Assesment of adherence to therapeutic guidelines in patients with chronic renal disease (CRD)

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SUMMARY

Objective: *The present study was designed to determine the degree of fulfilment of the therapeutic objectives recommended in the clinical guidelines in patients with chronic kidney disease (CKD) in a nephrology outpatient clinic and the treatment that the patients were receiving to control these objectives.*

Methods: *A descriptive, cross-sectional study was performed in unselected patients with CKD (stages 1-5) who attended the nephrology outpatient clinic of the Hospital General Universitario Gregorio Marañón for follow up between 1st January and 1st april 2006.*

Results: *Data from 600 patients with a mean age of 62.8 years (56.5% male) were collected. The distribution of patients according to the stage (S) of CKD was as follows: S1: 11.5%, S2: 18%, S3: 36.7%, S4: 27.5% and S5: 6.3%. The target blood pressure (BP) < 130/80 mmHg was reached in 35.5%. The target diastolic blood pressure was controlled in 70%. However, systolic blood pressure increasing significantly with age and the degree of renal failure was controlled only in 42%. Total cholesterol was ≤ 175 mg/dl in 33.3% of patients, LDL-cholesterol was ≤ 100 mg/dl in 40.6% of patients (53.6% with statins) and HDL-cholesterol was ≥ 50 mg/l in 64.1% of patients. Triglyceride level was related to renal function (p=0.04). Most of the patients (94%) had hemoglobin (Hb) levels ≥ 11 g/dl, because of a significant increase in the percentage of patients treated with erythropoiesis-stimulating agents as the degree of renal function is reduced. Target levels of calcium-phosphorus (CaXP) product (< 55 mg^2/dl^2) were maintained in all the stages at the expense of decreased Ca and increased P in relation to the decrease in glomerular filtrate (p = 0.001). Target Ca (8.4-9.5 mg/dl) was reached in 85% of cases (2% of patients in S3, 37% of patients in S4 and 54% in S5 were receiving calcitriol). Phosphorus levels were adequate in 80% of patients, but target levels of parathyroid hormone (PTH) were maintained only in 28.6% of patients in S3 (35-70 pg/ml), 14% of patients in S4 (70-110 pg/ml) and 28% in S-5 (115-300 pg/ml).*

Conclusions: *Anemia is the best controlled factor of all the factors related to renal function. The degree of control of blood pressure (BP) has improved in recent years. However, it is still poor, particularly the control of systolic blood pressure getting worse with renal failure and age. It is difficult to reach the target PTH, despite ade-*

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quate levels of Ca and P. Cholesterol levels, unlike triglyceride levels, do not depend on renal function and require an increse in the use and/or doses of cholesterol-lowering drugs.

Key words: **Chronic kidney disease. Therapeutic guidelines. Hypertension. Anemia. Calcium-phosphorus metabolism. Dyslipemia.**

EVALUACIÓN DEL CUMPLIMIENTO DE LAS GUÍAS TERAPÉUTICAS EN LA PRÁCTICA CLÍNICA EN PACIENTES CON ENFERMEDAD RENAL CRÓNICA (ERC)

RESUMEN

Objetivo: El presente estudio se diseñó para determinar el grado de cumplimiento de los objetivos terapéuticos recomendados por las guías de actuación clínica en los pacientes con ERC en una consulta externa de nefrología y el tratamiento que recibían los pacientes para el control de los mismos.

Métodos: Se realizó un estudio descriptivo y transversal con pacientes no seleccionados con ERC (estadios 1-5) que acudieron a revisión a la consulta ambulatoria de nefrología del Hospital General Universitario Gregorio Marañón entre el 1 de enero y el 1 de abril del 2006.

