Multicentric study on paired filtration dialysis as a short highly efficient dialysis technique

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SUMMARY

The PFD is a hemodiafiltration technique where ultrafiltration and dialysis are carried out in two separate chambers, thereby avoiding the negative interference which exists when convection and diffusion are carried out together. High efficiency purification is achieved using this technique and this allows the dialysis time to be shortened.

We studied a population of 35 patients from different centres treated with PFD over one year and evaluated the efficiency, clinical tolerance and possible complications of the technique. The patients were divided into two groups according to their body weight, interdialytic weight gain and quality of the vascular access. Group A (n = 18) had 3 weekly sessions lasting 180 mins; in group B (n = 18) the sessions lasted 150 mins. The following were used in both groups: an SG-3 (Sorin) filter, 0.5 sqm polisulphone filter for convection and 1.4 sqm filter of hemophan as dialyser. The volume of UF was 12 % of the body weight plus the interdialytic body weight gain. The composition of the reinfusion solution varied accordingly.

The Kt/V was = 1.0 and the PCR > 1.1 g/kg/day in all patients. All the analytic parameters measured, including the B-2-M, remained stable.

The tolerance to treatment was good and even improved over time in both groups.

There were no changes in the cardiovascular parameters measured by echocardiography. The nerve conduction velocity improved in both groups, particularly in group B ($p > 0.05$).

There were no clinical or technical complications.

Therefore, we conclude that PFD is an efficient form of dialysis treatment, which allows the dialysis time to be shortened and present excellent clinical tolerance.

Key words: ***Hemodiafiltration. Dialysis index.***

ESTUDIO MULTICENTRICO SOBRE LA PFD COMO TECNICA DE DIALISIS CORTA DE ALTA EFICACIA

RESUMEN

La PFD es una técnica de hemodiafiltración en la cual la ultrafiltración y la diálisis se realizan en dos cámaras independientes, evitando de esta forma la interferencia negativa

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entre convección y difusión. Con ella se consigue una alta eficacia depurativa, que permite acortar el tiempo de diálisis.

Se presenta un estudio multicéntrico en una población de 35 pacientes tratados con PFD a lo largo de un año, valorando la eficacia, tolerancia clínica y posibles complicaciones de la técnica.

Los pacientes se dividieron en dos grupos, en función de su peso corporal, ganancia interdialítica y características de su acceso vascular. En el grupo A (17 pacientes) se hicieron tres sesiones semanales de ciento ochenta minutos de duración; en el grupo B, la duración de la sesión fue de ciento cincuenta minutos. En todos los casos se usó un filtro SG-3 (Sorin): 0,5 m^2 de polisulfona como ultrafiltro y 1,4 m^2 de hemofán como dializador. El volumen de UF fue el 12 % del peso corporal más la ganancia interdialítica. La composición del líquido de reinfusión varió según las necesidades.

El Kt/V fue de = 1,0 y el PCR >1,1 g/kg/día en todos los pacientes. Todos los parámetros analíticos medidos, incluyendo la B-2-M, permanecieron estables.

La tolerancia a la técnica fue buena e incluso mejoró en ambos grupos a lo largo del tiempo.

No se registraron cambios en los parámetros cardiovasculares evaluados ecográficamente. La velocidad de conducción nerviosa mejoró en ambos grupos, especialmente en el grupo B ($p > 0,05$).

No hubo ningún tipo de complicaciones clínicas ni técnicas.

En conclusión, la PFD representa una forma de tratamiento dialítico eficaz, que permite acortar el tiempo de diálisis y tiene una excelente tolerancia clínica.

Palabras clave: ***Hemodiafiltración. Velocidad de conducción nerviosa. Indice de diálisis.***

Introduction

Paired filtration dialysis (PFD) is a relatively new form of hemodiafiltration utilized as renal replacement therapy for patients with chronic renal failure[1-3]. The technique consists in an extracorporeal blood purification obtained with a special two chamber dialyzer. In the first unit (polysulphon hemofilter) plasma water is removed by ultrafiltration. After total or partial reconstitution by reinfusion of replacement solutions, the blod is than countercurrently dialyzed in the second unit equipped with hemophan membrane. The patient weight loss can be achieved both in the dialyzer, maintaining a perfect balance between ultrafiltration and reinfusion in the first unit, or in the hemofilter by programming the difference between the ultrafiltrate and the amount of reinfused fluid. 6 to 9 liters are generaly exchange in pure convection during one session with an average production of 30 liter of ultrafiltrate per week[4].

