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Evolution and Trends in Peritoneal Dialysis

International Meeting, Croara di Gazzola (PC), October 27–28, 1989

Evolution and Trends in Peritoneal Dialysis

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Opening Address

Our first direct experience with peritoneal dialysis dates back 25 years. In Paris, 1968, at one of the first European Dialysis and Transplant Association (EDTA) Congresses, we reported on the question of protein loss, both in terms of quality and quantity. Each dialysis procedure resulted in a protein loss ranging from between 50 and 150 g, the profile varying from selective to nonselective as the case may be.

On the grounds of those early pathophysiological findings, we were against using peritoneal dialysis as an iterative means of therapy for chronic renal failure in the past, our earlier reservations being amply supported by the frequent infections and technical complications which occurred.

Long-term clinical results have shown these reservations to be unfounded. Despite the pathophysiological and clinical criticisms, not to mention the massive 'weight' in favor of extracorporeal hemodialysis, peritoneal dialysis has gradually taken its place among the forms of artificial substitution therapy in chronic renal failure. Peritoneal dialysis is no longer considered a second choice, but is today an alternative means of treatment.

This is one of the lessons that 25 years of renal replacement has taught us. The first lesson, however, is the general principle that it is far better to *prevent* than to *treat*. Research aimed at improving our knowledge of the mechanisms of onset *(primary prevention)*, at improving our ability to identify and combat the factors behind renal lesion progression *(secondary prevention)*, and at enhancing the use of substitution therapy in order to avoid systemic clinical complications once renal loss has occurred *(tertiary prevention)*, should be supported and given priority. For, despite miraculous results from many angles, all renal substitution therapy programs represent a sort of failure on the part of medicine as a whole, while the cost/benefit to society ratio

is at present largely disappointing. Experience shows that renal transplantation is far superior to artificial substitution, be it hemodialysis or peritoneal dialysis. Transplantation is the only nonillusory form of therapy in clinical terms, rehabilitating as it does from uremia: in social terms optimizing patient reentry to the home, and in logistic terms concering its better cost/benefit ratio.

True though this is, it is no less true that transplantation can only be performed in a kind of patient élite (no more than 30%). Artificial substitution predominates today and will predominate in the future owing to the shortage of donors. Moreover, without supportive artificial therapy, 98% of renal transplants would not have taken place, while over 50% of them would have had an unhappy outcome.

This last fact should be pondered more deeply by other organ transplant programs, where simultaneous artificial substitution does not exist. Against this background and reality, further study and research to improve the effect of renal artificial substitution therapy are both justified and are to be welcomed, aiming, for example, at improving biocompatibility, optimizing the time of starting treatment, and boosting artificial substitution by biological means in a form of 'hybrid' substitution therapy.

Recent research has shown that after years of hemodialysis, an immunological reaction may set in (a kind of immunological 'rejection' of dialysis), mainly affected by the nature of the artificial membrane used. This last fact, the long-term implications of which are hard to assess today, seems once again to favor peritoneal dialysis, the present status of which was unimaginable 10 years ago: i.e. the number of patients on CAPD growing steadily; indications for treatment including clinical situations (such as diabetes mellitus) which were once ruled out; clinical complications steadily dwindling; the risk of cross-infection lower than in hemodialysis; and profiles on postdialytic metabolic derangement certainly being no higher.

As with any treatment program, the results of CAPD largely mirror the 'credo' of whoever applies the program. And the doctor's credo, ethically, must be based on the reality of ascertained results, not on a priori dogma or prejudice – a fact I myself have sometimes to remember.

This outstanding contribution, from the excellent Karger series (which any nephrologist should zealously consult on his shelves), is a further proof of what the Italian School of Nephrology has to offer in terms of organizing ability, enthusiasm and dedication to work. Not surprisingly, the book is edited by Prof. Scarpioni who, with his School, is symbolic of these three qualities.

The Italian Society for Nephrology officially thanks Prof. Scarpioni for his efforts in organizing a meeting of this high scientific level, the results of which are reported herein. The value of CAPD is not only confirmed, but consolidated.

I wish to congratulate Prof. Scarpioni and his excellent co-workers, and I hope that CAPD, a lady among treatments, will accept my apologies.

Prof. *Vittorio Bonomini*
President,
Italian Society of Nephrology

Preface

This volume of *Contributions to Nephrology* is an updated review on peritoneal dialysis, mainly continuous ambulatory peritoneal dialysis (CAPD).

