An analysis of discharge drug prescribing amongst elderly patients with renal impairment

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Summary

Renal impairment is common amongst elderly patients and increases the risk of drug toxicity. Analysis of the discharge summaries of patients discharged from the geratology wards of an Oxfordshire hospital, showed that renal impairment was not referred to in 42% of patients with calculated creatinine clearances of 10–20 ml/min. A fifth of these patients, and 67% of patients with calculated creatinine clearances < 10 ml/min, had discharge drug prescriptions that contradicted the *British National Formulary* guidelines for prescribing in the presence of renal impairment. There should be increased awareness that, in elderly patients, normal serum creatinine concentrations do not exclude renal impairment and that several commonly prescribed drugs require dose adjustments or should be avoided in the presence of renal insufficiency.

Keywords: elderly; renal impairment; drug toxicity

Drug toxicity is a significant problem amongst elderly patients. This is partly due to reduced excretion of drugs and their metabolites from kidneys impaired by disease and age-related changes.¹ In the presence of renal insufficiency, toxicity from renally excreted drugs should be minimised by reducing doses or increasing the time interval between doses.² However, renal impairment is often missed in elderly patients, especially as decreasing muscle mass may prevent rises in serum creatinine concentration.¹ We have investigated the extent to which renal impairment is being recognised and drug doses adjusted for patients discharged from the geratology wards of a teaching hospital.

Patients and methods

The following information is routinely collected for patients discharged from the three geratology wards at the Radcliffe Infirmary, Oxford: weight, serum creatinine concentration and medication list. Where complete sets of data were available, creatinine clearance on discharge was calculated, using the Cockcroft-Gault formula³ (box 1), for patients discharged between 1 March 1993 and 1 March 1996, inclusive. The palliation of symptoms due to malignancy and/or end-stage disease (eg, cardiac failure, chronic obstructive pulmonary

The Cockcroft-Gault formula³

Calculated creatinine clearance =

$$\frac{(140 - \text{patient's age}) \times \text{patient's weight}^*}{72 \times \text{patient's serum creatinine concentration}^\dagger}$$

* measured in kg; † measured in mmol/l

Box 1

disease) often overrides concerns about drug toxicity. Patients receiving palliative care were therefore excluded from the following analysis. The discharge summaries of patients with calculated creatinine clearances of less than 20 ml/min, were reviewed for any reference to renal impairment (defined as a statement that the patient's renal function was compromised or that his/her discharge serum creatinine concentration was above 150 mmol/l, the upper limit of our laboratory's reference range). The discharge medication lists of these patients were reviewed against the *British National Formulary* guidelines for prescribing in the presence of renal insufficiency.² To enable such a review, moderate and severe renal impairment were defined, as in the *British National Formulary* guidelines, as creatinine clearances of 10–20 ml/min and less than 10 ml/min, respectively.

Results

Over the three years reviewed, 1875 patients (median age: 82.4 years; age range: 53.1–100.8 years; female/male ratio: 1.5) were discharged from the Radcliffe Infirmary geratology wards. Information to enable calculation of a discharge creatinine clearance was available for 1162 patients (median age: 82.1 years; age range: 53.1–100.8 years; female/male ratio: 1.5).

Excluding patients receiving palliative care, 96 (8.3%) of the 1162 patients (114 discharges) had moderate renal impairment (median age: 88.5 years; age range: 76.2–100.8 years; female/male ratio: 3.6), and six (0.5%) patients (10 discharges) had severe renal impairment (median age: 84.3 years; age range: 79.4–90.2 years; female/male ratio: 2.0). While the discharge summaries of all 10 patients with severe renal impairment contained some reference to the renal impairment, 66 (58%) of the 114 discharge summaries of patients with

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Table Drug prescriptions contradicting the *British National Formulary* guidelines for prescribing in the presence of reduced renal function

Drug	No of prescriptions	
	Moderate renal impairment group (n=96)	Severe renal impairment group (n=6)
Opiates*#		
Codeine phosphate/co-codamol	5	—
Co-proxamol	2	2
Co-dydramol	1	—
Nonsteroidal anti-inflammatory drugs†		
Ibuprofen	3	—
Diclofenac	2	—
Naproxen	1	2
Indomethacin	1	1
Fenbufen	1	—
Flurbiprofen	1	—
Nabumetone	1	—
Antibiotics*		
Trimethoprim	2	—
Cephadrine	1	1
Others		
Chlorpropamide†	3	—
Sulphinpyrazone†	2	—
Domperidone*	—	2
Ranitidine*	—	2
Colchicine†	—	1
Total	26	11

*The doses of these drugs had not been reduced, as recommended by the *British National Formulary* guidelines.²

#Co-codamol (1 tablet: codeine phosphate 8 mg, paracetamol 500 mg); co-proxamol (1 tablet: dextropropoxyphene 32.5 mg, paracetamol 325 mg); co-dydramol (1 tablet: dihydrocodeine tartrate 10 mg, paracetamol 500 mg).²

†The *British National Formulary* guidelines recommend that these drugs should be avoided in moderate and severe renal impairment.²

moderate renal impairment, did not contain any such reference.