The requirements of a modern renal replacement therapy can be summarised as follows: a) adequate clearances of small molecules with a Kt/V index >1[5], b) adequate clearances of larger molecules such as beta-2 microglobulin[6], c) adequate correction of acid-base balance[7], d) satisfactory control of the dry body weight[8], e) high biocompatibility[9], f) optimal clinical tolerance[10], and g) minimal dialysis treatment time. There is a certain agreement that different forms of hemodiafiltration can meet almost all these requirements even though few draw backs can be observed in this form of therapy. Among these, the possible backfiltration of contaminated dialysis fluid represent one of the potential hazards related to the use of highly permeable membranes. On the other hand not always the interference between diffusion and convection in a single hemodiafilter can be beneficial for the final efficacy of the treatment[11]. Paired filtration dialysis could in our view at least partially overcome such problems combining the advantages of diffusion and convection, but keeping these mechanisms separated and avoiding their negative interference.

In this paper we present a multicentric study carried out in a relatively large population of uremic patients using PFD as a short treatment. The study consists in a one year follow up of the treated population in terms of feasibility, adequacy of the therapy, clinical tolerance and possible complications. This clinical experience follows a detailed analysis carried out by our groups on the characteristics of the technique, its performance in different situations and its best condition of utilization[12].

Methods and population

35 uremic patients from three different dialysis. Centres were included in the study with a random selection. Patients were arbitrarily divided in two groups according to their vascular access condition, drinking habits weight and better vascular access that could be treated with high

blood flows were included in the group of 150 minutes/session schedule, while others were treated for 180 minutes/session and lower blood flows.

The characteristics of the two groups are summarised in table I. Table II summarises other parameters relating to the treated population and treatment schedule. The two groups were mostly differing in terms of body weight while age, dialytic age and residual renal function were not significantly different. As far as the treatment schedule is concerned, blood flow and ultrafiltration rate in the hemofilter, were significantly higher in group B where a shorter treatment time required a significantly higher efficiency. On the hand, the overall amount of fluid exchanged per session was similar in the two groups while the ultrafiltration rates in the dialyzer were significantly higher in patients of group A. In this group in fact, despite a longer treatment time, the remarkable interdialytic weight gain required larger ultrafiltration rates to reach the dry body weight at the end of each session.

In all patients a follow up of one year according to the prospective protocol reported in table III was carried out. Adequacy of treatment was evaluated in agreement with the mechanistic analysis of the American Cooperative Dialysis Study[13] and the relevant formulas. The results of the two groups are reported separately and compared even though a real comparison of the two groups was not the target of this study. The real aim of the study was to evaluate the performance of paired filtration dialysis in a wide population, its feasibility as a short highly efficient technique and the long term clinical results in a relatively large population. The use of a 150 or a 180 minutes schedule only represents one of the possibilities of personalization of the technique with a significant reduction of dialysis treatment time.

Table I. Characteristics of the two groups. (One year follow-up.)

	Group A (180 mins.)	Group B (150 mins.)
No. of patients entering the study	17 < 10 M 7 F	18 < 8 M 10 F
No. of patients completing the study	14< 10 M 4 F	18 < 8 M 10 F
Age (years)	52.46 ± 13.74	50.85 ± 17.6
Body weight	74.5 ± 16	61 ± 8.2
Residual renal function	0.51 ± 0.2	0.88 ± 0.18

Table II. Characteristics of the two groups. (One year average values).

	Group A	Group B
Treatm. Time (mins)	195 ± 25	158 ± 12
Device utilized	Sorin SG-3	Sorin SG-3
Blood flow (ml/min)	325 ± 25	351 ± 22
Dial. flow (ml/min)	500 ± 35	560 ± 30
HF ultraf. (ml/min)	44 ± 2.5	56 ± 8.1
Reinfusion (ml/min)	44 ± 2.5	56 ± 8.1
Tot. fluid exc. (ml)	8,750 ± 993	8,500 ± 1,200
Dial. UF rate (ml/min)	17.7 ± 14.1	11.3 ± 10.5
Dial. buffer (mMol/L)	Bic. 35 + Ac. 4	Bic. 35 + Ac. 4
Reinf. buffer (mMol/L)	Lactate 42	Bic. 50 – Lac. 40

Table III. Study design and controls.

