Continuous Ambulatory Peritoneal Dialysis in Diabetic Patients
The Relationship of Hypertension to Retinopathy and Cardiovascular Complications

JACQUES ROTTEMBOURG, MOHAMED REMAOUN, KALIL MAIGA, PAUL BELLIO, BELKACEM ISSAD, AMAR BOUDJEMAA, AND PIERRE-YVES COSSETTE

SUMMARY From August 1978 to December 1983, 51 insulin-dependent diabetic patients with end-stage renal disease were selected for treatment by continuous ambulatory peritoneal dialysis. There were 27 male and 24 female patients, with a mean age of 52.3 ± 13.5 years. Forty-five patients dialyzed themselves by continuous ambulatory peritoneal dialysis and six were treated by continuous cyclic peritoneal dialysis. All patients were treated at home. The cumulative duration of treatment was 65.6 patient-years; 14 patients were dialyzed for at least 24 months. Extrarenal complications were frequent at start of continuous ambulatory peritoneal dialysis, including hypertension in 48 patients, proliferative retinopathy in 50, and cardiovascular complications in 30. Age appeared to be the major risk factor, with success rates at 2 years of 78% in patients under age 50 years and only 50% in patients over age 50. The main cause of death was vascular and the main cause of transfer to other therapeutic modalities was abdominal complications or malnutrition or both. Excellent control of blood pressure, uremia, and blood glucose levels was obtained on a daily program of four exchanges. Improvement in visual status was frequently observed, mainly in the young population. In patients with juvenile diabetes, continuous ambulatory peritoneal dialysis should be part of an integrated program with transplantation, while in the elderly, the method offers a unique opportunity for them to treat themselves at home. (Hypertension 7 [Suppl II]: II-125–II-130, 1985)

KEY WORDS • insulin-dependent diabetes • end-stage renal failure

DATA presented at the last European Dialysis and Transplantation Association congress and during a recent international symposium entirely devoted to prevention and treatment of diabetic nephropathy clearly illustrated that diabetes is the only growing cause of end-stage renal disease (ESRD) in all of the industrialized countries. Indeed, a recent explosion in the acceptance of diabetic patients for dialysis and transplantation is observed when treatment facilities become available. Despite the very encouraging results achieved with transplantation, the majority of diabetic patients with ESRD are treated by dialysis. Continuous ambulatory peritoneal dialysis (CAPD) has been satisfactory for patients with insulin-dependent diabetes (IDD), and very encouraging results after 2 years have been reported. Therefore the time has come for a critical appraisal of the true advantages and shortcomings of CAPD in this population. Specific data are given about control of blood pressure, vision, and cardiovascular status.

Patients and Methods

Patients
Between August 1978 and December 1983, 51 unselected patients with IDD were trained in dialysis methods in an individualized unit of the Department of Nephrology of the Hôpital de la Pitié in Paris. They accounted for 30% of the 170 patients trained in CAPD during the same period and for 60% of the IDD patients treated by dialysis methods during the same period. The CAPD technique was the first choice of 46 patients, and 5 patients were transferred to CAPD from hemodialysis (HD) because of ocular (one patient), cardiovascular (three patients), and vascular access (one patient) problems. Forty-five of the 51 patients

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were trained in CAPD and the remaining six were also treated at home, mainly because of vision problems, with continuous cyclic peritoneal dialysis (CCPD). The data of these six patients were included in the CAPD series. As of December 1983, the cumulative duration of treatment was 65.6 patient-years, with an average time per patient of 17.1 ± 11 (SD) months (range 1–38 months). Fourteen patients were treated at least 2 years and four patients for 3 years.

At the beginning of treatment there were 27 male and 24 female patients whose mean age was 52.3 ± 13.5 years. The mean age when diabetes was discovered was 29.2 ± 15.2 years. The mean delay between discovery of diabetes and start of dialysis was 23 ± 17.6 years. The mean delay between the time that the serum creatinine level was 200 ± 50 μmol/L and the start of dialysis was 32.2 ± 12.8 months. Thirty-five patients had been treated with insulin since the discovery of diabetes and 16 had been treated temporarily with oral antidiabetic drugs. All patients were treated with insulin when dialysis was started.

Extrarenal complications at start of CAPD were extremely severe (Table 1).

