

Peritoneal dialysis as a therapeutic approach in congestive heart failure resistant to pharmacological treatment

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KEY WORDS

congestive heart failure, peritoneal dialysis

ABSTRACT

Given an increasing number of patients with congestive heart failure (CHF) refractory to diuretics, new and more effective therapeutic modalities are sought. Peritoneal dialysis (PD), which provides continuous, slow ultrafiltration, may be an alternative to hemodialysis in this population. The current paper, based on a comprehensive literature review, addresses the role of PD in improving the quality of life of patients with CHF.

Introduction Congestive heart failure (CHF) that is resistant to pharmacological treatment, especially with diuretics, is a problem of growing significance in everyday clinical practice. It represents type 2 cardiorenal syndrome (CRS). According to Ronco et al., it is characterized by chronic abnormalities in cardiac function causing progressive chronic kidney disease (CKD) with a decrease in glomerular filtration rate (GFR) below 60 ml/min/1.73 m².¹ The prevalence of CKD in chronic CHF has been reported at approximately 25%.² According to the European Society of Cardiology, the incidence of heart failure in Europe can be estimated at 0.4% to 2.0%, which translates into 500,000 to 750,000 patients in Poland.³

Periodic hemofiltration and, in the case of renal failure, classic hemodialysis are the 2 most common therapeutic modalities.⁴ However, it may be cumbersome because various modifications are required for individual patients. A method that could prove much more effective and simpler to employ is peritoneal dialysis (PD). Initially, it can be performed solely as peritoneal ultrafiltration, and in the case of concomitant renal failure, as a procedure of daily PD by means of continuous ambulatory PD (CAPD) or automated PD (APD).⁵⁻⁷ Several reports underscore the efficacy of PD as an approach providing daily, continuous, slow ultrafiltration in patients

with CHF.⁸⁻¹⁰ These promising results, together with over 30 years of our own experience in using CAPD as the only available method of home dialysis in Poland, prompted us to design our own clinical project in CHF.¹¹ Moreover, we recently showed that dialysis solution containing icodextrin as the osmotic agent is particularly efficient in transperitoneal water transport. It promotes long-lasting ultrafiltration, which may be particularly beneficial in CHF patients.¹²

Congestive heart failure and the kidneys CHF is a consequence of myocardial damage and ventricular filling impairment leading to hemodynamic dysfunction of the heart. In order to ensure proper cardiac output and restore correct homeostasis, compensation mechanisms are activated. Increased preload and afterload cause myocardial hypertrophy, which initially contributes to an increase in the stroke volume. However, the volumetrically overloaded heart requires a larger oxygen supply. Thus, in effect, insufficient oxygen delivery results in ischemia and progressive systolic dysfunction (cardiac dilatation) and a loss of myocardial compliance (diastolic dysfunction). A decrease in cardiac output activates neurohormonal mechanisms. The sympathetic nervous system, which attempts to compensate the imbalance, releases increased levels of noradrenaline and

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other catecholamines, and the renin-angiotensin-aldosterone (RAA) system becomes activated. As a consequence, the venous and arterial bed constricts and blood supply is redistributed to individual organs, particularly the brain and heart at the expense of other organs, for example the kidneys. A decreased GFR in the kidneys and activation of the RAA system lead to retention of sodium and water in the body. Clinically, this presents as overhydration, resistance to diuretics, oliguria, hyperazotemia, anemia, calcium and phosphate abnormalities, and hypertension. Such disturbances account for high mortality in CHF, because they are responsible for the vicious circle of events enhancing cardiac damage.^{1,13}

Peritoneal dialysis – the principles of peritoneal transport of sodium and water PD removes excess water mainly by means of osmotic ultrafiltration. The commonly used dialysis solutions contain glucose at different concentrations as an osmotically active substance. Glucose generates an osmotic gradient resulting in the transfer of water from the peritoneal vascular bed into the dialysate, which then flows into the dialysate container. Unfortunately, as the time of dialysis exchange extends beyond 4 h, its efficiency reduces due to a decrease of the osmotic gradient. It is caused by the absorption of glucose into the circulation and can by itself lead to hyperglycemia, hyperinsulinemia, and obesity. Icodextrin, a glucose polymer, has been shown to provide long and efficient ultrafiltration and, as opposed to glucose, to permeate blood only to a small extent.¹⁴

