Start of renal replacement therapy in a spanish department

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SUMMARY

Background: *Early nephrological referral and planned start of dialysis are associated with better prognosis after the beginning of renal replacement therapy (RRT). The aim of our study was to analyse patient clinical and analytic characteristics at the time of initiating dialysis and to evaluate if morbimortality was affected by planned start.*

Patients and methods: *We performed a retrospective study of all patients commencing RRT in a Spanish Hospital of The National Health System over two years (2003-2004). A total of 117 patients (47 female and 70 male) were included. We carried out a retrospective analysis of the demographic characteristics, patients' clinical and analytic conditions at the time of starting dialysis and hospitalization days and mortality in six months after starting dialysis. Patients were classified as planned (P) or unplanned (NP), depending on whether the first dialysis was planned or an emergency.*

Results: *Sixty five patients (56.4%) started dialysis in a planned group while 52 (43.6%) were unplanned. In the former group, 83.1% of the patients had a vascular or peritoneal access available when starting RRT, whereas in the later group only the 3.8% had it. Planned dialysis initiation was associated with a high level of serum haemoglobin, haematocrit, calcium and albumin ($p < 0.001$), and a low level of serum urea, creatinine ($p < 0.001$) and phosphate ($p < 0.05$). More patients of the unplanned group were admitted at hospital at the initiation of dialysis (90.4% vs 6.1%) and during the first 6 months (48% vs 15.3%). The period of hospitalization was longer for the unplanned group (23.6 days vs 3 days) ($p < 0.001$). The 6-months-mortality was lower in the planned group (4.6% vs 11.5%), whitout statistical difference.*

Conclusions: *Planned dialysis initiation is associated with better clinical and metabolical conditions, greater probability of a vascular or peritoneal access availability and lower rate of hospitalization and mortality within 6 months after starting RRT.*

Key words: ***Chronic renal failure. Morbidity. Mortality. Vascular access. Planned start to dialysis.***

COMIENZO DE TRATAMIENTO RENAL SUSTITUTIVO EN LA PROVINCIA DE CÁCERES

Introducción: *La derivación precoz al nefrólogo y el inicio programado de diálisis se asocian a un mejor pronóstico tras el comienzo del tratamiento renal sus-*

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titutivo (TRS). El objetivo de nuestro estudio fue analizar las características clínicas y analíticas de los pacientes al comienzo de diálisis y valorar si el inicio programado influía en la morbi-mortalidad a los 6 meses.

Pacientes y métodos: *Estudio retrospectivo que incluye los 117 pacientes que iniciaron TRS en nuestra provincia en los años 2003-2004 (47 mujeres y 70 varones). Se revisaron las características demográficas, los datos clínicos y analíticos al inicio, los ingresos hospitalarios y la mortalidad a los 6 meses. Los pacientes se dividieron en programados (P) y no programados (NP) dependiendo si la primera diálisis se realizó en situación de urgencia (NP) o si pudo ser diferida en el tiempo más de 24 horas (P).*

Resultados: *Sesenta y cinco pacientes comenzaron TRS de forma programada (56,4%) y 52 de forma no programada (43,6%). Los pacientes P presentaban acceso vascular o peritoneal útil en un porcentaje mayor (83,1%* vs *3,8%). El inicio programado de diálisis se asoció a un nivel más elevado de hemoglobina, hematocrito, calcio y albúmina (p < 0,001), y a una tasa más baja de urea, creatinina (p < 0,001) y fósforo (p < 0,05). Un menor número de pacientes del grupo P requirieron ingreso al inicio de TRS (6,1%* vs *90,4%), y también entre el 2° y el 6° meses (15,3%* vs *48%). Los días de hospitalización fueron significativamente inferiores en el grupo programado (3* vs *23,6) (p < 0,001). Aunque no hubo diferencias estadísticamente significativas, la mortalidad a los 6 meses fue menor en el grupo programado (4,6%* vs *11,5%).*

Conclusiones: *El inicio programado de diálisis se asocia a una mejor situación clínico-metabólica, una mayor probabilidad de acceso útil y un menor número de hospitalizaciones y tasa de mortalidad en los 6 meses posteriores.*

Palabras clave: ***Insuficiencia renal. Inicio de diálisis. Acceso vascular. Hospitalización. Mortalidad.***

