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Bulletin de la Dialyse à Domicile

Peritoneal dialysis in patients with refractory congestive heart failure

(Dialyse péritonéale chez les patients avec insuffisance cardiaque réfractaire)

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Résumé

L'insuffisance cardiaque est une pathologie dont la prévalence augmente régulièrement. En dépit des progrès de la prise en charge, un certain nombre de patients deviennent réfractaires aux traitements médicamenteux se manifestant alors par une résistance aux diurétiques avec persistance d'un syndrome congestif et installation ou aggravation d'une insuffisance rénale chronique. Une ultrafiltration à travers une hémodialyse ou une dialyse péritonéale peut être alors proposée pour traiter la surcharge hydro-sodée. La majorité des études ont pu démontrer l'efficacité de la dialyse péritonéale pour l'amélioration de la classe fonctionnelle, la diminution des hospitalisations, l'amélioration de la qualité de vie voire même une diminution de la mortalité. S'agissant d'une méthode de dialyse à domicile, elle est mieux acceptée par les patients. Il reste à déterminer le moment optimal pour initier ce traitement et les patients qui pourraient en bénéficier le plus à l'ère des nouvelles thérapeutiques de l'insuffisance cardiaque.

Mots clés : insuffisance cardiaque, dialyse péritonéale, surcharge hydro-sodée,ultrafiltration, icodextrine

Summary

Chronic heart failure is a growing problem. Despite progress in its management, many patients become refractory to therapies including diuretic resistance, major congestion, and worsening renal function. The only alternative to get rid of excess water and sodium is ultrafiltration, which can be achieved via hemodialysis or peritoneal dialysis (PD). The majority of studies have shown multiple benefits of PD as an improvement in functional class, a reduction in hospitalization leading to increased quality of life, and even a reduction in mortality. Being a home dialysis technique, it is more favorably accepted by patients. It remains necessary to confirm these potential positive outcomes and to identify patients who would benefit the most from this treatment in the era of new therapies available to date.

Key words : cardiac failure, peritoneal dalysis, hyperhydratation, ultrafiltration, icodextrin

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INTRODUCTION

The increase in the incidence of heart failure makes it a public health problem. In fact, the number of cases has doubled over the past thirty years. This increase, estimated at 5% per year, is explained by the presence of numerous cardiovascular risk factors, unhealthy lifestyles, and difficulties in terms of access to optimal medical treatment. The increase in life expectancy linked to medical progress also explains the increase in the prevalence of heart failure in the elderly population. Patients with advanced heart failure who can be considered refractory are estimated to be 1%–10% of all patients with heart failure who could be offered mechanical circulatory therapy and/or cardiac transplantation. However, only a small proportion of selected patients could benefit from these therapeutic options; a large number of patients cannot access these treatments because of age and comorbidities, thus being directed to palliative care.

Refractory heart failure may be retained in patients with NYHA stage III or IV dyspnea and who are unresponsive to maximal drug treatment with high doses of loop diuretics combined with thiazide diuretics and/or spironolactone, renin-angiotensin-aldosterone system inhibitors, beta-blockers, and water and salt restriction. The life expectancy of these patients is very limited, not exceeding one year, and it is burdened with high morbidity linked to numerous episodes of congestion leading to frequent and prolonged hospitalizations.