Baseline	* Patient registry. Anamnestic data. Vascular access evaluation.
Baseline and every 2 mths	* Biochemistry. * Acid-base status.
Baseline and monthly	* Treatment parameters. * Efficiency. * Recirculation.
Baseline and every 6 mths	* Cardiovascular evaluation. * Neurological evaluation.
Baseline and monthly	* Treatment tolerance: Blood pressure control. Frequency of hypotension. Frequency of side effects.

Results

In all cases the efficiency of the treatment was meeting the requirements for an adequate blood purification as proposed by Gotch et al.[14]. Table IV reports in detail the results concerning the urea kinetics in the studied groups. In both groups the Kt/V index was above 1 in presence of a Protein Catabolic Rate (PCR) higher than 1.1 g/24h/Kg b.w. These values were achieved with a stable urea clearance higher than 230 ml/min and a time average concentration of urea in the ranges considered safe by the American Cooperative Dialysis Study. In figure 1 the patients values are reported in relation to the classic nomogram of Gotch[14]. It can be noted that majority of the patients are in the area considered adequate for an optimal short dialysis treatment[13]. Once a month patients underwent recirculation measurement in their blood access and the correlation with the scheduled blood flow is reported in figure 2. Treatment time and clearances values were corrected for the amount of recirculation.

Table IV. Treatment efficiency. One year average values.

	Group A	Group B
BW	74.5 ± 16.1	61.03 ± 8.2
Urea K	236 ± 21	262 ± 13
Kt/V	1.16 ± 0.16	1.12 ± 0.13
PCR	1.21 ± 0.18	1.13 ± 0.16
TAC urea	59.1 ± 13.3	55.2 ± 9.8

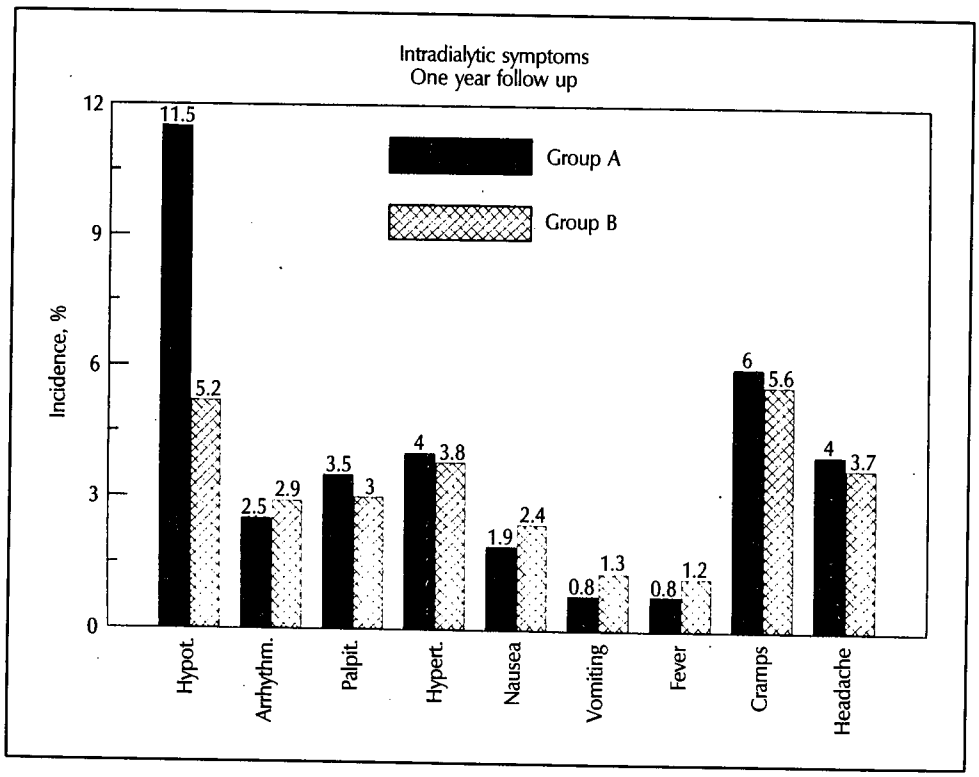

Fig. 1.—Porcentual Incidence of intradialytic symptoms observed in the two groups on the overall study period of one year.

