EVOLUTION OF RESIDUAL RENAL FUNCTION IN PATIENTS UNDERGOING MAINTENANCE HAEMODIALYSIS OR CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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Summary

A study has been carried out to compare over an 18 month period the residual glomerular filtration rate (GFR) measured by the creatinine clearance in two matched groups of 25 patients with end-stage renal disease. One group was treated by continuous ambulatory peritoneal dialysis, the other one by maintenance haemodialysis. GFR was similar in both groups immediately before starting dialysis therapy, respectively 4.3 ± 2.3 and 4.4 ± 2.4ml/min.

From the beginning of the dialysis treatment to the eighteenth month there was a significant and progressive decrease of GFR in the group of patients treated by haemodialysis, while in the peritoneal dialysis group GFR and peritoneal clearances remained stable.

Introduction

Residual renal function in patients with end-stage renal disease on maintenance dialysis is an important factor in the well-being of patients and in the determination of the dialysis schedule [1,2]. For the last four years continuous ambulatory peritoneal dialysis (CAPD) has offered to many patients an alternative to haemodialysis (HD). This study investigates the evolution of residual glomerular filtration rate (GFR), measured by creatinine clearance, of patients treated by CAPD in comparison to that of a matched group of patients treated by HD. In parallel, the evolution of the peritoneal clearances and protein losses were evaluated in the CAPD group.

Patients and methods

Patient characteristics

Fifty patients divided into two matched groups were studied over an 18 month period.
**Group I:** 25 patients (15 males, 10 females) treated by CAPD. At the start of dialysis, mean age was 61.6 ± 14.6 years, and mean body weight 63.2 ± 11.6kg. Primary renal diseases were chronic glomerulonephritis in 10 patients, chronic interstitial pyelonephritis in seven, diabetic nephropathy in four, nephroangiosclerosis in two, polycystic kidney disease in two. Daily dialysis was performed with a four exchanges schedule using commercial dialysis solutions, with three 2L 1.5% dextrose and one 2L 4.5% dextrose. Frusemide was given to 18 of the 25 patients at a mean daily dose of 325±125mg during the period of observation.

**Group II:** 25 patients (15 males, 10 females) treated by HD. Eighteen patients were dialysed in La Pitié Hospital. Seven patients were dialysed in other centres. These were selected from the data bank of the Diaphane Registry [3] to allow good matching of the two groups. At the start of dialysis mean age was 57.2 ± 13.2 years and mean body weight 62.0 ± 10.7kg. Primary renal diseases were chronic glomerulonephritis in 13 patients, chronic interstitial pyelonephritis in eight, nephroangiosclerosis in two, polycystic kidney disease in two. Dialysis therapy was carried out with a regimen of three dialysis sessions over 12 to 15 hours per week. In the 18 patients haemodialysed in La Pitié, frusemide was given in 14, at a mean daily dose of 425 ± 175mg/day.

There were no significant differences between the two groups according to sex, age, bodyweight and primary renal disease.

**Clearance studies**

The residual renal function expressed by GFR based on 24 hours creatinine clearance adjusted to a standard body surface area of 1.73m² was evaluated in each group just before dialysis therapy and every six months over an 18 month period. During the dialysis period, in the HD group, a 24 hour urine collection was performed on the last day of the longest period between two dialyses; blood samples for serum creatinine were obtained at the end of the urine collection period prior to the beginning of the next dialysis session. In the CAPD group, urine was collected over a 24 hour period on any day during the week, and blood samples were taken at the end of the urine collection period.

During the same period at the start of dialysis and every six months, the peritoneal clearances of phosphorus and creatinine were calculated as follows: the total daily peritoneal drainage volume was measured in a graduated cylinder (VD) divided by the time in minutes (t=1440min) multiplied by the dialysate concentration of the solute to be studied (D) and divided by the serum concentration (P):

\[
\text{Cml/min} = \frac{D \times VD}{P \times t}
\]

**Statistics**

Student’s paired t-test was used at each period to compare in the two groups differences between mean GFR expressed by creatinine clearances. Differences
<table>
<thead>
<tr>
<th>PERIOD</th>
<th>HD GROUP — 25 patients</th>
<th>CAPD GROUP — 25 patients</th>
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<tbody>
<tr>
<td></td>
<td>Body weight (kg)</td>
<td>GFR* (ml/min)</td>
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<tr>
<td>Before starting dialysis</td>
<td>57.2 ± 13</td>
<td>4.3 ± 2.3</td>
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<tr>
<td></td>
<td><strong>p&lt;NS</strong></td>
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<tr>
<td>6 months of dialysis</td>
<td>56 ± 12</td>
<td>2.7 ± 1.8</td>
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<td></td>
<td><strong>p&lt;0.04</strong></td>
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<tr>
<td>12 months of dialysis</td>
<td>57.5 ± 11</td>
<td>2.1 ± 1.5</td>
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<td></td>
<td><strong>p&lt;0.01</strong></td>
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<tr>
<td>18 months of dialysis</td>
<td>58.2 ± 12</td>
<td>1.3 ± 1.2</td>
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<td><strong>p&lt;0.01</strong></td>
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* GFR: Glomerular filtration rate expressed by creatinine clearance

