Evaluation of a pre-dialysis program in a renal unit of the city of Manizales, Colombia

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Abstract

Introduction: There is an increasing incidence and prevalence of patients with chronic kidney disease requiring replacement therapy, with poor outcomes and a high cost. Pre-dialysis programs allow the delay in the evolution of renal disease and reduction of cardiovascular events.

Objective: To assess the benefit of a pre-dialysis program in patients with Stage IV CKD, assisted at RTS renal unit in Manizales, Colombia.

Materials and methods: Retrospective cohort study. It was a complete database of clinical and paraclinical variables of the selected patients from the year of admission for three years. Statistical analysis was made with SPSS 12.0 software. Measures of central tendency (mean), of position (percentiles) and of dispersion (standard deviation, range) were used for the variables of a quantitative nature. The proportions for the variables of a qualitative nature were calculated.

Results: Control of systolic and diastolic blood pressure in the 3 and 2 years of monitoring, respectively, was statistically significant. Significance was observed during the monitoring of ferritin in the first and second years. In addition, there was a stable control of hemoglobin during the period of observation with minimal need for erythropoietin (23.07%). No patient initiated dialysis during the monitoring period.

Conclusion: A pre-dialysis program ensures greater adherence and control of targets in clinical and paraclinical variables in patients with chronic kidney disease.

Key words: Pre-dialysis, renal unit, chronic kidney disease, monitoring, Manizales, dialysis (MeSHsource).

Seguimiento de un programa de prediálisis en una unidad renal de la ciudad de Manizales

Resumen

Introducción: Existe una creciente incidencia y prevalencia de pacientes con enfermedad renal crónica que requieren terapia de reemplazo, con pobres resultados y alto costo. Los programas de prediálisis permiten retardar la progresión de la enfermedad renal y la reducción de eventos cardiovasculares.

Objetivo: Valorar el beneficio de un programa de prediálisis en pacientes con enfermedad renal crónica estadio IV, atendidos en la ciudad de Manizales.
Materiales y métodos: Estudio de cohorte retrospectivo. Se hizo una base de datos completa de variables clínicas y paraclínicas, de los pacientes seleccionados desde el año de ingreso, durante tres años. El análisis estadístico se hizo con el programa SPSS 12. Se utilizaron medidas de tendencia central (promedio), de posición (percentiles) y de dispersión (desviación estándar, rango) para las variables de naturaleza cuantitativa. Se calcularon las proporciones para las variables cualitativas.

Resultados: El control de la presión arterial sistólica y diastólica en los 3 y 2 años de control, respectivamente, fue estadísticamente significativo. Se encontró significancia en el control de la ferritina en el primero y segundo año. Se pudo observar un control estable de hemoglobina durante el período de observación con mínima necesidad de eritropoyetina (23,07%). Ningún paciente, en el tiempo de seguimiento, ingresó a diálisis.

Conclusión: Un programa de prediálisis asegura mayor adherencia y control de metas en variables clínicas y de laboratorio, en pacientes con enfermedad renal crónica.

Palabras clave: Prediálisis, unidad renal, enfermedad renal crónica, seguimiento, Manizales, diálisis (fuente DeCS).

Introduction

Chronic kidney disease (CKD) is a global public health problem. Only in the USA, 283,000 patients were on dialysis in 1996, and in 2010 figures recorded 650,000. The prevalence of CKD is rising, with the increased incidence of obesity, diabetes and arterial hypertension. Primary care physicians do not recognize CKD, and around 66% of them are unaware of the clinical practice guidelines (KDOQI). CKD progression and its associated morbidity and mortality can be reduced with optimal care. Late detection and treatment contribute to poor results. Latin American Nephrology and Hypertension Society (SLANH) has proposed a New Renal Health Model in our countries, which includes strategies of early referral and prevention of the progression of kidney disease. Adverse results from CKD can be prevented or delayed through interventions during earlier stages of the disease, such as the pre-dialysis program. This program’s objectives are defined and relate to the delay of the progression of CKD with adequate treatments of the different pathologies causing the disease, e.g. diabetes mellitus and arterial hypertension, to the prevention of uremia-related complications and to improve the quality of life of the patient.

The purpose of this paper is to determine whether the application of a protocol for controlling progression factors of CKD may bring benefit in the long term to the intervened patients.

Material and methods

Retrospective cohort study. Upon informed consent, the inclusion of patients in the pre-dialysis program was made from a renal unit in Manizales (Caldas/Colombia) which has a teaching-assistance agreement with Universidad de Caldas. Data which was averaged each year, and of over three consecutive years, were collected from the year of admission of each patient who met the inclusion criteria, for the analysis of qualitative and quantitative variables.

