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Continuous Ambulatory Peritoneal Dialysis Versus Automated Peritoneal Dialysis and Peritonitis in the Short and Very Long Term at Risk

Peritonitis (P) is the most important infectious complication in peritoneal dialysis (PD), but disagreement remains about the impact of PD modality on the frequency of P episodes.

We compared indices linked to P between patients on continuous ambulatory PD (CAPD) and those on automated PD (APD) in the short and very long term.

The study included 9 prevalent and 72 incident patients on CAPD (twin-bag system) and 37 incident patients on APD from 4 August 1995 to 31 March 2011. Data were collected prospectively from our database. The cumulative P rate (CPR) by weighted Student t-test ($p < 0.05$) expressed as the probabilities of remaining free of a first P episode and remaining free of all P episodes were compared by the Kaplan–Meier method (log rank $p < 0.05$). The proportion of patients with P (PPP) per group ($\chi^2 p < 0.05$) and the relative risk (RR) of P were also calculated.

The CAPD patients included 51 women and 30 men [mean age: 50.2 ± 14.21 years (range: 15 – 82 years); duration of treatment: 3579 patient–months (mean: 44.2 ± 34.2 patient–months); P episodes: 111] had a CPR of 0.38 episodes (1 episode in 31.35 patient–months) and a P rate per year (PRY) in the range 0.08 – 0.89 episodes. The APD patients [23 women and 14 men; mean age: 53.62 ± 13.61 years (range: 26 – 78 years); duration of treatment: 1718 patient–months (mean: 46.4 – 38.3 patient–months); P episodes: 46] had a CPR of 0.32 episodes (1 episode in 37.3 patient–months) and a PRY in the range 0 – 1.12 episodes. At 1, 3, 5, and 10 years respectively, a first P episode occurred in 73%, 36%, 23%, and 8% of CAPD and 72%, 59%, 35%, and 23% of APD patients (log-rank $p = 0.056$; CPR: $p = 0.01$; PPP: $\chi^2 p = 0.39$), for a RR of 0.83 linked to CAPD compared with APD.

A lower P frequency and a trend of less time to first P was observed for APD compared with CAPD. The CAPD patients did not show a higher risk of developing P than did the APD patients. For comparisons between the modalities, CPR is a reliable index in the very long term at risk. Depending on the size of the population and the time at risk, the PRY obtained on short follow-up could result in a misinterpretation of the performance of each treatment modality.

Key words
Peritonitis rate, CAPD, APD, coagulase-negative peritonitis

Introduction
From the beginning of continuous ambulatory peritoneal dialysis (CAPD), constant headway has been made in clinical and laboratory management, antibiotic pharmacokinetics, and catheter and device technology, with the goal of avoiding contamination of the peritoneal cavity (1–4). Nevertheless, peritonitis is the most important clinical complication of peritoneal dialysis (PD) and the cause of 15% of the technique failure and 2% – 3% of the mortality in PD (5,6). Likewise, coagulase-negative micro-organisms remain the most prevalent cause of peritonitis episodes, especially those involving intraluminal contamination, in which the skill of the patient during the exchange procedure plays the most important role.

With the advent of automated PD (APD), important advances for patient lifestyle and dialysis
adequacy were achieved, making the most of the transport characteristic of the peritoneal membrane. In addition, because of the less-frequent connections in APD, the risk of patients making mistakes during the connection and disconnection procedures was lessened, with new hope for reductions in the peritonitis rate. However, there is still disagreement about the impact of PD modality on the frequency of peritonitis episodes (7–21). In the present prospective study, we compared some indices linked to peritonitis between CAPD and APD, and we evaluated the impact of modality on those assessments in the short and very long term at risk.

**Methods**

The study included 9 prevalent and 72 incident patients on CAPD (twin-bag system) and 37 incident patients on APD who were admitted to our PD program from 4 August 1995 to 31 March 2011 and who had undergone treatment for at least 3 months. Data for those patients were collected prospectively from our database.