Resultados: Se recogieron los datos de 600 pacientes con una edad media de 62,8 años (56,5% varones). La distribución de los pacientes según los estadios (E) de ERC fue: E1: 11,5%, E2: 18%, E3: 36,7%, E4: 27,5% y E5: 6,3%. El objetivo de presión arterial (PA) < 130/80 mmHg, se alcanzó en el 35,5%. La PA diastólica estaba controlada en el 70%. Sin embargo la PA sistólica que aumenta significativamente con la edad y con el grado de insuficiencia renal, únicamente se controló en el 42%. El 33,3% de los pacientes presentaba cifras de colesterol-total ≤ 175 mg/dl, el 40,6% de LDL-colesterol ≤ 100 mg/dl (53,6% con estatinas) y el 64,1% de HDL-colesterol ≥ 50 mg/l. El nivel de triglicéridos se relacionó con la función renal (p = 0,04). La mayor parte de los pacientes (94%) tenía cifras de Hb ≥ 11 g/dl, gracias a un aumento significativo en el % de pacientes tratados con agentes estimulantes de la eritropoyesis conforme disminuye el grado de función renal. El CaxP se mantuvo en cifras objetivo (< 55 mg^2/dl^2) en todos los estadios a expensas de disminución del Ca y aumento del P en relación con la disminución del filtrado glomerular (p = 0,001). El objetivo de Ca (entre 8,4-9,5 mg/dl) se alcanzaba en el 85% de los casos (2% de pacientes en E3, 37% de E4 y 54% de E5 recibían calcitriol). Los niveles de fósforo fueron adecuados en el 80%, pero sólo 28,6% de los pacientes en E-3 mantuvo cifras objetivo de PTH (35-70 pg/ml), 14% en E-4 (70-110 pg/ml) y 28% en E-5 (115-300 pg/ml).

Conclusiones: De los factores relacionados con la función renal la anemia es el mejor controlado. El grado de control de la PA aunque ha mejorado en los últimos años, sigue siendo pobre, sobre todo de la PA sistólica que empeora con la insuficiencia renal y la edad. Es difícil alcanzar el objetivo de PTH, a pesar de cifras adecuadas de Ca y P. Los niveles de colesterol, al contrario que los niveles de triglicéridos, no dependen de la función renal y requieren incrementar el uso y/o dosis de fármacos hipocolesterolemiantes.

Palabras clave: **Enfermedad renal crónica. Guías terapéuticas. Hipertensión. Anemia. Metabolismo calcio-fósforo. Dislipemia.**

INTRODUCTION

In recent years, several scientific societies have elaborated action guidelines in Nephrology aiming at improving the quality in the management of patients with chronic renal disease (CRD); among these guidelines there are those elaborated by the Spanish Society of Nephrology (SEN),[1] the European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA),[2] the National Kidney Foundation/Dialysis Outcomes Quality Initiative (K/DOQI).[3,4,5]

These guidelines comprise therapeutic goals based on scientific evidence and reflect the best situation that our patients should reach to prevent the development and progression of CRD, improve organic dysfunction and associated comorbidity.[6,7,8] However, in clinical practice it is not always possible to reach the recommended goals. On the other hand, there are currently very few data on the level of adherence to therapeutic goals targeted by clinical practice guidelines in non-dialyzed patients with CRD.

PATIENTS AND METHODS

Study design

An observational, cross-sectional, descriptive study was elaborated. Data on 600 non-selected consecutive patients were collected at the time they attended the nephrology outpatient clinic at the Gregorio Marañón University Hospital from January 1st to April 1st 2006.

Patients

Patients were male and women aged 17-90 years, with CRD at stages 1-5 and with previous follow-up for at least 6 months at the nephrology clinic. Patients managed with renal replacement therapy or renal transplantation were excluded, as well as those with acute or subacute renal failure.

Variables

General data were gathered for each patient: age, gender, weight, diabetes mellitus. Physical examination was carried out including measurement of arterial blood pressure (BP). BP was determined according to the recommendations of the *European Society of Hypertension*.[9] In brief, we undertook two BP measurements with the patient sitting after a 5-minutes resting period, with a calibrated mercury sphingomanometer or a validated oscilometric device. The reference value was the average of the two measurements.