Peritoneal dialysis has attracted the interest of nephrologists since its beginning as a useful and reliable technology for the treatment of chronic uremia.

In March 1978, more than 10 years ago, we organized, in Piacenza, the First International Symposium on Chronic Peritoneal Dialysis. Now with 10 years' experience, we have repeated the meeting to discuss the current status of peritoneal dialysis, CAPD and continuous cycling peritoneal dialysis (CCPD), exchanging opinions, experiences and prospectives of this therapy that has been proved to afford effective survival and rehabilitation.

CAPD has permitted management of patients failing hemodialysis; in addition, it has greatly facilitated the treatment of uremic children and old patients. In several patients, particularly those who have diabetic nephropathy, it has become the treatment of choice. Every year there has been a steady increase of patients actively on CAPD/CCPD. Dropouts due to death or transfer to hemodialysis have been fewer than newly registered patients. We do not yet know if CAPD care maintains a patient on dialysis as long as hemodialysis, but we do know that CAPD is the only home dialytic care that has rapidly increased while, at the same time, hemodialysis is decreasing as home care.

L. Lino Scarpioni

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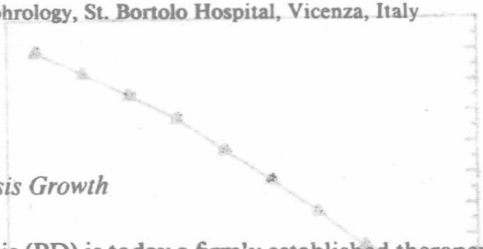

Peritoneal Dialysis Growth

Peritoneal dialysis (PD) is today a firmly established therapeutic modality for end-stage renal disease (ESRD). The worldwide diffusion grows progressively both in terms of total number of patients and in terms of the percentage of global patients on renal replacement therapy [1].

The overall population treated by a substitute therapy has increased by about 10% per year during the last 3 years. The number of patients on continuous ambulatory peritoneal dialysis (CAPD) over the same period has shown a dramatic but steady increase throughout the world (fig. 1). At the end of 1988 there were over 43,000 patients alive on this treatment, representing about 13% of the total dialysis population [1].

The regional distribution of PD patients is depicted in figure 2: over two-thirds of the treated patients live in North America and Europe. The last third is distributed among Latin America, Asia, Africa and Oceania. It can be noted that on these continents the majority of CAPD patients belongs to a very small number of countries. This suggests that for a large number of countries with fewer facilities a PD program could be developed in the near future.

The percentage of CAPD patients on the global regular dialysis treatment (RDT) in different countries is depicted in figure 3. In very large and/or in underdeveloped countries CAPD patients represent a very high percentage of the total treated patients. However, CAPD also plays an important role where the renal replacement therapy program is well developed. In these

countries, like Scandinavia, the integrated program of ESRD allows patients on hemodialysis (HD) to be switched when necessary to CAPD or vice versa and makes the probability of transplant in only a few years very high.

On the contrary, in well-developed countries with a very effective RDT program such as France, Italy, Germany and Japan, a very low percentage of CAPD patients is reported. This seems mainly due to a different fee of reimbursement for CAPD vs. HD provided by the National Health Service. In Europe, 11.4% of dialysis patients are on CAPD and one-third of them are in the UK (fig. 4). In this country, following

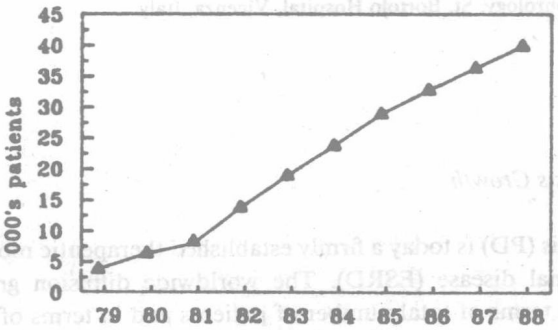

Fig. 1. Worldwide PD growth.