Peritonitis was defined as the presence of cloudy dialysis effluent with white blood cells exceeding 100/mm³ and a differential count showing more than 50% polymorphonuclear cells (22). Continuous variables are expressed as mean ± standard deviation. The cumulative peritonitis rate (CPR) and the peritonitis rate per year (PRY) were measured in both groups of patients. A weighted t-test was used to compare the CPR between the groups, taking into account the peritonitis rate for each patient and the time at risk as weights (23). To calculate time to first peritonitis per group, we used the product-limit estimation method of Kaplan–Meier, in which a first episode of peritonitis was considered the endpoint. The same method was also used to determine the probability of remaining free of all peritonitis episodes, with each event being considered an endpoint. In both measurements, the resulting curves were compared using the log-rank method. The chi-square test was used to analyze the proportion of patients with peritonitis in each group. Statistical significance was considered at $p < 0.05$. In addition, we calculated the relative risk for peritonitis between the two PD modalities.

**Results**

The study enrolled 118 PD patients. Table 1 shows their characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient group</th>
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<tbody>
<tr>
<td></td>
<td>CAPD</td>
</tr>
<tr>
<td>Sex (men/women)</td>
<td>30/51</td>
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<tr>
<td>Age (years)</td>
<td>Mean 50.2±14.21</td>
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<td></td>
<td>Range 15–82</td>
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<td>Time at risk (patient–months)</td>
<td>Total 3579</td>
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<td></td>
<td>Per year (range) 103.5–304.3</td>
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<td>Mean time on PD (months)</td>
<td>44.2±34.2</td>
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**Table 1** Characteristics of the study patients

Peritonitis

| Total episodes | 111 | 46 |
| Cumulative rate | 0.38 | 0.32 |
| Annual rate (range) | 0.08–0.89 | 0–1.12 |
| Coagulase-negative rate | 0.14 | 0.07 |

CAPD = continuous ambulatory peritoneal dialysis; APD = automated peritoneal dialysis.

The CAPD group consisted of 51 women and 30 men [mean age: 50.2 ± 14.21 years (range: 15 – 82 years); 16.3% with diabetes; overall time on treatment: 3579 patient–months (mean: 44.2 ± 34.2 patient–months; average per year of follow-up: 282 ± 84 patient–months)]. This group experienced 111 peritonitis episodes, with 50 patients (61.7%) experiencing at least 1 episode, for a CPR of 0.38 episodes (1 episode every 31.35 months) and a PRY in the range 0.08 – 0.89 episodes (Figure 1). The coagulase-negative peritonitis rate was 0.14 episodes (1 episode in 83 months).

The APD group included 23 women and 14 men [mean age: 53.62 ± 13.61 years (range: 26 – 78 years); 16.2% with diabetes; overall time on treatment: 1718 patient–months (mean: 46.4 ± 38.3 patient–months; average per year of follow-up: 114.5 ± 53.5 patient–months)]. This group experienced 46 peritonitis episodes, with 19 patients (51.3%) experiencing at least 1 episode, for a CPR of 0.32 episodes (1 episode in 37.3 patient–months) and a PRY in the range 0 – 1.12 episodes (Figure 2). The coagulase-negative peritonitis rate was 0.07 (1 episode in 171.8 patient–months).

The CPR comparison between the modalities reached statistical significance ($p = 0.01$). The proportion of patients who presented with peritonitis did not show statistical significance between the groups.
and the relative risk was 0.83 for CAPD compared with APD.

At 12, 36, 60, and 120 months respectively, survival to a first peritonitis was 73%, 36%, 23%, and 8% in the CAPD group, and 72%, 59%, 35%, and 23% in the APD group (log-rank \( p = 0.056 \), Figure 3). At 12, 36, 60, 84, 120, and 140 months respectively, the probability of remaining free of all peritonitis events was 85%, 47%, 24%, 9%, 4%, and 2.4% in the CAPD group, and 82.5%, 57.7%, 38%, 30.3%, 13.8%, and 4.1% in the APD group (log-rank \( p = 0.039 \), Figure 4).

Discussion
As mentioned earlier, peritonitis continues to be the most important infectious complication of the PD renal substitutive therapy. Regardless of the advantages of the APD modality with respect to other aspects of the treatment, it introduced a new challenge into peritonitis control. Thus, observational, retrospective, randomized, and other studies with varied population samples making comparisons between peritonitis rates in APD and CAPD did not take long to emerge.

