Drug therapy in the elderly

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Abstract

Drug dosage in the elderly requires an understanding of the age-dependent changes in drug disposition and sensitivity. The most important pharmacokinetic alteration is a decline in renal function, the elderly should therefore be treated as renally insufficient patients. Metabolic clearance is primarily reduced with drugs that display high hepatic extraction, whereas the metabolism of drugs with low hepatic extraction usually is not diminished. The reduction of metabolic clearance is especially pronounced in malnourished or frail patients. The water content of the aging body decreases, the fat content rises. Hence the distribution volume of hydrophilic drugs may be reduced in the elderly, resulting in increased plasma concentrations. In contrast, the distribution volume of lipophilic drugs is increased, their plasma concentrations may decrease. Intestinal absorption of most drugs is not altered in the elderly. Aside of these pharmacokinetic changes, one of the characteristics of old age is a progressive decline in counterregulatory (homeostatic) mechanisms. Therefore, drug effects are attenuated less, the responses are usually stronger than in younger subjects, the rate and intensity of adverse effects are higher. Examples of drug actions augmented in this manner are postural hypotension with agents that lower blood pressure, dehydration and electrolyte disturbances in response to diuretics, bleeding complications with oral anticoagulants, hypoglycemia with antidiabetics, and gastrointestinal irritation with non-steroidal anti-inflammatory drugs. The brain is an especially sensitive drug target in old age. Psychotropic drugs, anticonvulsants, and centrally acting antihypertensives may impede intellectual function and motor coordination. Hence drugs should be used restrictively in geriatric patients.

Keywords: Aging; Elderly; Pharmacokinetics in the elderly; Pharmacodynamics in the elderly; Drug dosage; Gerontopharmacology; Drug metabolism; Renal drug excretion; Pharmacokinetic dosage guidelines

1. Introduction

Generally, elderly are more susceptible to drug effects, adverse drug reactions are observed 2–3 times more frequently in geriatric patients than in younger adults (Turnheim, 1998) Aside from senescence, this problem is attributed in part to multimorbidity and polypharmacy in old individuals. To avoid drug interactions and compliance problems, drug regimes for the elderly should be as simple as possible, 1 or 2 treatments per day should be the goal. But the primary question is not which drug to prescribe and at what dosage, but whether a drug is necessary at all.

As a consequence of the age-dependent decline in physiological functions and changes in the composition of the organism, we are confronted with pharmacokinetic and pharmacodynamic mechanisms of altered drug responses in old age.

2. Pharmacokinetic changes and dosage guidelines

The most important pharmacokinetic change in the elderly is the reduction in renal drug elimination, as glomerular filtration rate, tubular secretion, and renal blood flow are reduced Disregarding the reduction in drug elimination by the kidneys in the elderly will result in increased drug serum levels. In fact, the decline in renal function is closely related to the incidence of adverse drug reactions (Lindeman, 1995; Mühlberg and Platt, 1999).
For drugs with linear pharmacokinetics, the reduction in renal drug excretion in old age can be compensated by correcting the maintenance dose, $D_m$, by the factor $Q$:

$$D_m' = D_m k_c/k_e = D_m Q,$$

(1)

where $k_e$ is the elimination rate constant. The prime, $'$, designates the values in old age. Renal elimination of most drugs is closely correlated with the endogenous creatinine clearance, $\text{CL}_{CR}$, therefore the dose adjustment factor $Q$ can be calculated from:

$$Q = Q_0 + (1 - Q_0) \frac{\text{CL}_{CR}'}{\text{CL}_{CR}},$$

(2)

where $Q_0$ is the non-renal elimination fraction or $k_e^{\text{NR}}/k_e$, $k_e^{\text{NR}}$ being $k_e$ in anuric patients (Turnheim, 1991). Alternatively $Q$ can be obtained from convenient nomograms that relate $\text{CL}_{CR}$ and $Q_0$ (Dettli, 1974; Spring, 1975). Values for $Q_0$ are listed in appropriate reference handbooks (for instance Dettli, 1996; Fichtl, 2001).

$\text{CL}_{CR}'$ as a function of age and serum creatinine concentration, $C_{CR}$ (in mg/dl), may be calculated from the Cockroft and Gault equation (1976):

$$\text{CL}_{CR}' = \frac{(140 - \text{age}) \times \text{bodyweight}(\text{kg})}{72 C_{CR}}.$$

(3)

This equation gives a value for the creatinine clearance in men, that for women is obtained by multiplication with 0.85 to account for the lower skeletal muscle mass in women. It has to be emphasized that the creatinine clearance calculated using Eq. (3) represents an average value for an individual in a certain age group. The only way to be certain about the creatinine clearance in a given person is to actually measure it.