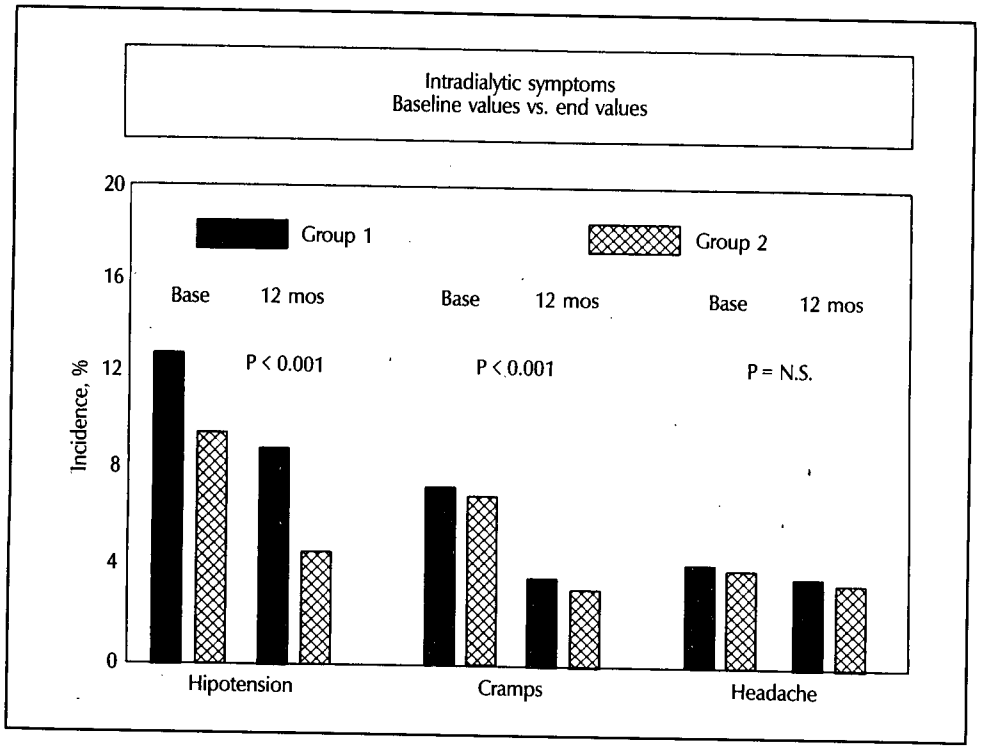

Fig. 2.—Comparison of the percentual incidence of some symptoms at the beginning of the study and after 12 months of short dialysis therapy.

Patient's blood chemistry displayed a stable behaviour over the year of observation (Table V). Hct and Hb showed a significant increase but three patients underwent Epo therapy during the study period. Figure 3 displays the beta-2-microglobulin levels in the two groups measured in blood samplew drawn predialysis at the end of the long interval. No changes occurred in both groups even though a wide variation was observed among individuals. Figure 4 reports the average values expressed in percentage of complications and intradialytic symptoms observed during the study. A remarkably low incidence of intradialytic symptomatology was observed in both groups. The slightly higher incidence of hypotension observed in group A could be related to the higher rate of net ultrafiltration recorded in this group as previously suggested by us[15]. Comparing the incidence of hypotension, cramps and headache in both groups between the first and the last trimester of the study we could observe a significant reduction of these symptoms in the last period of observation as displayed in figure 5. In Table VI the cardiovascular parame-