Piraino and Sheth raised interesting questions about the comparisons between peritonitis rates in CAPD and APD in a review of studies worldwide, in which patient populations, time at risk, and results varied (24). Previously, Mactier had made similar
observations in a review of single-center and multicenter studies with populations on CAPD and on both treatment modalities, including an interesting description of the factors that influence reported peritonitis incidences (25). In both reviews, as well as in other published articles, a remarkable disparity in the peritonitis rates was observed.

In terms of the “value” of the peritonitis rate, the total patient–months in a large patient sample probably guarantee reliability in both the short and the long term. When the patient population is smaller, the value of the peritonitis rate over the long term will probably be reliable, but as Vonesh emphasized, infection rates are likely to be underestimated if the patients are followed for only a short time (26). In a study with 25 patients (13 CAPD, 12 APD) followed for 6 months, Bro et al. (12) showed 2 peritonitis episodes in the CAPD group (0.31 episodes per patient–year) and 1 peritonitis episode in the APD group (0.17 episodes per patient–year). A possible conclusion might be “for peritonitis, APD is a better modality of treatment,” but is that assertion really true? In a contrasting short-term study, Basile and De Padova concluded that indications for APD should not include a reduced peritonitis frequency (27). Caution with respect to the conclusions of trials with a short follow-up was also emphasized by Nessim and Bargman (28). It is difficult to establish a conclusion about treatment impact in the short term because the performance of each modality could be misinterpreted, especially in single-center studies, in which the patient population is usually small. Several statistical studies have commented on this dilemma, but no definitive conclusion has yet been reached about the minimal number of patient–months needed to draw an inference.

In our study involving patients on both treatment modalities followed for a very long period, with close surveillance of peritonitis (Figures 1 and 2), the evolution of the CPR, the peritonitis rate per year, and the peritonitis frequency per year can be seen. It is important to pay attention to the variability of the peritonitis rate year by year, but the cumulative curve is important in assessing the evolution of a PD program with respect to peritonitis.

Another method used to evaluate the impact of peritonitis in a PD program and to compare CAPD with APD is the time to a first episode of peritonitis. Rodríguez–Carmona and coworkers (7) observed a higher peritonitis rate in CAPD than APD (0.64 episodes/patient–year vs. 0.31 episodes/patient–year) and better survival to a first episode of peritonitis in APD. A trend favoring APD over CAPD was also observed by de Fijter et al. (14). Similar results were found by, among others, Huang and coworkers (16) and our group (Figure 3). The lower peritonitis frequency in the patients on APD compared with the patients on CAPD and the probability of remaining free of all peritonitis episodes during the time at risk was statistically significant in favor of APD, an observation that supports the trend to a longer time to a first peritonitis episode in APD. Proportionally, however, CAPD patients did not show a higher risk for developing peritonitis than APD patients did, and thus the number peritonitis episodes per patient plays an important role during the time at risk. It is therefore important to emphasize the higher coagulase-negative peritonitis rate in CAPD than APD in our study, which to some extent supports the risk of infection during the more frequent fluid exchange procedures in the former modality, as others have observed (29).

Conclusions

In comparing PD modalities, the CPR is a reliable index over the long term at risk. It is unwise to make comparisons of the peritonitis frequency between CAPD and APD in the short term unless the size of patient population, and the sum of the months at risk, is representative enough to reach truthful conclusions about the number of peritonitis episodes. In the long term, the CPR is an accurate reflection of the smooth running of a PD program with respect to infectious complications. The probability of remaining free of peritonitis is a reliable index reflecting patient compliance with training received. Control of coagulase-negative micro-organisms might close the gap in peritonitis rates between the dialysis modalities.

To facilitate self-assessment of a PD program, it will be necessary to determine the minimal number of patient–months needed in both the short and long term to evaluate the peritonitis rate.

Disclosures

The authors have no financial conflicts of interest to declare.

References

1 Peritonitis in continuous ambulatory peritoneal dialysis (CAPD): a multi-centre randomized clinical


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