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## **Suplemento**

# PD and HD in combination

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### **SUMMARY**

Peritoneal dialysis (PD) and hemodialysis (HD) are the most used therapies for endstage renal disease (ESRD). Peritoneal dialysis offers the advantages of long, slow, continuous ultrafiltration and preserve residual renal function (RRF) one of the most important factors affecting outcomes in PD. In contrast, HD offers superior solute removal but with undesirable cardiovascular tolerance of high rates of sodium and water removal. Peritoneal dialysis (PD) represents an effective way to maintain residual renal function and should be the first choice dialysis technique. However, with the loss of RRF, some limitations of PD alone in controlling the uremic state appear. Combination of the two techniques therapies, PD + HD (also called bimodal dialysis BMD), is the simplest way to deal with these limitations. The general prescription for BMD should be 5-6 days of PD and 1 or 2 HD sessions weekly. One of the most important controversy is how to evaluate the adequacy of the combined treatment: some Authors adopted the equivalent renal clearance (EKR), first transforming the weekly PD adequacy index (Kt/V), and then evaluating total clearance from both modalities. However, the EKR may overestimate the dialysis dose. Thus to accurately track dialysis dose some use the total effluent (PD, RRF, and HD) sampling method to yield Kt/Vef and creatinine clearance (CCref).

Key words: Peritoneal dialysis. Hemodialysis. Bimodal dialysis. Adequacy. Ultrafiltration loss. Residual renal function.

### INTRODUCTION

Peritoneal dialysis is considered to be the technique that better allows patients to maintain the residual renal function the main determinant in patients' outcome. One of the most important aspects of PD is represented by the elevated number of patients' drop out. The Italian PD Study Group presented a census of the PD population and indicated the magnitude of the «drop out» problem. In particular they indicated all the causes that lead to the technique withdrawal.<sup>1</sup>

On the total number of drop outs transplantation accounts for 19.86%, death for 41.86%, transfer to HD for 34.5%. In the transfer to HD group catheter's related problems accounted for 8.15%, peritonitis 37.36%, UF loss 15.73%, poor adequacy

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#### RESUMEN

La diálisis peritoneal (DP) y la hemodiálisis (HD) son los tratamientos más utilizados para la nefropatía terminal (NT). La diálisis peritoneal ofrece la ventaja de una ultrafiltración prolongada, lenta y continua y conserva la función renal residual (FRR), uno de los factores más importantes que influyen en los resultados de la DP. En cambio, la HD elimina mejor los solutos pero con una tolerancia cardiovascular deficiente de los elevados porcentajes de eliminación de sodio y agua. La diálisis peritoneal (DP) representa un método eficaz para mantener la función renal residual y debe ser la técnica de diálisis de primera elección. Sin embargo, con la pérdida de la FRR, se manifiestan algunas limitaciones de la DP aislada para controlar el estado urémico. La combinación de las dos técnicas, DP + HD (también denominada diálisis bimodal, DBM), es la forma más sencilla para superar estas limitaciones. La prescripción general de la DBM debe ser 5-6 días de DP y 1 ó 2 sesiones de HD a la semana. Uno de los aspectos que suscitan más controversia es cómo se debe evaluar la idoneidad del tratamiento combinado: algunos autores han adoptado la depuración renal equivalente (EKR), primero transformando el índice de idoneidad de la DP semanal (Kt/V) y luego determinando la depuración total de ambas modalidades. Sin embargo, la EKR puede sobrevalorar la dosis de diálisis. Así pues, para determinar con exactitud dicha dosis algunos autores utilizan el método de muestreo del efluente total (DP, FRR y HD) para obtener el Kt/Vef y el aclaramiento de creatinina (CCref).

Palabras clave: Diálisis peritoneal. Hemodiálisis. Diálisis bimodal. Adecuación de la diálisis. Pérdida de ultrafiltración. Función renal residual.