The laboratory work-up included: complete blood count, serum creatinine, fasting serum glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, calcium, phosphorus, PTH, and urine analysis for quantification of proteins in 24-hour urine. Serum creatinine was determined using a Hitachi auto-analyzer and serum PTH by IRMA for intact PTH. Renal glomerular filtration rate was calculated by the abbreviated MDRD formula[10] and patients were classified depending on the glomerular filtration rate in the different stages established in K/DOQI guidelines.[11]

Pharmacological therapies received by each patient with erythropoiesis stimulating factors, iron supplements, anti-hypertensive drugs, renin-angiotensin system blockers, statins, phosphorus chelating agents or calcitriol were registered.

Objectives

The main goal of the study was to assess the level of adherence to therapeutic goals recommended in the clinical practice guidelines for CRD (in patients not submitted to renal replacement therapy) at a nephrology outpatient clinic.

The secondary objectives were:

- Clinical and demographic analysis of the CRD population attended at the nephrology clinic of the Health Care Area 1 of Madrid.
- Analysis of the current status of patients attending the nephrology clinic with regards to anemia, blood pressure, calcium-phosphorus metabolism/PTH, and lipids management according to the degree of CRD.
- Analysis of the pharmacological therapy received according to the level of control of the different clinical and analytical studied parameters and its adherence to the recommended objectives.
- Analysis of the degree of biochemical control in our patients for each of the studied items and treatment received at each CRD stage in order to identify the poorest controlled stages and trying to improve them in clinical practice by a better clinical intervention.

The following parameters were considered as optimal control according to the therapeutic intervention guidelines:

Table I. General characteristics of the patients

Cr	1.8 ± 1.14 mg/dL
eGFR	49 ± 30 mL/min
SBP	136 ± 22 mmHg
DBP	75 ± 11 mmHg
Rx with anti-HT medication	1.9 ± 1.2 drugs/pt.
ACEI/ARA-II	72% of the patients
Total cholesterol	196 ± 48 mg/dL
LDL-cholesterol	112 ± 37 mg/dL
HDL-cholesterol	57 ± 16 mg/dL
Triglycerides	131 ± 77 mg/dL
Rx with statins	50% of the patients
Hb	13.6 ± 1.7 g/dL
Ht	40.0 ± 51%
Rx whit ESF	16.8% of the patients
Rx with iron salts	16.7% of the patients
Ca	9.1 ± 0.5 mg/dL
P	3.5 ± 0.7 mg/dL
PTH	139.5 ± 166 pg/mL
Rx with P-chelating agents	6% of the patients
Rx with vitamin D	18.7% of the patients

- BP control:
  - Blood pressure at the clinic < 130/80 mm Hg or < 125/75 when proteinuria is > 1g/day.
- Dyslipidemia management:
  - HDL-cholesterol > 50 mg/dL.
  - LDL-cholesterol < 100 mg/dL.
  - Total cholesterol < 175 mg/dL
  - Triglycerides < 150 mg/dL
- Anemia management:
  - Hemoglobin > 11g/dL
  - Hematocrit > 33%
- Management of Ca-P metabolism
  - Calcium 8.4-9.5 mg/dL
  - Phosphorus 2.7-4.6 mg/dL (stages 1,2,3,4); 3.5-5.5 mg/dL (stage 5)
  - Ca × P product < 55
  - PTH 35-75 pg/mL (patients at stage 3); 70-110 pg/mL (patients at stage 4); 150-300 pg/mL (patients at stage 5)

Table II. Characteristics of the patients with adequately and poorly controlled blood pressure (BP)

