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Research Article

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Is peritoneal dialysis an effective treatment for cardiorenal syndrome with decompensated heart failure? A single center experience

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Abstract

Introduction and Objectives: *ultrafiltration techniques have shown promise in the treatment of diuretic-resistant heart failure (HF). The aim of this study was to describe a center experience in treating refractory HF with peritoneal dialysis (PD).*

Methods: *we performed a retrospective study of 14 patients presenting symptoms and signs of refractory congestive HF despite optimal pharmacological therapy, all excluded as candidates for heart transplantation. Baseline characteristics, laboratory data, Charlson score, and transthoracic doppler-echocardiogram results were collected. PD adequacy was evaluated through peritoneal equilibrium test results.*

Results: *12 patients were males and 2 females, with a median age of 72.13 years. The mean following time was 52.5 months. Symptoms of HF improved in 5 patients, with an upgrade of New York Heart Association (NYHA) Functional Classification and improvement in ejection fraction. NHYA remained the same in 6 PD treated individuals, despite and improvement of absolute ejection fraction. At the beginning of PD, the mean Charlson Score value was 5.7 ± 2.3, which reduced to 5.3 ± 2.6 by the end of observation time ($p<0.01$; $r=0.984$). Six patients presented one episode of decompensated heart failure needing hospitalization, with a median length of stay of 2 days. During the observation period 2 patients died, 1 from an acute hemorrhagic stroke and the other with a septic shock.*

Discussion: *PD treatment in refractory HF seems to be effective since it improves quality of life and functional class.*

Keywords: Cardio-Renal Syndrome, Heart Failure, Peritoneal Dialysis, Diuretic Resistance.

Introduction

Heart failure (HF) is a public health problem which prevalence has been rising globally as a result of an increase in longevity. It is a deadly and costly disease with a high symptom burden and decreased quality of life [1]. Fluid retention and congestion are hallmarks of decompensated HF, and diuretics are a cornerstone of these patients management. With chronic therapy diuretic resistance is common and it's defined by an attenuation or absence of the maximal diuretic effect that ultimately limits sodium and chloride excretion [2,3]. Most patients with treatment-resistant HF have underlying cardiorenal syndrome (CRS). Numerous interventions have been tried to overcome diuretic resistance, including furosemide adjustment (higher dose, more frequent administration and change route to intravenous), sequential nephron blockage, intravenous inotropic therapy, dual chamber pacing or resynchronization therapy [2,4] Extracorporeal ultrafiltration (EUF) has been used for acute decompensated diuretic-resistant HF with a favorable outcome. However, it is not recommended as long-term treatment in CRS due to hemodynamic complications, high cost, and vascular access-related problems [5]. Peritoneal dialysis (PD) is a home-based therapy that achieves salt and water removal though two important physiologic processes: diffusion that leads to solute clearance and convection that removes water from the blood stream into the peritoneal cavity [6]. The reasons why PD is a great therapeutic option for CRS are multiple. It offers gentle ultrafiltration with minimal impact on hemodynamics that result in a lower degree of neurohumoral stimulation and in slower decline of renal function, factors known to be associated with survival. Peritoneal ultrafiltration leads to effective continuous solute clearance, such as potassium, allowing better up-titration of HF pharmacological treatment. This technique is also not associated with myocardial stunning and seems to achieve a reduction in inflammatory burden [7-9].

The aim of this study was to describe a single-center experience in using PD to treat CRS patients with decompensated HF and analyze the safety of this technique in this group of patients, especially regarding infections.