Water and sodium overload is a common problem of most patients with refractory heart failure and represents the first cause of hospitalization. It also contributes to the progression of heart failure. Renal dysfunction and resistance to diuretics are often associated with fluid overload, making congestion difficult to control, thus worsening the prognosis [1, 2]. At this level, the therapeutic options remain rare and limited. Among them, peritoneal dialysis (PD) was first used in 1949 and has been gaining interest gradually over the past twenty years. Different clinical cases, small series, and often retrospective studies have reported favorable outcomes with PD in patients with different types of cardiomyopathy responsible for congestive heart failure with preserved or reduced ejection fraction [3]. Data from the French-language Peritoneal Dialysis Registry (RDPLF) shows a marked increase in the use of PD for cardio-renal syndrome over the past ten years. Indeed, between 2010 and 2021, the percentage of patients treated by PD for cardio-renal syndrome was multiplied by 3.5, going from 2.2% to 7.7%. In this population, cardio-renal syndromes are clearly more observed in men in 74.2% of cases than in women (25.8%), while the other nephropathies responsible for chronic renal failure treated by PD are mainly reported in women in 62% of cases (men in 38%). The average age of these patients is 75.2 ± 9.8 years, while the average age of the other patients treated by PD is 66 ± 17 years. Thus, based on this data, we propose a review of the literature on the place of PD in the treatment of congestive heart failure.

I. RENAL DYSFUNCTION AND RESISTANCE TO DIURETICS IN HEART FAILURE

The pathophysiology of kidney failure associated with heart failure has two main mechanisms. For many years, decreased cardiac output and fluid redistribution in heart failure were considered the primary causes of renal dysfunction through decreased renal perfusion, the activation of the sympathetic nervous system, and renin/angiotensin/aldosterone, thus causing water and sodium retention to preserve renal function and the glomerular filtration rate. In the long term, these mechanisms induce harmful effects on the heart and kidneys by activating the mechanisms of fibrosis, apoptosis, oxidative stress, and inflammation (Figure 1).

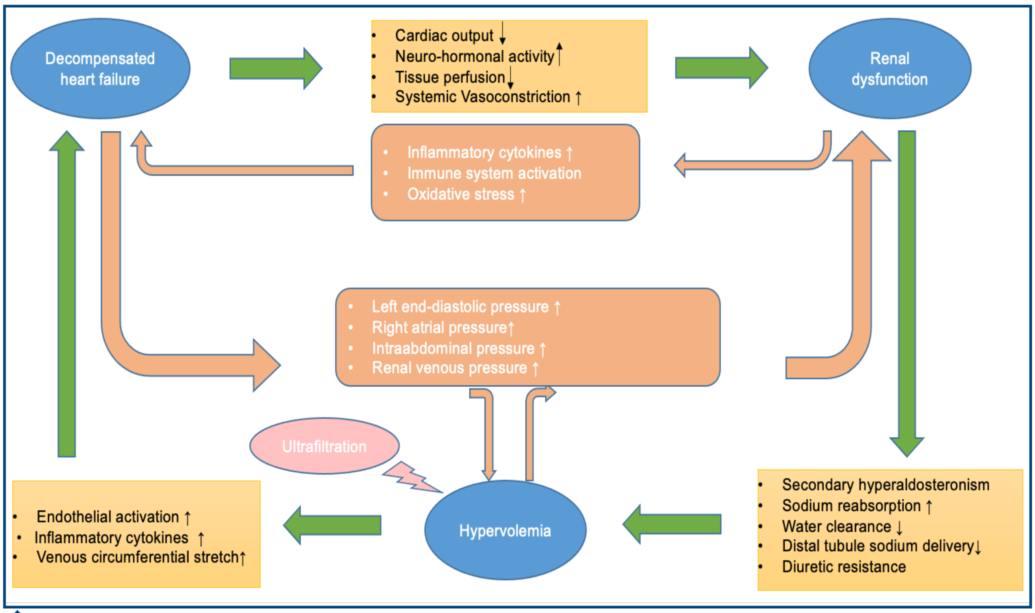

Fig. 1: Bidirectional axis linking heart failure, renal dysfunction and congestion in cardiorenal syndrome