### Methods

Training for CAPD and CCPD took place in a separate unit with a nursing staff especially devoted to this task. The training period lasted an average of 22 days (12–32 days). Treatment was conducted through a double-cuff Tenckhoff catheter (supplied by Quinton Instruments, Seattle, WA, USA); we preferred the curled type. The composition of the dialysate and features of the bag have been described. In most cases, CAPD was carried out with four exchanges per day using three 2-liter bags with 1.5% dextrose concentration and one 2-liter bag with 4.5% dextrose concentration. The CCPD was conducted by the family of the patient or a trained nurse with a cycler machine dispensing three to four 2-liter bags overnight while fluid was left in the peritoneal cavity during the daytime.

Considering the daily peritoneal absorption of about 100 g of dextrose and the daily loss of about 10 g of protein through the dialysate effluent, the patients were asked to eat a diet with a carbohydrate content ranging between 130 and 150 g/day and a protein content of about 1.5 g/kg of body weight per day. Water and salt intake was adjusted according to residual renal function, clinical state of hydration, and blood pressure values. Furosemide was administered orally with the aim of preserving residual urinary output.

Patients and their relatives were trained to measure the blood sugar level with the finger-prick technique on the Glucometer Ames (Ames Miles Division, Paris, France). During the initial training, control blood sugar was measured four times per day at each exchange. At home, only two measurements were performed routinely by the patients, but every 2 weeks they were required to take six readings at 0800, 1100, 1400, 1800, 2000, and 2200 hours. Our goal was to obtain a fasting blood glucose level of less than 10 mmol/L. During CAPD, insulin was administered exclusively through the peritoneal route with a special injection site on the line of the bag. Insulin schedules according to time and meals are shown in Table 2 for patients treated by CAPD. Patients treated by CCPD received subcutaneous injections of regular insulin twice daily and a mixture of regular and long-acting insulin once daily.

### Results

#### Survival Rates, Cause of Dropout, Technical Complications, and Hospitalization

The overall rates of patient survival and technique success according to age are given in Figure 1. At 2 years the survival rate of all patients was 63%. In 19 patients under age 50 years (mean age 39 ± 8 years) the technique success rate at 2 years was 78% and in 27 patients over age 50 years it was only 50% (mean age 61.5 ± 8 years). The dropout rate including deaths and transfers to other therapeutic modalities increased with age. A total of 14 patients transferred from hemodialysis for the following reasons: inability to manage the technique, 5 patients; recurrent peritonitis, 4; sclerosing peritonitis, 2; malnutrition, 1; bowel perforation, 1; and loss of ultrafiltration, 1. (Three of these patients died during the 2 months after transfer.) The causes of transfer of patients to HD were mainly due to abdominal complications or malnutrition. Five patients were unable to handle the technique, and as they could not care for themselves at home, they were transferred in the early phase of HD. Later causes of transfer were severe abdominal complications including recurrent peritonitis, sclerosing encapsulating peritonitis, loss of ultrafiltration, and malnutrition. The 13 deaths were from the following causes: myocardial infarction, 3 patients; gangrene and sepsis, 6; cerebrovascular accident, 1; malnutrition, 1; liver insufficiency, 1; and bowel perforation, 1. This one abdominal death occurring in a patient treated with CAPD was caused by an acute abdominal complication related to a perforated sigmoid diverticulum.

The overall frequency of peritonitis was 86 episodes, one every 9.6 patient-months. In 68 patients a pathogen was isolated: 47 gram-positive, 26 gram-
TABLE 2. Estimation of Daily Insulin Requirement and Carbohydrate Intake from Food and Dialysate in Insulin-Dependent Diabetic Patients Treated with CAPD

<table>
<thead>
<tr>
<th>Components</th>
<th>Timing of bag exchange and meals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0700 hours</td>
</tr>
<tr>
<td>Dextrose concentration of the 2-L bag (%)</td>
<td>1.5</td>
</tr>
<tr>
<td>Routine dextrose absorption per 2-L bag (g)</td>
<td>25</td>
</tr>
<tr>
<td>Routine carbohydrate intake per meal (g)</td>
<td>30</td>
</tr>
<tr>
<td>Regular insulin routinely injected (IU)</td>
<td>18</td>
</tr>
</tbody>
</table>

Table showing the components and timing of bag exchange and meals with corresponding values for different time periods.

Main Clinical Values

Hypertension

At the start, 48 patients were hypertensive. Three patients previously treated by hemodialysis and transferred to CAPD because of cardiovascular complications such as hypotension and cardiac failure were normotensive. Ninety-three percent received hypotensive drugs, including diuretics, 36 patients; beta blockers, 25; central sympatholytic agents, 29; vasodilators, 18; and converting enzyme inhibitors, 5. At start of CAPD, three patients (7%) were normotensive without any therapy, 17 (37%) were normotensive with treatment including mostly three to four drugs; and 26 (56%) were hypertensive despite intensive treatment.

