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BRIEF REPORT

Adjusting the dosage of medication in institutionalised elderly patients with renal failure

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KEYWORDS
Chronic renal failure;
Pharmaceutical care;
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Abstract
Objective: To design a programme for pharmaceutical care for the elderly with renal failure in 3 nursing homes in the region of Valencia.
Method: A 9-month long, prospective study into pharmaceutical interventions was carried out. The study assessed the development of renal function and the effectiveness of drug dosage adjustment with pharmacokinetics affected by renal failure in patients with creatinine clearance below 30 mL/min.
Results: Fifty-two residents of 251 centres presented creatinine clearance lower than 30 mL/min. Forty-seven out of 74 pharmaceutical interventions were accepted. The drugs which were mainly used were: diuretics, antibiotics, anti-inflammatories, antiemetics, and ranitidine. Although the process of renal disease continued its course, in most cases the follow-up parameters of effectiveness and safety (in terms of renal toxicity) were maintained within the established limits.
Conclusion: The interventions carried out showed, in most cases, to be safe (renal toxicity) and effective, with some exceptions which required more individual follow-up.

PALABRAS CLAVE
Insuficiencia renal crónica;
Atención farmacéutica;

Ajuste de dosificación de medicamentos en pacientes ancianos institucionalizados con insuficiencia renal

Resumen
Objetivo: Describir un programa de atención farmacéutica en ancianos con insuficiencia renal en 3 centros sociosanitarios de la Comunidad Valenciana.

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Sociosanitario;
Geriatría

Método: Estudio prospectivo de 9 meses de las intervenciones farmacéuticas realizadas, para evaluar la evolución de la función renal y la efectividad del ajuste posológico de fármacos con farmacocinética afectada por insufi ciencia renal en pacientes con aclaramiento de creatinina inferior a 30 ml/min.
Resultados: Cincuenta y dos residentes de los 251 valorados presentaron aclaramiento de creatinina inferior a 30 ml/min. De las 74 intervenciones farmacéuticas realizadas, se aceptaron 47. Los fármacos mayormente implicados fueron: diuréticos, antibióticos, antiinflamatorios, antieméticos y ranitidina. Aunque el progreso de la enfermedad renal sigue su curso, en la mayoría de los casos los parámetros de seguimiento de la efectividad y la seguridad (en términos de toxicidad renal) se mantienen dentro de los límites establecidos.
Conclusión: Las intervenciones realizadas se muestran en la mayoría de los casos seguras (toxicidad renal) y efectivas, con alguna excepción, que requiere un seguimiento más individualizado.

Introduction

One of the most commonly reported and predictable changes associated with ageing is decreased renal function. Mild chronic renal failure (CRF) (glomerular filtration [GF>40 mL/min) is generally asymptomatic, but when the GF is <30-40 mL/min, important disorders begin to appear.[1]

One of the consequences is that it is more difficult to eliminate many drugs, especially those excreted renally. A population study in the United Status which obtained data from 15 625 non-institutionalised adult patients estimated that CRF with a GF<60 mL/min has a prevalence of 4.6%. One noteworthy aspect is the association between advanced age and an increased prevalence of GF<60 mL/min.[2] It is extremely important to design early CRF detection strategies, keeping in mind the factors involved in CRF's evolution, including pharmacological treatment. Therefore, in patients with an altered renal function who are on multiple medications, nephrotoxic drugs should be avoided and dosages adjusted accordingly.[3]

This article describes a pharmaceutical assistance programme for elderly CRF patients which evaluates the effectiveness and change in renal function for each pharmaceutical intervention administered.

Method

Prospective study over 9 months (April-December 2006). An action programme was designed to identify drugs that should be substituted and/or have their dosages adjusted in elderly CRF patients. The programme has been implemented in three health centres. It includes 251 residents (69.7% women), with an average age of 81.6 years.

When the resident is admitted to the health centre, his/her medications are recorded along with anthropometric statistics, clinical diagnoses, etc. He/she schedules an analysis to record serum creatinine (Crser) and calculates creatinine clearance (Clcr) using the Cockroft-Gault equation.[4]

Men: $Clcr = (140 - age) \times weight / 72 + (Cr_{ser})$
Women: $Clcr = (140 - age) \times weight / 72 + (Cr_{ser}) \times 0.85$

In patients with grade III obesity, the weight-adjusted dose is calculated as follows[5]:

$WD = W_{ideal} + 0.4 (W_{current} - W_{ideal})$
W_{ideal} men: $56.2 + 0.555$ (height [cm] $-$ 152.4)
W_{ideal} women: $53.1 + 0.535$ (height [cm] $-$ 152.4)

Once Clcr has been calculated, we consider values below 30 ml/min, since most elderly patients present Clcr below 50 ml/min. Once an episode or CRF has been identified, either when registering at the centre or when modifying treatment, the patient becomes part of the programme. A dosage adjustment programme was designed based on an exhaustive bibliographic study,[6-9] and an alert system was set up on a computer programme (Sinphos®, Grifols). We performed follow-up on the pharmaceutical interventions prescribed by the doctor. There was no follow-up for drugs that required a dosage adjustment for a short-term, non-nephrotoxic treatment.