INTRODUCTION

Although there are many factors that have an influence on the prognosis of patients starting renal replacement therapy (RRT), the clinical status at the time of dialysis onset is considered one of the most important ones[1]. In this sense, there have been a number of publications that highlight the importance of early referral to the nephrologist and the benefits of appropriate pre-dialysis care[2-6]. This include not only measures aimed at slowing renal failure (RF) progression or treating cardiovascular risk factors, but also an adequate preparation of patients for the initiation of RRT, such as information on the different dialysis techniques and transplantation, the creation of a valid and functioning vascular or peritoneal access at the time of starting, and of psychological support allowing an initiation the least dramatic as possible.

In spite of all this, a high percentage of patients are referred late to Nephrology Departments, which prevents from a scheduled dialysis onset and creation of an adequate vascular or peritoneal access[4, 6-8]. Sometimes patients are even seen for the first time by a nephrologist at the time of starting RRT, which sometimes occurs for emergency conditions such as volume overload, severe laboratory impairments, or severe uremic symptoms.

We have considered it may interesting knowing the characteristics of patients starting on RRT in our province, both in a planned and in a non-planned manner. For this, we carried out a retrospective study aiming at analyzing the clinical and laboratory characteristics of patients at the beginning of RRT and assessing how programmed dialysis onset would have an influence on 6-months evolution with regards to mortality and morbidity.

PATIENTS AND METHODS

This is a retrospective study in which we analyzed all patients starting RRT in our province during the period 2003-2004. One hundred and seventeen patients were included. They were 47 (40.2%) women and 70 men (59.8%), with a mean age of

63.9 ± 15.2 years (range 18-89). The follow-up time since dialysis onset was 6 months or until death or renal transplantation occurred, if this happened before.

Patients were divided into two groups: Programmed (P) or non-programmed (NP). A patient was considered to be programmed (P) when dialysis was planned with time and non-programmed (NP) when the first dialysis was started for an emergency condition or was not appropriate to delay it for more than 24 hours. Emergency causes were the presence of severe uremic symptoms, volume overload, and severe analytical impairments.

The patients' origin was assessed, and they were divided into four groups: advanced chronic renal failure (ACRF) clinic, nephrology clinic, transplantation (if the patient was followed only at the transplantation center and at the specific renal transplantation clinic), and unknown (when initiation of RRT occurred within the following 30 days of the first visit to the nephrologist).

Demographic characteristics (age and gender), clinical data (etiology of renal failure, systolic and diastolic BP, presence of a valid vascular or peritoneal access at dialysis onset, type of RRT (peritoneal dialysis vs. hemodialysis), admission requirement at the beginning and total days of hospitalization required, and number of hospitalizations within the following 6 months and their cause (categorized in infectious, cardiovascular, and others), laboratory data at RRT onset (urea, creatinine, creatinine clearance calculated by the Cockcroft-Gault formula, calcium, phosphorus, iPTH, bicarbonate, iron, ferritin, transferrin saturation index, transferrin, hematocrit, hemoglobin, and albumin), and mortality within the 6 months following dialysis onset.

Statistical Analysis

Data were analyzed with the statistical package SPSS for Windows, version 11.0. Data are expressed as mean ± SD. Student's t test was used for quantitative data and the Chi-squared test for qualitative data. It was assumed that a statistical significance was reached with a p value < 0.05.

RESULTS

Between January 1st of 2003 and December 31st of 2004, 117 patients started on RRT at our province. They were 47 women and (40.2%) and 70 men (59.8%), with a mean age of 63.9 ± 15.2 years (range 18-89).

Out of the 117 patients, 65 (56.4%) started on RRT in a programmed manner, and 52 (43.6%) did so in a non-programmed manner. Mean age and gender distribution were similar in both groups (63.5 years in group P and 64.4 years in group NP; 41.5% of women in P, and 35% in NP, respectively).

The causes of NP initiation were presence of severe uremic symptoms in 19 patients (36.5%), volume overload in 14 (27%), and severe analytical impairments in 19 (36.5%).

Most of the patients of group P came from the ACRF clinic (83.1%), whereas patients in the NP group came from the nephrology clinic (30.8%) or did not have a previous nephrology follow-up (53.8%). Only two patients in group P were considered of unknown origin (3.1%) (table I).

