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Prescribing Drugs for the Elderly: Reaching Therapeutic Goals

SUMMARY

The positive aspects of drug use by the geriatric population are balanced by concerns about harmful effects of the drugs. Physiologic changes that accompany aging alter the pharmacology of many drugs, but problems of compliance, adverse reactions and polypharmacy are of equal importance. The authors of this article examine aspects of drug delivery in the elderly and make suggestions for improving prescribing practices. (*Can Fam Physician* 1986; 32:2633–2637.)

SOMMAIRE

Les aspects positifs de l'usage de médicaments chez la population gériatrique sont contrebalancés par les préoccupations engendrées par les effets nocifs des médicaments. Les changements physiologiques qui accompagnent le vieillissement altèrent la pharmacologie de nombreux médicaments, mais les problèmes de compliance, d'effets secondaires et de polypharmacie sont d'égale importance. Les auteurs de cet article discutent des divers aspects de la prescription de médicaments chez les personnes âgées et font des suggestions pour améliorer les habitudes de prescription.

Key words: geriatrics, pharmacotherapy, prescribing

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THE POSITIVE ASPECTS OF therapeutic drug use by the growing geriatric population are balanced by the concerns about harmful effects of drugs in the elderly. These concerns are well-founded. The belief that the function of geriatricians is to take patients off drugs prescribed by other doctors may inappropriately cause the overly cautious physician to under-medicate, or withhold effective medications, simply because the "patient is too old".

Surveys of practising physicians reveal serious deficiencies in knowledge of geriatric pharmacotherapy.[1] Many excellent reviews address the specific problems of drugs in the elderly, and research in this area is progressing. There is an increased awareness of the problems and challenges, and drug manufacturers are now beginning to recommend specific dosing schedules for elderly patients. Nonetheless, basic prescribing errors frequently occur. "Start low and go slow", an invaluable clinical maxim, roughly allows for the altered disposition and distribution of drugs in the elderly, but it should be emphasized that problems relating to compliance, adverse reactions and polypharmacy must be considered as of equal, and in some cases of greater, importance.

Drug Distribution and Disposing

Pharmacokinetics attempts to quantify the absorption, distribution and elimination of drugs and to predict precisely the plasma concentration of the drug. *Pharmacodynamics* quantifies the organism's response to a given concentration of drug. A basic understanding of how aging affects the pharmacokinetics and pharmacodynamics of drugs is essential to optimum prescribing for the elderly.[2, 3]

The plasma concentration of a drug is a function of dose per unit time divided by clearance. A high dose and short dosing interval or decrease in clearance rate would result in a greater drug concentration. The dosing schedule must therefore be adjusted according to the clearance so that the desired drug concentration is obtained. The clearance of a drug is

independent of the manner of its distribution throughout the body; it is related to the ability of the kidneys and liver to dispose of the drug.

The drug half-life, a related but different value, is of importance in defining the rate of achieving a steady state, or the rate of recovery from the effects of a drug when its use is discontinued, but should have little effect on a physician's choice of drug dosage or the interval of administration.

Renal and Hepatic Clearance of Drugs

Renal function is known to decline with aging; the mean glomular filtration rate decreases by approximately 35%.[3] Predicting appropriate drug-dosing intervals for drugs cleared by the kidneys may be difficult. The serum creatinine depends on lean body mass and is not always an accurate predictor of renal function in the older patient. Measurement of the 24-hour creatinine clearance is cumbersome and rarely practical. Several nomograms and formulae are available to predict the creatinine clearance. In practice an educated guess is often made, and drug dosage and interval are decided on the basis of the patient's body size, age and serum creatinine. The shortcomings of these approaches are apparent in the commonly encountered toxicity associated with renally cleared drugs such as digoxin and aminoglycosides. The situation is further complicated by the fact that renal clearance is modified by factors such as changes in intravascular volume, blood pressure, intercurrent illness and concomitant use of other drugs.