Table V

	Group A				Group B			
	Base	**4**	**8**	**12 mths.**	**Base**	**4**	**8**	**12 mths.**
Na	137 ± 2.0	138 ± 1.6	139 ± 1.9	138 ± 1.8	138.8 ± 4.1	137.6 ± 3	137.3 ± 5.3	136.5 ± 3.3
K	5.4 ± 0.5	5.6 ± 0.4	5.3 ± 0.5	5.4 ± 0.5	5.4 ± 0,6	5.4 ± 0.7	5.7 ± 0.6	5.3 ± 1.5
Cl	100 ± 4.1	99.1 ± 3.6	98 ± 4.5	100 ± 4.5	97.9 ± 2.2	102 ± 3,9	103.3 ± 4.9	98.6 ± 4.3
Ca	9.3 ± 1	8.9 ± 0.9	9,3 ± 1.1	9.2 ± 1.1	9.5 ± 1	9.6 ± 1.1	9.5 ± 0.9	9.5 ± 0.9
BUN	85.7 ± 15	90.9 ± 17	91.7 ± 17	92.4 ± 18	86.2 ± 13	92.5 ± 20	83.1 ± 14	87.2 ± 18
Creat.	13.5 ± 4	12.9 ± 3	12.7 ± 3	13.2 ± 4	12.1 ± 2.2	12.9 ± 4.1	12.3 ± 1.9	12.4 ± 2.6
Uric acid	8.6 ± 2.0	8.0 ± 2.1	7.6 ± 1.9	8.6 ± 2.0	7.9 ± 1.9	8.0 ± 1.3	8.2 ± 1.5	8.0 ± 1.6
Phospates	5.2 ± 0.7	5.0 ± 0.9	6.1 ± 1.0	5.2 ± 1.3	5.1 ± 1.1	6.0 ± 1.5	5.8 ± 1.0	5.5 ± 1.2
Tot. prot.	6.1 ± 0.8	6.0 ± 0.9	6.0 ± 0.8	5.9 ± 0.9	6.2 ± 1.2	6.4 ± 0.9	6.1 ± 0.9	6.0 ± 1.0
Albumin	2.5 ± 0.2	2.5 ± 0.3	2.46 ± 0.2	2.51 ± 0.1	2.47 ± 0.3	2.51 ± 0.2	2.63 ± 0.4	2.49 ± 0.4
Htc	22.4 ± 4.0	25.2 ± 5.0	26.5 ± 3.0	30.5 ± 4.0*	22.8 ± 5.1	23.3 ± 3.7	23.8 ± 3.4	24.6 ± 3.3**
Hb	7.6 ± 2.0	7.9 ± 1.5	8.6 ± 2.0	8.9 ± 2.1*	7.6 ± 1.7	7.8 ± 1.4	7.7 ± 1.1	8.2 ± 1.0**
pH	7.38 ± 0.06	7.40 ± 0,07	7.39 ± 0.08	7.40 ± 0.06	7,37 ± 0.02	7.35 ± 0.05	7.35 ± 0.03	7.36 ± 0.06
HCO_3	23.4 ± 3.1	24.0 ± 3.2	23.0 ± 2.8	24.1 ± 3.2	20.5 ± 3.2	19.7 ± 2.1	18.9 ± 2.1	20.1 ± 3.1
PTH	270 ± 130	285 ± 125	280 ± 146	300 ± 150	431 ± 140	320 ± 111	388 ± 131	350 ± 125
Alk. Ph.	81.1 ± 20	94.3 ± 12	86 ± 18	85.3 ± 22	85.2 ± 22	84.5 ± 18	89.6 ± 21	91 ± 36