	BP < 130/80 mmHg	BP < 130/80 mmHg	P (Odds ratio)
Prevalence [n.º (%)]	213 (35.5%)	387 (65.5%)	
Age (years)	51.3 ± 19.0	64.8 ± 14.8	< 0.001
Diabetes [n.º (%)]	57 (37.1%)	97 (62.9%)	< 0.001
Proteinuria (g/day)	0.10 ± 0.33	0.30 ± 0.68	0.004
Creatinine clearance (mL/min)	77.6 ± 33.4	44.3 ± 27.5	0.000
Systolic BP (mmHg)	123.7 ± 21.9	138.4 ± 22.2	0.001
Diastolic BP (mmHg)	74.8 ± 12.7	75.4 ± 11.2	0.714
Num. Anti-HT drugs	1.1 ± 0.8	2.2 ± 1.2	0.001
Total cholesterol (mg/dL)	198.1 ± 46.1	195.6 ± 48.1	0.523
LDL-cholesterol (mg/dL)	112.2 ± 38.7	111.3 ± 34.4	0.987
Hemoglobin (mg/dL)	14.3 ± 1.7	13.55 ± 1.5	0.001
PTH	75.4 ± 68.7	150.6 ± 178.2	0.001

Data analysis

Qualitative variables are expressed as distribution frequencies and quantitative variables as mean ± SD. When necessary, the chi-squared test or Fisher's exact test were used to compared the proportions of qualitative variables. The Student's t test and the variance analysis were used to compare the means of quantitative variables. A multifactorial logistic regression model was created using candidate prediction factors ($P < 0.05$) that were associated with the different analyzed parameters. All statistical tests were two-tailed and a p value < 0.05 was considered to be statistically significant. The SPSS statistical software, version 11.5 for Windows, was used for the statistical analysis.

RESULTS

General data

Of the 600 patients included in the study, 339 (56.5%) were men and 261 (43.5%) were women, with mean age 62.8 ± 16.2 years. It was surprising that the age range was wide, from 17 to 90 years. One hundred and fifty-four patients (25.7%) had diabetes mellitus and 64.5% hypertension (AHT). The

Table III. Independent risk factors for poor blood pressure (BP) control

Variables	B	SE	Exp (B)	95% CI	P
Age	0.002	0.011	1.022	1.000-1.044	0.005
Creatinine clearance	-0.020	0.006	0.980	0.968-0.992	0.001
Diabetes	-1.313	0.634	0.269	0.078-0.933	0.003

patients' distribution by CRD stages was as follows: stage 1: 69 (11.5%); stage 2: 108 (18%); stage 3: 220 (36.7%); stage 4: 165 (27.5%); and stage 5: 38 (6.3%).

Mean values for the studied parameters of studied patients are summarized in Table 1.

Blood pressure (BP) management

35.5% of the patients included into the study had BP < 130/80 mmHg. Systolic BP was < 130 mmHg in 42%, whereas diastolic BP < 80 mmHg was observed in 70% of the patients studied. Table 2 shows the comparison of patients' characteristics categorized into arterial BP < 130/80 or > 130/80 mmHg. Patients with uncontrolled BP were older, diabetics, with higher level of renal failure, higher proteinuria levels, and received a greater number of antihypertensive drugs. Patients with poorer BP control had lower Hb levels and higher PTH levels, which is in relation with the strong association existing between the increase in BP levels and the decrease in GFR. The variables independently associated with the lack of BP control upon carrying out the multifactorial analysis were glomerular filtration rate, DM, and age, as shown in Table 3. We observe that poor BP control in our pa-

tients is mainly due to poor control of systolic BP, which progressively and independently increases as patient's age increases. As shown in Table 4, as the patients' mean age increases, as well as SBP values as GFR decreases in the different CRD stages, the number of antihypertensive drugs necessary to achieve BP control also increases.

About BP control in patients with proteinuria > 1g/day, which accounted for 9% of all studied patients, only 17% achieved adequate BP control with BP values < 125/75. This poorer control is related with higher mean age (67 ± 3.4 years) and higher percentage of diabetic patients (33%), apart from more severe proteinuria, among patients with proteinuria > 1 g/day. Both variables, age and DM, as well as the increase in systolic BP, are independently associated in the multifactorial analysis, P < 0.005 as shown in Table 5.

Anemia management

Ninety-five percent of the patients studied were able to reach Hb levels > 11g/dL and Ht > 33% as recommended in the guidelines.

