

PHARMACEUTICAL CARE OF THE ELDERLY

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The older patients to whom pharmacists provide long-term medication often have multiple diseases which, together with polypharmacy, present increased problems of adverse drug reactions and the risk of poor patient concordance with medication. Treatment for older people is often prescribed to relieve symptoms rather than to control completely or cure a condition and patients may have difficulty understanding the limitations of drug therapy. The patient's effort to maintain independence is set against a potentially increasing burden of disease, which may threaten their quality of life. The therapy of one condition can interfere with the control of another and the presence of co-morbidity complicates the assessment of drug therapy in the elderly. Restrictions on dexterity and memory can impair the reliability of patients to take their medicines. Pharmacokinetic and pharmacodynamic changes associated with ageing and disease add emphasis to the need for individualisation of care

(1) DRUG USE IN ELDERLY PATIENTS

There are opportunities presented by current NHS policy for pharmacists to expand their services to meet the needs of special patient groups in the population. The continuing need to improve the use of medication in older people has been highlighted by a recent update of the Royal College of Physicians' report on medication for older people (see "Further reading"). When defined as aged over 65 years, older people constitute almost a fifth of the population and represent the majority of high users of the pharmacy, receiving nearly half of all prescription items. The "very elderly", those aged 75 years and more, are targets for medical screening programmes and periodic review. Pharmaceutical care requires attention to the

health changes brought about by ageing, including the social and behavioural changes patients face.

The varying impact of different morbidity with age means that chronological age alone forms an unreliable basis for prescribing decisions. For some drug treatments, older patients may derive specific benefit and denial of treatment on the grounds of age alone may be unjustified. Patients should be assessed as individuals while at the same time encouraged to be involved active-

ly in decision making about their own drug therapy. Greater involvement relies on the patient's understanding of their disease and knowledge of their drug therapy.

Pharmacists have an opportunity to educate patients about their condition, their medication and how to cope with both. The Royal Pharmaceutical Society's report "Compliance to concordance" emphasises how pharmacists and other health care professionals must move from the concept of patient compliance to patient concordance,

where increasing attention is placed on gaining patient participation in drug therapy decisions. That includes addressing patient attitudes to drug therapy and taking the time to negotiate with them ways of improving treatment outcomes. Patients' appreciation of the benefits as well as the risks of medication are necessary for them to take part in the decision to add or discontinue treatments.

Two thirds of older people receive regular medication and this commonly includes cardiovascular

PRESCRIPTIONS AND THE ELDERLY

- Older people (over 65) account for 18 per cent of the total UK population. They are responsible for only 19 per cent of medical consultations but receive 45 per cent of all prescribed medicines
- Seventy-eight per cent of all prescribed medicines are issued by repeat prescriptions
- The targeting of pharmaceutical services to patients must deal with the fact that for each pharmacy there are about 800 people over 65 years old
- Twenty-two items/year are dispensed per elderly person
- Half those on repeat medication receive four or more concurrent items
- Older people are three times more likely to be admitted to hospital with an adverse drug reaction

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agents, antihypertensives, analgesics and anti-inflammatories, sedatives and gastrointestinal medicines. Patients in residential and nursing homes tend to receive laxatives, analgesics, major tranquillisers and benzodiazepines. Pharmacists must develop systems for identifying those most at risk of medication-related problems. Systematic approaches to delivering pharmaceutical care require pharmacists to identify subgroups of patients with defined needs and at particular risk.

There are several ways in which pharmacists are developing services designed to tackle the problems associated with polypharmacy. These include conducting repeat prescribing medication reviews in the GP's surgery, visiting patients at home, providing individual patient care to those in nursing homes, and the introduction of local "brown bag" schemes in the pharmacy, where patients are invited to bring in their medication for systematic pharmacy review.

DRUG HANDLING AND AGEING

Drug absorption Drug absorption is theoretically reduced in the elderly as loss of mucosal intestinal surface, decrease in gastrointestinal blood flow and reduced gastric acidity all occur with ageing. However, while nutrient absorption (calcium, iron and thiamine) is known to be compromised by age, there are few examples of specific drug absorption problems of demonstrable clinical significance. More commonly, co-existing disease and drug-related causes of reduced gastric emptying, such as the decreased gastrointestinal motility produced by anticholinergic agents, are likely to affect the rate rather than the extent of drug absorption.

Drugs undergoing high first pass metabolism (such as propranolol) may have a higher bioavailability in the elderly due to changes in liver blood flow and hepatic function (see below).

Drug distribution

Drug distribution is affected by the changes in body composition associated with ageing, particularly the increase in adiposity which rises from 18 per cent in young adults to 36 per cent in elderly men and from 36 per cent to 48 per cent in women. The volume of distribution for lipid soluble drugs

Case study 1: Concordance in older people

Older patients need help to understand their medication, including the benefits and how to take their medicines

Mr W. M. is an 83-year-old widower who has been admitted to hospital on bendrofluazide 5mg and aspirin 75mg each morning, ranitidine 150mg twice daily, nifedipine 10mg three times daily and isosorbide mononitrate 20mg three times daily. He is complaining of worsening angina and is not coping with taking all of his tablets. Each morning he puts all the tablets he requires for the day in a pillbox and takes one of the tablets when he thinks it is the right time.