Hepatic drug clearance is more difficult to predict than is renal clearance.[3] There are no readily available laboratory measurements that accurately correlate with the liver's capacity to clear drugs. The oxidative metabolism of many drugs is decreased with aging, but conjugative reactions are little altered. Drugs are metabolized by one or both pathways in sequence, and their relative effect on hepatic clearance depends on the specific chemistry of each drug. However, inter-individual variability, smoking or the concomitant use of other drugs that either inhibit or induce hepatic enzymes are of relatively greater importance than age-related changes.

If the effect of aging on hepatic clearance of a given drug is unknown, it is safest to assume that it will be to decrease clearance. Furthermore, like renal clearance, hepatic clearance is not a static property, but is subject to modulation by drugs and external influences which can induce or inhibit hepatic enzymes, decrease effective hepatic mass, or decrease blood flow.

Absorption and Distribution of Drugs

Most drugs are absorbed from the gastrointestinal tract by passive diffusion. Despite predictions to the contrary, age-related changes in gastrointestinal function, such as decreased gastric acid secretion, motility, and reduced active transport processes, have little or no effect on drug absorption.[3] However, pathological changes in gastrointestinal function may have profound effects on the absorption of certain drugs. For example, mucosal edema of the gut, occurring in congestive heart failure, can significantly impair the absorption of furosemide and other cardio-active agents.[4]

The decrease in lean body mass and the increase in adipose tissue which occur with aging, can change the distribution of certain drugs.[2, 3] Fat-soluble drugs such as diazepam and phenothiazines have an increased volume of distribution, whereas drugs that are more water soluble have a decreased volume of distribution.

These changes have no major effect on the steady state concentration, but have an effect on the rate of attainment of the steady state. Such factors determine the optimum time to monitor drug levels or reassess therapy. Haloperidol, a highly lipid-soluble compound with a half-life of up to 35 hours, may produce profound extrapyramidal symptoms weeks after initiation because once fat stores are saturated, serum levels increase dramatically, thereby causing unanticipated cumulative effects. Similarly, the recovery period after withdrawing medication may be quite prolonged (Case 1). On the other hand, a decreased volume of distribution for water-soluble drugs such as alcohol accounts, at least in part, for the apparent increased sensitivity to acute dosings in the elderly.

The volume of distribution of highly protein-bound drugs is decreased in elderly patients because of the age-related decline in plasma albumin concentration.[3, 5] The changes become more pronounced when there is poor nutrition, chronic illness or severe debilitation. The major implication of this decreased plasma drug-binding capacity is that therapeutic and toxic plasma concentrations of drugs can be shifted to lower ranges in the elderly.[5]

Unfortunately, even if one could accurately predict and control drug concentration, age-related and inter-individual variability in pharmacodynamics preclude precise prediction of individual patient response. It is generally believed that elderly patients are more sensitive to a given concentration of drug, and studies on the sedating effect of the diazepines and the anticoagulant effect of coumadin support this premise.[6, 7] However, findings of decreased sensitivity to beta-receptor agonists and antagonists in some older subjects indicates that this is not true in all cases.[8] Continued research in this area will undoubtedly yield important, clinically relevant findings.

Compliance

Approximately 30% to 50% of patients of all ages are non-compliant, a problem that physicians largely underestimate.[9] Elderly patients are no better or worse than younger patients in this regard.[10] However, the factors that lead to non-compliance in the geriatric population may be quite different from those that influence younger individuals. 'Compliance' in the present context is used in the broadest sense and includes over- or under-medication both voluntarily and as a result of error. More than 50% of ambulatory patients make significant medication errors.[11, 12] Identified risk factors include aging, living alone, multiple diagnoses and general debility. Adding to this is the occasional problem of errors of prescribing and dispensing that occur despite the shared concerns of physicians and pharmacists about appropriate drug delivery for the elderly.