In contrast to renal drug excretion, the effect of age on hepatic drug metabolism continues to be a controversial issue. In vitro, no consistent relationship has been found between age and the activity of microsomal cytochrome P450 enzymes (CYP) that are responsible for phase-I metabolism (Le Couteur and McLean, 1998). Under in vivo conditions, on the other hand, the metabolic clearance of some drugs is decreased by 20–40% (examples are amiodarone, amitriptyline, triazolam, fentanyl, nifedipin, warfarin, and verapamil), whereas that of others is unchanged (for instance alfentanil, diazepam, paracetamol [acetaminophen], celecoxib, diclofenac, citalopram, and risperidone), apparently irrespective of which CYP enzyme is involved (Turnheim, 2003). This discrepancy has been attributed in part to the property of high or low extraction of the drug by the liver. Drugs that are extensively ‘cleared’ from the blood by the liver display an age-related decrease in metabolic clearance as blood flow through the liver declines in the elderly. The metabolic clearance of drugs with low hepatic extraction, on the other hand, is usually not altered, since it is not dependent on hepatic hemoperfusion but on the tissue content of metabolizing enzymes (Le Couteur and McLean, 1998).

In general, the interindividual variation in metabolic drug clearance by CYP enzymes or phase-I reactions exceeds the decline caused by aging.

The nutritional status of a patient has a marked influence on the rate of drug metabolism. In frail elderly, drug metabolism is diminished to a greater extent than in elderly with normal body weight (Walter-Sack and Klotz, 1996; Vestal, 1997).

The intestinal absorption of most drugs that permeate the gastrointestinal epithelium by diffusion is not diminished in the elderly to a clinically relevant extent. Compounds that permeate the intestinal epithelium by carrier-mediated transport mechanisms may be absorbed at a lower rate in the elderly, e.g. calcium, iron, vitamins, and possibly nucleoside drugs (Turnheim, 1998).

Although there is atrophy of the epidermis and dermis in the aged with a reduction in barrier function of the skin, the rate of transdermal drug absorption may be diminished in elderly because of reduced tissue blood perfusion (Trautinger, 2001). This holds also true for absorption from the subcutaneous and muscular tissue. Intramuscular injections should be avoided generally in this age group because of erratic absorption and the high risk of sterile infiltrates.

Body water content falls by 10–15% until the age of 80. The volume of distribution of hydrophilic drugs therefore decreases, the equivalent doses given to younger individuals will result in higher plasma concentrations. This, for instance, is the case for aspirin, tubocurarine, edrophonium, famotidine, lithium, but also ethanol (Turnheim, 1998). Use of diuretics may reduce the extracellular space even further, leading to accentuation of toxic drug effects.

Body fat, on the other hand, increases on average from 18 to 36% in men and from 33 to 45% in women (Vestal, 1997). Thus, although the fat content is higher in women than in men, the relative change in the volume of distribution for lipophilic drugs is more marked in men than in women. Examples for drugs with increased volumes of distribution in old age are amiodarone, diazepam, teicoplanin, and verapamil (Turnheim, 1998).

Very old individuals lose weight and become frail, a fact that is frequently over-looked as low weight patients frequently receive higher doses per unit body weight than heavier patients. Hence low body weight, in addition to advanced age, constitutes a risk factor for over medication (Campion et al., 1987).

Age-dependent changes in plasma protein binding are generally not clinically relevant, as drug elimination increases when the free (unbound) drug concentration is enhanced. A decrease in plasma protein binding may therefore obscure an age-related decrease in drug clearance.
The dose adjustment to account for a decline in total clearance can be obtained from

\[ D'_{m} = D_{m} \frac{f\text{CL}'}{f\text{CL}}, \]  

where \( f \) is the drug bioavailability and \( \text{CL} \) the total clearance that is equivalent to \( V \cdot k_{e} \). Average values for \( f, V, k_{e}, \) and \( \text{CL}/f \) for a number of agents in old and young adults have been published previously (Turnheim, 1998). It should be noted that Eq. (4) takes into account age-dependent changes of \( V \) and \( f \) in addition to \( k_{e} \), whereas Eq. (1) compensates only for altered \( k_{e} \).