In spite of this good anemia management, even in advanced stages of CRD, a decrease in hemoglobin and hematocrit levels was observed in our patients as CRD progresses. That made necessary that requirements for therapy with erythropoiesis-stimulating factors (ESF) and with iron supplements were higher as glomerular filtration rate decreases in order to reach therapeutic goals. As shown in Table 6, as CRD progresses Hb levels decrease, the percentage of patients with anemia (Hb < 11 mg/dL) increases, which results in an increase in the percentage of patients treated with ESF and iron supplements. In patients receiving ESF, this therapy achieved that 80% of the patients had Hb levels > 11g/dL and 60% above 12 g/dL. As

Table IV. BP management, antihypertensive therapy, and mean age by CRD stage

	Mean SBP (mmHg)	% SBP < 130 mmHg	Mean DBP (mmHg)	% DBP < 80 mmHg	% BP < 130/80 mmHg	Age (years)	Num. of drugs/patient
Stage 1	125 ± 20	62%	76 ± 11	63%	53%	41 ± 15	0.9 ± 1.2
Stage 2	131 ± 20	52%	77 ± 10	66%	44%	55 ± 16	1.3 ± 1.1
Stage 3	138 ± 23	39%	75 ± 12	70%	32%	68 ± 2	2.1 ± 1.2
Stage 4	139 ± 22	34%	72 ± 9	81%	28%	70 ± 11	2.4 ± 1.1
Stage 5	142 ± 20	29%	76 ± 11	70%	27%	63 ± 14	2.5 ± 1.1
All patients	136 ± 22	42%	75 ± 11	70%	35%	62 ± 16	1.9 ± 1.2

Table V. Independent risk factors for having proteinuria > 1 g/day

Variables	B	SE	95% CI	P
Age	-0.002	0.011	0.000-0.002	0.003
Systolic blood pressure	0.001	0.000	0.576-0.887	0.000
Diabetes	0.001	0.009	0.044-0.080	0.001

Fig. 1.—¡¡¡¡FALTA TRADUCCION PIE DE FIGURA!!!.

shown in Table 7, patients with the highest degree of anemia were diabetics, women, and thus, those receiving more therapy with ESF and iron supplements. These variables were independently related with the risk for anemia. Upon carrying out the multifactorial analysis, we observed that GFR was not independently associated with the risk for having anemia in spite of the fact that Hb levels decrease occurs as CRD progresses. This fact is related with early correction of anemia with ESF from early CRD stages, which conditions that a high percentage of patients do not have anemia, even at advanced stages.

Management of lipid metabolism

From our sample, 33% of the patients had total cholesterol levels < 175 mg/dL, 40% had LDL-cholesterol < 100 mg/dL and 64% HDL-cholesterol > 50 mg/dL. Only 47% of the patients on therapy with statins achieved LDL-cholesterol < 100 mg/dL, as recommended in the guidelines. Levels of total cholesterol, HDL-cholesterol and LDL-cholesterol were not associated with renal function, whereas triglycerides levels did independently related with renal function level increasing as GFR decreased (p < 0.001). Table 8 shows the data on lipid management at different CRD stages and therapy with statins; we observe that the percentage of patients with adequately controlled total cholesterol and
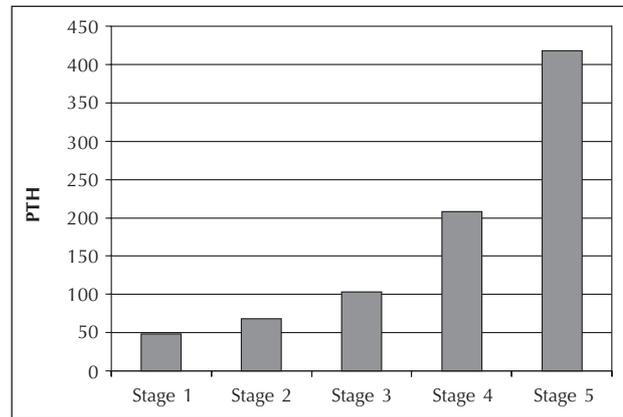
LDL-cholesterol, as well as their corresponding levels, did not differ between the different stages of CRD, whereas we did observe a progressive increase in triglycerides levels with decreasing GFR.