** P: Peritoneal
in mean values were also subjected to paired t-test analysis for measurements in
the CAPD group of the creatinine and phosphorus clearances and protein losses.
The null hypothesis was rejected at p less than 0.05.

Results

The evolutions of GFR and peritoneal clearances are given in Table I. Just before
dialysis therapy there was no difference in GFR between the two groups while
differences at 6, 12 and 18 months were highly significant. Urine volumes follow
similar changes. During CAPD treatment daily urine output remained stable:
800 ± 400ml before dialysis, 950 ± 540 at six months, 950 ± 520ml at 12 months
and 725 ± 500ml at 18 months. During HD treatment daily urine volume de-
creased from 830 ± 380ml before dialysis to 600 ± 320ml at six months, 450 ±
180ml at 12 months and 220 ± 140ml at 18 months. Fourteen patients out of 25
were almost anuric 18 months after starting treatment.

The mean peritoneal clearances of creatinine and phosphorus measured
during the training period of CAPD and regularly at six month intervals remained
stable. Values were not influenced by the incidence rate of peritonitis. During
the same period no clinical modification of the ultrafiltration rate was detected
and satisfactory water and sodium balances were maintained without increase in
the number of 4.5% dextrose concentration bags. Peritoneal protein losses were
stable at around 10g/day.

Discussion

A progressive decrease in urine output during the first years of treatment by HD
is a common finding [2]. In contrast stable residual renal function in patients
treated by CAPD is not frequently reported. Our comparative study between
two matched groups demonstrates that over an 18 month period a significant
and progressive decrease of GFR is observed in the group of patients treated by
HD while GFR remained stable in patients treated by CAPD.

In dialysed patients the remaining function of the existing renal mass is
important. It helps to maintain a good water and electrolyte balance without
too rigid diet restrictions. It represents an estimation of certain non-excretory
functions of the kidney such as synthesis of erythropoietin and the final con-
version of vitamin D to its active form [4]. It plays a major role in the daily
excretion of the so-called middle molecules [5]. Residual renal function is
considered as an index influencing the weekly dialysis time of patients on HD
[1].

Determination of GFR in haemodialysed patients is difficult. Creatinine
clearance has been shown to be very close to inulin clearance at the low level
of GFR observed in such patients but rigid precautions dealing with collection
of urine and timing of blood samples are required [6]. In our study during the
dialysis period, creatinine clearances were measured over a 24 hour period the
day before haemodialysis. Only one blood sample was taken at the end of the
period.
Such a method is exposed to errors and cannot be compared exactly with the 24 hour creatinine clearance determined in patients treated by CAPD with a stable plasma creatinine concentration and urine volume. Nevertheless the methods used were similar throughout the period of study. Small errors in the measurement of the GFR cannot explain the progressive and highly significant differences between the evolution of the GFR of the two groups.

There are very few reports in the literature regarding the evolution of the GFR of dialysis patients: Milutinovic et al [6] reported only seven patients over a period longer than one year with a mean creatinine clearance of 2.42ml/min at start of dialysis and 1.65ml/min after one year. Recently the EDTA Registry [7] collected information on residual renal function recording only the daily urinary volume on the day prior to dialysis in the two most common primary renal diseases: glomerulonephritis and pyelonephritis. There is a progressive decrease in the proportion of patients with high urinary volumes. The residual daily urine volume was higher in patients with pyelonephritis but a progressive reduction with time on dialysis was also observed. The deterioration of GFR is partly related to progressive evolution of the primary renal disease [4], but factors such as hypertension, overhydration, nephrotic syndrome, severe hypotensive episodes during dialysis sessions, variations in body weight and haemodynamic status may accelerate the deterioration in the HD group.

A stable GFR in patients treated by CAPD can be related to the constant high plasma osmolality with a stable high plasma urea concentration and to the absence of acute fluid shifts similar to that observed during haemodialysis. The routine administration of frusemide to our patients may also contribute in maintaining a large urine output. Control series are required to analyse the true efficacy of the drug. The daily prescription of frusemide to haemodialysed patients does not always prevent the reduction of urine volume.