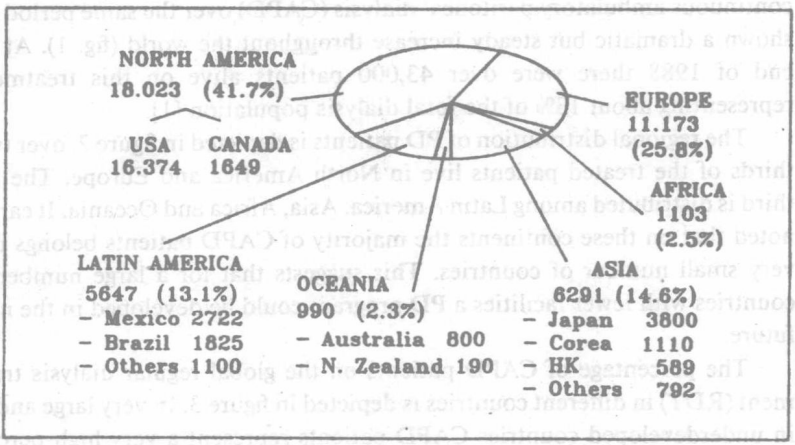

Fig. 2. Regional distribution of the PD population.

restriction of the HD program for economical reasons, PD growth has increased constantly in the last years and has almost completely substituted for home HD. The same trend of substituting home HD has been registered in other European countries, e.g. Italy, and in the USA. In Italy, the PD diffusion varies in the different regions and the majority of patients are in the north (fig. 5).

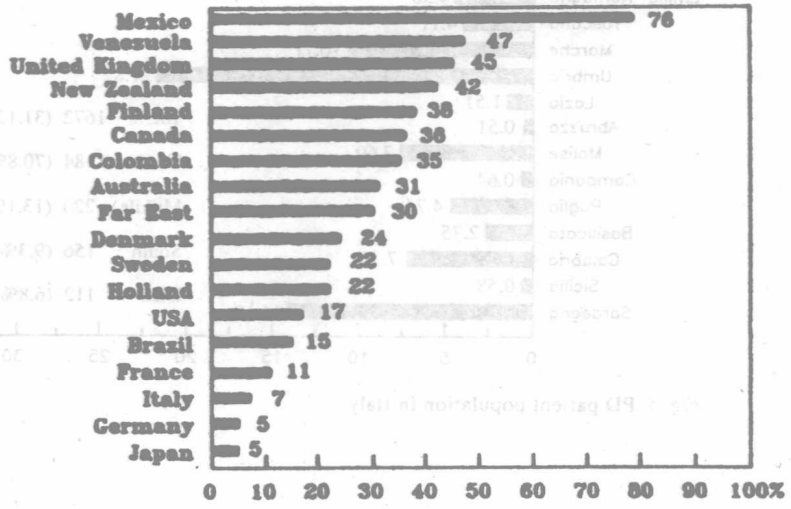

Fig. 3. PD patients as a percentage of the total dialysis population.

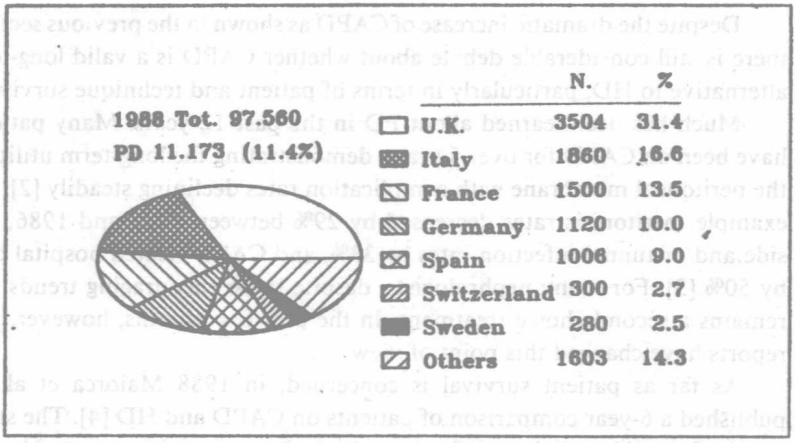

Fig. 4. RDT population in Europe.