Nephrotoxic drugs

Follow-up on renal function using serum urea values and GF at time of intervention and at six months: beta-lactams, quinolones, non-steroidal anti-inflammatories, and angiotensin converter enzyme inhibitors.

Drugs requiring a dosage adjustment for long-term treatment

1. Diuretics and anti-hypertensive drugs: follow-up on blood pressure (BP) at time of intervention, at 1 week, 1 month, and 3 months. Criterion for high BP: values above 140/90 mm Hg (stage 1 arterial hypertension [AH],[10] or cases in which a patient in stage 1 passes to stage 2 (AH>160/100 mm Hg).
2. Alopurinol: follow-up on uric acid values at the time of intervention and at 6 months. Criterion for uric acid increase: values above 7 mg/dL (reference laboratory [RL]).
3. Anti-diabetic drugs: follow-up on glucose values at the time of intervention and at 6 months. Criterion for high

Table 1 Spanish Nephrology Society's proposed classification of different renal function stages according to glomerular filtration (GF) and associated renal damage

Stage	Description	GF, mL/min	Renal damage
Normal	Increased risk	>90 with CKD risk factors	
1	Renal damage with normal or high GF	>90	Albuminuria, proteinuria, haematuria
2	Renal damage with normal or low GF	60-89	Albuminuria, proteinuria, haematuria
3	Renal damage with normal or low GF	30-59	Chronic renal failure Early renal failure
4	Severely diminished GF	15-29	Chronic renal failure Advanced renal failure Terminal pre-CKD
5	Renal failure	<15 (or dialysis)	Renal failure, uraemia, terminal kidney disease

glycaemia: values above 120 mg/dL (RL). Drug dosage adjustments in elderly institutionalised patients with renal failure.

4. Digoxin and anti-epileptics: follow-up on plasma values at time of intervention, at 1 month and at 6 months.

Evaluating renal function

1. GF is calculated based on Clcr and uses as a reference the classification scheme proposed by the Spanish Society of Nephrology (SEN)[11] (Table 1). Given that most of our patients are in stage 2 or above, a change in renal function stage is considered to indicate a worsening condition.
2. Urea: worsening is indicated by values above 50 mg/dL (RL).

Results

Out of the total of 251 patients that were evaluated, 52 (20.7%) of the elderly residents presented CRF (Clcr<30 mL/min).

Seventy-four pharmaceutical interventions took place, and 47 were accepted. These included 7 changes in treatment, 37 dosage adjustments, and 3 cases of discontinuing the treatment. The index of acceptance by the medical staff was 63.5%.

Table 2 shows the most frequently involved medications.

Table 3 presents analytic data and blood pressure recorded during follow-up on the intervention.

Of the 47 interventions that were performed, long-term follow-up (at least 6 months) could be carried out for 33; the rest of the interventions only involved a treatment modification during a brief time.

We evaluated treatment safety for those 33 interventions with follow-up according to whether or not renal function decreased (Table 1). There was a change in renal function stage in 5 interventions (2 in the same patient). If we observe urea values, we see that 18 show values above 50 mg/dL at 6 months from the intervention, although in 15 these values were already above 50 mg/dL at the time of intervention, and the rest remained constant or even decreased (10 interventions).

Table 2 Drugs most frequently involved in interventions for medication-related problems in institutionalised elderly patients with renal failure

Treatment group	No. of interventions
Diuretics	15
Antibiotics	12
Ranitidine	6
Anti-inflammatories	6
Antihemetics	6
Potassium	5
Alopurinol	4
Antihypertensives	4
Antihistamines	4
Antidepressants	3
Digoxin	3
Memantine	2
Alendronat	1
Analgesics	1
Antidiabetics	1
Antiepileptics	1

Regarding the effectiveness of the treatment, we can use the abovementioned parameters from the 14 cases in which effectiveness can be evaluated objectively to show that the treatment was effective in 12 cases.

Discussion

Data obtained from the Kidney Disease Registry at the SEN corroborates that Spain has one of the highest CRF rates among European countries, and that the magnitude of the problem, which is linked to the ageing population, could increase in the near future.

