Rev. Colomb. Nefrol. 2016; 3(1): 18 -23. http//www.revistanefrologia.org

Research article

http//doi.org/ 10.22265/acnef.3.1.237

Late-onset renal failure because of angiotensin blockade in 51 patients with chronic kidney disease

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Late-onset renal failure from angiotensin blockade in 51 chronic kidney disease patients

Abstract

Introduction: In this research, we describe the outcome of the glomerular filtration rate (GFR) in patients with hypertension and chronic kidney disease(CKD), in whom the angiotensin converting enzyme inhibitors (ACE-i) or angiotensin receptor blockers (ARB) were suspended after sudden deterioration of their GFR; this information is based on the Onuigbo 2005 report related to late onset renal failure after angiotensin blockade (so called Lorffab syndrome).

Materials and methods:a series of Hispanic patients attended in an outpatient department were followed in a clinic of prevention of kidney disease, with hypertension and stable CKD stages 3 and 4, who suffered a sudden deterioration of unknown origin of their GFR, and who were followed prospectively after withdrawing ACE-i or ARB.

Results: 51 patients were sampled, the mean age 81 years (SD 7); 32 females (63%)were followed-up after withdrawing the above medications during 240 days (of 129). As a result, their CKD were due to hypertensive nephrosclerosis in 37 patients (73%), diabetes in 11 (22%), chronic glomerulo nephritis in 1 (2%) and unknown origin in 2 (3%).

ACE-i or ARB were withdrawn:losartan in 34 patients (67%), enalapril in 13 (25%), irbesartan in 2 (4%), captopril and telmisartan in 1 (2%). A Doppler ultrasound of renal arteries after Lorfabb syndrome was suspected were normal in 17 of the 17 cases performed. Compared to baseline measurements, GFR improved in 35 patients (69%), was stable in 7 (14%) and worsened in 9 (18%).

Conclusions: In very old hypertensive patients with stages 3 and 4 of CKD who were taking ACE-i or ARB, presented with sudden deterioration of their GFR; there was an improvement in kidney function after withdrawing these medications. However, some bias to these results are the low number of patients and that Doppler ultrasound was performed in only 33% of patients.Our observations ask for further studies.

Keywords: Late onset renal failure, RAAS blockers, Lorffab syndrome, Chronic kidney disease, ARB, ACEi.

Received: May 8th, 2016 Accepted: May 15th, 2016

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Deterioro renal tardío por bloqueo de angiotensina en enfermedad renal crónica

Resumen

Introducción: Teniendo en cuenta el trabajo de Onuigbo, en 2005, sobre un empeoramiento súbito de aparición tardía de la función renal en pacientes con enfermedad renal crónica (ERC), previamente estables, quienes venían siendo tratados con bloqueadores de angiotensina (denominado síndrome Lorffab), se describen los resultados de la evolución de la tasa de filtración glomerular (TFG) en pacientes con hipertensión y ERC, en los cuales los inhibidores de la enzima convertidora de angiotensina (IECA) o bloqueadores de los receptores de angiotensina (ARA) se suspendieron después de que presentaron un deterioro repentino de su TFG.

Materiales y métodos: Se describe una serie de pacientes hispanos de dos centros de seguimiento ambulatorio para la prevención de ERC, hipertensos y en estadios 3 y 4 de su ERC, quienes venían previamente estables y sufrieron un deterioro repentino de origen desconocido de su TFG, y que fueron seguidos de forma prospectiva después de retirarles los IECA o ARA.

Resultados: 51 pacientes, edad media 81 años (DE 7), 32 mujeres (63%), seguimiento 240 días (DE 129) después de suspendidos los medicamentos anteriores. Causas de ERC: nefroesclerosis hipertensiva en 37 pacientes (73%), diabetes en 11 (22%), glomerulonefritis crónica en 1 (2%) y de origen desconocido en 2 (3%). La creatinina sérica y el TFG (CKD-EPI).

Los IECA o ARA retirados fueron: losartán en 34 pacientes (67%), enalapril en 13 (25%), irbesartán en 2 (4%), captopril y telmisartán en 1 cada uno (2%). La ecografía doppler de las arterias renales después de sospechado el síndrome Lorfabb fue normal en todos los casos. En comparación con las mediciones de referencia, la TFG mejoró en 35 pacientes (69%), permaneció estable en 7 (14%) y empeoró en 9 (18%).

