INVITED ARTICLE

DRUGS AND THE ELDERLY

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ABSTRACT

Prescribing for the older individual requires a great deal of thought. Multiple pathology is usually associated with multiple drug taking and therefore a high risk of adverse drug reactions. Physiological changes have important bearing on drug usage. Constant vigilance is required to ensure safe prescribing.

Keywords : Adverse drug reaction, compliance, drug distribution, renal function, polypharmacy

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INTRODUCTION

"I do not wish two diseases, one nature made and one man made"

Napoleon I (1769-1821)

The elderly suffer more disability and disease than younger people and are prescribed more medication.

In 1980, for example, in Britain, twice as many prescriptions were dispensed to the elderly as the national average[1]. Multiple pathology is almost always associated with polypharmacy.

It has been estimated that in Britain, 75% of the population over the age of 75 years is on regular medication. Two thirds of these regular drug-users take one to three drugs regularly and one third take four to six drugs regularly[2,3].

There is no reason to suggest that the situation is any different in Singapore.

Polypharmacy in the elderly causes concern because of the associated increased incidence of adverse drug reactions. The mortality from this form of iatrogenic diseases rises disproportionately with age.

It is suggested that two groups of drugs cause nearly two thirds of all reactions; drugs acting on the circulation (hypotensive agents, digoxin, diuretics) and drugs acting on the brain (hypnotics, tranquillisers and antidepressants).

The factors contributing to the high incidence of adverse reactions are listed in Table I.

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Table I

Factors Contributing to High Adverse Reaction Rate	
1)	Inaccurate diagnosis
2)	Uncritical assessment of need of treatment
3)	Excessive prescribing
4)	Repeat prescribing without clinical reassessment
5)	Altered pharmacokinetics and sensitivity
6)	Patients' expectations
7)	Poor compliance

Unchecked polypharmacy can convert a competent individual into a confused incontinent bed-bound patient.

COMPLIANCE

Compliance is the extent to which a person's behaviour coincides with medical advice. Compliance depends on the participation of the patient, carer, pharmacist and doctor. To aid compliance the patient must have the mental capacity to understand the aims of treatment and the motivation to follow the treatment. To understand the aims of treatment the patient or carer must receive adequate explanation from the medical practitioner. The treatment should be as pleasant as possible. An elderly patient with swallowing difficulties may experience true physical difficulty trying to comply. The taste of the preparation may be too horrible to take particularly on a long term basis.

The pharmacist can aid compliance by ensuring that the patient or carer can understand the instructions on the tablet bottle. Patients and carers run into problems when they receive prescriptions from various doctors, some using generic names, some using trade names. The pharmacist can help prevent confusion. The pharmacist can enquire about pre-existing medication before supplying over-the-counter drugs.

The doctor should ensure that the patient has been given full information regarding possible side effects. The doctor should endeavour to identify all drugs taken by each individual regardless of how many other clinics are attended. Actually seeing all the tablets and tablet bottles is vital. Written instructions to the patient or carer may be useful.

Health education programmes could highlight the dangers of doctor or clinic "hopping".

Whenever possible the drug list should not include more than 3 drugs and even then the compliance of the 3rd drug may only be 50%. Whenever possible a twice daily regime should be recommended. A more frequent regime will be associated with decreasing compliance.

PHARMACOKINETICS

Pharmacokinetics includes drug absorption, distribution and metabolism.

Absorption of orally administered drugs is occasionally slower in the elderly, but this is rarely of importance.

However, it is worth noting that a large fluid volume swallowed at the time of drug taking improves absorption and prevents oesophageal stasis. Co-existing disease may delay absorption. Congestive cardiac failure may be associated with intestinal mucosal oedema and decreased splanchnic blood flow.

Pain or emotional upset may delay gastric emptying.

The prescribing of antacids may reduce the absorption of drugs normally absorbed in the stomach. Antacids cause a high gastric pH which will favour rapid gastric emptying (Table II).

Table II

Drugs Affected by Concomitant Antacid Prescription
Chlorpromazine
Diflunisal
Ciprofloxacin
Rifampicin
Pivampicillin
Tetracycline
Chloroquine
Iron
Penicillamine

Anticholinergics delay gastric emptying and will therefore delay absorption of drugs normally absorbed in the small intestine eg. madopar.

The main changes affected drug distribution are summarised in Table III.

Table III

Body Changes Affecting Drug Distribution	
1)	Lean Body Mass ↓
2)	Fat Mass ↑
3)	Organ Blood Flow ↓
4)	Plasma proteins ↓ (including albumin)
5)	Body water ↓

The distribution of a drug is influenced by the degree of protein binding and by its lipid solubility.

Ageing is associated with a decrease in serum albumin which is further decreased by chronic disease and immobility. There may be increased availability of albumin bound drugs eg. salicylates, phenytoin, pethidine and prednisolone. Where side effects are thought to be dose related eg. prednisolone, the elderly may be at greater risk.

