

Peritoneum: A Noble Membrane in Long-Term Dialysis Treatment

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The durability of the peritoneum as a dialysis membrane is as yet an unanswered question. Peritonitis episodes have an important effect in long-term treatment. To evaluate survival of the peritoneum for dialysis, we analyzed peritoneal failure related to technique dropout because of peritonitis, inadequate dialysis, and ultrafiltration disorders.

We retrospectively analyzed data for 89 peritoneal dialysis patients who had been treated for at least 3 months [52 women, 37 men; mean age: 50.91 ± 13.72 years (range: 22 – 81 years)] from August 4, 1993, to July 1, 2008. The Kaplan–Meier method was used to measure peritoneum survival, with only a definitive switch to hemodialysis or death from peritonitis, ultrafiltration failure, or inadequate dialysis as endpoints.

Total treatment time was 5008 patient–months (mean: 55 ± 44 patient–months), and the historical annual rate of peritonitis was 0.37 per year at risk (1 episode in 32.52 patient–months). Of the 89 patients, 19 dropped treatment because of peritonitis and 1 because of ultrafiltration failure. Peritoneum survival was 98.8%, 93.7%, 87.6%, 66.9%, 46.4%, and 33.8% at 1, 3, 5, 8, 10, and 14 years.

In the 15 years of our program, peritoneum failure represented less than 1.5% of drop-out causes annually. The peritoneum is a reliable membrane to reach dialysis targets in long-term therapy.

Key words

Peritoneal function, drop-out, membrane, long-term survival, peritonitis rate

Introduction

The effectiveness of the peritoneum as a filtering membrane in the dialysis procedure was demonstrated by Ganter in 1923. Among other considerations, peritoneal clearance of the biochemical disturbances

in uremic patients and the possibility of ultrafiltration by osmotic components in the solution introduced the idea of peritoneal dialysis (PD) into the treatment of end-stage renal disease patients. From the beginning of the 1980s, important advances were made in peritoneal access, peritoneal solutions, devices to avoid entry of germs into the peritoneal cavity, and knowledge of pharmacokinetic and peritoneal physiology, among others. However, in the nephrology community, doubts about the durability of the peritoneum in long-term replacement therapy remain (1).

To evaluate survival of the peritoneum in terms of dialysis, we analyzed “peritoneum failure,” in which, through lack of adequacy and inability to meet ultrafiltration (UF) targets to continue PD, membrane function and irreversible peritonitis determined dropout from the method.

Patients and methods

All incident PD patients who were admitted to our PD program from August 4, 1993, to July 1, 2008, and who underwent treatment for at least 3 months were included in the study. The data were retrospectively analyzed, and continuous variables are expressed as mean \pm standard deviation. To calculate peritoneum survival, we used the product-limit estimation method of Kaplan–Meier, in which death from peritonitis during PD or within 90 days after stopping treatment and a definitive switch to hemodialysis (HD) because of peritonitis, ultrafiltration failure, or inadequate dialysis were considered endpoints. Transplantation, loss to follow-up, and transfer to HD or death from other causes were censored. In regard to patient survival, death was considered an endpoint only during PD or within 90 days after stopping PD treatment; technique survival estimates used transfer to HD or death related to PD therapy as endpoints. Transplantation, loss to follow-up, and partial recovery of renal function were censored.

Peritonitis was defined as the presence of cloudy dialysis effluent with more than 100 white blood cells

per cubic millimeter, and a white blood cell differential count exceeding 50% polymorphonuclear cells (2). The peritonitis rate was calculated by dividing the total patient-months by the total number of peritonitis episodes occurring during treatment. The condition of irreversible peritonitis leading to discontinuation of PD was considered membrane failure.

In general terms, adequacy assessment in our PD program is performed mainly by taking into account the first weekly total Kt/V urea after the initial dialysis prescription. The treatment scheme varies depending on the presence of residual renal function (RRF) and optimization according to peritoneal transport type measured by the Twardowski method 45 – 60 days from the onset of PD (3). Adaptive changes in the dialysis prescription, either by increasing the volume of dialysate or the number of exchanges, are performed gradually, in a non compulsive way, trying to reach the targets proposed in the guidelines from the Kidney Disease Outcomes Quality Initiative as published during the period of study, and seeking the understanding and compliance of patients in the context of quality of life (4). Initial and final adequacy indicators were compared by paired *t*-test, with significance set at $p < 0.05$.

Ultrafiltration tests were performed in patients who were suspected of having complications from chronic volume overload (5). The net ultrafiltration rate was estimated using the net negative balance before infusion and after effluent drainage in each exchange. Ultrafiltration failure was defined as a net ultrafiltration below 400 mL using 3.86% glucose during a 4-hour exchange (5). Definitive ultrafiltration failure was considered when the 24-hour ultrafiltration volume failed to satisfy the individual patient's requirements for a negative daily balance.

Results

We retrospectively reviewed 89 PD patients [52 women, 37 men; mean age: 50.91 ± 13.72 years (range: 22 – 81 years)] for this analysis. The overall treatment duration was 5008 patient-months (mean: 55 ± 44 patient-months).