After 1 year of CAPD treatment, 17 of 31 patients (55%) were strictly normotensive without drug therapy (if one excludes diuretics to prevent residual renal function). Fourteen (45%) took antihypertensive drugs, but in smaller amounts than previously; of these, 10 were normotensive and 4 remained hypertensive. After 2 years, 11 patients of 14 (79%) were normotensive and 3 were treated either with beta blockers and central sympatholytics or central sympatholytics and vasodilators (Table 3).

In eight patients with major autonomous neurologic disorders, severe postural hypotension was observed and was augmented when rapid ultrafiltration is induced by using dialysate with a high dextrose concentration. Sodium supplement or albumin infusion may sometimes be necessary in such instances.

Visual Status

Visual status was assessed at start of treatment and after at least 6 months of CAPD (range 6–38 months) in 46 patients. At each ophthalmic visit the best corrected visual acuity for each eye was determined, a thorough ophthalmic examination was completed, and retinopathy was documented by multiple-field stereophotography (one per year). The visual acuities were grouped into functional stages: 1) reading visual acuity, 20/10 to 20/50; 2) impaired visual acuity, 20/70 to 20/100; 3) ambulating visual acuity, 20/160 to count-
TABLE 3.  Evolution of Blood Pressure and Hypotensive Therapy in 46 Patients Treated with CAPD for More Than One Month

<table>
<thead>
<tr>
<th>Period (mo)</th>
<th>Patients (n)</th>
<th>0-1</th>
<th>6</th>
<th>12</th>
<th>24</th>
<th>36</th>
</tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine systolic</td>
<td>46</td>
<td>173±42</td>
<td>150±30</td>
<td>149±30</td>
<td>146±32</td>
<td>137±28</td>
</tr>
<tr>
<td>Diastolic</td>
<td>37</td>
<td>96±27</td>
<td>85±14</td>
<td>86±17</td>
<td>83±16</td>
<td>89±13</td>
</tr>
<tr>
<td>Orthostatic systolic</td>
<td>31</td>
<td>165±63</td>
<td>143±25</td>
<td>136±22</td>
<td>144±28</td>
<td>138±35</td>
</tr>
<tr>
<td>Diastolic</td>
<td>14</td>
<td>90±35</td>
<td>90±16</td>
<td>82±12</td>
<td>86±18</td>
<td>80±16</td>
</tr>
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</table>

Patients taking antihypertensive drugs

<table>
<thead>
<tr>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>93</td>
</tr>
<tr>
<td>19</td>
<td>51</td>
</tr>
<tr>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>1</td>
<td>25</td>
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ing fingers; 4) minimal visual function, hand motions to light perceptions; and 5) no visual function, no light perception. All but one patient had proliferative retinopathy, 64% were in stages 1 and 2, and 36% in stage 3. Results on visual function and visual course are shown in Table 4. Visual acuity measurements in 46 patients showed the following distribution: stage 1, 30 eyes; stage 2, 26 eyes; stage 3, 22 eyes; stage 4, 7 eyes; stage 5, 5 eyes.

Visual course over the period of study gave the following results: visual improvement was noted in 14 eyes (mainly in young patients under 50 years old) due to spontaneous resorption of vitreous hemorrhage, photoagulation, and surgical vitrectomy. Deterioration of visual function occurred in 17 eyes due to numerous events (some patients experienced more than one): recurrent vitreous hemorrhage, 5 eyes; cataract, 6 eyes; macular degeneration, 3 eyes; and anterior segment neovascularization, 3 eyes.

Cardiovascular Complications

Complications were categorized as cardiac, cerebrovascular, and peripheral vascular. Extrarenal complications, mainly cardiovascular, were noted at the start of CAPD. During treatment, the condition of most patients improved, but one died within the first month of treatment of cerebrovascular accident; 3 died of myocardial infarction after 1, 15, and 27 months of treatment; and 16 suffered from angina pectoris, mainly during the short period of fluid overload.

During observation, 11 patients of 46 required 23 amputations. These were exclusively in the lower limb, including 5 toes, 5 forefeet, 12 legs at different levels, and 1 thigh. Diffuse necrotic skin lesions were observed in four patients. Six patients died after amputations.