Methods

Retrospective study of 14 patients with diuretic resistant HF, in a single-unit PD program. Patients started PD between November 2009 and November 2017 and the follow-up included the period from the first day of PD until May of 2019. Inclusion criteria were age ≥ 18 years old; symptoms and signs of severe refractory congestive HF despite optimal pharmacological therapy; non-end stage kidney disease; absence of criteria for a heart transplant; heart failure diagnosis by echocardiographic structural abnormality, systolic dysfunction, diastolic dysfunction, or a combination of these abnormalities in patients with resting or/and exertional symptoms of heart failure. The following data were registered at the beginning and at the end of follow up: New York Heart Association (NYHA) functional classification, estimated glomerular filtration rate (eGFR) through CKD-EPI formula; Charlson's Comorbidity Index; Doppler-echocardiography (DE) with determination of left ventricular ejection fraction (LVEF). Hospitalizations due to decompensated heart failure, their length of stay and peritonitis rates were also accounted during PD treatment. Demographic characteristics, previous comorbidities, etiology of HF and PD prescription were recorded at baseline. PD adequacy was evaluated through peritoneal equilibration test (PET) with classification of peritoneal transport type by creatinine and urea dialysis-to-plasma (D/P) ratio, dialysis dosage by measurement of the ratio between dialyzer urea clearance over time and patient's volume of urea distribution (Kt/V), ultrafiltration by free water removal 1 hour after a 3.86% dextrose solution dwell (UF 3.86%), residual creatinine clearance, and normalized protein catabolic rate (nPCR).

Numerical data are presented with median and interquartile range (IQR) or mean and standard deviation (SD) according to its distribution. The level of significance used was $p<0.05$ (two-sided). All data was analysed using SPSS Statistics® version 23.0.

The study was approved by the ethical committee of the local hospital, and written consent was obtained from all patients. All personal information were analyzed according to data protection law.

Results

We followed a cohort of 14 patients with HF, 12 were males (85.7%) and 2 females (14.3%). Patients' characteristics are described on Table 1.

Table 1: Patients baseline characteristics.

Characteristics	N (%)
Male Gender	12 (85.7)
Median age (years)	72.13 (IQR 42.5-75.38)
Mean following time (months)	52.5 (SD 18-95)
Comorbidities	
Hypertension	7 (50)
Diabetes mellitus	7 (50)
Myocardial infarction	3 (21.4)
Hepatitis C infection	2 (14.3)
Etiology of heart failure	
Arterial hypertension	7 (50)
Ischemic cardiopathy	3 (21.4)
Valvular cardiopathy	3 (21.4)
Congenital cardiopathy	1 (7.1)
IQR: Interquartil range; SD: Standard deviation	

Referring to PD treatment itself, 11 patients started PD *ab initium* but 3 (21.4%) started treatment with EUF, which was suspended due to hemodynamic instability. PD prescription is summed on

Table 2 and the type of solutions refers to patients last therapeutic scheme. Only one patient was on automated peritoneal dialysis and another one on assisted peritoneal dialysis. All patients were treated with icodextrin solutions (ICO).

Table 2: Peritoneal Dialysis prescription and efficacy.

PD precription	N (%)
PD first	11 (78.6)
PD modality	
CAPD	13 (92.9)
APD	1 (7.1)
Assisted Peritoneal Dialysis	1 (7.1)
Type of solutions	
ICO 1 night exchange	6 (42.9)
ICO + glucose 1.36 + 1.36 + 2.27 + 2.27%	5 (35.7)
ICO + glucose 1.36 + 1.36 + 1.36%	2 (14.3)
ICO + glucose 1.36 + 2.27 + 2.27+ 3.86%	1 (7.1)
Total volume PD solutions (L)	8 (IQR 6.72-8.64)
Residual diuresis (mL)	1364.3 (SD 849.1-1879.52)
Kt/v	2 (IQR 1.93-2.64)
nPCR (g/Kg/day)	0.93 (SD 0.8-1.06)
Fluid removal (mL)	1940 (SD 1456.7-2423.3)
D/P	0.66 (SD 0.60-0.72)
UF after a 3.86% glucose solution (mL)	709.2 (SD 524.6-893.8)
GFR (mL/min/1.73m^2)	4.71 (SD 3.3-6.1)
APD: Automated peritoneal dialysis; CAPD: Continuous ambulatory peritoneal dialysis; D/P: Four-hour dialysate/plasma creatinine; GFR: Glomerular filtration rate; ICO: Icodextrin solution; Npcr: normalized protein catabolic rate; PD: peritoneal dialysis; UF: ultrafiltration.	

