ± 18.24 months.

Among the 35 patients, 62.9% (n = 22) were males, 22.9% (n = 8) had diabetes mellitus (DM), 85.7% (n = 30) hypertension and 20% (n = 7) were smokers. 68.6% (n = 24) were undergoing Automated Peritoneal Dialysis (APD), 51.4% (n = 18) used bicarbonate-based PD solution and 31.4% (n = 11) icodextrin solution.

More than one-third (n = 13) of the patients were in OH status and 20% (n = 7) had OH/ECW over 15%. For nutritional status, 74.3% (n = 26) had serum albumin superior to 3g/L.

During the follow-up period, there were 7 episodes of peritonitis (Table 1).

Chi-square Independence test showed that there was an association between OH and the risk of peritonitis ($P < .05$). Patients that had

Table 1. Demographic Characteristics of the Patients

General Characterization (n = 35)	
Male Sex, n (%)	22 (62.9)
Mean Age ± SD, y	53.46 ± 11.83
Mean Time in PD ± SD, mo	12.49 ± 18.24
Patients with Peritonitis, n (%)	7 (20)
Risk Factors	
Diabetes Mellitus, n (%)	8 (29.9)
Hypertension, n (%)	30 (86.7)
Cigarette Smoking, n (%)	7 (20)
OH, n (%)	13 (37.1)
OH/ECW > 15%, n (%)	7 (20)
Median Albumin (IQR), g/L	3.3 [IQR = 2.1 to 4.3]
PD Settings	
APD, n (%)	24 (68.6)
ACPD, n (%)	11 (31.4)
HCO_3^- Solution, n (%)	18 (51.4)
Icodextrin Solution, n (%)	11 (31.4)

Abbreviations: ACPD, ambulatory continuous peritoneal dialysis; APD, automated peritoneal dialysis; g/L, gram per liter; HCO_3^-, Bicarbonate; IQR, interquartil range; no, number; OH, overhydration; OH/ECW, overhydration / extracellular water; PD, peritoneal dialysis; SD, standard deviation.

Table 2. Chi-Square Independence Test Results

	With Peritonitis	Without Peritotinis	*P*
Mean OH ± SD, L	3.6 ± 3	0.3 ± 1.4	< .05
OH / ECW > 15%, n (%)	4 (57.1)	3 (10.7)	< .05
HCO_3^- Solution, n (%)	1 (14.3)	17 (60.7)	< .05
DM, n (%)	0	8 (28.6)	< .05
Cigarette Smoking, n (%)	2 (28.6)	5 (17.9)	< .05
CCI, n (%)	5 (71.4)	4 (14.3)	< .05
Albumin < 3 g/L, n (%)	5 (71.4)	4 (14.3)	< .05

Abbreviations: ACPD, ambulatory continuous peritoneal dialysis; APD, automated peritoneal dialysis; CCI, charlson comorbidities index; DM, diabetes mellitus; g/L, gram per liter; HCO_3^-, bicarbonate; IQR, interquartil range; L, liter; no, number; OH, overhydration; OH / ECW, overhydration / extracellular water; PD, peritoneal dialysis; SD, standard deviation.

OH/ECW over 15% had a higher peritonitis rate ($P < .05$).

Nutritional parameters, as previously suggested, were also involved in peritonitis risk: an association between serum albumin lower than 3 g/L and peritonitis risk was proven ($P < .05$).

We also found that DM ($P < .05$), cigarette smoking ($P < .05$), OH ($P < .05$), PD solution ($P < .05$), and CCI ($P < .05$) were associated with the risk of peritonitis (Table 2).

Increasing age, gender, hypertension and PD modality were not associated with risk for peritonitis.

DISCUSSION

An association between OH and the risk of peritonitis was established. These results confirmed the observations from a Southern Chinese cohort that found that patients who are overhydrated were found to have higher rates of peritonitis,[5] as well as similar observations to the study conducted by Santhakumaran *et al.*[10]

As in the EuroBCM study we found a negative association between serum albumin and OH. As this is a cross-sectional cohort it is however impossible to determine whether low albumin is a consequence or a cause of OH.[7]

As the clearance of toxin and fluid removal are moderately gentle and continuous in patients on PD, their dietary and fluid intake are less restricted when compared with patients on Hemodialysis.[1] In our cohort we confirmed that the majority of our patients were well nourished and without hypoalbuminemia. Nevertheless, a PD patient developing malnutrition may gradually acquire extracellular water accumulation to balance loss of body cell mass or body fat mass while this hydration fails to become clinically obvious until fluid excess is considerably overt. Hypoalbuminemia has been a recognized marker for increased mortality, as shown by Ong *et al.* the baseline hypoalbuminemia is an important risk for subsequent peritonitis.[11] Our work confirms Ong *et al.* observations, since we established an association between hypoalbuminemia and the risk of peritonitis.