In recent years, it has been proposed that the increased pressure in the renal veins caused by fluid overload is the cause of renal dysfunction in this situation [4]. This increase in pressure reduces the net gradient at the level of the glomerular filtration mechanism, thus causing a decrease in the rate of glomerular filtration and thus reducing the elimination of water and sodium, aggravating renal congestion [5]. This congestion is the first cause of the poor prognosis in these patients and is considered to have a significantly greater impact than other risk factors such as renal failure. It has thus been demonstrated that patients without congestion had a better prognosis regardless of the presence or absence of renal insufficiency. In contrast, the risk of mortality and readmission is increased in patients with persistent chronic congestion alone or associated with impaired renal function. Patients receiving high-dose decongestant therapy during an episode of cardiac decompensation had a lower six-month mortality rate even though this therapeutic strategy was associated with impaired renal function [6]. Thus, congestion control is associated with a better prognosis, hence reducing the rate of hospitalization and preventing the worsening of renal function secondary to fluid overload [7].

Loop diuretics are the mainstay of treatment for congestive heart failure. High doses are well tolerated and allowed in most cases to promote the clinical improvement of the patient as well as fully prevent water and sodium retention. Failure to achieve decongestion despite increasing the diuretic dose is defined as a state of diuretic resistance, with a prevalence ranging from 21% to 35%, and this diuretic resistance is independently associated with mortality risk [8].

Many mechanisms have been implicated in the development of diuretic resistance. Variations in pharmacodynamics and pharmacokinetics through changes in the absorption, distribution, metabolism, and elimination of diuretics have been implicated in this resistance. The chronic administration of loop diuretics decreases sodium reabsorption from the loop of Henlé and increases the delivery of large amounts of sodium from the distal tubule. This will be responsible for hypertrophy of the tubular cells and an increase in the reabsorption of sodium responsible for a decrease in natriuresis, this phenomenon being called the “braking phenomenon” [8] (Figure 2).

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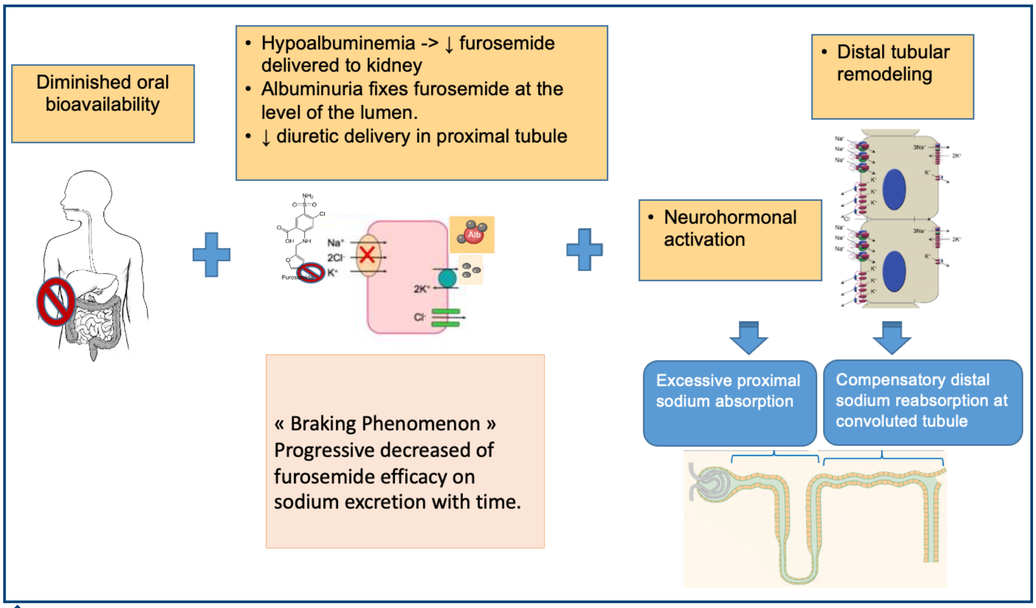

Fig. 2: Mechanisms of resistance to diuretics in cardiorenal syndrome

When high doses of loop diuretics are insufficient to obtain a reduction in water and sodium overload, it is essential to use diuretics acting on other segments of the nephron, in particular thiazides, antagonists of mineralocorticoid receptors, and now type 2 sodium/glucose transport inhibitors (iSGLT2). This last therapeutic class is particularly effective in reducing the risk of mortality in this population category and has demonstrated beneficial effects on both the heart and the kidneys.