Causes of Medication Errors

Some medication errors are the direct result of the patient's inability to read, comprehend or remember instructions.[2] Identifying such disabilities may be the first clue to the exis-

tence of non-compliance. The ideal solution in some cases may be to provide continued supervision, but this is neither practical nor desirable in every case. Alternative solutions such as drug schedules and maps, or multiple-dose pill boxes can be very helpful. If the patient is unable or unwilling to take medications reliably, it may be wiser, in some cases, to withhold therapy altogether rather than risk medication error.

Lack of compliance is often the result of the patient's poor understanding of the purpose of, and expectations for, a particular therapy. This is especially important when the physician is dealing with chronic illnesses such as hypertension or diabetes that commonly occur in the older population. Symptoms may be mild or absent, and so the patient may have difficulty understanding the need for medications. Similarly, the patient may not understand the diagnosis: "Why are my feet swollen if I have problems with my heart?" A clear, careful explanation of the problem, the purpose of therapy, and the expected outcome, given in simple terms that the patient can understand, is invaluable for improving compliance.

The form and packaging of therapeutic products are often significant factors in drug use. Child- and tamper-proof packaging are known to create difficulties, especially when patients are debilitated by arthritis, impaired vision or neurological problems.[13, 14] There would be little use in prescribing an anti-inflammatory drug in suppository form for an arthritic who lacks mobility to properly insert it.

Elderly patients often have great difficulty swallowing pills and capsules because of decreased salivation or impairment in the swallowing mechanism caused by disease. Supplying medications in alternative forms such as elixirs sometimes leads to more difficulties because accurate dose measurement and administration are less certain. Likewise, crushing pills and opening capsules does not always ensure that the prescribed dose will be consistently ingested and may interfere with the appropriate delivery of some controlled-release preparations. Time spent coaching elderly patients on when and how to take their medication can sometimes make the difference between therapeutic success and failure (Case 2). For example, a few sips of water or other appropriate fluid before the pill is taken, with a generous amount of fluid to follow, can improve chances of the drug arriving at its site of absorption.

Aerosolized medications such as bronchodilators or steroids are effective in the treatment of chronic obstructive lung disease and asthma, with relatively little systemic absorption. The use of spacer devices such as the Aerochamber® can greatly improve drug delivery to the site of action in patients who, without these devices, lack the required co-ordination for puffer use.[15]

Polypharmacy and adverse drug reactions are endemic in the geriatric patient population. Each of these problems can have a major effect on patient compliance. Each of these areas will now be examined more closely.

Adverse Drug Reactions

Adverse drug reactions (ADRs) may be defined as any undesirable reaction caused by medication. These reactions result because of exaggeration of the intended therapeutic response, an unrelated toxic effect, or an interaction with a second therapeutic agent. In addition to being a potential factor that can lead to patient non-compliance, it has been estimated that ADRs play a significant role in over 10% of geriatric hospital admissions, and in some cases represent the sole reason for admission.[16]

Because many diseases can have atypical presentations in the elderly, ADRs may be more difficult to identify in this age group.[17] Drugs must always be considered in the etiology of virtually any problem presenting in the elderly. Failure to recognize ADRs can result in the addition of more drugs rather than the appropriate withdrawal of the offending agent. The consequences of ADRs may be more severe, and recovery may be less complete in this age group. Consider, for example, the morbidity and mortality associated with falling in the elderly, a condition in which ADRs have been strongly implicated. Tardive dyskinesia resulting from the use of phenothiazines is usually not completely reversible (Case 2).

