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Hyperkalaemia and impaired renal function in patients taking spironolactone for congestive heart failure: retrospective study

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Spironolactone reduces disease and death in patients with severe congestive heart failure and is well tolerated with regard to renal function and serum potassium concentrations.[1] Guidelines recommend taking spironolactone in addition to angiotensin converting enzyme inhibitors and β blockers,[2 3] but since spironolactone can lead to renal dysfuction or hyperkalaemia, we followed up a cohort of patients taking spironolactone to identify predictors of harmful effects.

Participants, methods, and results

We selected 125 consecutive patients from the congestive heart failure outpatient clinic of Frederiksberg University Hospital, Copenhagen (table).[4] We included only patients with a left ventricular ejection fraction (LVEF) of no more than 45% or patients who were taking spironolactone. We started 65 patients on spironolactone; 60 patients were already taking spironolactone when they were referred. We measured blood electrolytes at baseline and then every two months. The study started in September 1999 and lasted 2 years. We analysed data using χ^2 tests, Student's *t* tests, and multiple logistic regression.

At baseline, 93 (74%) patients were receiving potassium supplementation. We stopped supplements in 66 (71%) patients and gradually reduced dosages in the others. We observed each patient for a mean 370 days; total observation was for 73.0 patient years. We saw each patient a mean 11.1 times (mean 22.9 days between visits).

Mean peak serum creatinine concentration was 167.6 (SD 11.9) μmol/l, and mean peak potassium serum concentration was 5.0 (0.4) mmol/l. A total of 73 (58%) patients, had serum creatinine >130 μmol/l, and 23 (18%) had >220 μmol/l. Relative to baseline, 69 (55%) patients had their serum creatinine concentrations increase by 20%, 30 (24%) by 50%, and 11 (9%) by 100%. A total of 45 (36%) patients had potassium serum concentrations >5 mmol/l, 21 (17%) patients >5.5 mmol/l, and 13 (10%) >6 mmol/l.

Patients taking spironolactone before referral did not differ significantly from those we started at the clinic in terms of severe hyperkalaemia (8.3% *v* 10.8%, P=0.63) or azotaemia (23.3% *v* 24.6%, P=0.81). We found a mean weight loss of 1.3 kg.

We logistically regressed azotaemia (defined as a 50% increase in serum creatinine concentration) with age, sex, New York Heart Association function class (NYHAFC), LVEF, and use of angiotensin converting enzyme inhibitors and β blockers. Age (odds ratio 1.74 (95% confidence interval 1.03-2.91) for each

Baseline characteristics of the heart failure population studied (n=125)

Characteristic	Value
Mean (range) age (years)	72.9 (46.5-90.6)
No (%) of women	34 (27)
Mean (SD) left ventricular ejection fraction (%)	29 (5)
Mean (SD) creatinine concentration (μmol/l)	118 (7)
Mean (SD) serum potassium (mmol/l)	4.2 (0.3)
No (%) in New York Heart Association function class:	
I	7 (6)
II	55 (44)
III	58 (46)
IV	5 (4)
No (%) taking:	
Converting enzyme inhibitor or angiotensin receptor blocker	108 (86)
Potassium supplements	93 (74)
Digitalis	48 (38)
β blockers	49 (39)

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decade of age) and lower LVEF (0.94 (0.89 to 0.99) for each 10% increase) were independent risk factors for azotaemia.

For severe hyperkalaemia (serum potassium >6.0 mmol/l) we added to the model baseline serum creatinine concentration and whether the patient was taking potassium supplementation. In this analysis the NYHAFC (3.36 (1.17 to 9.69) for each class) and lower LVEF (0.37 (0.15 to 0.95) for each 10% increase) were predictive factors.

Comment

Taking spironolactone for congestive heart failure is associated with considerably more frequent side effects than previously thought.[1] Age, lower LVEF, and higher NYHAFC are predictors of hyperkalaemia and azotaemia.

Excessive diuresis might be an important cause of renal dysfunction while taking spironolactone. One way of dealing with renal dysfunction secondary to spironolactone may be to reduce doses of concomitant diuretics.

In the future, drugs such as eplerenone may replace spironolactone, but the risks of hyperkalaemia and renal insufficiency may be equally high.[5] We found that adverse effects with spironolactone were common. We recommend that particular caution is taken in elderly people with LVEFs below 20%, potassium supplementation should be discontinued, changes in body weight should raise concern, doses in concomitant diuretic regimens may need adjustment, and continuous laboratory monitoring remains inevitable.

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Increasing hospital admissions for systemic allergic disorders in England: analysis of national admissions data

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Epidemiological studies indicate that the prevalence of allergic disorders such as allergic rhinitis, asthma, and eczema have increased during recent decades in many Western countries.[1] Although anecdotal reports suggest that the prevalence of systemic allergic conditions may also be changing, only limited evidence exists to support this assertion.[2] We report on trends in admissions for anaphylaxis, angio-oedema, food allergy, and urticaria, analysed by using national hospital discharge statistics from 1990-1 to 2000-1.

Methods and results

We obtained hospital admissions data from the hospital episode statistics system.[3] This database records episodes of care after admission to hospital and assigns a primary diagnosis on discharge based on the international classification of diseases (ICD).[4] Data are available by financial year (1 April-31 March). Diagnoses were classified using the ninth revision (ICD-9) up to March 1995 and using the tenth revision (ICD-10) thereafter.

We identified admissions for anaphylaxis, angio-oedema, food allergy, and urticaria (ICD-9 codes: 995.0, 999.4, 995.1, 693.1, 708; ICD-10 codes: T78.0, T78.2, T80.5, T88.6, T78.3, L27.2, T78.1, L50). We calculated age and sex standardised admission rates and used rate ratios to quantify the changes over the 11 year period. We tested for time trend by fitting simple linear regression models to the standardised rates for each condition.

A total of 49 300 admissions for systemic allergic conditions occurred during the 11 year study period (urticaria: 19 250; anaphylaxis: 13 230; food allergy: 8690; angio-oedema: 8180). Total admissions for these four disorders increased from 1960 admissions in 1990-1 (0.02% of all admissions) to 6752 in 2000-1 (0.06%) (figure).

The largest increases in rates have been for anaphylaxis and food allergy. Anaphylaxis rates rose from 6 to 41 per million between 1990-1 and 2000-1, and food allergy rates rose from 5 to 28 per million over this period. The greatest number of admissions was for urticaria, although increases in admission rates