Creatinine and phosphorus peritoneal clearances and protein losses remained stable during the period of observation and were not influenced by the rate of peritonitis episodes [8,9]. Although increased protein losses are routinely observed during peritonitis, prompt therapy as described by Oreopoulos et al [10] maintains base line peritoneal transport properties.

It is too early to predict what will be the residual renal function and the peritoneal clearances of patients after many years of treatment by CAPD. The most recent results observed in our department are encouraging. Among 18 patients on CAPD for at least two years, GFR remained stable in 10. A slow deterioration was observed in eight patients with a mean creatinine clearance at two years of 2.08 ± 1.25ml/min. Within the limited period of observation a persisting residual renal function of a few millilitres per minute is, in our experience, a major contributing factor to the well-being of patients successfully treated by CAPD.

References

1 Milutinovic J, Strand MJ, Casaretto A et al. Trans ASAIO 1974; 20: 410
3 Degoulet P, Le Grain M, Reach I et al. Nephron 1982; 31: 103
Open Discussion

CANTAROVICH (Buenos Aires) I would like to ask a question and make a comment. Are any of your patients free of dialysis for any period of time?

ROTTEMBERG During the study period?

CANTAROVICH Yes.

ROTTEMBERG Never.

CANTAROVICH The comment is we undertake three daily changes routinely and we have observed that eight per cent of our patients on CAPD are able to discontinue dialysis for periods from three months to two years. We compared these patients with those on haemodialysis who had practically the same aetiology and only 1.8 per cent of these patients were able to discontinue dialysis. As Dr Rottembourg has shown, improvement in renal function is a challenge to be analysed in CAPD patients.

LOWRIE (Boston) I believe that you may have severely underestimated the residual clearance in your haemodialysis patients. I understand that you use the pre-dialysis value as the plasma value, and I think it would be more appropriate to use the average value which occurs during the interdialysis interval.

ROTTEMBERG Yes, I agree with your remark, but we used the same protocol during the entire period of observation, from the first measurement before the onset of dialysis therapy to the last measurement eighteen months after. The possible error made by underestimation of the creatinine clearance in the haemodialysis patients is reproduced every six months. Despite this fact there is a decrease in the haemodialysis group whereas there is not a decrease in the CAPD group.

DRÜEKE (Paris) The problem is to know whether the initial renal function was the same in the two patient groups. If you underestimate the function in the
haemodialysis patients the initial clearance and the initial function would not be the same in both groups. This might be important.

ROTTEMBOURG The first measurement of the creatinine clearance is performed in the two groups before onset of any dialysis therapy. Urine collection is obtained in both cases during a 24 hour period.

LEGRAIN (Paris) Dr Drueke we can answer your question. Before starting dialysis there was no dialysis at all. It was a 24 hours urine collection period, so that CAPD and HD were comparable. The remarks of Dr Lowrie are correct, it does not apply before starting dialysis. The creatinine clearance of the two groups before starting dialysis was calculated in the same way and was 4.3 and 4.4ml/min.

RINGOIR (Chairman) Your findings suggest you have a better removal of middle molecules in CAPD group than in the haemodialysis group.

ROTTEMBOURG I think that is another problem. I am not sure that we remove more middle molecules or what we call middle molecules. We have made other studies in other groups of patients treated by CAPD or haemodialysis comparing removal of molecules between 300 and 500 daltons and the removal is similar. I am not sure that we remove more middle molecules during CAPD.

KRAMER (Germany) Sorry to come back to the measurement of creatinine clearance. I think pre-dialysis determinations are performed in a steady state, and the same is true on CAPD. If you subsequently treat a patient with haemodialysis and you use only the pre-dialysis creatinine this is not a steady state and so you may make an underestimation.

ROTTEMBOURG I agree with you but we could not collect urine every day during eighteen months for 25 patients. It was quite difficult to obtain regular urine collection by the patient. I thought that by taking the longest period without dialysis a twenty-four hour urine collection overestimated the mean daily output, and by taking creatinine concentration pre-dialysis we overestimated the serum concentration.

GAHL (Paris) The natural course of chronic renal disease is a further deterioration of the residual renal function with time. Perhaps somebody has an explanation why in the peritoneal dialysis group reported in this study the residual renal function did not decrease but remained absolutely stable with time.
PART X

Guest Lecture  THE ROLE OF IMMUNOLOGICAL PARAMETERS IN KIDNEY TRANSPLANTATION

Chairmen  H Brynger
           J B Dausset