Inclusion criteria:
• Diagnosis of stage IV CKD (GFR 15-30 ml/minute).
• Record in the database of the renal unit.
• Stay of at least 3 consecutive years from admission to the program.

Exclusion criteria:
• Attrition during monitoring.
• Non-acceptance of informed consent.
• Patients diagnosed with ischemic nephropathy whose renal function improved after discontinuation of nephrotoxic drugs.

The statistical analysis was performed using SPSS 12.0, licensed for use at Universidad de Caldas.
Measures of central tendency (mean), of position (percentiles) and of dispersion (standard deviation, range) for variables of quantitative nature, and proportions were calculated for qualitative variables. The bivariate analysis was performed using the statistical software Epi-Info.

**Results**

An instrument of data collection was developed, and it allowed to describe the main clinical and paraclinical variables during the three years of monitoring (Table 1). 26 patients met the inclusion criteria.

Control of systolic blood pressure in the three years of monitoring, and of diastolic blood pressure in the 2 years of monitoring, was statistically significant. Significance was observed during the monitoring of ferritin in the first two years. In addition, there was a stable control of hemoglobin (Hb) during the observation period. Control of intact parathyroid hormone (iPTH) between the first and second year was statistically significant, maintaining levels under 110 pg/ml. Phosphorus levels remained normal during the three years of monitoring and uncorrected total calcium normalized on the third year of monitoring. Stable fasting blood glucose was observed during the three years of monitoring with averages under 100 mg/dl. At this time, glycated hemoglobin was not recurrent because of the administrative procedures of the different health entities, and the admission was irregular for different patients, hence this data was eventually excluded. Even without a statistical significance, the lipid profile remained stable with a decrease of 20 mg/dl, approximately, in total cholesterol levels, and a proximity to target LDL, triglycerides increased in non-significant levels and HDL decreased by 6 mg/dl during the three years, without greater statistical or clinical impact.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>p 1-2</th>
<th>p 1-3</th>
<th>p 2-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS</td>
<td>149.846,23.255</td>
<td>133.769,17.025</td>
<td>134.923,26.785</td>
<td>0.0064</td>
<td>0.0368</td>
<td>0.8537</td>
</tr>
<tr>
<td>PAD</td>
<td>80.154,13.034</td>
<td>73.808,8.755</td>
<td>73.385,14.765</td>
<td>0.0445</td>
<td>0.0858</td>
<td>0.9005</td>
</tr>
<tr>
<td>BUN</td>
<td>43.038,18.008</td>
<td>45.296,19.608</td>
<td>44.115,20.204</td>
<td>0.6673</td>
<td>0.8400</td>
<td>0.8315</td>
</tr>
<tr>
<td>Cr</td>
<td>2.346,0.816</td>
<td>2.285,0.760</td>
<td>2.292,0.646</td>
<td>0.7814</td>
<td>0.7924</td>
<td>0.9716</td>
</tr>
<tr>
<td>TFG</td>
<td>24.231,7.056</td>
<td>24.4,0.69</td>
<td>23.731,3.884</td>
<td>0.8856</td>
<td>0.7529</td>
<td>0.8084</td>
</tr>
<tr>
<td>Hb</td>
<td>12.454,1.861</td>
<td>12.250,1.830</td>
<td>13.123,1.422</td>
<td>0.6919</td>
<td>0.1515</td>
<td>0.0605</td>
</tr>
<tr>
<td>Ferritin</td>
<td>150.423,113.74</td>
<td>270.885,196.80</td>
<td>199.008,124.23</td>
<td>0.0094</td>
<td>0.1476</td>
<td>0.1216</td>
</tr>
<tr>
<td>Potassium</td>
<td>90.920,25.098</td>
<td>98.385,33.694</td>
<td>96.538,27.249</td>
<td>0.3693</td>
<td>0.4430</td>
<td>0.8288</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>4.638,0.543</td>
<td>4.612,0.630</td>
<td>4.681,0.583</td>
<td>0.8740</td>
<td>0.7843</td>
<td>0.6836</td>
</tr>
<tr>
<td>Calcium</td>
<td>7.535,3.969</td>
<td>7.961,3.388</td>
<td>8.962,2.891</td>
<td>0.6975</td>
<td>0.1447</td>
<td>0.2972</td>
</tr>
<tr>
<td>iPTH</td>
<td>170.038,183.83</td>
<td>106.115,68.111</td>
<td>109.308,64.858</td>
<td>0.0368</td>
<td>0.1185</td>
<td>0.8633</td>
</tr>
<tr>
<td>Uric acid</td>
<td>6.058,1.852</td>
<td>5.973,1.360</td>
<td>6.604,1.215</td>
<td>0.8511</td>
<td>0.2146</td>
<td>0.0838</td>
</tr>
<tr>
<td>TC</td>
<td>201.423,57.016</td>
<td>187.26,195</td>
<td>189.808,43.584</td>
<td>0.2467</td>
<td>0.4131</td>
<td>0.7794</td>
</tr>
<tr>
<td>LDL</td>
<td>115.423,56.653</td>
<td>98.846,28.912</td>
<td>107.538,35.908</td>
<td>0.1899</td>
<td>0.5516</td>
<td>0.3410</td>
</tr>
<tr>
<td>HDL</td>
<td>56.885,30.464</td>
<td>54.423,22.341</td>
<td>49.192,21.615</td>
<td>0.7410</td>
<td>0.2987</td>
<td>0.3950</td>
</tr>
<tr>
<td>TGD</td>
<td>166.731,63.866</td>
<td>176.769,66.995</td>
<td>169.692,85.435</td>
<td>0.5827</td>
<td>0.8880</td>
<td>0.7410</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.630,0.409</td>
<td>3.608,0.350</td>
<td>3.788,0.432</td>
<td>0.8358</td>
<td>0.1817</td>
<td>0.1050</td>
</tr>
</tbody>
</table>
From the total of the 26 patients analyzed, who met the inclusion criteria, the highest prevalence was for arterial hypertension (46.15%) as a cause of CKD, followed by diabetes mellitus (34.61%) and obstructive uropathy (19.23%), with a higher frequency in males (53.8%) with a mean age of 74.1.