14.33%. Inability to reach adequacy targets and ultrafiltration loss accounts together for the 30,06%. The only measure available to diminish the risk of uremic complications is increasing the dose of dialysis but this has the potential to augment the negative impact of high dialysis solution volumes on the peritoneal membrane. An alternative to increasing the dose of dialysis<sup>2-6</sup> is to combine PD with hemodialysis (BMD). Many Authors<sup>3,5,7,9-11</sup> have adopted bimodal dialysis with different scheduled programs. The most used is a 6 days PD with 1 day HD and in some cases 5 days PD and 2 days HD. For example, although only limited outcomes data are currently available concerning combined therapy, BMD has rapidly gained popularity mostly in Japan but also in other Countries.

BMD is a feasible treatment for ESRD. It is associated with adequate solute removal and good hemodynamic/volume control. Underdialysis has been established as a major predictor of reduced survival for both HD and PD.<sup>12</sup> It is of concern that, in the absence of residual function, only a minority of PD patients are capable of reaching adequate levels of small molecule clearance, without the use of automated PD.<sup>13</sup>

Table I. Adequacy data reported by different authors in BMD								
Author	Measure	PD	BMD	р	Ref			
Kavanishi H, 2007	WKt/V <sub>EKR</sub>	$1.53 \pm 04$	$2.72 \pm 0.3$	< 0.001	(7)			
	WKt/V <sub>ef</sub>	$1.55 \pm 04$	$2.27 \pm 0.3$	< 0.001				
	WCCr <sub>ef</sub>	$42.0\pm7.7$	$60.3 \pm 9.2$	< 0.001				
Hoshi H, 2006	WCCr	45	63	< 0.01	(8)			
Kanno Y, 2003	CCr	$48 \pm 2$	> 60	< 0.05	(9)			
Kavanishi H, 2002	WKt/V (+ RRF)	$1.64 \pm 0.22$	$2.22 \pm 0.25$		(3)			

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The role of residual function, allowing both continuous solute clearance and fluid removal, is increasingly recognized to be of utmost importance. As a technique, PD allows slow continuous ultrafiltration, but less efficient solute removal. In contrast, HD allows highly efficient solute removal, but at the expense of interdialytic fluid overload and precipitous ultrafiltration.

The use of both modalities at the same time allows partial separation of the two essential components of effective renal replacement therapy (RRT), fluid removal and solute clearance. Solute removal can be enhanced by the addition of high efficiency, euvolemic, short-time HD sessions. Bimodal dialysis aims to use both PD and HD in an optimized fashion, exploiting each technique's particular strengths within a setting of good patient acceptability. The potential benefits of such therapy might include good control of blood pressure, minimization of the increase in left ventricular mass (LVM), reduced need for potentially harmful antihypertensive medications, optimized preservation of residual renal function (RRF), all as a result of the maintenance of slow continuous peritoneal ultrafiltration.

## **QUALITY OF LIFE**

Hashimoto<sup>11</sup> prospectively assessed quality of life (QOL) in 6 PD patients before and after initiation of BMD using a modified Kidney Disease Questionnaire by Laupacis.<sup>14</sup> This self-administered questionnaire measured five health status dimensions like fatigue, depression, relationship with others, frustrations and physical symptoms. In all 6 cases BMD therapy was well tolerated, without discomfort; it also improved symptoms related to uremia. Improvements in QOL scores were observed in each dimension except the physical symptoms dimension this one due to a high pre-QOL score (fig. 1).

## **ADEQUACY**

Table 1 shows adequacy data reported by different Authors: surely there is an increasing in adequacy targets but it is evident that there is no possibility of comparison between the different studies because of different adequacy evaluating methods.