We observe a increase in the percentage of patients receiving therapy with statins as GFR decreases, which was significant with the multivariate analysis, likely related with more intensive therapy and a more stringent control of patients at more advanced CRD stages.

Management of Ca-P metabolism/PTH

Almost all patients from our sample (99.5%) had a Ca × P < 55. This control is achieved at the expense of a progressive decrease in Ca levels and an increase in P levels as CRF decreases. Seventy-three percent of the patients had Ca levels 8.4-9.5 mg/dL. The percentage of patients with adequately managed Ca is similar at all CRD stages, in spite of the decrease in Ca levels at more advanced CRD stages due to the increase in therapy with calcium supplements and calcitriol.

Table VI. Anemia control by CRD stage

	Ht (%)	Hb (g/dL)	Hb < 11 g/dL % pts	Rx ESF % pts	Rx FE salts % pts
Stage 1	41.6 ± 4.3	14.3 ± 1.4	2	0	1.5%
Stage 2	43 ± 4.2	114.7 ± 1.5	1.8	0	1.8%
Stage 3	40.2 ± 5.4	13.7 ± 1.8	5	12.7	11%
Stage 4	38 ± 4.5	12.9 ± 1.48	7.9	30	29%
Stage 5	36.6 ± 4.3	12.4 ± 1.5	15.8	63	59%

Table VII. Independent risk factors for having anemia

Variables	B	SE	Exp (B)	95% CI	P
Gender (female)	1.575	0.549	4.830	1.861-12.532	0.001
Diabetes	-1.280	0.432	0.278	0.119-0.648	0.003
Rx ESF	1.103	0.549	3.014	1.027-8.843	0.004
Rx Fe salts	1.202	0.405	3.328	1.503-7.365	0.003

Eighty-percent percent of the patients reached P levels recommended in the guidelines (P: 2.7-4.6 mg/dL at stages 3 and 4; P: 3.5-5.5 mg/dL at stage 5), although this percentage of patients decreases as GFR increases and P and PTH levels increase. About PTH control, which increases as GFR decreases, we observe that the percentage of patients with PTH within levels recommended in the guidelines decreases as CRD progresses (stage 3: 29% of the patients with controlled PTH; stage 4: 14.5%; and stage 5: 13%) (Figure 1), making necessary more therapy with phosphorus chelating agents, calcium supplements and vitamin D (calcitriol) at more advanced CRD stages in order to reach adequate control (Table 9).

Ca, P, and PTH levels were independently related with renal function degree upon carrying out the multivariate analysis, as well as therapy with p.o. calcium supplements, calcitriol, and phosphorus chelating agents.

DISCUSSION

BP control is a essential factor for reducing the cardiovascular risk and halting or delaying progression of renal disease in patients with CRD.[12] Proper BP management still is a difficult challenge in these patients.[13] In our sample, 35% of the patients achieved BP goals set at BP < 130/80 in the guidelines. In spite of this deficient control currently, BP control has been improved in recent years. This improvement may be evident if we compare these current results with those obtained in a study with similar characteristics done at our clinic in the year 2003, on a sample of 1004 patients. In that study, only 24% of the patients achieved BP < 130/85.[14] The better current BP control is related with intensification of anti-hypertensive therapy since, as compared with the first study, the current percentage of patients with 3 or more anti-hypertensive therapy has significantly increased and currently no single hypertensive patient is not receiving anti-hypertensive therapy. The lack of BP control was related with advanced age, the presence of DM, and poorer renal function, i.e., a greater cardiovascular risk.[15] Insufficient BP control was mainly due to failing of controlling systolic BP, which was significantly related with patients' age, increasing with progressing CRD stages. Patients with more advanced CRD stages received a higher number of antihypertensive therapy, although this did not achieve to improve BP control. In conclusion, although we have improved BP management in recent years by intensifying therapy, BP management still is one of the main challenges in clinical practice, particularly in older patients and higher level of CRD.

