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Renal function in patients treated with a combination of renin-angiotensin blockers and thiazide diuretics. Is this appropriate?

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To the Editor,

The combination of renin-angiotensin system blockers and thiazide diuretics is the most used in antihypertensive treatment when the patient is not undergoing monotherapy. These diuretics are known not to be very effective in renal failure. Therefore, renal function should be evaluated prior to their prescription and periodically during use, due to the fact that their effectiveness is slight in patients with creatinine clearance rates below 30ml/min. Furthermore, after reviewing the available literature, the use of diuretics in patients with severe renal failure is controversial. For example, the study published by Karadsheh et al[1]. concludes that the use of thiazide diuretics should not be ruled out as an antihypertensive treatment option in patients with advanced chronic renal failure. On the other hand, Chan et al[2]. state that their use should not be recommended in these patients since their findings do not support their effectiveness. Agarwal at el.[3] suggest that more randomised clinical trials are needed for the recommendation of their use in severe renal failure, as they can cause volume depletion, hyponatraemia, hypokalaemia, hyperkalaemia and acute renal failure.

In light of what has been discussed, it would be interesting to analyse whether creatinine clearance in patients treated with thiazide diuretics is taken into account in regular clinical practice.

The objective of our study is to calculate creatinine clearance in hypertensive patients treated with thiazide diuretics in combination with renin-angiotensin system blockers.

Thus, a cross-sectional study was designed selecting 100 essential hypertensive patients (42 males, 58 females), with mean age 68.8±9.3 years, treated with a combination of renin-angiotensin system blockers and thiazide diuretics. The patients were randomly selected from the hypertensive patients of three primary care quotas from an urban health centre in the Region of Murcia. Firstly, any record of creatinine clearance in the last ten years was checked for in all the patients' clinical history. Creatinine clearance was then calculated using the Crockcroft formula and stratified according to the KDOQI (Kidney Disease Outcomes Quality Initiative) stages (Table 1)[4].

The results show that only 11% (11) of the hypertensive patients studied had strictly normal renal function, 6 % (6) had hyperfiltration >110ml/min/1.73m^2, 47 % were stage 2 KDOQI (60-89ml/min/1.73m^2), 36% (36) were stage 3 KDOQI (30-59ml/min/1.73m^2) and there were no patients in stage 4 (15-29ml/min/1.73m^2) or 5 (<15ml/min/1.73m^2). Of all the patients, 15% (15) displayed creatinine levels above the laboratory's reference values, which are <1.3mg/dl in males and <1.2mg/dl in females. No patient had creatinine above 1.8mg/dl. Prevalence of hidden kidney failure in the sample analysed was 15% (15) (glomerular filtration rate [GFR] <60ml/min/1.73m^2 and creatinine within the normal range provided by the laboratory). Regarding the diuretics used, 41% (41) of patients were treated with 12.5mg hydrochlorothiazide, 25% (25) with 25mg hydrochlorothiazide, 20% (20) with 1.5mg indapamide, and 14% (14) with 2.5mg indapamide. None of the 100 patients had creatinine clearance in their clinical history.

As discussion, firstly the high prevalence of hidden renal disease found in our study must be pointed out, probably due to it being carried out in primary care and on essential hypertensive patients. Elsewhere, in a study carried out by Fácila et al[5]. approximately 10% of the hypertensive patients monitored by cardiology presented hidden renal failure.

Table 1. Classification of chronic renal failure according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines.

KDOQI Stage	Description	GFR (ml/min/1.73m²)
1	Renal damage with normal or increased GFR	≥ 90
2	Renal damage with slight GFR reduction	60-89
3	Moderate GFR reduction	30-59
4	Severe GFR reduction	15-29
5	End-stage chronic renal failure	<15 or on dialysis

GFR: glomerular filtration rate.

This detection of renal dysfunction at earlier stages (even when creatinine level is normal) is very important, since it not only prompts a necessary adjustment in the dosing of numerous drugs (digoxin, beta-blockers, anticoagulants, etc.) and the monitoring of the possible appearance of toxic effects, but it also constitutes a risk factor for cardiovascular morbidity and mortality. Otero et al[6]. detected 13% of hidden renal disease using the MDRD equation on 1059 patients older than 18.

Another aspect worth highlighting is the lack of systematic GFR in our sector; furthermore, we did not detect the use of thiazide diuretics with GFR <30ml/min/1.73m² in any case, therefore, they are being used correctly. Nonetheless, we observed that hydrochlorothiazide suitability as a drug combined with renin-angiotensin system blockers is a combination likely used too frequently; occasionally, by only taking into account the disorders associated with hypertension, another combination could be used which would benefit the patient more without having to monitor renal function. As an example, in a patient with cerebrovascular disorder, calcium antagonists could be the best option for combining with renin-angiotensin system blockers.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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