Most significantly, an improvement in the parameters related to nutrition status was only observed in the group of patients treated with megestrol acetate.

Conflicts of interest

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

1. Locatelli F, Fouque D, Heimburger O, Drücke TB, Cannata-Andía JB, Hörl WH, et al. Nutritional status in dialysis patients: a European consensus. Nephrol Dial Transplant 2002;17:563-72.
2. Fernández Lucas M, Teruel JL, Burguera V, Sosa H, Rivera M, Rodríguez Palomares JR, et al. Tratamiento de la anorexia urémica con acetato de megestrol. Nefrologia 2010;30:646-52.
3. Yeh SS, Marandi M, Thode HC, Levine DM, Parker T, Dixon T, et al. Report of a pilot, doubleblind, placebo-controlled study of megestrol acetate in elderly dialysis patients with caquexia. J Ren Nutr 2010;20:52-62.
4. Burrowes JD, Larive B, Cockram DB, Dwyer J, Kusek JW, McLeroy S, et al. Effects of dietary intake, appetite, and eating habits on dialysis and non-dialysis treatment days in hemodialysis patients: cross-sectional results from the HEMO study. J Ren Nutr 2003;13:191-8.
5. Lopes AA, Elder SJ, Ginsberg N, Andreucci VE, Cruz JM, Fukuhara S, et al. Lack of appetite in haemodialysis patients - associations with patients characteristics, indicators of nutritional status and outcomes in the international DOPPS. Nephrol Dial Transplant 2007;22:3538-46.

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Hyperkalaemia in hospitalised patients. How to avoid it?

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To the Editor,

Hyperkalaemia is a serious electrolyte disorder whose incidence is increasing, especially among the elderly, in which renin release is reduced and to whom drugs favouring hyperkalaemia, such as renin-angiotensin-aldosterone system inhibitors (RSAA) or non-steroidal anti-inflammatory drugs, are regularly administered[1,2,3]. It is not uncommon for several of these drugs to be used simultaneously in a patient, increasing thus the risk of hyperkalaemia[4].

We decided to study the epidemiology of hyperkalaemia in patients admitted to a hospital centre, carrying out a cross-sectional observational prevalence study over a year (01/06/2009-31/05/2010), which included adults with principal or secondary hyperkalaemia diagnosis in the discharge report.

Demographic variables, the origin of hyperkalaemia and trigger factors, among others, were studied.

Hyperkalaemia was considered of domiciliary origin if the patient presented hyperkalaemia on admission and of hospital origin if the potassium readings were within the normal range on admission and hyperkalaemia developed during admission.

Hyperkalaemia was defined as mild if potassium was below 5.9mmol/l, as moderate if it was between 6-6.9mmol/l and as serious if it was above 7mmol/l.

The possible causal factors for hyperkalaemia were reviewed, with a maximum of two from the following: acute renal failure (ARF), administration of potentially hyperkalemic-inducing drugs, potassium supplements, heart failure (HF) or the escape of potassium from cells.

Associated history and predisposing factors for hyperkalaemia included arterial hypertension, chronic HF, chronic kidney disease (CKD), diabetes mellitus, chronic liver disease and volume depletion.

Out of the 11 856 adult patients admitted in the study period, hyperkalaemia diagnosis figured in the discharge report of 96 patients (0.8%). Detection of hyperkalaemia by the laboratory was higher: 26% (3098/11 856) of the patients presented potassium levels above the range (5.1-12.8mmol/l). Hyperkalaemia was mild in most cases (n = 2715 [87.6%]), moderate in 303 (9.8%) and serious in 80 (2.6%).

Of the 96 patients with hyperkalaemia identified in the discharge report, the disease evolved during hospital stay in 32 of the cases (33.3 %). Among the precipitating factors, drugs and/or ARF were responsible for hyperkalaemia in 80.2% of the patients. Mean age was 74 (14.3) [19-97] years and 59.4% were female.

We found an accumulated hyperkalaemia incidence of 0.81% of the admissions in a year. It is an underestimated incidence, given that detection was made based on diagnoses at discharge and many cases of hyperkalemia were not included in the diagnoses in the discharge report. Only 15.4% (59/383) of moderate and serious hyperkalaemia detected by the laboratory (K≥6mmol/l) were included in the discharge reports. This indicates a possibility for improvement, since the discharge report, the mean of communication between various activity levels, must be as complete as possible.

Hyperkalaemia was more frequent in older patients, in diabetics and in patients with CKD, and was frequently of multifactorial origin, combining comorbidity factors and drugs.

76 % of patients with hyperkalaemia were on treatment with a potentially hyperkalaemic-inducing drug, and of these, 54.8 % were taking two or

Table 1. Drugs associated with the appearance of hyperkalaemia.

Drugs	n/(%)
ACEi	39/(40.6)
Potassium-sparing diuretics	30/(31.3)
ARA II	23/(24)
Betablockers	19/(19.8)
Digoxin	15/(15.6)
Heparin	7/(7.3)
NSAID	6/(6.3)
Oral potassium	5/(5.2)
Renin inhibitors	3/(3.1)
Trimethoprim	3/(3.1)
Calcineurin antagonists	1/(1)

NSAID: non-steroidal anti-inflammatory drugs; ARA II: Angiotensin II receptor antagonists; ACEi: angiotensin-converting enzyme inhibitors.