The etiology of renal failure is shown in Table II for both groups. A higher frequency of glomerular diseases and polycystic renal disease is observed in group P, whereas systemic diseases predominated in group NP. Both diabetic nephropathy and vascular nephropathy had a similar incidence in both groups.

Hemodialysis was the initial technique in all patients in the NP group, whereas it accounted for 81.5% of the cases in the P group.

The group P patients received IV iron therapy, erythropoietic agents, phosphorus chelating agents, and calcium and vitamin D supplements in a higher percentage than patients in group NP, as well as protein restriction diets (0.6-0.7 g of proteins/kg/day).

When we revised the presence of a valid access at the beginning of RRT, we could observe that only 16.9% of the patients in group P were lacking an access versus 96.2% of the patients in group NP (table I). The average waiting time for creation of a vascular access was similar in both groups since at our Hospital vascular and peritoneal accesses are done by request ranking without taking into account whether the patient is included or not in RRT.

About the laboratory data, we found that group P had higher hemoglobin, hematocrit, calcium, and albumin levels, and lower levels of urea, creatinine, and phosphorus, all of them with an statistical significance ($p < 0.001$, but for phosphorus, $p < 0.05$) (table III).

About hospitalizations, we did not consider programmed hospitalizations for creation of the vascular or peritoneal access or for training of patients starting on PD therapy, since we considered they were elective admissions that depended on the distance of the patient's home to the hospital. As a general rule, at our Center patients are not admitted for creation of native AVF but they do so for prosthetic AVF, for 24 hours. For placement of peritoneal

Table I. Clinical and demographical characteristics of the patients at the beginning RRT

	Group P (N = 65)	Group NP (N= 52)	P
Age, years (mean ± SD)	63.5 ± 13.6	64.4 ± 17.2	NS
Sex: female	27 (41.5%)	20 (35%)	NS
male	38 (58.5%)	32 (65%)	
SBP (mmHg)	145.8 ± 24.3	156.1 ± 29.2	< 0.05
DBP (mmHg)	80 ± 14.8	77.1 ± 14.8	NS
Type of initial dialysis: HD	53 (81.5%)	52 (100%)	< 0.001
PD	12 (18.5%)	0 (0%)	< 0.001
Waiting time for performance of vasc/perit access (days)	28.1 ± 20.3	28.2 ± 18.8	NS
Useful access	54 (83.1%)	2 (3.8%)	< 0.001
Origin: ACRD clinic	54 (83.1%)	7 (13.5%)	< 0.001
nephrology clinic	6 (9.2%)	16 (30.8%)	< 0.001
trasplant	3 (4.6%)	1 (1.9%)	NS
unknown	2 (3.1%)	28 (53.8%)	< 0.001
Treatment with IV Fe	33 (50.8%)	7 (13.5%)	< 0.001
Treatment with erythropoietic agents	44 (67.7%)	8 (15.4%)	< 0.001
Mortality at 6 months	3 (4.6%)	6 (11.5%)	NS

SBP: systolic blood pressure; DBP: diastolic blood pressure; HD: hemodialysis; PD: peritoneal dialysis; ACRD: advanced chronic renal disease.

they stay at the hospital for 24-48 hours. Table IV shows the data corresponding to hospitalization. We observe that only 4 patients (6.1%) in group P required hospitalization at the beginning of RRT versus 47 (90.4%) in group NP. Upon reviewing admissions between months 2 and 6, 10 patients (15.3%) in group P had one admission, whereas 25 patients (48%) in group NP did so. The causes for hospitalization were mainly infectious, including vascular access-related infections (58.8% in group P and 37.8% in group NP). About hospitalization days, both at the beginning and after the second month, we found that programmed patients had significantly less hospitalization days than non-programmed patients (3.0 ± 8,7 *vs*. 23.6 ± 17.9), (p < 0.001).

Within 6 months of RRT onset, 3 patients (4.6%) in the group P and 6 patients (11.5%) in the group NP died, not reaching statistical significance. No patient was transplanted within this period.