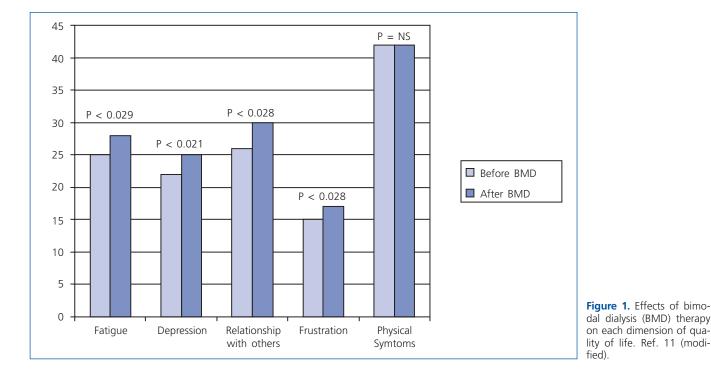
When PD is combined with HD, the dialysis dose by weekly HD must be converted to a continuous treatment value to obtain the total dialysis dose. The equivalent renal clearance (EKR) of urea (in millilitres per minute) proposed by Casino et al.<sup>15</sup> is used as a conversion method. The calculated HD dose is added to the dialysis dose achieved by 5-6 days of PD per week to obtain the total weekly dialysis dose for evaluation.3 Alternatively, Vonesh16 suggested the urea reduction rate to calculate a combined PD and HD dose and Hamada and colleagues showed the usefulness of direct sampling of the total HD and PD effluent.17

More recently Debowska et al.<sup>18</sup> performed computer simulations using a variable-volume, two-compartment urea kinetic model for 1-week treatments with 1) HD with three sessions (HD3), 2) continuous ambulatory PD (CAPD), 3) 6 days of CAPD and 1 day with HD session (BMD1) and 4) 5 days of CAPD and 2 days with HD (BMD2). Four dialysis adequacy indices like KT/V, stdKT/V, fractional solute removal (FSR), and equivalent clearance (EKR) were analyzed using four different reference methods for normalization of urea amount and concentration: 1) peak value, 2) peak average value, 3) time average value, and 4) treatment time average value. The analyses show that a proposed simplified rule of adding one third of weekly FSR for HD3 for each dialysis session and one seventh of weekly FSR for CAPD for each PD day for prediction of weekly FSR for BMD provides a fair prediction, although some corrections may be necessary, depending on the chosen reference method. They concluded that theoretically correct adequacy indices for BMD may be defined and calculated by using numerical simulations. Thus evaluation of adequacy in BMD is still difficult and to be widely discussed and accepted.

## **CONCLUSIONS**

In the presence of RRF, PD therapy with an optimal PD dose can maintain good nutrition status; however, as RRF declines, so does solute clearance, and nutrition status deteriorates. At this point, increasing the PD fluid volume results in increased removal of low-molecular-weight solutes only, and peritoneal deterioration may accelerate while nutrition status remains poor. In patients without RRF, a BMD regimen is recommended for maintaining an optimal dialysis dose and good nutrition status with less risk of peritoneal deterioration from an increase in PD fluid volume. The main barrier to this was complications with the access required

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for the dual therapy. The requirement for the formation of an arteriovenous fistula and insertion of a PD catheter is a potential shortcoming, exposing the patient to the possible complications of both. With the use of BMD patients' symptom scoring demonstrated a marked improvement. Patients treated with BMD certainly appeared to have good control of hypertension (with a reduction in the number of antihypertensive agents required).

Bimodal dialysis appears to be capable of delivering adequate RRT, with levels of small molecule clearance, hypertension control, and modulation of volume status comparable to HD or PD alone. Furthermore, the technique may have the advantage of helping to maintain RRF (when in patients with RRF a euvolemic HD session is scheduled) and certainly increases flexibility of RRT.

Finally the assessment of blood purification presented some difficulty. There are no data to determine what an adequate small molecule clearance would be with reference to currently accepted thresholds for the reduction of long-term mortality. Clearly, further comparative studies are required to investigate these potential applications.

#### **Conflict of interest statement**

I, Roberto Dell'Aquila, declare not to have conflict of interest.

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