Table 3 Follow-up on pharmaceutical interventions for medication-related problems in institutionalised elderly patients with kidney failur

Intervention	GF_1, mL/min	GF_2, mL/min	Urea1, mg/dL	$Urea_2$, mg/dL	BP_{before}, mm Hg	BP_{week}, mm Hg	BP_{month}, mm Hg	$BP3_{months}$, mm Hg
Interventions in diuretic treatments. Proposal: replace hydrochlorothiazide and/or spironolactone with ASA diuretics								
1	45	42	51	52	140/80	155/80	140/80	140/80
2	36.3	59	113	39	130/80	120/65	120/70	120/70
3	27.3	24.6	80	76	150/50	110/56	150/80	160/80
4	48	48	22	21	150/90	150/80	109/60	140/70
5	42.4	41.5	65	80	100/50	–	–	100/60
Interventions in antihypertensive treatment. Proposal: dosage adjustment								
1	34.1	25.4	97	305	130/70	100/35	130/70	115/75
2	46.9	54.8	91	66	130/60	110/50	120/60	100/60

Itervention	GF_1, mL/min	GF_2, mL/min	$Urea_1$, mg/dL	$Urea_2$, mg/dL	$Uric_1$, mg/dL	$Uric_2$, mg/dL
Interventions in alopurinol treatment. Proposal: dosage adjustment						
1	34.1	25.4	97	305	4.5	6.3
2	36.3	59	113	39	3.2	8
3	36.3	47.1	69	65	10.6	6.7

Intervention	GF_1, mL/min	GF_2, mL/min	$Urea_1$, mg/dL	$Urea_2$, mg/dL
Interventions in NSAIDs treatments. Proposal: replace with paracetamol or opioids				
1	45	42	51	52
2	38.4	42.2	51	52
3	35.6	30.3	143	110
Interventions in treatment with ranitidine. Proposal: dosage adjustment				
1	49.5	49.5	113	39
2	63.7	64.5	51	48
3	27.3	24.6	80	76
4	51.4	51.4	52	28
5	51.4	60	94	74
Interventions in treatment with antibiotics. Proposal: dosage adjustment				
1	64.5	64	48	59
2	32.7	22.7	136	233
3	30.4	18.7	52.6	32.4
4	51.4	51.4	52	28
5	41.9	41.3	86	78
6	47	46.7	34	33
7	46.2	51.4	43	36
Interventions in treatment with metoclopramide. Proposal: dosage adjustment				
1	51.9	50.6	32	51
Interventions in treatment with antidepressants. Proposal: dosage adjustment				
1	51.9	50.6	32	51
2	41.9	41.3	86	78
3	53	51.9	34	33

Intervention	GF_1, mL/min	GF_2, mL/min	$Urea_1$, mg/dL	$Urea_2$, mg/dL	$Level_1$	$Level_2$
Interventions in treatment with digoxin (μg/mL): Proposal: dosage adjustment						
1	36.3	59	113	39	0.7	0.8
2	51.4	51.4	52	28	1.2	1.6
3	45.7	45.7	41	49	0.6	1

Intervention	GF_1, mL/min	GF_2, mL/min	$Urea_1$, mg/dL	$Urea_2$, mg/dL	$Glucose_1$, mg/dL	$Glucose^2$, mg/dL
Interventions in treatment with antidiabetics. Proposal: replace with a different sulphonylurea drug						
1	34.9	35.1	32	35	110	83

1 indicates before intervention; 2, six months after intervention; BP, blood pressure; GF, glomerular filtration; NSAIDs, non-steroidal anti-inflammatory drugs.

One of the fundamental aspects in the follow-up of pharmaceutical treatment in elderly patients is evaluating whether that treatment is consistent with the dosage and/or guidelines indicated by the patient's Clcr. After carrying out the intervention, it is appropriate to follow up on both the safety and the effectiveness of this treatment.

Within this context, if we analyse the data obtained from our study, we see that approximately 21% of all patients have a Clcr below 30 mL/min, which is similar to other percentages described in the bibilography.[1-3,12,13]

As for the index of acceptance by the medical staff, we see that the resulting value is not very high[14-16]; this may be due to the fact that most of the proposed interventions were adjustments to the dosage, which could lead to distrust for the treatment's effectiveness on the part of staff members. Consequently, we are considering doing follow-up on the interventions that were accepted and carried out in order to evaluate both their effectiveness and the evolution of renal function in the case of treatments that were modified.

Upon evaluating the evolution of renal function with each treatment, the results indicate that renal function in these patients is already significantly impaired, and that the kidney disease continues to progress despite the pharmaceutical treatments administered.

Regarding the effectiveness of these treatments, and taking the directives of the Joint National Committee[10] into consideration, we observe that where there were interventions in diuretic and anti-hypertensive treatments, all patients maintained BP values below the set limits at 6 months, even when BP was above the limit at the time of intervention, except in 1 case in which the systolic pressure was above 140 mm Hg. Furthermore, for interventions in digoxin and oral anti-diabetic drug treatments, we see that pharmacokinetic values (in the first case) and fasting glucose levels (in the second) remained within the established limits.

Three interventions were made in alopurinol treatment; in 2 cases, uric acid values at 6 months were lower than 7 mg/dL and in the other it was higher than that amount.

Therefore, we can conclude that the majority of the interventions the pharmaceutical specialist carried out to modify treatments so as not to exacerbate renal failure seem to be safe and effective where renal function is concerned; however, there are exceptions in which it is appropriate to re-adjust the dosage and/or guidelines to obtain the desired results. For this reason, it is recommended that a multi-disciplinary team carry out an individual follow-up of reference values (pressure, analysis).

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