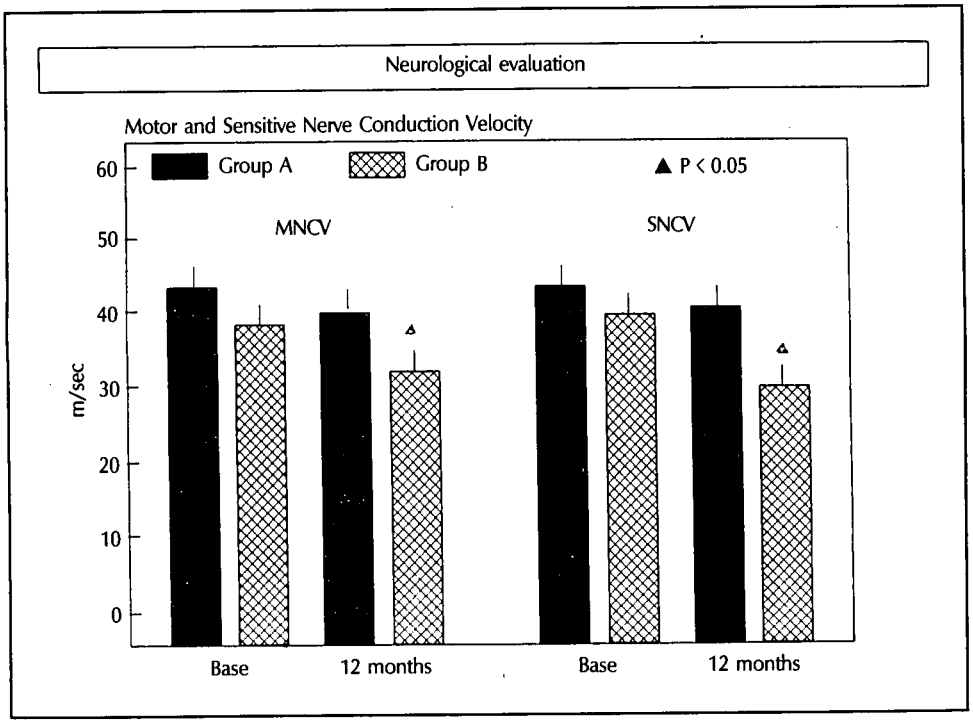

Fig. 3.—Neurological evaluation by motor and sensitive nerve conduction velocity. A significant improvement could be noted in group B.

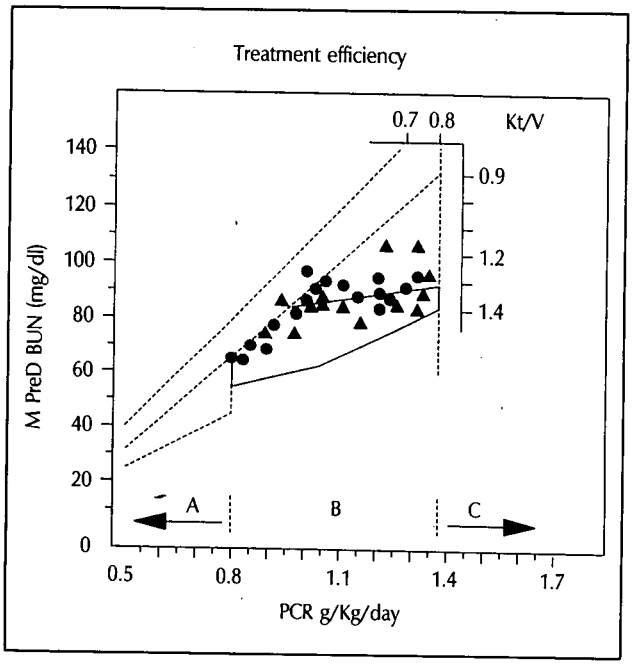

Fig. 4.—Treatment efficiency evaluation in each patient according to Gotch et al. (See reference 13).

Table VI. Cardiovascular evaluation.

	Base	12 m	Base	12 m
Aortic valve:				
L. atr.·diam.....	3.65	3.80	3.71	3.60
Left ventricle:				
Enddiast. diam..:	5.95	5.80	5.83	5.85
Endsyst. diam.....	3.47	3.50	3.60	3.58
Stroke vol.	85.0	83.1	88.1	86.0
Septum IVS.....				
Diast. thikness.....	1.21	1.24	1.28	1.26
Syst. thikness.....	1.68	1.71	1.59	1.64
Left ventr. function:				
Ejection fract.....	64.9	65.6	67.4	69.3

Group A (p = N.S.). Group B (p = N.S.).

ters investigated by echocardiography are reported in the two groups. No significant changes could be noted after 12 months of short dialysis treatment and this is especially important in the group B where the average blood flow was higher. In figure 6 the neurological evaluation carried out by a motor and sensitive nerve conduction velocity is reported in the two groups. It is important to note that no deterioration of the nerve conduction velocity took place in the study period while a slight improvement was noted in group B ($P < 0,05$). The same trend was present in group A but it was not statistically significant.

No technical complications occurred during the study period and the monitors utilized for ultrafiltrate and reinfusion fluid balance showed a remarkable reliability without special maintenance procedures.

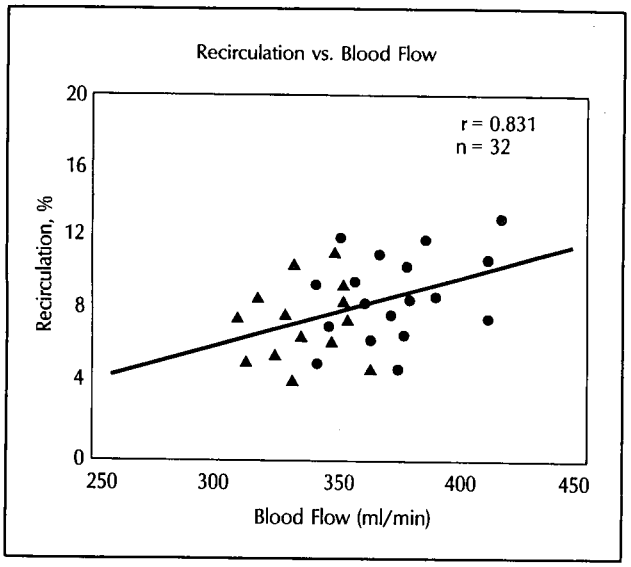

Fig. 5.—Average recirculation values in each patient in relation to the utilized blood flow.