Of the 89 patients initiated onto PD, 60 (67.41%) had previously been treated with HD [mean duration: 45.18 ± 40.16 patient-months (range: 5 – 216 months)]. Anuria was present in 41 of the 89 patients (46%). The primary diseases in the group were diabetes mellitus (14.6%), hypertensive nephrosclerosis (13.5%),

polycystic kidney disease (7.8%), glomerulonephritis (24.7%), unknown (22%), lupus nephritis (9%), and others (7.8%).

The historical annual rates of peritonitis for patients on continuous ambulatory PD (CAPD) and automated PD (APD) were 0.43 (1 in 28.1 patient-months) and 0.24 (1 in 50 patient-months) respectively, but in the last year of the study, the global peritonitis rate and frequency were 0.23 and 51.87 respectively. Peritonitis caused 19 patients to go off PD treatment, and of those 19, 6 died and 13 transferred to HD. Table I shows the organisms causing peritonitis.

No patient was transferred to HD because inadequate dialysis. Table II shows the mean initial and final peritoneal urea clearances and weekly total Kt/V urea in patients with anuria and with RRF. In addition, the mean value of the final measured weekly total Kt/V urea for the 19 patients that dropped out because of peritonitis was 2.07 ± 0.4 . Ultrafiltration failure as a cause of drop-out was observed in 1 patient.

Analysis showed a peritoneum survival of 98.8%, 93.7%, 87.6%, 66.9%, 46.4%, and 33.8% at 1, 3, 5, 8, 10, and 14 years (Figure 1). For the same intervals, patient survival was 97%, 81%, 70%, 53%, 50%, and 31%, and technique survival was 96%, 85%, 79%, 58%, 40%, and 29% (Figure 2).

Discussion

Chronic PD is an established form of renal replacement therapy; however, the durability of the peritoneum to function as a dialysis membrane is as yet unanswered. Among the many things that affect the life of the peritoneal membrane, PD solution dwells and long-term exposure to high glucose concentrations in the solutions cause macroscopic and microscopic

TABLE I Drop-out for peritonitis

<i>Micro-organism</i>	<i>Death</i>	<i>Transfer to HD</i>
<i>Staphylococcus aureus</i>	—	1
Coagulase-negative staphylococci	—	3
<i>Pseudomonas aeruginosa</i>	—	3
Other gram-negative	2	3
<i>Candida</i>	2	2
Negative culture	2	1
TOTAL	6	13

HD = hemodialysis.

TABLE II Adequacy indicators

<i>Patients</i>	<i>Initial</i>	<i>Final</i>	<i>p Value</i>
With RRF			
Peritoneal urea clearance	50.52±18.77	61.65±19.75	<0.05
Weekly Kt/V urea	2.74±0.78	2.42±0.65	>0.05
Renal urea clearance	39.94±23.26	20.98±23.99	<0.05
Anuric			
Peritoneal urea clearance	68.18±12.39	65.66±14.51	>0.05
Weekly Kt/V urea	2.11±0.47	2.02±0.36	>0.05

RRF = residual renal function.

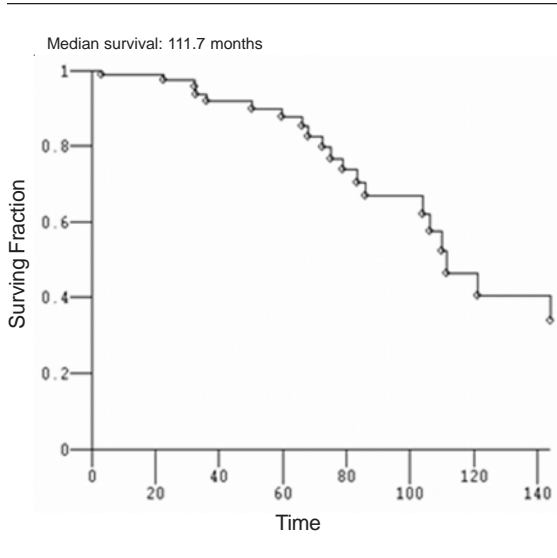


FIGURE 1 Peritoneum survival.

changes in the peritoneal cavity. Beneficial effects may be expected with the new osmotic solutions without dextrose, but long-term use of icodextrin PD solution still requires further investigation.

There are various reasons for drop-out from PD (peritonitis, catheter infections, hyperglycemia, leakage, hernias, patient or partner choice, obesity, and so on), but inadequate ultrafiltration and molecule clearance are the intrinsic causes in which the peritoneal membrane is truly responsible for dialysis continuity through membrane filtration.