II. ULTRAFILTRATION AS AN ALTERNATIVE TO DIURETICS

Ultrafiltration can be achieved through two methods: hemodialysis or PD. In acute decompensated heart failure, extracorporeal ultrafiltration has been compared in randomized studies to pharmacological treatment without it being possible to demonstrate a beneficial effect of ultrafiltration and with a greater number of side effects, including worsening renal failure [9, 10]. This extracorporeal ultrafiltration has only been used in acute heart failure and has not been tested beyond 90 days.

A. Place of peritoneal dialysis

PD has been proposed in the treatment of refractory heart failure given its ability to allow ultrafiltration, thus optimizing blood volume. This method can be used at home, and given the fact that it allows a gradual and continuous gentle reduction of excess water and solute, this gives it a minimal hemodynamic impact, thus reducing renal venous pressure and decreasing interstitial edema. Other effects of PD would be the clearance of factors associated with myocardial dysfunction such as TNF Alpha, MDF, IL-1, and IL-6, among other factors [11]. These factors have a molecular weight between 500 and 30,000 Daltons, passing easily through the peritoneal membrane. The purification of these factors positively affects the half-life of myocardial cells.
The elimination of water alone is insufficient to improve the prognosis of heart failure because

sodium is the major determinant of extracellular volume and has a fundamental role in the development of congestion. The sodium extraction in DP can be obtained by the osmotic gradient generated by the infusion of a glucose dialysate. The use of an icodextrin solution (Extraneal®) producing a colloid osmotic gradient makes it possible to obtain maximum sodium extraction. Depending on the patient, CAPD or APD can be used, bearing in mind that CAPD allows greater sodium extraction than APD in whom the supine position, recruit a larger surface of the peritoneal membrane for the exchanges. Different therapeutic regimens can be proposed—either a single infusion of icodextrin solution associated or not with the infusion of another bag of isotonic or hypertonic glucose dialysate during the day or even two bags of this type of dialysate depending on the severity of associated renal failure.

Among the main benefits reported in studies using PD in congestive heart failure alongside the decrease in water and sodium overload with a parallel reduction in weight, there is a clear improvement in the NYHA class of heart failure moving from 3 or 4 to 1 or 2, along with a very clear reduction in the frequency and duration of hospitalizations by 90% in most studies [12, 13]. All these benefits are responsible for improving the quality of life. Some degree of improved cardiac function has sometimes been reported. However, in most studies, there is no correlation between improvement in symptoms and a significant improvement in cardiac performance [14]. Recently, a study involving 32 patients found a significant improvement in NYHA functional class as well as a small but still significant increase in LVEF after 6 months of PD treatment attributed to the decrease in cardiac preload by the ultrafiltration obtained [15].
The decreases in renal venous congestion and intra-abdominal pressure have been associated with a restoration of the efficacy of diuretics and a slowing down of the deterioration of renal function. The economic impact of the reduction in hospitalizations is not negligible, and the overall cost of PD treatment for congestive heart failure is lower than the cost generated by the repeated hospitalizations of patients [14].

The mortality of patients with refractory heart failure and treated conventionally is 75% at one year in different cohorts. An improvement in patient survival has been reported, in particular by Nunez, who reported a lower rate of mortality and readmission of patients treated with PD compared to diuretic medical treatment after one year of follow-up [3]. Despite the potential benefits of PD, not all patients could benefit from it. The usual contraindications of PD will be a limiting factor associated with a greater anesthetic risk given the general situation of the patient. The development of the insertion of the peritoneal catheter under loco-regional anesthesia of the TAP block type will make it possible to lift the brake of a general anesthesia and not challenge the patient any longer.