Conclusiones: En pacientes ancianos hipertensos, con ERC estadios 3 y 4, que estaban tomando IECA o ARA, y que presentaron deterioro repentino de su TFG, hubo una mejoría en su función renal después de la retirada de estos medicamentos. Sin embargo, hay varios sesgos a estos resultados: el escaso número de pacientes y que el ultrasonido doppler se realizó en solo el 33% de ellos. Nuestras observaciones obligan a la realización de nuevos estudios.

Palabras clave: Síndrome de deterioro renal tardío, bloqueadores SRAA, Lorffab, enfermedad renal crónica, ARA-II, iECA (fuente DeCS).

Introduction

There is no doubt that the Angiotensin-converting enzyme inhibitors (ACE-i) and the antagonists of the angiotensin without receptor (ARA) have been considered as the cornerstone in patient management with chronic kidney disease (CKD), especially when there is proteinuria and arterial hypertension (HTA).In fact, all current guidelines about arterial hypertension of different agencies and countries include the handling of several types of ERC. However, both groups of drugs can lead to the presentation of a slight decrease of renal function during the beginning of its useage[1,2],which is usually reversible and that is offset by the benefits in the long term that have already been amply described in many studies over the past thirty years.

The presence of late renal deterioration by the useage of the drugs referred to above is referred to as Lorffab Syndrome (by its initials in English. Onuigbo and collaborators since 2005 have warned patients of the late onset renal failure from angiotensin blockade)[3].Unfortunately, their comments had not been of relevance, as far as we know, there are no other publications exploring the theme.

Objectives

Around 400 patients on dialysis were attended to in two renal departments, 3000 patients in medical follow-up through ambulatory consultation and 1300 patients consultation per month attended were observed in previous years by our group in Medellin, Colombia between 2010 and 2012.We decided to actively seek possible cases in order to collect and evaluate the validity of the existence of this syndrome. This purpose arose because of many isolated cases related to the late deterioration of kidney syndrome.

Materials and Methods

This is an observational study corresponding to a cohort of ambulatory patients attended to in two centers dedicated to the control and follow-up of CKD patients in Medellin, Colombia, classified in stages 3 and 4, who regularly attended to follow –up consultations (usually every 2 to 4 months), between January 2010 and December 2012. Patients with suspected renal insufficiency due to the late start by blocking angiotensin were included, the following findings were discovered

- Taking ACE inhibitors or ARA.
- GFR stable in at least two previous visits.
- Deterioration of GFR >25% compared with basal values.
- We could not find a cause to explain the deterioration, such as diarrhea, loss of volume, use of contrast material or antibiotics, use of NSAIDS.

According to the formula CKD-EPI, the GFR was calculated. In the same laboratory with the method Jaffee automatized, the serum creatinine was determinant. ARA or ACEI were removed in these patients. In all patients, follow-up was carried out, in different periods, in accordance with the doctor in charge decision. EPITABLE statistical software was used to calculate the difference between the average levels of serum creatinine and GFR.

Results

From approximately 2,500 patients with ERC in stages 3 and 4, we found the following results : 51 patients met the inclusion criteria. The mean follow-up was 240 days (129), 32 patients were women and 19 men with a mean age of 81 years (7). The etiological diagnosis of the ERC was Hypertensive Nefroesclerosis in 37 patients (73%), diabetic nephropathy in 11 (22%), glomerulo nephritis in 1 (2%) and other causes in 2 (3%), as shown in Figure 1. The ACEI were used in 14 patients (27%) and ARA in 37 (73%), specifically enalapril in 13 (25%), captopril in 1 (2%), losartan in 34 (67%),irbesartan in 2 (4%) and telmisartan in 1 (2%), information showed in Figure 2.

Renal vascular Doppler was applied in 17 patients (33%), but all of them had negative as diagnosis for significant stenosis (considered if> 60%) of the renal arteries. No risk factors were found nor additional triggers to explain the deterioration of the renal