During the evolution of our program, through advances in disconnect systems and a continuous patient education program regarding the routes of infection control, we observed an improvement in the frequency of infectious complications, especially those involving

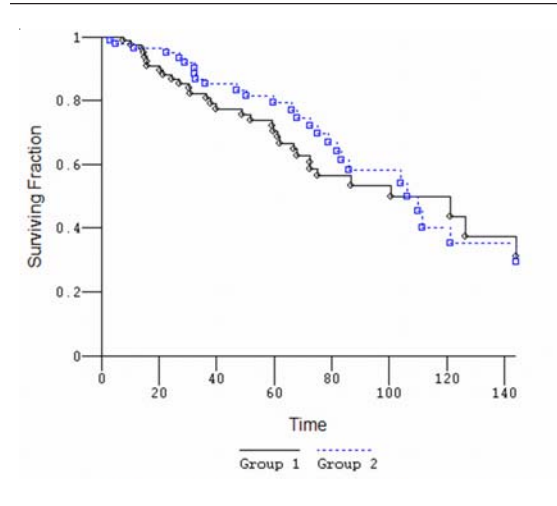


FIGURE 2 Patient and technique survival.

gram-positive micro-organisms. In addition, with the advent of automated PD, the peritonitis rate declined even further (Figure 3). In fact, patient drop-out caused by gram-positive peritonitis was 21%, but gram-negative and *Candida* micro-organisms caused 63% of drop-out.

From the beginning of solute transport studies of the peritoneal membrane, weekly Kt/V urea and weekly creatinine clearance took on importance as indicators of adequacy and, likewise, controversy regarding which is the best measure (6,7). Targets for both indicators were raised, based on observations of survival improvement and less morbidity (8). However, starting with the ADEMEX study, in which the mortality rate showed no significant difference with increased peritoneal clearance and a lower patient survival than had been seen in other experiences, lower adequacy targets were suggested (9,10).

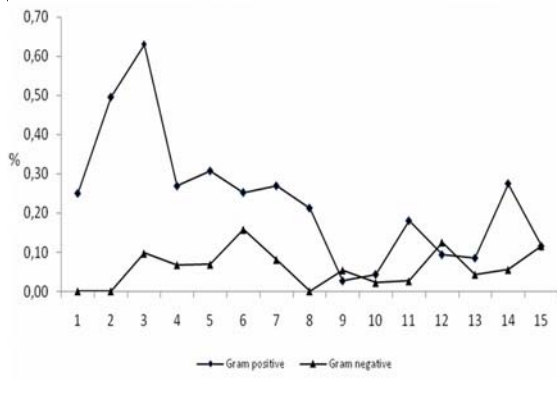


FIGURE 3 Gram-positive and gram-negative peritonitis rate in each program year.

In patients who are beginning substitutive therapy on PD, adequacy levels are probably more likely to be reached, given the contribution of RRF to small-solute clearance. However, these adequacy levels tend to decline because of a progressive reduction in RRF, especially in large patients. Researchers suggested incremental and continuous adaptation to obtain acceptable adequacy indicators (11,12). In patients with RRF, we have always considered a gradual and adaptive dialysis prescription based on the progressive decline in urine output. We begin with the Kidney Disease Outcomes Quality Initiative (KDOQI) targets proposed for small-solute clearance and with the patient's individual requirements for daily ultrafiltration that contribute to blood pressure control and volume homeostasis, and we modify the exchange volumes, dwell time, and solution tonicity. The term "adequacy of dialysis" involves not only reaching a small-solute clearance indicator, but also gaining better control of all aspects of the typical alterations of the uremic syndrome and of a patient's overall well-being.

Similarly, in previous studies in our group of anuric patients, we found that, to obtain the aforementioned objectives, the equation

$$\frac{\text{Initial dialysate volume (L)}}{\text{Body surface area (m}^2\text{)}}$$

was significantly higher in anuric patients than in those with RRF [6.50 ± 0.95 vs. 5.4 ± 0.91 respectively, $p < 0.05$ (13,14)]. During the study period, the mean values of adequacy indicators were

higher than the minimal levels proposed in the most recent KDOQI guidelines (10). Therefore, in patients with a weekly Kt/V urea below 1.7, gradual corrections in the dialysis prescription were performed to reach targets of 2, 2.1, and 2.2 in CAPD, continuous cycling PD, and nightly intermittent PD respectively.

Changes in ultrafiltration and solute transport might be expected in the follow-up of PD patients; the causes typically mentioned are variations in mass transfer area coefficient and lymphatic absorption and also the effect of long-term therapy (5). In the evolution of our study, we observed changes in solute transport characteristics, and we used, in the daily prescription, glucose solutions that were more hypertonic to contribute a net negative balance. Only 1 patient was transferred to HD because of ultrafiltration failure.

Conclusions

In considering so-called long-term therapy, the efficiency of the method is, in general terms, determined by the permanence of the treatment. The patient's survival is probably one of the most reliable indicators of the functioning of a health system; however, in chronic PD, technique survival, morbidity, medical and psychological complications, and other factors add "end-points" that are not linked to membrane function. The percentage probability of peritoneum survival observed in the present study shows that the peritoneum is a reliable membrane for long-term therapy.

By consensus, 5 years under treatment is probably considered "long-term" in renal substitutive therapy, and no long-term randomized prospective studies show outcome data for more than 4 years (15). Penetration of chronic PD in Argentina is lower than it is in other Latin American countries, and no long-term studies of more than 10 years' follow-up have been published (16). We believe that the present retrospective study of 15 years of close follow-up provides stimulating information that dispels doubts about the efficiency of the therapy and that can promote the growth of PD.

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