Lipophilic drugs eg. propranolol, imipramine and cimetidine tend to bind to glycoproteins and lipoproteins. If several lipophilic drugs are prescribed together, there will be an increased chance of displacement from binding sites and increased chance of side effects (Table IV).

Table IV

Lipophilic Drugs Displaced by Cimetidine
Nifedipine
Propranolol
Metformin
Benzodiazepines

HEPATIC METABOLISM AND ELIMINATION

Elimination and hepatic inactivation of many drugs are reduced in the elderly as a result of age-related changes in renal and hepatic function. Water soluble polar drugs are excreted unchanged by the kidneys but lipid-soluble drugs need to be metabolised to water soluble compounds before excretion. The rate of metabolism controls the duration of action of a single dose and the steady state concentration reached by multiple dosing.

Metabolism occurs by either oxidation, hydroxylation or acetylation.

The first two processes undergo age related changes rendering them less efficient. Reduced plasma clearing has been documented for chlormethiazole, chlordiazepoxide and propranolol.

Renal blood flow decreases with age, being reduced by approximately 45% by the age of 65 years. If excretion is impaired than the steady state concentration is likely to be increased.

The steady state concentration of propranolol tends to be increased by a factor of 4 comparing a 40 year old and a 70 year old.

Procainamide, pethidine, nitrofurantoin and allopurinol all produce metabolites which tend to accumulate in the presence of renal impairment.

It is well to remember that urea and creatinine estimations do not provide reliable estimation of renal function in the older individual.

PHARMACODYNAMICS

The responses of the target organ to a given drug are only understood in a very basic way at present. Research in this area is extremely difficult to perform. The study of receptors is a developing science.

Pharmacodynamic changes are thought to be responsible for the increased sensitivity to drugs with ageing.

Increased plasma concentration of noradrenaline has been documented in the elderly. This increased sympathetic nervous system activity is thought to cause changes in adreno receptors[6]. Decreased sensitivity to agonists has been documented in ageing Beta adreno receptors[7]. The increased levels of circulating noradrenaline may result in down regulation of beta-receptors.

In the central nervous system, the reduction in endogenous neurotransmitters is thought to be implicated in the increased response of CNS receptors occurring with advancing age.

In advanced Parkinson's disease dyskinesias may be produced by low doses of dopamine agonists. This may be related to compensatory increases in post-synaptic dopamine receptors. Neuroleptic agents are thought to alter receptors thus leading to chronic tardive dyskinesias. Further study is required in this field. The elderly show an increased sensitivity to benzodiazepines[8]. It is postulated that this increased sensitivity is related to a reduction in a neurotransmitter, possibly gamma-amino-butyric acid.

Table V
Drugs Which Commonly Cause Problems in the Elderly

Drug	Problems	Reason
Digoxin	Toxicity	Reduced clearance
Disopyramide) Procainamide)	Toxicity	Reduced clearance
Diuretics (Loop)	Urinary incontinence	Urgency of micturition
Propranolol	Nightmares, Confusion	Lipid soluble
Hydralazine) Prazosin)	Postural hypotension	Reduced homeostasis
Warfarin	Many drug interactions	Protein binding
Diazepam) Nitrazepam)	Daytime drowsiness	Increased sensitivity
Phenothiazines (including those used for vertigo)	Extrapyramidal effects	Increased sensitivity
Tricyclic antidepressants	Postural hypotension Anticholinergic effects (confusion, constipation, urinary retention)	Increased sensitivity
Tetracyclines	Renal failure	Smaller functional reserve
Long acting sulphonylureas especially chlorpropamide	Hypoglycaemia especially at night	Reduced clearance
Oral iron-salts	Constipation, nausea, anorexia	
Non-steroidal anti-inflammatory drugs	Na+ retention, gastric toxicity Hypertension Heart failure aggravated	Antagonise anti-hypertensive agents Decrease glomerular filtration rate Inhibition of prostaglandins Diuresis prevented

NEW DRUGS

New drugs present particular problems as clinical trials rarely involve adequate numbers of elderly individuals.

Adequate information on safety and efficacy is often lacking. If a new drug is used in an elderly person then special vigilance is required.

CONCLUSION

The need for any treatment should be carefully considered. The treatment regime should use as few drugs as possible. It may be necessary to sacrifice some treatments to ensure that the essential ones are taken reliably.

At each repeat prescription, the continuing need for the drug should be reassessed.

There may be benefits from using a restricted list for elderly patients so that each drug is known and its effects in the elderly appreciated (Table V).

The patient may benefit from simple clear written instructions and memory aids may be helpful. Thought should be given to the blind, the poor-sighted and the arthritic. Bubble and blister packs may be difficult to negotiate.

Before discharge from hospital a period of supervised self-administration of drugs may help elderly patients establish correct medicine taking.

It is not sufficient to have a knowledge of basic pharmacology. Safe prescribing for elderly patients requires a knowledge of the age related changes in drug handling and an understanding of the practical problems involved in drug taking.

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