The highest comorbidity was arterial hypertension in 96.2% of patients, followed by diabetes mellitus in 30.8% and, in order of frequency: benign prostatic hypertrophy in 23.1% of patients, hyperlipidemia in 19.2%, smoking in 15.4% and hyperuricemia in 3.8%.

34.2% of patients had or were initiated on angiotensin converting enzyme inhibitors or angiotensin II receptor antagonist, 88% of patients had loop diuretic, 61.53% required allopurinol and 23.07% received erythropoietin (EPO) during monitoring.

Regarding proteinuria, it was present in 19.2% of patients in the first year, and in the second and third year of monitoring it was in 3.8% and 11.5%, respectively (Table 2).

Below are the figures showing the overall GFR, the group of patients with CKD with a high blood pressure cause, diabetic nephropathy and obstructive cause (Figures 1-4).

The GFR mean in the starting year of the pre-dialysis program was 24ml/min, it was stable in the second year, and for the third year it had a lower than expected decline, 1 ml/min/year.

### Table 2.

<table>
<thead>
<tr>
<th>Proteinuria in the three years of monitoring of the total of patients</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>19.2%</td>
<td>3.8%</td>
<td>11.5%</td>
</tr>
<tr>
<td>NO</td>
<td>80.8%</td>
<td>96.2%</td>
<td>88.5%</td>
</tr>
</tbody>
</table>

### Discussion

The risk of progression of CKD is high in patients with poor glycemic and blood pressure control, and high levels of proteinuria. Early detection of CKD,
Figure 2.
Evolution of CKD in patients with hypertensive nephrosclerosis.

Figure 3.
changes in lifestyle, including smoking cessation, weight loss, a healthy diet and control of the modifiable risk factors may slow the progression of CKD and of the associated cardiovascular disease.3

A late referral to the nephrologist (less than 3 months before the start of dialysis) can cause anemia, mineral and bone disorder, dislipoproteinemia and malnutrition in the patient with diabetic or hypertensive nephropathy; 70% of patients belatedly referred to the nephrologist suffer more serious complications. A case-control study showed that patients with late referral to nephrology and to the pre-dialysis group had higher acidosis, hypocalcemia, hyperphosphatemia, anemia, fluid overload and hypertension, than the patients who were referred early.

Treatment of arterial hypertension in pre-dialysis stage seeks to reduce the progression of CKD and morbidity and mortality. In the study group, control of systolic blood pressure during the 3 years and of diastolic blood pressure during the 2 years was statistically significant. It is known that even a moderate pressure drop represents reduction in the risk of progression of CKD. High blood pressure is an important independent predictor of the decline of renal function in the general population.5

There are several guidelines that lead us towards a therapeutic target in the treatment of hypertension. The Eighth Joint National Committee (JNC 8)6 proposes a value under 140/90 for patients with CKD, regardless of age. KDIGO guidelines of 20137 also recommend that value, but only for normoalbuminuric (A1) patients, and for microalbuminuric (A2) or macroalbuminuric (A3) patients a target pressure of less than 130/80 is recommended. Australian recent guideline (KHA-CARI) also supports the latter recommendations8. The above recommendation is not based on evidence for pre-dialysis patients. Therefore, the target blood pressure beneficial for this population5 has been evaluated in the study group PREPARE-1 (The PRE dialysis PAatient REcord-1). 89% of patients in stages IV-V did not reach target blood pressure levels, despite 92% of them were treated with antihypertensive drugs. High levels of systolic and diastolic blood pressure were associated with rapid progression of CKD. Therefore, every 10 mmHg of increase is associated, respectively, with 1.09 and 1.16 of increase in the risk of entering renal replacement therapy5. Glomerular hypertension induced by arterial thickening and protein-induced hyperfiltration is an explanation for the association of arterial hypertension with chronic renal failure9.