On assessment, all of the medication he is taking is still required, but there is scope for some rationalisation to allow the medication to be taken in once or twice daily routines. On hospital discharge he is maintained on bendrofluazide 5mg, aspirin 75mg, amlodipine 5mg and isosorbide mononitrate SR 50mg, all each morning, and diclofenac 75mg/misoprostol 200µg (Arthrotec 75) twice daily (morning and night). Mr W. M. was helped with a Dosett box as a compliance aid containing a week's supply of his medicines. This helped him to remember his medication and allowed a home help to check he was taking it.

consequently be decreased, leading to higher plasma concentrations of polar drugs such as lithium, cimetidine and many antibiotics. The use of diuretics may further exacerbate this problem.

Since the elderly have a decreased lean body mass, the volume of distribution of drugs that are highly bound to muscle, notably digoxin, is reduced and plasma concentrations increased.

Changes in volume of distribution alone tend to affect the loading doses of drugs and dose intervals rather than overall total daily maintenance doses.

The elderly may have a reduction in plasma albumin of as much as 25 per cent, resulting in a higher free (active) concentration of drug for highly bound agents, such as phenytoin, digoxin and warfarin, which can result in an increased drug effect. Such cases may remain undetected by therapeutic drug monitoring in which both the free and the bound drug concentrations are routinely measured.

CHRONIC DISEASES ASSOCIATED WITH ELDERLY PEOPLE

FOR EACH COMMUNITY PHARMACY IN THE UK THERE ARE ESTIMATED TO BE:

- 800 people over 65
- 350 people over 74
- 75 people over 85
- 60 patients with heart failure
- 60 patients with stroke
- 12 patients with Parkinson's disease
- 50 diagnosed non-insulin dependent diabetics
- >50 undiagnosed diabetics
- 150 patients with rheumatoid arthritis
- 75 patients with glaucoma

tends to increase, leading to a prolonged half-life of drugs such as psychotropic agents, particularly benzodiazepines.

Total body water can decrease by up to 15 per cent in older patients and the volume of distribution of water-soluble drugs may

Drug metabolism Drug metabolism is reduced with advancing age due to a loss of liver mass (and therefore the number of functioning hepatocytes) and reductions in liver blood flow. Phase 1 metabolic pathways, such as microsomal oxidation and reduction, are more susceptible to age-related change than phase 2 conjugation pathways. Potentially those drugs whose liver metabolism is blood flow dependent, such as propranolol, may be susceptible to increases in bioavailability due to reduced first pass metabolism.

However, the clinical significance of age on drug handling by the liver is difficult to judge and the effects of concomitant disease make age-related changes in hepatic function unpredictable. The problem of identifying patients at risk is partly due to the lack of reliable markers of "liver function". The laboratory markers, such as "liver enzymes", reveal changes in structure rather than test specifically for changes in function.

A generally high hepatic capacity for drug metabolism casts doubt on the clinical significance of age-related changes in the absence of liver disease.

Renal elimination

Renal elimination is more predictably affected by ageing. Glomerular filtration rate (GFR, normally 100-140ml/min) declines by 1 per cent per year from age 40. It is further affected by

SOME DRUGS LARGELY DEPENDENT ON RENAL ELIMINATION WHICH MAY REQUIRE DOSAGE ADJUSTMENT

Aciclovir	Amiloride	Aminoglycosides	Atenolol
Atropine	Baclofen	Captopril	Cephalosporins
Chlorpropamide	Chloroquine	Ciprofloxacin	Clonidine
Cimetidine	Digoxin	Dipyridamide	Doxycycline
Enalapril	Ethambutol	Flecainide	Flucytosine
Fruzemide	Gold	Lithium	Metformin
Methotrexate	Midazolam	Nadolol	Nalidixic acid
Nitrofurantoin	Penicillamine	Penicillins	Procainamide
Primidone	Ranitidine	Tetracycline	Thiazide diuretics
Triamterene	Trimethoprim		

concomitant disease affecting the kidneys directly or indirectly through renal blood flow. Creatinine clearance (Clcr) is a suitable indicator of GFR.

In practice, creatinine clearance is more often estimated from serum creatinine rather than measured from urinary output. In the elderly, who have a reduced muscle mass, serum creatinine concentrations within the normal range are compatible with marked renal function impairment (see Panel below).

Plasma urea (reference range approximately 3-6mmol/L) is used routinely to screen for impaired renal function but it is a poorer marker of reduced GFR than serum creatinine because it can be increased by dehydration or gastrointestinal bleeding and decreased by liver dysfunction.

Estimation of the patient's renal function to assess the need for any dosage reduction requires the use of a predictive equation. The equation of Cockcroft and Gault has been shown to be as reliable as the direct measurement of creatinine clearance from 24 hour urine collection in routine practice.