Elderly patients are at greater risk for ADRs than are younger persons. Hurwitz found that the incidence of ADRs more than doubled in hospitalized patients over 80 years of age as compared with those under 60.[18] The reasons for this discrepancy are manifold. The existence of multiple pathologies increases the likelihood of exacerbation of an existing disease state. Elderly patients may be more sensitive to some toxic effects. The concomitant use of a greater number of medications is known to increase the incidence of ADRs. Evidence suggests that there is a "threshold" number of drugs (5–7), above which the number of ADRs increases markedly.[19] Most ADRs involve cardiovascular or psychotropic drugs, agents in common use in the elderly. Approximately 75% of nursing-home residents receive at least one of these agents.[3]

The finding of ADRs does not always necessitate the discontinuation of the implicated agent. Risks must be weighed against benefits in each case. Often it is preferable for a patient to tolerate an ADR in order to enjoy the therapeutic benefit of a drug. An example of a tolerable ADR might be the dysgusia associated with captopril, an agent that is highly effective in the treatment of congestive heart failure. Patients can be trained in certain manoeuvres that can minimize some drug side-effects. The dangers of postural hypotension can be decreased by instructing patients to rise to the standing position gradually and with support.

Although as a general principle it is ill-advised to attempt to ameliorate an adverse drug reaction by the addition of a second agent, there are some circumstances where this attempt is warranted. The use of anticholinergic agents to counteract the extrapyramidal side-effects of phenothiazines, or the treatment of significant diuretic-induced hypokalemia by the addition of potassium supplements, are examples.

Polypharmacy

Because of the increase in illness and disease that occurs with advancing age, it is not surprising that the number of medications used also increases with age. Indeed, it is not unusual for a geriatric patient to be taking more than 10 medications simultaneously. Many chronically ill patients with several diagnoses often require complicated therapeutic regimes for adequate symptom control. However, diagnostic errors or failure to recognize ADRs result in prescribing of additional med-

ications rather than the more appropriate revision of existing theraptutic regimens. The "additive" approach may unnecessarily complicate therapy.

When patients receiving multiple medications are assessed, the question often arises whether such polypharmacy is warranted. Medical histories may be poorly documented or unavailable, and some patients cannot recall details of their medical past. Since compliance decreases and the incidence of ADRs increases with the number of drugs taken, simplifying therapy can in some cases significantly improve the patient's well-being (Case 3).

Review of a patient's compliance may reveal a number of unnecessary medications that are not being taken regularly and hence can be discontinued immediately. Other medications are best tapered with close monitoring of symptoms. It has recently been shown that rapid discontinuation of benzodiazepines is associated with withdrawal reactions that can be minimized when the medication is gradually decreased.[20] It has been shown that digoxin and diuretics, two of the most commonly used drugs in the geriatric age group, can successfully be withdrawn in selected patients.[21, 22] Many antihypertensive agents that are traditionally given four times daily are as effective when administered once and twice daily as in the more frequent doses. Avoidance of long-acting preparations sometimes prevents prolonged periods of unwanted side-effects.

Some drug-related problems require admission to hospital for a close monitoring of symptoms. Visits to a Geriatric Day Hospital or frequent office assessments can be well suited to this type of approach. Current studies have shown that hospitalization does not significantly decrease the number of drugs being taken, and indeed the number of drugs is often greater after discharge.[23] As recognition of this problem increases, expertise of physicians in simplifying drug regimens will improve. Polypharmacy as a distinct medical problem is a valid reason, in some cases, for seeking a specialist consultation.

Case History 1

D.W., a 76-year-old woman living in her own home, presented to another hospital with urinary tract sepsis. The sepsis resolved with antibiotics. However, she became agitated and was treated with haloperidol 3 mg daily. She was unable to return home and was discharged to a nursing home seven weeks later.

Approximately one year later she was admitted to the Behavioural Neurology ward at Baycrest Hospital because of continued deterioration. She had lost 40 lbs. in weight, was not eating well, and was poorly motivated. Examination showed a thin woman with bradykinesia, cogwheel rigidity, a shuffling gait, tardive dyskinesia, akathisia and mild cognitive impairment.

Haloperidol was discontinued, and over the ensuing period she made a slow but steady recovery. Attempts to treat her with levodopa 50 mg plus carbidopa 12.5 mg twice daily produced confusion and paranoid ideation, without any salutory effect. After nine weeks she was discharged to her own home. A follow-up visit three weeks later showed further evidence of improvement in gait, mood and cognitive ability.