Thus, BCM helps to identify early or occult OH. Furthermore, the lower serum albumin level of malnourished patients inevitably caused a lower colloid osmotic pressure in the blood, which certainly aggravated the fluid retention in the tissue space.[5] On the other hand, down-titrating the target weight of dialysis patients, to reach euvolemia, puts them at risk for potential volume depletion.[2] Bio impedance analysis cannot distinguish between the intravascular and extravascular fluid, consequently, attempts to normalize tissue OH in hypoalbuminemic PD patients may lead to intravascular volume depletion.[2]

Substantial fluid overload is indeed a prevalent problem in PD patients, and more attention should be given to its assessment and correction.[7]

Our statistical analysis also established an association between bicarbonate-based PD solution, DM, cigarette smoking, CCI and the rate of peritonitis. These associations should be further studied in larger cohorts.

The cause of the association between OH and higher peritonitis incidence is unclear. OH is prevalent in our patients undergoing PD and is a modifiable risk factor for peritonitis.

The BCM is an economical tool that provides objective data to help the nephrologist in assessing the hydration and nutritional status of patients on dialysis. It should be used in association with a physical exam and treatment results to achieve the normo hydrated status in those patients.

This cohort was small, which is one of the limitations of our work, preventing our observation to be generalized to the whole PD population. Further research is needed to investigate the subpopulation of PD patients who could definitely benefit from routine BCM fluid management, with larger samples to confirm these observations and verify the correlation between peritonitis from enteric organisms and over hydration as performed by Santhakumaran *et al.*[10]

CONCLUSION

OH is prevalent in our patients undergoing PD and it is a modifiable risk factor for peritonitis. The bio impedance analysis is economical and should be used in association with a physical exam and treatment results to achieve the normo-hydrated status in those patients.

Notification

This study presented in part at the EuroPD 2017 Congress held October 4 to 6, 2017 in Dublin, Ireland.

REFERENCES

1. Li JSC, Chan JYH, Tai MMY, et al. Hydration and nutritional status in patients on home-dialysis—A single centre study. J Ren Care. 2018; 44(3):142-151.
2. Oh KH, Baek SH, Joo KW, et al. Does routine bioimpedance-guided fluid management provide additional benefit to non-anuric peritoneal dialysis patients? Results from compass clinical trial. Perit Dial Int. 2018; 38(2):131-138.
3. Li PK, Ng JK, Uk M, Mcintyre CW. Inflammation and Peritoneal Dialysis. Semin Nephrol. 2017; 37(1):54-65.
4. Oei E, Paudel K, Visser A, Finney H, Fan SL. Is overhydration in peritoneal dialysis patients associated with cardiac mortality that might be reversible? World J Nephrol. 2016; 5(5):448.
5. Guo Q, Lin J, Li J, et al. The effect of fluid overload on clinical outcome in southern chinese patients undergoing continuous ambulatory peritoneal dialysis. Perit Dial Int. 2015; 35(7):691-702.
6. Shu Y, Liu J, Zeng X, et al. The Effect of Overhydration on Mortality and Technique Failure among Peritoneal Dialysis Patients: A Systematic Review and Meta-Analysis. Blood Purif. 2018; 610041:350-358.
7. van Biesen W, Williams JD, Covic AC, et al. Fluid status in peritoneal dialysis patients: The European body composition monitoring (EuroBCM) study cohort. PLoS One. 2011; 6(2):1-9.
8. Fein P, Chattopadhyay J, Paluch MM, Borawski C, Matza B, Avram MM. Enrollment fluid status is independently associated with long-term survival of peritoneal dialysis patients. Adv Perit Dial. 2008; 24:79-83.
9. O'lone EL, Visser A, Finney H, Fan SL. Clinical significance of multi-frequency bioimpedance spectroscopy in peritoneal dialysis patients: Independent predictor of patient survival. Nephrol Dial Transplant. 2014; 29(7):1430-1437.
10. Santhakumaran T, Samad N, Fan SL. Hydration status measured by BCM: A potential modifiable risk factor for peritonitis in patients on peritoneal dialysis. Nephrology. 2016; 21(5):404-409.
11. Ong LM, Ch'Ng CC, Wee HC, et al. Risk of peritoneal dialysis-related peritonitis in a multi-racial asian population. Perit Dial Int. 2017; 37(1):35-43.
12. Salzer WL. Peritoneal dialysis-related peritonitis: challenges and solutions. Int J Nephrol Renovasc Dis. 2018; Volume 11:173-186.
13. Ceri M, Mert M, Dursun B. Peritonitis due to streptococcus sanguinis in automated peritoneal dialysis. Iran J Kidney Dis. 2020; 14(3):243-244.
14. Kerschbaum J, König P, Rudnicki M. Risk factors associated with peritoneal-dialysis-related peritonitis. Int J Nephrol. 2012; 2012(April).
15. Niebauer J, Volk H, Kemp M, et al. Endotoxin and immune activation in chronic heart failure : a prospective cohort study. 1999; 353:1838-1842.
16. Hassan MO, Duarte R, Dix-Peek T, et al. Correlation between volume overload, chronic inflammation, and left ventricular dysfunction in chronic kidney disease patients. Clin Nephrol. 2016; 86(S1):131-135.
17. Sandek A, Bauditz J, Swidsinski A, et al. Altered Intestinal Function in Patients With Chronic Heart Failure. 2007; 50(16).
18. John B, Tan BK, Dainty S, Spanel P, Smith D, Davies SJ. Plasma volume, albumin, and fluid status in peritoneal dialysis patients. Clin J Am Soc Nephrol. 2010; 5(8):1463-1470.

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