There was a relieve in symptoms of HF in 5 patients (patient 8, 11, 12, 13 and 14), with an improvement of NYHA functional class and in LVEF (Figure 1). NHYA remained the same in 6 PD treated individuals, despite and improvement of absolute LVEF value (Table 3). HF progressed with worsening NYHA class and LVEF in 3 patients. However, there was a global significant increase in absolute LVEF value with PD treatment (p=0.016; r=0.63).

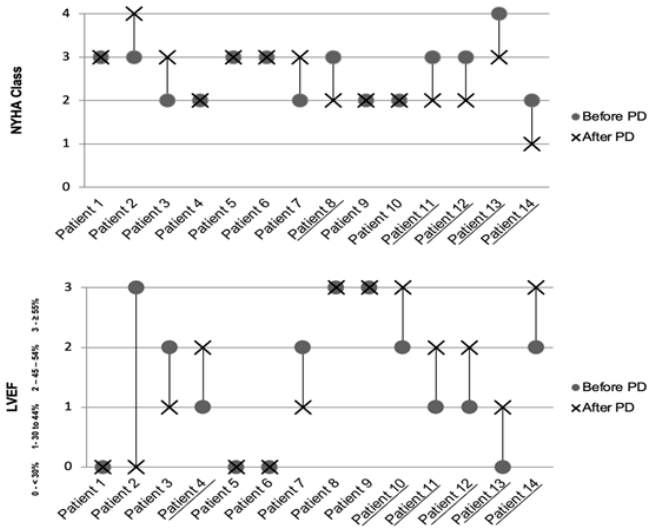

Figure 1: Variation of NYHA class and LVEF with PD treatment. LVEF: Left Ventricular Ejection Fraction; NYHA: New York Heart Association; PD: Peritoneal dialysis.

Table 3: Absolute left ventricular ejection fraction value.

Patient	Ejection Fraction (%)		Patient	Ejection Fraction (%)	
	Before PD	After PD		Before PD	After PD
1	<25	27	8	56	75
2	55	29	9	59	67
3	46	35	10	51	63
4	44	51	11	33	49
5	27	29	12	31	52
6	<25	28	13	<25	41
7	45	43	14	50	72
PD: Peritoneal dialysis.					

During the observation period 7 patients were transferred to HD. In 3 cases this was led by peritonitis episodes and in 4 by ultrafiltration failure. Six patients presented one episode of decompensated heart failure needing hospitalization with a median length of stay was 2 days. Two patients died, one from an acute hemorrhagic stroke and the other with septic shock. The mean survival time was 62 ± 14.1 months (range 52-72).

Estimated GFR (p=0.114) and diuresis (p=0.084) at baseline and at the end of follow-up were not significantly different. On the other hand, Charlson Comorbidity Index (Figure 2) a mean value of 5.7 at the beginning of PD which reduced to 5.3 by the end of observation time (p<0.001; r=0.98).

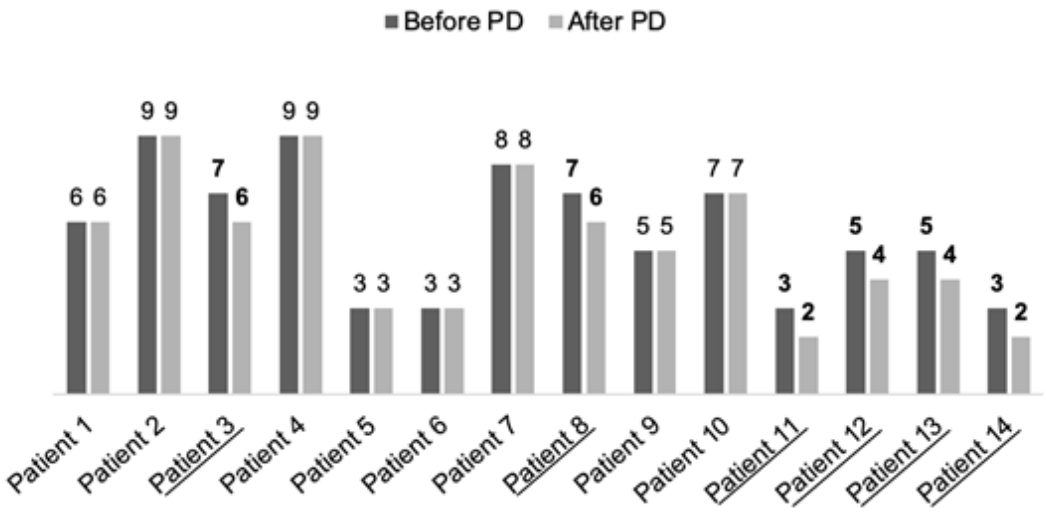

Figure 2: Variation of Charlson Comorbidity Index with PD treatment. PD: Peritoneal dialysis.