Amongst the patients with moderate and severe renal impairment, there were, respectively, 26 drug prescriptions (20 patients, 23 discharges) and 11 drug prescriptions (four patients, eight discharges) that contradicted the *British National Formulary* guidelines (table). Sixteen of the contradicting prescriptions (13 patients, 13 discharges) for patients with moderate renal impairment and all 11 contradicting prescriptions for patients with severe renal impairment, accompanied discharge summaries that referred to the patient's renal insufficiency but did not warn that the implicated drugs were being used despite coexisting renal impairment.

Discussion

The formula used in this study to identify renal impairment, has been shown to correlate well with measured creatinine clearance.⁴ However, because its calculation of creatinine clearance is based on the patient's weight, the formula may underestimate the renal function of very light patients.⁴ To avoid recruiting patients who might thus have been erroneously diagnosed with renal impairment, we excluded from our analysis patients with calculated creatinine clearances between 20 and 50 ml/min (ie, the criterion used by the *British National Formulary* guidelines to define mild renal impairment²).

Our findings support the view that renal impairment is often missed in elderly patients with normal serum creatinine concentrations.¹ Such omissions could explain the fact that one

Proposed guidelines for identifying and managing elderly patients at risk of drug toxicity because of renal impairment

Preceding discharge,* each patient will have his/her creatinine clearance calculated using the Cockcroft-Gault formula.³ All patients with creatinine clearance values of less than 50 ml/min will have their medications reviewed against the latest *British National Formulary* guidelines for prescribing in the presence of renal impairment. The final decision to stop or replace a contraindicated medication will be made on an individual patient basis, taking into consideration, in particular, the degree of renal impairment and whether the patient is at the end stage of a terminal illness.

Unless a calculation or formal measurement has been performed recently, patients with known renal impairment will still benefit from calculation of their creatinine clearances before discharge. It is important to quantify the degree of renal impairment as certain drugs are only contraindicated with moderate and/or severe impairment.²

* The decision to calculate the creatinine clearance before discharge as opposed to, eg, on admission, is based on two factors. Firstly, because a patient's general state of health will usually have been optimised before discharge, any factors (eg, dehydration and malnutrition) that may spuriously alter the patient's calculated creatinine clearance value will be minimised. Secondly, the calculation of creatinine clearance is less likely to be overlooked if it is incorporated into the 'routine' discharge procedure that each patient undergoes.

Box 2

third of the drug prescriptions for our patients with moderate renal impairment contradicted the *British National Formulary* guidelines. However, the remaining two-thirds of these prescriptions and all the contradicting prescriptions amongst our patients with severe renal impairment, had been made despite acknowledgement of coexisting renal impairment. The commonest contradicting prescriptions were opiates and nonsteroidal anti-inflammatory drugs (NSAIDs). Using opiates in the setting of renal impairment results in the accumulation of their metabolites and hence, an increased risk of side-effects, in particular

Learning/summary points

- a normal serum creatinine concentration does not exclude renal impairment in the elderly patient
- the Cockcroft-Gault formula provides a rapid and accurate means of estimating creatinine clearance
- the possibility of 'occult' renal impairment should always be considered when prescribing drugs, in particular opiates and NSAIDs, to elderly patients

Box 3

respiratory depression.⁵ Both codeine⁶ and dihydrocodeine,⁷ which are constituents of two of the three opiate preparations identified in this study (table), have been reported to cause prolonged narcosis in patients with renal impairment. NSAIDs can exacerbate existing renal impairment and can, in their own right, cause renal damage, eg, tubulo-interstitial nephritis.⁸

The risks of drug toxicity amongst elderly patients with renal impairment, could be reduced by increasing awareness that renal impairment can accompany normal serum creatinine concentrations, and that prescribing

opiates and NSAIDs in the presence of renal impairment is potentially dangerous. To further minimise drug toxicity, the creatinine clearances of elderly patients could be routinely calculated on deciding their discharge and their drug prescriptions reviewed before discharge. We plan to disseminate these guidelines (box 2) within our unit and to review their effects on the recognition of renal impairment and on discharge drug prescribing in a future study.

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Images in medicine

A fortunate adverse drug reaction

A 21-year-old woman presented with this isolated lesion suggestive of superficial skin necrosis of her left lower leg. She was hospitalised and a skin biopsy demonstrated limited purpura fulminans. A thorough search failed to reveal the presence of any infection or thrombophilic state, leading to a clinical suspicion of an unusual manifestation of drug hypersensitivity. The patient's history included Arnold-Chiari malformation, mild mental retardation and 'recurrent seizures' for which she had been prescribed phenytoin (600 mg/day, serum levels 16 µg/dl) a couple of months earlier. Close observation and electroencephalogram studies during the attacks revealed them to be 'pseudoseizures'. Phenytoin was discontinued with no ill effects and the skin lesion gradually cleared spontaneously.

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