Table 2. Recommendations for avoiding hyperkalaemia.

Avoid uncontrolled combination of potentially hyperkalaemic-inducing drugs in populations at risk: elderly, diabetics, CKD patients
If using anti-aldosterone agents in the presence of CKD with GFR < 60ml/min/1.73m^2, spironolactone dosage should not exceed 25mg/24h and eplerenone dosage should not exceed 50mg
Avoid using NSAID in any patient at risk of developing hyperkalaemia. If used, monitor serum potassium levels
Faced with symptoms of volume depletion, suspend RSAA inhibitor drugs
Monitor serum potassium levels in all patients at risk of hyperkalaemia, on increasing or introducing a new hyperkalaemic-inducing drug. If the level of potassium in saline reaches 5.5mmol/l, reduce the drug dose and re-determine the serum potassium level
Determine renal function in patients at risk of hyperkalaemia using formulae that estimate GFR. Risk increases substantially if GFR is <30ml/min/1.73m^2
A diet low in potassium and avoiding potassium supplements is recommended

NSAID: non-steroidal anti-inflammatory drugs; CKD: chronic kidney disease; GFR: glomerular filtration rate; RAAS inhibitors: renin-angiotensin-aldosterone system inhibitors.

more drugs. We found a statistically significant correlation (P<.01) between the number of potentially hyperkalaemic-inducing drugs and the seriousness of hyperkalaemia. Although hyperkalemia risk is low in studies with RSSA drugs in monotherapy[5], we have to take into account that the patients in these studies were carefully selected and underwent close monitoring, and therefore the results can not always be extrapolated to daily clinical practice. Angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists are, at present, one of the most frequent causes of hyperkalaemia, particularly in patients with other predisposing factors. Special attention should be paid to patients with dual or triple renin-angiotensin-aldosterone system blocking, since recent studies show that the risk of hyperkalemia is higher[6]. Meta-analysis on the safety of using aliskiren administered in combination with other RSSAs also observed a greater risk[7].

The drugs are shown in Table 1, highlighting potassium-sparing diuretics as the second most frequent cause, 66.6 %, mostly (27/39) with spironolactone and in high dosis (100mg).

It is of relevance in our study that 73 % of the patients presented ARF and, of these, 50 % were attributed to pre-renal origin. Renal hypoperfusion favours hyperkalaemia due to the reduction of sodium and water supply to the renal tubules, where it is exchanged for potassium, decreasing its excretion. In these cases, hyperkalaemia could be prevented by a warning on the drug leaflet of RSSA inhibiting drugs, similar to that which appears in metformin in relation to the risk of lactic acidosis, whereby it is recommended to temporarily stop the drug in situations that predispose renal failure, such as intense diarrhoea, vomiting or iodine contrast administration, among others.

We believe that our study, although it has many limitations, deals with an important topic from the points of view of patient safety and prevention, mainly directed at clinics, for improving this type of patient management. Table 2 shows recommendations for preventing hyperkalaemia, which could be summarised in the best use of potentially hyperkalaemic-inducing drugs in populations at risk (elderly, diabetics, CKD) that suffer volume depletion.

Conflicts of interest

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

1. Palmer BF, Levi M. Effect of aging on renal function and disease. In: Brenner BM, editor. Brenner & Rector's The Kidney. Vol. 2, 5th ed. Philadelphia: W.B. Saunders, 1996. pp. 2274-96.
2. Muzzarelli S, Maeder MT, Toggweiler S, Rickli H, Nietlispach F, Julius B, et al. Frequency and predictors of hyperkalemia in patients ≥60 years of age with heart failure undergoing intense medical therapy. Am J Cardiol 2011;109:693-8.
3. Braden GL, O'Shea MH, Mulhern JG, Germain MJ. Acute renal failure and hyperkalaemia associated with cyclooxygenase-2 inhibitors. Nephrol Dial Transplant 2004;19:1149-53.
4. Uijtendaal EV, Zwart-van Rijkom JE, van Solinge WW, Egberts TC. Frequency of laboratory measurement and hyperkalaemia in hospitalized patients using serum potassium concentration increasing drugs. Eur J Clin Pharmacol 2011;67:933-40.
5. Weir MR, Rolfe M. Potassium homeostasis and renin-angiotensin-aldosterone system inhibitors. Clin J Am Soc Nephrol 2010;5:531-48.
6. Mann JF, Schmieder RE, McQueen M, Dyal L, Schumacher H, Pogue J, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet 2008;372:547-53.
7. Harel Z, Gilbert C, Wald R, Bell CH, Perl J, Juurlink D, et al. The effect of combination treatment with aliskiren and blockers of the renin-angiotensin system on hyperkalaemia and acute kidney injury: systematic review and meta-analysis. BMJ 2012;344:e42.

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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.