The choice of patients who can benefit from PD remains imperfectly specified. Nevertheless, patients with NYHA stage 3 to 4 heart failure having repeated episodes of water and sodium overload (requiring frequent hospitalizations or the use of intravenous diuretics) or not/imperfectly responding to a combination of diuretics and presenting with heart failure refractory to optimized medical treatment and having no contraindication to PD may benefit from this therapy. The impact of iSGLT2 on the prognosis of these patients remains to be assessed in the coming years, and this would make it possible to redefine the place of PD in these patients if necessary. To date, the use of these drugs is not recommended in patients with severe renal impairment with a GFR <25 mL/min.

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B. Peritoneal dialysis and degree of chronic renal failure

About 50% of patients with chronic heart failure have impaired renal function, while 16% of patients with congestive heart failure have had glomerular filtration rates of less than 30 mL/min and 39% between 30 and 50 mL/min.

Among patients with non-end-stage chronic renal failure, most studies have not demonstrated a correlation between survival and renal function level. Thus, Courivaud et al. reported in one of the largest studies of PD in heart failure that patients with severe renal impairment were significantly older and less frequently treated with aldosterone receptor antagonists but that these conditions did not influence the survival of these patients [12]. However, other studies have found no association between survival and GFR level, and there is no statistically significant difference between GFR level before and after PD treatment [13,14,16-19]

The theoretical advantages of PD over hemodialysis in this indication can be raised. Myocardial stunning secondary to hemodynamic phenomena is present in patients receiving hemodialysis treatment even in the absence of significant coronary artery disease. This situation leads to a reduction in long-term systolic function, thus increasing the risk of heart failure. PD is not associated with this phenomenon [20]. The continuous nature of PD makes it possible to limit variations in serum potassium and to continuously monitor the potassium stock, which may constitute an advantage to allow the use of potassium-sparing diuretics such as mineralocorticoid receptor antagonists and inhibitors of the renin-angiotensin-aldosterone system [16,17]. The absence of an arteriovenous fistula eliminates the deleterious hemodynamic effects of a possible high flow of the fistula. Better preservation of residual renal function is much more often observed in PD than in hemodialysis.

Several studies have reported better survival rates of patients with heart failure on hemodialysis than on PD [21]. This difference may be due to the persistence of a relative hypervolemia that went unnoticed in patients treated with PD, as shown by the EURO BCM study, which found that only 40% of patients on PD were euvolemic [22]. This underlines the importance of a continuous and regular evaluation of the fluid overload in these patients; the clinical evaluation of the fluid overload can be faulted, while the use of bioimpedance could prove useful for the evaluation of blood volume and its therapeutic management.

Improvement in the left ventricular ejection fraction after the initiation of PD has been reported by several authors but not found by others. While the improvement in the functional state of the patients was observed under PD, the improvement in morbidity was only observed in patients with heart failure with preserved left ventricular ejection fractions. Other authors have found that mortality was more frequent in patients whose left ventricular function was stable and did not improve during the first year of PD treatment [17, 18]. However, it should be kept in mind that the vast majority of studies are essentially observational and retrospective, thus limiting the generalizability of the results.

Finally, right ventricular dysfunction associated with major water and sodium retention in the form of ascites, edema of the lower limbs, severe pulmonary arterial hypertension, and tricuspid insufficiency with preserved renal function could constitute a preferred indication for treatment with PD.

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CONCLUSION

PD is an accessible and effective form of treatment among the therapeutic options for patients with heart failure refractory to optimal drug treatment. The most impressive results include the improvement of morbidity, with a very significant reduction in hospitalizations, the improvement of the patient's functional state and quality of life, and the possible improvement of the prognosis. Quite often, this technique is offered to patients as a last resort. Patients who could benefit the most from this treatment and the impact of iSGLT2 on the prognosis of these patients remain questions that should be answered in the coming years.

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

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