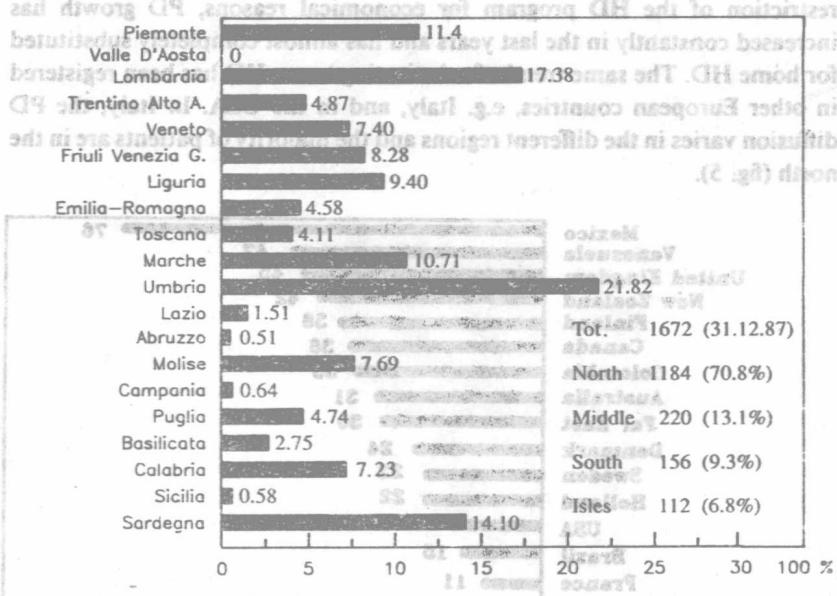

Fig. 5. PD patient population in Italy.

Patient and Technique Survival

Despite the dramatic increase of CAPD as shown in the previous section, there is still considerable debate about whether CAPD is a valid long-term alternative to HD, particularly in terms of patient and technique survival.

Much has been learned about PD in the past 12 years. Many patients have been on CAPD for over 5 years, demonstrating the long-term utility of the peritoneal membrane with complication rates declining steadily [2]. For example, peritonitis rates decreased by 29% between 1982 and 1986, exit side and/or tunnel infection rates by 33%, and CAPD-related hospital days by 50% [3]. For many nephrologists, despite these encouraging trends, PD remains a second choice treatment. In the past few months, however, new reports have changed this point of view.

As far as patient survival is concerned, in 1988 Maiorca et al. [4] published a 6-year comparison of patients on CAPD and HD [4]. The study was performed in a dialysis unit where the patients were either treated by HD or CAPD.

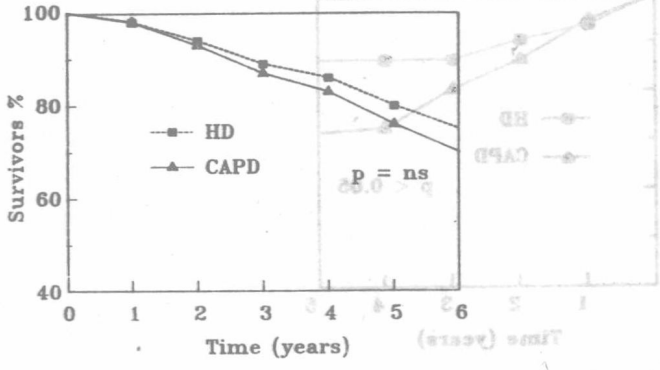

Fig. 6. Estimated patient survival.

Table 1. Weekly clearances and TAC urea

	CAPD	HD
Urea clearance, liters/week	67	> 100
Creatinine clearance, liters/week	50	> 100
Inulin clearance, liters/week	40	7
TAC urea, mg/dl	60–70	50–70 (f Kt/v)

Cox's proportional hazard regression model was utilized to evaluate patient and technique survivals corrected for pre-treatment risk factors. Overall patient survival between CAPD and HD did not differ. Subsequently this study was extended to another five dialysis units in which the same policy had been followed [5]. Over 850 patients (480 on CAPD and 373 on HD) have been studied for a period of 6 years using Cox's analysis. As shown in figure 6, no difference between the two groups was observed in the survival curves. A detailed analysis of this study is published further on in this book.

These data first demonstrate that the patient long-term survival in CAPD and in HD is comparable when the risk factors of the two populations are considered.

However, from a theoretical point of view, HD is a very efficient treatment, mainly for small solutes if compared with CAPD.