Figure 1

Causes of chronic kidney disease (CKD) in studied patients

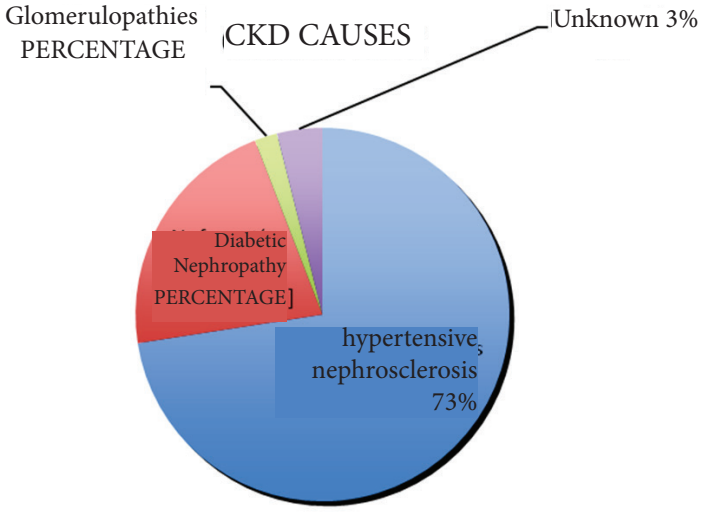
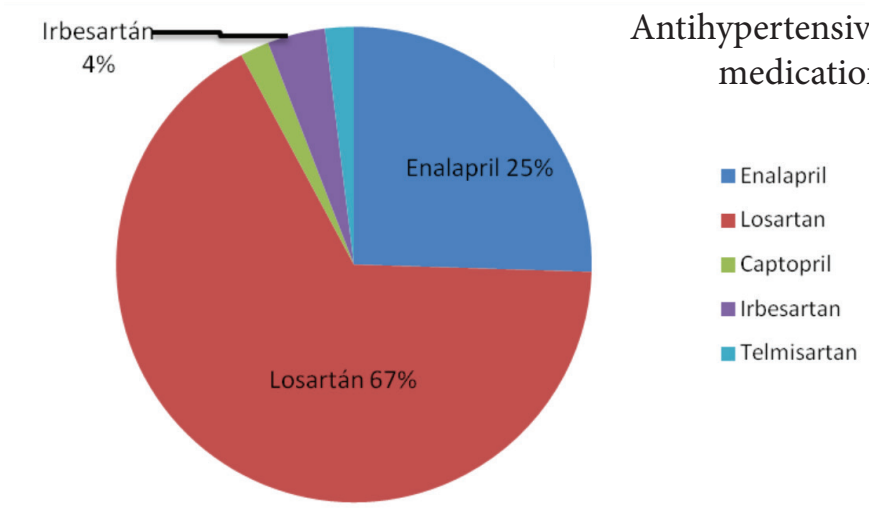


Figure 2
Antihypertensive medication used in patients



function in this sample, as recent hypovolaemia, diarrhea, use of NSAIDS, nephrotoxic drugs or contrast media.

The basal serum creatinine, creatinine at the time of diagnosis of Lorffab and creatinine levels during the follow-up after IECA or ARA interruption. IECA or ARA were: 1.83 (0.51); 2.38 (0.71); and 1.66 (0.55) mg/dL respectively. The GFR baseline, at the time of diagnosis of Lorffab and monitoring after the suspension of ACE inhibitors or ARA were: 35 (6), 25 (2), 40 (6) mL/min, respectively (Figure 3).

We found a significant improvement after the interruption of the drug in comparison with the baseline serum creatinine (-0.2 mg/dL[p=<0.0005]). Similar results were found with the TFG(4 mL/min [p=<0.0005]).

Discussion

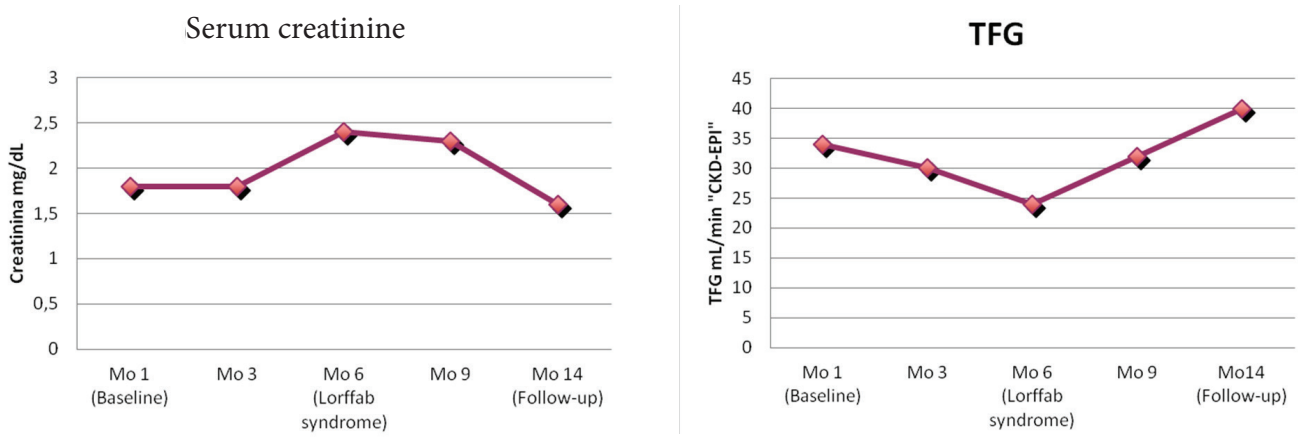
In spite of renal-protector effect, widely known for decades, blockers renin-angiotensin-aldosterone system (RAAS), such as ACE inhibitors and ARA, gave as a result that in a population of patients who are very elderly, with CKD stages 3 and 4.In addition to the progressive deterioration of the GFR with time, the blockade of the RAAS can lead to more rapid loss of kidney function in some patients. This decline of GFR> 25% of the initial value was not associated with other usual triggers, such as infection, contrast media, hypovolemia or consumption of NSAIDS, among others.