Table II. Etiology ore renal failure

Etiology	Scheduled (%)	Non-scheduled (%)
DN	16 (24.6%)	16 (30.8%)
GN	16 (24.6%)	7 (13.5%)
UN	9 (13.6%)	5 (9.6%)
CTIN	6 (9.2%)	7 (13.5%)
VASC	6 (9.2%)	5 (9.6%)
PCRD	7 (10.8%)	1 (1.9%)
SYST	1 (1.5%)	8 (15.4%)
CGN	4 (6.1%)	2 (3.8%)
Others	0 (0%)	1 (1.9%)

DN: diabetic nephropathy; GN: glomerulonefritis; UN: unknown; CTIN: chronic interstitial nephropathies; VASC: vascular nephropathies; SYST: systemic disease; PQ: polycystic renal disease; CGN: chronic graft nephropathy.

Table III. Laboratory characteristics of the patients at the beginning of RRT

	Group P (N = 65)	Group NP (N = 52)	P
Urea (mg/dl)	185.4 ± 47.1	255.8 ± 82.5	< 0.001
Creatinine (mg/dl)	6.6 ± 1.6	8.6 ± 3.7	< 0.001
Creatinine clearance (ml/min)	10.6 ± 3.0	9.3 ± 4.4	NS
Calcium (mg/dl)	8.8 ± 0.9	8.0 ± 0.9	< 0.001
Phosphorus (mg/dl)	5.3 ± 1.3	6.0 ± 1.8	< 0.05
Bicarbonate (mEq/1)	22.3 ± 4.0	21.4 ± 6.4	NS
Albumin (g/dl)	3.4 ± 0.6	2.8 ± 0.6	< 0.001
Iron (mcg/1)	64.2 ± 32.0	63.4 ± 35.1	NS
Ferritin (ng/ml)	216.1 ± 189.6	348.0 ± 351.1	< 0.05
Transferrin saturation index (%)	24.3 ± 11.7	29.0 ± 16.5	NS
Hematocrit (%)	33.4 ± 5.0	28.1 ± 4.6	< 0.001
Hemoglobin (g/dl)	11.1 ± 1.6	9.3 ± 1.5	< 0.001
iPTH (pg/dl)	310.8 ± 242.2	305.2 ± 183.1	NS

Table IV. Data from hospitalization

	Group P (N = 65)	Group NP (N = 52)	P
Patients being admitted at the beginning of dialysis	4 (6.1%)	47 (90.4%)	< 0.001
Patients with hospitalization between 2-6 months	10 (15.3%)	25 (48%)	< 0.001
Num. of hospitalizations or infectious origin between months 2-6	10 (58.8%)	14 (37.8%)	NS
Días de hospitalización (total)	3.0 ± 8.7	23.6 ± 17.9	< 0.001

NS: not significant.

DISCUSSION

The incidence of patients starting on RRT varies among regions within our country. In the year 2002, the lower range corresponded to Aragon with 89 pm and the upper range to the Balearic Islands with 170 pmp[8]. Our data from 2003-2004 report an incidence of 142 pmp/year.

In spite of what has been previously mentioned about the benefits of early referral to the nephrologist, we found a high percentage of patients (43.6%) beginning RRT in a NP way. Although the criterion to define programmed dialysis was different from the one used by other authors, who consider it as the presence of a useful vascular or peritoneal access[3, 8, 10], the outcomes are virtually similar. Using this latter criterion, our incidence of programmed dialysis would be 47.8%.

Since renal failure is a progressive disease, such an elevated figure of NP dialysis onset is striking. Certainly, there are inevitable situations that may lead to emergency start of dialysis, such as non-recovered acute renal failure or an acute episode of a previous RF for several reasons. However, in almost one third of NP patients the etiology was diabetic nephropathy, a readily detectable pathology and than can be referred in early stages. In many cases, these patients, which often times are older and present associated comorbid risk factors, are disregarded by other specialists for RRT[11].

The RF etiology did not show important differences between both groups; similar to other studies[8, 10], most of the patients in group P had glomerulonephritis or diabetic nephropathy as the underlying disease, and there was a high incidence of diabetic patients and systemic diseases in the NP group.

About patients origin, only 2 patients in group P lacked a previous nephrology follow-up or it was shorter than one month, which occurred in more than half of the patients in the NP group. Most of the patients in group P were followed at the ACRF clinic.