Table 1 depicts the different weekly clearances obtained with the two techniques. CAPD is more effective in removing middle-sized molecules, while weekly clearances of small solutes are at least twofold in HD. Accord-

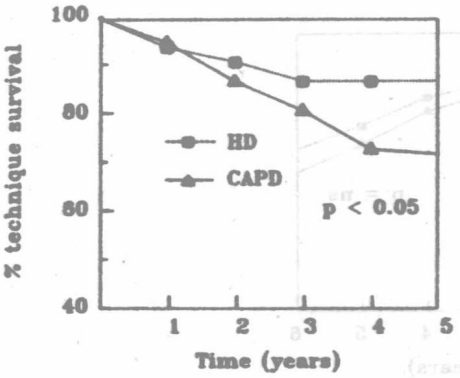

Fig. 7. Estimated technique survival.

ing to the NCDS [6] recommendations, time averaged concentration (TAC) of urea and Kt/v are important parameters to evaluate dialysis efficiency. Patients on CAPD present a TAC urea quite similar to those of HD well-dialyzed patients. In a continuous treatment, like CAPD, the average value of urea corresponds to the maximum. In an intermittent treatment, like HD, the urea level progressively increases from the end of one dialysis session to the beginning of another, and the patients' values remain above those of CAPD patients for at least half of the interdialytic time. However, as far as the Kt/v for the same PCR is concerned, it should be noted that all the CAPD patients should be considered underdialyzed.

Consequently, CAPD patients should present a higher mortality and morbidity rate than HD patients. This does not fit with the multicentric study presented above. Some explanations can be given for these discordant data.

First of all the Kt/v is not a suitable index for a continuous treatment [7]; furthermore, CAPD provides better middle molecule clearances, preserves diuresis better than HD and maintains the blood biochemistry and acid-base status stable over time. This peculiar characteristic of CAPD could explain why a low-efficiency treatment can guarantee the same survival as a more efficient one.

The 6-year multicentric comparison study between CAPD and HD showed a significantly better technique survival for HD patients at 5 years (fig. 7). The most important reasons for abandoning the technique were

peritonitis, catheter malfunction and peritoneal membrane failure. As far as the peritonitis rate is concerned, the data obtained by the Italian CAPD study group using the Y set [8] with disinfectant were recently confirmed by a Canadian controlled trial [9].

The goal of 1 episode/2 years/patient peritonitis should now be the standard result in the CAPD population. However, we believe that such a result could be further improved, thus reducing the infection-related technique failure.

For a longer peritoneal viability, further results can be expected by morphological and functional studies on the peritoneal membrane, In fact, there is more and more evidence that the peritoneal membrane is not only a linear foil of the bowel, but it is also a living organ producing many substances and hormones [10]. In this field something new can be expected in the near future.

The acidity of the solution should be avoided when the bicarbonate-buffered dialysate is commercially available. The practical use of alternative osmotic agents and/or amino acids could reduce the use of glucose in the solution. In fact, the high concentrations and the degradation products of glucose negatively affect the peritoneal membrane. Furthermore, the high glucose reabsorption from the solution causes metabolic derangements mainly in the diabetic population. Finally, new materials for bags are needed to avoid the release of plasticizers from PVC.

Transplant

One of the most important obstacles to CAPD diffusion in the past decade has certainly been the reluctance of patients to enter a PD program due to the risk of exclusion from kidney transplant.

In fact, the transplant units did not take into account patients treated by PD for some hypothetical problems. The presence of the catheter, which is a foreign body in the abdomen, was considered a risk in an immunosuppressed patient. The relapse of a previous silent peritonitis and/or the development of a new episode, if dialysis treatment were needed, was the second argument.

Finally, the less immunodeficiency of the CAPD vs. the HD population was emphasized, thus suggesting a greater immunological response against the transplanted kidneys.

In recent years many transplant programs have included PD patients, and the results obtained in the UK, USA, Australia and our country have not

shown any difference between the two populations [11–14]. We believe that this is the basic consideration for both patients and nephrologists. These results certainly remove an important obstacle to PD diffusion.

In conclusion, three established points have been reached in recent years. They are: patient survival comparable to HD, reduced rate of peritonitis, and good results obtained with kidney transplantation. Other problems such as technique survival and long-term peritoneal membrane viability remain to be solved. However, on the basis of the above considerations we believe that CAPD can play a role equal to HD in the treatment of ESRD. This should be useful both in countries that are lacking in facilities and in those with well-developed transplant programs.

We believe, therefore, that it is ethical that more and more dialysis units should offer their patients both CAPD and HD treatments.

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