PD results in the removal of water as well as sodium ions, as illustrated by the “sodium sieving” phenomenon. The peritoneal membrane contains 3 types of pores: ultra small, small, and large. Initially, water permeates through ultra small and small pores as a result of high osmotic pressure due to the presence of high concentration of glucose in the dialysis solution. At the same time, water molecules carrying sodium ions travel exclusively through small pores. This initial stage of PD is described as convective transport of sodium. As the peritoneal exchange progresses and the glucose osmotic gradient disappears, sodium transport occurs through diffusion. The sodium concentration gradient (blood – hypernatremia/fluid – hyponatremia) forces sodium permeation from the blood into the dialysate. Disappearance of glucose gradient in the first stage is a direct reason why shorter and more frequent peritoneal exchanges are preferred when glucose solutions are used. However, the procedure should be long enough to allow the second phase (sodium diffusion) to take place.¹⁵

As normal blood volume and arterial pressure are achieved, the cardiac load decreases. Sympathetic nervous system activity returns to baseline levels, and the serum angiotensin II level decreases. At the same time, responsiveness to diuretic treatment is restored.^{10,15}

Peritoneal dialysis in congestive heart failure In 1949, Shneerson et al. published the first report on peritoneal irrigation as a life-saving procedure in a CHF patient.¹⁶ Since then, over 300 cases of patients with CHF resistant to standard pharmacotherapy, successfully treated with the use of PD, have been described. In a prospective study on 20 patients with CHF and baseline GFR of 14.84 ± 3.8 ml/min, Gotloib et al. demonstrated that PD as a procedure of APD (3–8-hour sessions per week) provided a stable dehydration effect, and thus improved hemodynamic cardiac parameters. Clinically, it translated into a significant improvement in the patients’ physical and mental state, increased exercise capacity as measured by improved New York Heart Association (NYHA) functional class IV to class I, decreased left ventricular diastolic diameter, raised left ventricular ejection fraction (LVEF), lower right ventricular systolic pressure (RVSP), and improved diuretic efficacy. However, this protocol had to be preceded by 2 to 5 sessions of continuous venous/venous hemofiltration of sequential hemofiltration.¹⁰

Bertoli et al. described 2 CHF patients in NYHA class III and class IV without concomitant end-stage renal failure, put on a continuous peritoneal ultrafiltration on an overnight, single, 12-hour exchange regimen with a dialysis solution containing icodextrin. After 12 months, the authors have observed an improvement in patients’ physical and mental state, while echocardiography revealed a significant increase in LVEF. Moreover, throughout the whole follow-up period the patients did not require hospitalization.¹⁷

Ryckelynck et al. published a report on 15 patients with heart failure refractory to standard therapy (11 in NYHA class IV and 4 in NYHA class III). CAPD solutions in 2 l bags were administered as follows: in 7 patients – 1 overnight exchange every 24 h with concentrated solution (3.85% glucose), in 4 patients – 1 overnight exchange every 48 h with concentrated fluid, in 1 patient – 3 day-time exchanges every 24 h with isotonic solution (1.36% glucose), and in 2 patients – a full CAPD program, i.e., 3 day-time exchanges with isotonic solution plus 1 overnight exchange with concentrated solution within 24 h. One patient was put on an overnight APD with a cyclor. The mean body weight loss was 5.2 kg and was associated with restored responsiveness to diuretics in 12 of 15 patients. In addition, the signs and symptoms of heart failure, namely edema and ascites, disappeared, which significantly improved patients’ physical and mental state (out of 10 patients in NYHA class IV: 6 moved to NYHA class II, 4 to NYHA class III, 5 patients in NYHA class III moved to class II). Echocardiography showed an increase in LVEF in 3 of 7 patients, in 2 it was stable, and in the remaining 2 subjects it decreased. Furthermore, the authors reported lower hospitalization rate in all studied patients.¹⁸

Takane et al. described 16 patients with severe CHF and end-stage renal failure who were started on renal replacement therapy using the CAPD

method. All patients were treated for 12 months with a regimen comprising 4 exchanges of 2 l per 24 h (8 l in total) with the use of 1.5% or 2.5% dextrose solutions. At the same time, patients received standard treatment with loop diuretics and RAA blockers. A beneficial effect of CAPD on patients' general condition was achieved, as expressed by increased exercise capacity (NYHA class III to II in 11 patients, class II to I in 4 patients, and class III to II in 1 patient) and LVEF (31%–44%). In addition, arterial blood pressure was better controlled. Daily diuresis increased from 470 to 550 ml (mean values) and GFR from 46 to 60 ml/min/1.73 m².¹⁹