Discussion

Since the first use of PD in humans by Ganter, this technique has been used for several clinical conditions [10]. The interest of PD for HF is original from the 1940s, when Scheierson used peritoneal irrigation to treat intractable edema of cardiac origin [11]. In 1964 Mailloux et al. were pioneers in the successful treatment of nonuremic refractory congestive HF with peritoneal ultrafiltration [12]. Since then, various studies have been carried out to evaluate the role of PD in refractory congestive HF. Whether PD improves survival is still a topic of dispute. Some studies demonstrated a remarkable survival advantage of PD, with 1-year survival rates as high as 85% and mean survival time of 24 ± 15 months [13]. However other trials have discrepant conclusions with a survival at the end of the first year with this technique as low as 12.5% [14-16]. In our study the survival was much higher than the ones reported, probably due to our inclusion criteria. We selected individuals with refractory congestive HF despite optimal pharmacological therapy which included patients with persistent symptoms during daily physical activity (NYHA class II), for less than ordinary physical activity and at rest (NYHA III and IV respectively). However, most studies analyzed patients with predominant NHYA classes III or IV and consequently worst prognosis [17-22].

We also compared our patients Charlson Comorbidity index at beginning of PD and at the end of follow-up period. A significant reduction in this score after treatment with PD suggests a beneficial

effect of this technique not only in short-time but also on 10-year predicted survival. There are limited data comparing the survival of refractory congestive HF patients treated with peritoneal dialysis to those with a conservative medical management and it is unknown whether a therapeutic strategy including PD improves the survival rate for this patient population.

In most of our surviving patients there was an improvement in functional status by a decrease in NYHA class. Several studies confirmed a symptomatic relieve with a reduction in NYHA grading after starting PD [7,16-19]. Weather this is really due to improvement in cardiac muscle function is still a question. We used LVEF as a parameter of cardiac function and our result was a value significantly higher with PD treatment. There are reports of amelioration in LVEF as high as from 29.3% to 48.5%, some even observed in patients with lower baseline LVEF [12,15,25].

A low rate of hospital stays is a key to judge the success of any PD regimen for resistant HF. The majority of the PD studies have confirmed marked reduction in presentations and hospital bed days, for fluid overload and congestive symptoms, after institution of this therapy [13,22,23]. Similarly, our patients had a median length of hospital stay of 2 days. Results are variable but can be as impressive as a reduction of 90% in the number of days of hospitalization due to decompensated HF, after started PD therapy [15]. This achievement has a considerable impact on quality of life but also on these patients cost of care [18].

One major concern about the application of PD in decompensated HF is the potential high rates of technique failure and complications, such as peritonitis. Of the total 14 patients, 7 had at least 1 peritonitis episode during the mean following time of 52.5 ± 25.3 months. In 3 patients the recurrency of this infection led to PD drop out and 4 patients had to change to EUF due to peritoneal ultrafiltration failure. Like others, our results showed good technique survival without a higher peritonitis rate [5,23,24].

In our group of patients, PD was a safe and effective technique in relieving resistant HF symptoms, with improvements in LVEF measured by doppler-echocardiography and in 10-years predicted survival, without worsening renal function. This study has several limitations as it is a retrospective and nonrandomized trial with a small number of patients, including those with mild HF symptoms. Also, diagnosis of CRS was clinical which can lead to misclassification and/or underestimation of other etiologies for renal failure rather than heart disease.

Our study corroborates the accumulating evidence that points to PD as a beneficial adjunct to medical therapy in patients with chronic refractory HF without end-stage renal disease. This home-based therapy can efficiently extract sodium-rich fluid resulting in decongestion which provides a better functional status and quality of life with significant savings in health-care expenditure for CRS patients.

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