Case History 2

T.H., an 81-year-old woman, was admitted to Baycrest Hospital because of palpitations and chest pain. She had a history of paroxysmal atrial fibrillation controlled by digoxin 0.25 mg daily. Because of occasional chest pain, isosorbide dinitrate 10 mg four times daily had been prescribed, nine weeks earlier. The patient had not understood her physician's instructions and took isosorbide dinitrate instead of digoxin. After admission, digoxin was restarted, and control of the ventricular rate was obtained.

During the next few days the patient experienced episodic chest pain while walking. Isosorbide dinitrate was discontinued and verapamil begun. Because of the potential interaction between verapamil and digoxin, her daily digoxin dose was adjusted to 0.125 mg.[24] On this regimen her rate remained controlled, and she experienced no further episodes of chest pain. She was discharged to her own home 10 days after admission.

Case History 3

A 78-year-old man was referred with a seven-month history of confusion. He had developed a three-year history of angina pectoris and had been hospitalized because of a myocardial infarction three months before being assessed. Hospitalization was complicated by confusion and disorientation. His only other problem was parkinsonism, for which he had been treated for a year. His medications included levadopa/carbidopa 100/25 three times daily, enteric-coated aspirin 650 mg twice daily, diltiazem 60 mg four times daily, allopurinol 300 mg daily, hydrochlorothiazide combined with amiloride (Moduret®), one tablet every other day, digoxin 0.125 mg daily, nitropaste four times daily, ranitidine 150 mg at night, and diazepam 5 mg twice daily p.r.n.

Other than generalized weakness, the only positive findings on physical examination were mild cognitive impairment and parkinsonism. Laboratory investigations showed mild azotemia, hyperkalemia and the digoxin level in the toxic range. Diazepam and Moduret® were discontinued. The dose of enteric-coated aspirin and diltiazem was decreased, and digoxin was held for three days, then restarted at 0.625 mg daily. Two weeks later there was marked improvement in the patient's general functional ability. Azotemia had improved and hyperkalemia and digoxin toxicity had resolved. Allopurinol is now being tapered, as the serum uric acid is in the normal range.

Suggestions for Improving Prescribing Practices

To improve prescribing practices, we suggest that physicians:

1. *Arrive at an accurate diagnosis.* This is often difficult in the older patient. Problems of obtaining an adequate history, the atypical presentation of certain illnesses, and frequent coexistence of multiple pathologies are common problems. The physician is in the best position to make a wise choice of therapeutic options when standing on a firm diagnosis. However, this ideal may not be possible in every case, since investigations are sometimes taxing for a debilitated patient. The alternative approach of instituting therapy for palliation or symptom control is quite acceptable in some cases.
2. *Set clear therapeutic goals.* Clear therapeutic goals should be set not only in terms of the desired results of therapy, but also in terms of the timeframe of treatment.

3. *Review the patient's drug regimen periodically.* The frequency of such review is determined by the therapeutic plan, the patient's reliability, the severity of illness, and the complexity of the drug schedule. Periodic reviews should include a check of the patient's compliance. Educate patients to bring with them *all* of their medications in the bottles, including those not currently used and non-prescription drugs. This practice provides valuable information about exactly what drugs the patient has access to, the names of pharmacies and other physicians the patient may be seeing, compliance, and potential errors involving look-alike drugs or drugs that have changed appearance. The patient can be quizzed about how and when each medication is taken, and this affords the physician the opportunity to dispose of drugs not being used.

4. *Evaluate for the presence of ADRs.* This is made easier if a limited practice formulary is used, and if the physician is familiar with drug effects and side-effects.

5. *Recognize problems related to polypharmacy and address the problems.* The physician should address the problem of "too many drugs" as he or she would address any presenting medical complaint.

With the increased average age of our population, problems in drug prescribing will increase. Alterations in drug pharmacology in the elderly are important, but focusing attention on the larger issues of appropriate drug prescribing will enhance the great value of modern therapeutics in the geriatric population. ◉

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