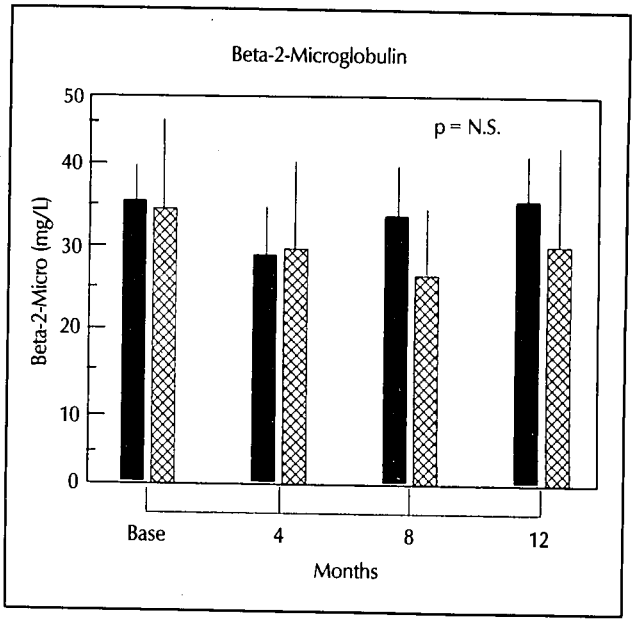

Fig. 6.—Beta-2-Microglobulin Plasma Levels in patients of both groups during different periods of the study.

Discussion

Several criticisms have been rised to the wide use of short highly efficient dialysis techniques. Most of them were related to the risks of underdialysis in the patients, to the difficulty in achieving the right dry body weight and finally to the potential risks linked to the use of high blood flows. On the other hand the increasing number of elderly patients undergoing chronic renal replacement therapy also arises some concerns about the feasibility of such efficient dialysis techniques in patients with poor compliance to fluid restriction and special diet. In this paper we wanted to test the feasibility of a relatively new form of therapy in a large number of patients with a parallel reduction of dialysis treatment time. To be able to proof the feasibility of higly efficient hemodiafiltration in unselected patients, we used the two chamber technique also called paired filtration dialysis. The treatment time was scheduled according to the patients's body weight, to their drinking habit and to their vascular access condition. In this way we could identify two groups that were both receiving a short dialysis treatment, but the reduction of treatment time was strictly personalized. Therefore the results are presented for the two groups but are not comparable eachother. In both groups paired filtration dialysis appeared to be a reliable form of renal replacement therapy. Convection and diffusion were obtained separately but in agreement to a precise dialytic prescription. No pyrogenic reactions were noted and this fact could probably be at least in part in relation to the absence of backfiltration in this form of therapy. Dialysis treatment time could be shortened as low as 150 minutes/session in a selected group of patients with smaller size and well functioning vascular access. On the other hand in a non selected group of patients with bigger size and less efficient A-V fistulas, the treatment time could also be reduced in the range of three hours/session. We therefore concluded that in the majority of patients paired filtration dialysis could represent a reliable form of short dialysis treatment. The efficiency in removing small solutes is adequate and the efficacy in removing larger molecules by convection is satisfactory. The whole sistem present biocompatible membranes and no risks of backfiltration are encountered. The correction of uremic acidosis is excellent and it can be modulated by modifying the composition of the replacement solution. Ultrafiltration rates are well tolerated and the clinical stability of the patient is good. The major draw backs of the method are represented by the cost of the two chamber device and the cost of the replacement solution even though there are no significant differences with other forms of hemodiafiltration.

Finaly, the method in our view might present a great potential for the future in the sense that the ultrafiltrate could provide an on-line sample of plasma water that could be continuously analyzed and might be used to operate a complex biofeedback on the dialysate composition, on the ultrafiltrate rate and therefore on the patient's clinical stability.

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