The Panel on p687 shows some commonly prescribed drugs largely dependent on renal elimination for which dose adjustment may be needed in the elderly.

Pharmacodynamic changes Pharmacodynamic changes are due to changes in the responsiveness of the target organ, giving rise to an increased or decreased effect of a given dose compared with that seen in a younger patient. These changes may be due to a change in receptor binding or a decrease in receptor number. Enhanced sedation from benzodiazepines and decreased antihypertensive effectiveness of beta-blockers are examples of pharmacodynamic changes in receptor responsiveness seen in the elderly.

Clinical data on the use of a new drug in elderly patients is usually limited and clinical

Case study 2: The use of digoxin

Digoxin is still commonly prescribed and remains a cause of toxic symptoms

Mrs M. W. is a 74-year-old widow taking digoxin for cardiac failure and atrial fibrillation. She is also receiving frusemide 80mg daily and verapamil 40mg three times daily. Normally an active sociable woman who manages at home independently, she has become moody and withdrawn lately since a hospital admission. On inquiry she also complained of poor appetite and loose stools.

Digoxin toxicity (in this case manifesting as effects on mood, nausea and diarrhoea) may be precipitated by interaction with verapamil which increases digoxin plasma concentrations by reducing the volume of distribution and the clearance of digoxin from the body. The patient's digoxin concentration should be measured to confirm digoxin toxicity and the plasma potassium should also be checked to assess the possible contribution of hypokalaemia to the exacerbation of digoxin toxic effects.

The digoxin concentration was 3.2 nmol/L (reference range 1.3-2.6 nmol/L) and the serum potassium 2.8 mmol/L (reference range 3.5-5.5 mmol/L). The digoxin dose was halved and the frusemide substituted with a potassium-sparing diuretic combination of frusemide with amiloride. Mrs M. W.'s mood and appetite improved over the next week.

cal evidence about changes in drug responsiveness must await the accumulation of experience with the drug after marketing. A cautious approach to the use of new agents in the elderly is therefore justified and suspicions of unwanted effects deserve to be documented in pharmacy records and medical case notes. Pharmacists must ensure any suspected adverse reactions are formally reported.

ADVERSE DRUG REACTIONS IN THE ELDERLY

In elderly patients, the number of serious adverse drug reactions reports to the Committee on Safety of Medicines is more than twice that in patients under 40 years old. Although older patients are not considered to be at greater general risk of non dose-related (idiosyncratic) adverse effects, there are notable exceptions; for instance, older patients are at greater risk of antibiotic-associated colitis. More importantly, susceptibility to dose-related adverse reactions increases due to changes in drug handling associated with ageing. Furthermore, the greater exposure of older patients to drugs simply increases the risk of adverse drug reactions.

The detection of adverse effects in the elderly is complicated by both the co-mor-

bidity and the polypharmacy that are prevalent in geriatric medicine. Unwanted drug effects may add to the co-morbidity of age and co-existing disease may mask the presence of underlying drug-related clinical effects. Co-morbidity and polypharmacy therefore make detection of adverse drug effects more difficult. Moreover, the tendency to overprescribe in the elderly may result in the inappropriate use of one drug to treat the adverse effects of another. In practice, expedients aimed at reducing the number of prescribed medications in an elderly population can reduce the number of ADRs.

The Panels below show examples of sub-optimal and inappropriate prescribing that were highlighted by the Royal College of Physicians in its recent report on drug use in the elderly.

CAUSES OF SUB-OPTIMAL PRESCRIBING IN OLDER PEOPLE IDENTIFIED BY THE RCP¹

- Inadequate clinical assessment leading to incorrect diagnosis
- Failure to record current medication, including OTCs
- Failure to monitor response to treatment
- Failure to document previous adverse drug reactions
- Excessive prescribing
- Inappropriate prescribing
- Failure to review repeat medication
- Failure to take account of altered pharmacokinetics and pharmacodynamics

EXAMPLES OF INAPPROPRIATE PRESCRIBING CITED BY THE RCP¹

- Phenothiazines for dizziness due to postural hypotension
- Major tranquillisers for acute confusional states
- L-dopa for non-Parkinsonian tremor
- Antibiotics for viral upper respiratory tract infections
- L-dopa for phenothiazine or metoclopramide induced Parkinsonism
- Benzodiazepines for insomnia due to depression
- Loop diuretics for dependent oedema

Estimating renal function

The serum creatinine reference range (70-110µmol/L) can be deceptive:

- A serum creatinine of 90 µmol/L in a 70kg, 29-year-old woman is compatible with a creatinine clearance of 90 ml/min
- A serum creatinine of 90 µmol/L in a 53kg, 80-year-old woman is compatible with a creatinine clearance of 35 ml/min

The Cockcroft and Gault equation takes into account age-related changes in the estimation of creatinine clearance:

$$\text{Clcr} = \frac{[140 - \text{Age}] \times \text{Bodyweight (kg)} \times F}{\text{Serum Creatinine (}\mu\text{mol/L)}}$$

where F = 1.03 females and 1.23 males