Discussion

During the past 5 years it was well demonstrated that CAPD could offer patients with insulin- and non-insulin-dependent diabetes with ESRD excellent control of both uremia and blood glucose levels, and their complications.9-14 For these reasons, since 1978 many institutions have selected CAPD as the preferred mode of home dialysis for diabetics.15 Nevertheless, two major drawbacks have limited its extensive use: patients who are partially or totally blind find the technique difficult to manage despite intensive training14 and the dropout rate is high because of the severe and sometimes lethal abdominal complications.16

The most recent data published, including our own results,8, 10, 17 demonstrate that if one considers not only patient survival rate but the technique's success rate, the results obtained with CAPD can compete favorably with those obtained in a diabetic population of the same mean age treated not only by hemodialysis and intermittent peritoneal dialysis6-18-19 but by transplantation. The only exception is represented by the excellent graft survival rate when using a living related donor.6 The dropout rate, including deaths and transfers, is largely influenced by age, the major risk factor. In our series, the technique success rate at 2 years with

<table>
<thead>
<tr>
<th>Stage</th>
<th>Acuity</th>
<th>Baseline</th>
<th>Final</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>1</td>
<td>20/10 ±20/50</td>
<td>30</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>20/70-20/100</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>20/160-counting fingers</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>Light perception</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>Totally blind</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Totals 92 100 92 100
CAPD was 78% for patients under age 50 years and only 50% for those over age 50. Patients transferred mainly because of technical problems.

Excellent clinical status with good control of blood pressure, satisfactory values of major biological variables, and good nutrition are routinely obtained in many patients with CAPD on a daily program of four exchanges, including only one 2-liter bag with high dextrose concentration. Extracellular fluid volume can be controlled by changing the dialysate formulation, principally by increasing the dextrose concentration. In our experience with the regimen described, daily fluid removal was found to be 1200 ± 230 ml/day and the sodium balance negative on 80 ± 25 mmol/day. Our results agreed with those of other studies dealing with diabetics showing a good control of blood pressure by CAPD. This control seems to be progressive with time: 7% of patients at start of CAPD, 55% at 1 year, and 79% at 2 years were normotensive without any medication. Rapid control of hypertension was also associated with a relatively high frequency of symptomatic orthostatic hypotension. Despite a progressive increase in body weight after 1 and 2 years of treatment, arterial blood pressure had no tendency to return toward high levels. This increase in body weight may probably be attributed not only to a gain in lean body mass but to expanded extracellular volume. Some of these patients became hypotensive, suggesting sodium depletion and hypovolemia. Further studies are required to explain this phenomenon: is there a depletion of pressor substance with a high molecular weight? is there any disturbance in the vascular reactivity with CAPD?

Rapid deterioration of visual function is one of the major threats to diabetic uremic patients who undergo maintenance hemodialysis therapy. Poor control of hypertension and blood glucose level, and the metabolic disturbances induced by diabetes and uremia, together with the deleterious effect of heparin are claimed by these authors as being responsible for the progression toward blindness often encountered in these patients. With CAPD the reports improve: Khanna et al. reported improvement in 3 of 19 eyes and deterioration of 4 of 30 eyes. Good control of blood pressure and blood glucose levels, no acute shifts in body weight or osmolality, and no intensive use of heparin enabled patients to maintain visual acuity at the same level as at the start of CAPD. In addition, active therapy such as scatter photocoagulation and surgical vitrectomy can often clearly alter the natural course of diabetic retinopathy.

Vascular complications remain the main cause of death among diabetics treated by all forms of dialysis and after transplantation. Adequate prevention seems possible through an early program of foot care. Excluding diabetic patients from treatment is no longer acceptable when the therapeutic facilities are available. Several treatment modalities now offer increasing numbers of diabetic patients with ESRD longer survival, decreased morbidity, and better rehabilitation, and at a lower cost for the community, and CAPD should be one of the therapies available. It is probably the only dialysis method that diabetics can perform themselves at home. With acceptable rates of peritonitis and diminution of peritoneal complications, CAPD could really be the dialysis method of choice. An integrated program CAPD-transplantation could become the preferred supportive treatment for those with juvenile diabetes. Although tedious precautions are required to avoid peritoneal infection, CAPD offers a unique opportunity to treat elderly diabetics at home and ensure the best control of diabetes, uremia, and hypertension.

Thus while CAPD may be the best treatment selection for some diabetics, all forms should be available to give each patient a good first choice.

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