In 2007, Diez Ojea et al. published a report on 5 patients with severe heart failure and chronic kidney disease (GFR <60 ml/min/1.73 m²) treated with various CAPD regimens, including that with icodextrin solution. Similarly to previously mentioned studies, patients reported improved physical and mental state (decrease in NYHA class, and in RVSP, increase in LVEF). In addition, an increase in the GRF from 16 to 33 ml/min/1.73 m² was detected together with a reduction in the hospitalization rate.²⁰

The most recent report by Basile et al. has described 4 patients with CHF (NYHA class IV) and with varying degrees of chronic renal failure, treated with overnight PD exchanges using icodextrin solution (including 1 patient who also received a day-time exchange with 1.36% glucose solution). The authors observed an improvement in the physical and mental state in all patients (NYHA class IV to II), a statistically significant increase in daily diuresis (from 587.5 to 1700 ml) and a reduction in serum creatinine levels (from 3.55 to 2.37 mg/dl). Echocardiography showed an increased LVEF in 1 patient, stable in 2, and decreased in 1. Furthermore, the authors reported a lower hospitalization rate.²¹

There is a limited number of publications addressing the issue of removing cardiac injury markers into the dialysate. These markers include medium molecular mass molecules (between 500 and 20,000–30,000 Da) such as atrial natriuretic peptide (ANP), tumor necrosis factor- α (TNF- α), myocardial depressant factor, as well as interleukin (IL)-1 and IL-6. It has been suggested that removal of these molecules inhibits myocardial remodeling and myocyte apoptosis.²² A study conducted by Zemel et al., supervised by Krediet at the Academic Medical Center of Amsterdam, on a group of 20 stable patients put on CAPD demonstrated that TNF- α and its receptors TNF- α I and TNF- α II diffuse into the dialysate from the blood. Removal of these molecules is independent of their local production, for example in dialysis-associated peritonitis, and their transport directly correlates with their molecular mass – the smaller it is, the larger the ratio of their dialysate level to serum level (D/S).²³ Fincher et al. conducted their study on 19 stable patients on CAPD, in which D/S for ANP was measured in the 90th minute of a standard dialysis

exchange. They demonstrated significantly higher baseline ANP values in patients on CAPD as compared with healthy controls. In the 90th minute of the exchange, ANP could be still detected in the dialysate, and its level correlated with its baseline serum level.²⁴

Conclusions Patients with type 2 CRS developed as a consequence of CHF constitute a new and unique niche group within the kidney disease spectrum, as the above data strongly suggest. Depending on the degree of GFR reduction, continuous peritoneal ultrafiltration or one of the forms of long-term PD might be used as an alternative to different modifications of HD. Our original case report published in the *Polish Archives of Internal Medicine* describes the case of a patient with terminal CHF who has been successfully treated with PD for 7 months. We observe that numerous prerequisites need to be considered while designing such a therapeutic regimen. These prerequisites include hemodialysis pretreatment prior to implanting the peritoneal catheter, proper training, and education for the patient and his family as well as logistic and financial coverage by the insurance companies.²⁵ Nevertheless, the development of an efficient dialysis-based management of CHF resistant to diuretic therapy is destined not only to advance scientific and clinical knowledge, but also to bring about measurable economic benefits resulting from a reduced hospitalization rate and shortened length of hospital stay in this patient group.

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Dializa otrzewnowa jako metoda leczenia zastoinowej niewydolności serca odpornej na leczenie farmakologiczne

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SŁOWA KLUCZOWE

ultrafiltracja
otrzewnowa,
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STRESZCZENIE

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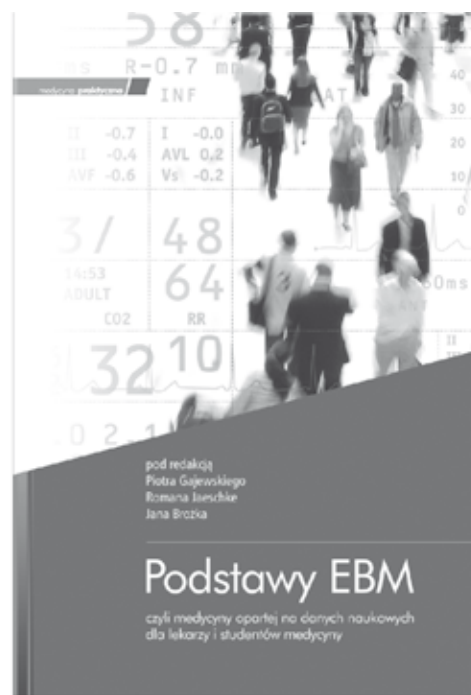
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