Among all factors related with CRD, anemia is the one best currently managed. Ninety-five percent of the patients had HB levels > 11 g/dL. Patients with higher level of anemia were women, diabetics, and patients with poorer renal function. In spite of a progressive fall of Hb levels as renal function deteriorates, we achieve good anemia management even at more advanced CRD stages thanks to the use of ESF, which increases as GFR falls. In conclusion, in recent years we have improved anemia management in CRD

Table VIII. Levels of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides by CRD stage. Statins therapy

Stages	Total cholesterol (mg/dL)	Total cholesterol % < 175 mg/dL	LDL-Chol. (mg/dL)	LDL-Chol. % < 100 mg/dL	TG (mg/dL)	Age (years)	% Rx Statins
Stage 1	196 ± 41	30.9%	113 ± 28	41%	58 ± 13	118 ± 64	35
Stage 2	202 ± 38	25.2%	120 ± 31	30%	58 ± 18	125 ± 62	32
Stage 3	193 ± 56	38.4%	108 ± 43	47%	57 ± 17	132 ± 91	56
Stage 4	191 ± 41	34.5%	109 ± 34	45%	55 ± 15	132 ± 66	60
Stage 5	207 ± 53	31.6%	120 ± 43	41%	55 ± 12	157 ± 81	60

Table IX. Levels of calcium, phosphorus, and PTH by CRD stage and therapy with oral calcium and calcitriol

	Ca (mg/dL)	% Ca control	P (mg/dL)	% P control	Ca p.o. % of treated pts	Calcitriol % of treated pts	% PTH control
Stage 1	9.1 ± 0.5		3.3 ± 0.46				
Stage 2	9.3 ± 3.2		3.2 ± 0.49				
Stage 3	9.1 ± 0.5	71%	3.3 ± 0.57	89%	5.5%	2%	28.8%
Stage 4	9.1 ± 0.5	74%	3.7 ± 0.7	80%	8%	37%	14.5%
Stage 5	8.7 ± 0.7	71%	4.8 ± 0.7	74%	19%	45%	13%

patients as therapy with ESF becomes more universal, achieving good control even at more advanced stages of CRD.[16] This good anemia management achieved is important not only to improve the clinical condition of our patients but also to slow CRD progression.[17]

About lipid metabolism management, it is poorly managed for all total cholesterol, HDL- and LDL-cholesterol levels, and at all levels of CRD, in spite of therapy with statins. Levels of total cholesterol, HDL- and LDL-cholesterol were not related with CRF, presenting similar levels at all CRD stages. However, triglycerides do significantly increase as renal failure progresses, being independently associated with the multifactorial analysis.

Therapy with statins significantly and independently increases as GFR decreases, and this does not seem to be related with LDL-cholesterol levels (which did not vary at different CRD stages) but with a more stringent management of all cardiovascular risk factors associated with CRD and with a more intensive follow-up with a higher number of clinical visits in those patients with more advanced CRD stages.

In spite of statins therapy, almost 50% of treated patients did not achieved LDL-cholesterol levels < 100 mg/dL; so that we believe that the statins use should be increased in these patients to achieve better lipid control and decrease their high cardiovascular risk.[18]

About management of Ca-P metabolism/PTH, we observe, as expected, that Ca, P, and PTH levels are independently related with GFR, as well as therapy with calcitriol and phosphorus chelating agents, which increases as CRD progresses. In spite of the fact that almost patients in our sample had Ca × P < 55 mg/dL^2, control of PTH levels was very poor, particularly at more advanced CRD stages. It is likely that PTH management will improve in the future with the use of new drugs acting on PTH without inducing hypercalcemia, by contrast with what happens with calcium-mimetic agents. There are currently several on-

going studies on the effect of these drugs on CRD patients. Similarly, it is expected that the update of the SEN and K/DOQI guidelines in relation with bone and mineral metabolism impairments in chronic renal disease will modify the goals for PTH making them more suitable to clinical reality and will be able to include the recommendations on the indications for therapy with calcium-mimetic agents in non-dialysis treated patients.

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