Our results show similar mean age in both groups, although other authors find that NP patients tend to be older[8]. Although the mean age of the group was 63.3 years, 26.7% o the patients were 75 years and older. In the EDTA Registry of the year 2003, similar figures are found in most of the European Union countries[12], which highlight the old age of patients starting on RRT.

The dominant technique was HD, although we did not find significant differences between both groups. Whereas HD represented the bulk of NP dialyses, it only reached 81.5% in programmed dialyses. This highlights the lack of pre-dialysis education and possibility of making a choice about the preferred dialysis technique in the NP group, although patients were informed about RRT options once HD has been started, and even those referred by the ACRF clinic (7 patients, 13.5%) had already been informed (table I). The outcomes from the study carried out by the Spanish Group of Chronic Renal Disease highlighted that when patients received information about dialysis options, the percentage of those choosing PD was higher than when they were not informed[13]. Although no patient in the NP group started RRT with PD, within the following 6 months, 8 patients switched to PD after receiving information about it. Only one patient starting on HD was switched to HD during the follow-up due to sever pain during fluid infusions and drainage.

Only two patients in the NP group had a valid access at the time of starting dialysis, whereas this happened in 83% of the patients in the P group.

About the laboratory data, patients in the P group had better metabolic condition with lower urea and creatinine levels, with creatinine clearances closer to the current DOQI guidelines recommendations[14, 15]. Similarly, they had better calcium-phosphorus and anemia control, related with a higher percentage of patients receiving therapy with erythropoietic agents, phosphorus chelating agents, and vitamin D in this group. Another important observation is that serum albumin was significantly higher in group P, which reflects a better nutritional status in these patients. Metcalfe *et al.*[10] showed by logistic regression analysis that serum albumin was one of the factors with a significant effect on mortality within 90 days of dialysis onset, together with the way of starting dialysis and

comorbidities. This has been confirmed by other authors[16] who consider that albumin level is a marker of nutritional status and of chronic disease and inflammation, identifying those patients with higher mortality risk.

The initial hospitalization was significantly more frequent in the NP group, occurring in more than 90% of the patients, whereas hospitalization was required in 6% of the patients starting dialysis in a programmed way. Although hospitalizations during months 2-6 did not show such a marked difference, it also was statistically significant. Our hospitalization results are lower than those found by others[8], except for initial hospitalization in the NP group. We must stress that we did not observe any difference in hospitalizations due to infectious causes, including vascular access-related infections, considering that the rate of transient catheters was close to 100% in the NP group and below 20% in the P group.

We have not analyzed the estimated costs for both groups, but we just have to look at the outcomes relating to hospitalization days within the first 6 months (3 days in the P group vs. 23.6 days in the NP group) to realize on the important economic burden that represents starting dialysis in a non-programmed manner. In his analysis of cost of late referral to the nephrologist, Jungers[2] estimates that considering the direct and indirect costs derived from late referral, up to 10% of the expenditures originated by chronic dialysis could be saved by means of better pre-dialysis patient's management. He estimates that this figure could account for more than one billion dollars per year in the USA.

No patient was transplanted within the 6 months of follow-up, and 9 died. Although mortality was much higher in the NP group, the low number of patients precluded reaching statistical significance.

The revised data highlight the importance of starting dialysis in a programmed manner, from both a clinical and economic perspective. In order to start RRT in planned manner, patients need to be referred early to Nephrology Departments and received adequate pre-dialysis care that includes those measures aimed at slowing the progression of RF, controlling cardiovascular risk factors, appropriately managing anemia, preventing metabolic impairments, preserving a good quality of life, informing about the different dialysis techniques of RRT, and correctly preparing the patient for the technique hew/she may have chosen. Therefore, it is important to spare no efforts and resources to make primary care physicians and other specialists (mainly endocrinologists, cardiologists, and internists) aware of the convenience of early referral to the nephrologist and of the benefits of adequate pre-dialysis care if we want to improve the condition in which our patients start dialysis, and therefore the intermediate- and long-term prognosis.

In summary, programmed dialysis onset has been associated with better clinical and metabolic situation, better nutritional status, higher probability of a valid vascular or peritoneal access, and lower hospitalization and mortality rates within the 6 following months.

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