Figure 4.
Evolution of CKD in patients with obstructive cause.

Obstructive cause

<table>
<thead>
<tr>
<th>GFR ml/min</th>
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<tbody>
<tr>
<td>18</td>
</tr>
<tr>
<td>19</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>21</td>
</tr>
<tr>
<td>22</td>
</tr>
<tr>
<td>23</td>
</tr>
</tbody>
</table>

1 Series 1

1 2 3
In the present study, we found significance during the monitoring of ferritin in the first two years. To date, there is no certainty about the value of serum ferritin recommended in patients with CKD stage IV. In dialysis patients, values over 150 mg/dl are accepted. A stable control of Hb was observed during monitoring with minimal need for EPO in 23.07%. Hb normal concentration protects against deterioration of renal function (Reno-protection). The decrease of Hb rate is a known factor of renal fibrosis. In turn, CKD causes anemia of multifactorial etiology: a decrease on EPO secretion by endothelial cells of peritubular capillaries and differentiated tubule-interstitial fibroblasts, iron deficiency, intravascular hemolysis, reduced erythrocytes life span, a decrease on medullary erythropoietic activity. EPO, by itself, exerts a renoprotective role with its antioxidant and cardioprotective effect, by improving bioavailability of nitric oxide, which brings its therapeutic effect beyond anemia correction. EPO decreases tubule-interstitial injury with the inhibition of inflammation, interstitial fibrosis and tubular apoptosis. Therefore, Nobuharu Fujiwara’s study concludes how recombinant EPO may be effective in reducing renal damage, atherosclerosis and oxidative stress in anemic patients in pre-dialysis.

Monitoring of PTHi between the first and second year was statistically significant. It remained stable in the second and third year of monitoring, from what can be inferred that it delayed the risk of secondary complications of CKD. Skeletal disorders are frequent in the course of CKD, and are caused by disorders of calcium-phosphorus metabolism and by the existence of hyperparathyroidism. Hyperphosphatemia contributes to an abnormal bone metabolism and to cardiovascular calcification, which are components of the syndrome of mineral and bone disorders associated with CKD. In vitro studies show that phosphorus directly stimulates vascular smooth cells towards its osteoblast differentiation and expression of bone-related proteins, which are involved in the development and progression of cardiovascular calcification. Control of serum phosphorus in the values recommended by KDOQI guidelines (2.7 to 4.6 mg/dl in stages 3 and 4 of CKD) contributes to the reduction of cardiovascular morbidity and mortality. Treatment with phosphate binders is independently associated with improved survival of patients newly admitted to hemodialysis, which has been extrapolated to patients in pre-dialysis monitoring, although to date none of the phosphate binders has been approved by the Food and Drug Administration (FDA) for use in patients without dialysis replacement therapy.

Global GFR figure shows a similar linear decrease to that reported in the tests. The curve in the group of patients with CKD with obstructive cause is the expected. Yet, once there is renal injury, the disease then progresses and recovers in some proportion. In CKD with hypertensive cause, a linear decrease with decreasing GFR of approximately 10 ml/min/year is expected, if there’s no antihypertensive treatment. In the present study, we can not explain the increase in the second year of monitoring and the later decrease of GFR. It may be explained by the coexistence of diabetes mellitus or other cause, in which case etiology would be mixed or less likely because of glomerular hyperfiltration phenomenon expected in less advanced stages of CKD. The decline in the curve of patients with diabetic nephropathy with a later trend to stabilization is not expected in this patient group. We may assume a mixed etiology not certified by the advanced renal injury and, at the time of stabilization, this explains how the proper application of a pre-dialysis program allows a delay in the progression of CKD.

The limitations of this study include sample size, monitoring time and lack of inclusion of variables such as weight, glycated hemoglobin (HbA1c) and quantitative proteinuria for a further analysis to better assess the factors associated with the progression of CKD.

**Conclusion**

A pre-dialysis program ensures a greater adherence and control of targets in clinical and laboratory variables in patients with CKD. Monitoring of systolic blood pressure is clinically and statistically significant as an intervention variable. Even if it is not represented in international target values, a moderate decrease is known to represent a reduction of
the risk of renal events. No patient initiated dialysis during the monitoring time.

This is the first step towards future studies that assess the time of initiation of dialysis.

**Interest conflict**

The authors declare no conflict of interest.

No funding was required for the conducting of this study.

**Bibliographical references**