This cohort of patients showed a significant improvement or stabilization ofrenal function in 82% of the cases in 8 months (2-17) of monitoring and they did not improve the renal function in 18%, attributing to recent cases to the natural evolution of the ERC. In 17 cases submitted to duplex of renal arteries due to suspicion of renal-vascular hypertension, significant stenosis was not found in any of them.

The published studies about the decline of GFR when blockers are used as RAAS in patients of a very advanced age with ERC are overwhelmingly poor. As far as we know, a report with an observational follow-up of 100 patients of advanced age (71 years) was described at first by Onuigbo[3]; in this research he reported progression to end-stage kidney disease and the improvement of the TFG in the remaining 74% (initial 23.9 ± 9 [7-47]and end 39.2

Figure 3

Variables of renal function over time, in patients included in this study.



As it is showed above, Serum creatinine, down section, renal function estimated based on CKD equation: glomerular filtration rate : Mo. Follow up.

± 15.4 [17-89]mL/min/1.73 m2), 26 (3-46) months after leaving the RAAS blockers (p=0.001)in 16 of patients (16%). Our results agree with the ones suggested by Onuigbo, et al.

The study we conducted has several limitations: it is an observational and retrospective study, with a small number of patients sampled and there was an absence of image studies of the renal artery in 66% of cases.

So, it should be noted that Lorffab syndrome occurs with greater incidence in populations over the age of75 years, with ERC of diabetic and hypertensive etiologies. Both diseases are associated with the hypothesis that explains the pathogenesis of the syndrome Lorffab, concerning the injury of the kidney's microvasculature, which leads to a hemodynamic phenomenon similar to the mechanism of the stenosis of the renal artery which is the same mechanism that would explain the abrupt renal deterioration described here.

We do not know if the suspension of the RAAS blockers in these patients result in an increase in cardiovascular events, the progression to end-stage kidney disease or its effect on mortality.

Finally, with this study we confirm the existence of this syndrome, but we must stress that is limited to the population described and, although its incidence in our case was low (around 2 per cent of the patients evaluated), it is highly suspected in any elderly patient that is taking RAAS blockers and presenting a progressive and rapid deterioration of their GFR, without kidney noxas existence to explain it. In these cases, a very simple measure is used to withdraw the blocking drugs of the RAAS and re-assess after one or two months of treatment. This can positively affect the quality of life, by delaying the onstart of renal replacement therapy; reduce health costs and prevent complications inherent to the beginning of dialysis.

Unfortunately, the diagnostic methods imaginative results are unreliable in these cases and, the radiologists usually rejects them with contrast media with the danger of further worsening the TFG. Therefore, we recommend that, in case of a marked renal deterioration, without apparent cause, in an old man who was previously stable in his renal function and that used ACEI or ARA; it is preferable to remove those medicines, at least as evidence, and to re-assess the patient two or three months again. The improvement

of their GFR should be avoided these medicines in the future is confirmed. Also, we do not recommend the use of duplex color of renal arteries in the study of these cases because of its low sensitivity and specificity to detect significant stenosis.

Finally, it must be clear that this observation applies to an elderly patient population, and it should not be extended to any person who takes ACE inhibitors or ARA, drugs that have been very useful in many kidney diseases and handling of the HTA4solely and exclusively .

Conflict of Interest

All authors state that they do not have any conflict of interest.

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