Using mean clearance values for the calculation of dosage with Eq. (4) will give average adjustments. Individual dosages can be obtained from the clearance in a given patient by measuring the area under the plasma concentration-time curve (AUC) and using the equation

\[ \text{CL}'/f' = \frac{D}{\text{AUC}^e}, \]  

where \( D \) is the dose administered. Alternatively, the individual clearance of a drug can be obtained from the steady-state drug serum concentration, \( C^{ss} \):

\[ \text{CL}'/f' = \frac{D_{m}}{C^{ss}e}, \]  

where \( \text{CL} \) and \( \text{CL}/f \) stand for the clearance after intravenous or peroral drug administration.

3. Pharmacodynamics

The pharmacokinetic guidelines for dose adjustment in the elderly given above disregard changes in the sensitivity to an agent. Aside from its concentration at the site of action, the magnitude of a drug effect depends on the number of receptors in the target organ, the ability of the cells to respond to receptor occupation (signal transduction), and on counter-regulatory processes that tend to preserve the original functional equilibrium. Thus, in addition to pharmacokinetics, the pharmacodynamics of a drug have to be considered in the elderly. An increase in drug sensitivity has to be assumed when the response to a given serum concentration is enhanced.

Age-related changes in pharmacodynamics may occur at the receptor or signal-transduction level or homeostatic mechanisms may be altered.

3.1. Receptor properties

A reduction in response to \( \beta \)-adrenoceptor agonists has been reported for the elderly, since the sensitivity of the myocardium to catecholamines is lower. Apparently \( \beta \)-adrenoceptors are downregulated in old age by increased serum noradrenaline levels, possibly because of diminished presynaptic \( \alpha_2 \)-adrenoceptor activity and augmented noradrenaline release. The decreased antihypertensive effect of \( \beta \)-adrenoceptor blockers may be related to the lower renin levels in the elderly. Responsiveness of adenosine \( A_1 \)-receptors, which mediate cardio-protective effects, is also reduced as is the activity of heart muscarinic receptors (Hämmerlein et al., 1998; Swift, 1990; Turnheim, 1998).

In contrast to effects mediated by \( \beta \)-adrenoceptors, responses to nitrates do not appear to change with age (Verhaeverbeke and Mets, 1997).

In the central nervous system the number of dopamine \( D_2 \) and cholinergic receptors is decreased in the elderly (Wong et al., 1997), as will be discussed below.

3.2. Homeostatic mechanisms

One of the fundamental characteristics of aging is a progressive reduction in homeostatic mechanisms. Hence, following a pharmacological perturbation of a physiological function, more time is required to regain the original steady-state as counter-regulatory measures are reduced. Therefore, drug effects are attenuated less in the elderly, the reactions may be stronger than in young individuals and the incidence of adverse drug effects is higher, despite the general decline in receptor number or responsiveness.

A typical example for the consequences of the decrease in homeostatic mechanisms is the increased susceptibility of elderly patients to postural hypotension in response to drugs that lower arterial blood pressure (Turnheim, 1998). Drug-induced orthostatic reactions, that are estimated to occur at a frequency of 5–33% in geriatric patients, contribute to the risk of syncope and falls. When assessing orthostatic hypotension in the elderly, drug treatment should always be reviewed. 11% of cases of syncope in the elderly are reported to be drug-induced (Verhaeverbeke and Mets, 1997). In addition, peripherally acting antihypertensives such as calcium-channel blockers or loop diuretics may be associated with lower intellectual scores in the elderly (Turnheim, 1998). But untreated, elevated blood pressure may also be associated with cognitive impairment (Amenta et al., 2002).

Do the aged benefit from antihypertensive therapy? At the present time, it would appear reasonable to treat elderly patients with hypertension, particularly those with evidence of target organ damage (Duggan, 2001). According to the recently published ALLHAT study (2002), thiazide diuretics are superior to calcium channel blockers and ACE (angiotensin converting enzyme) inhibitors with respect to prevention of cardiovascular complications in hypertensive patients, irrespective of age.

The role of ACE inhibitors in geriatric patients is debatable as renin secretion is decreased in this age group, but there is clinical evidence for a beneficial effect of these agents (Ahmed et al., 2002). Digoxin is recommended in patients with heart failure not adequately responsive to ACE-inhibitors and diuretics, and in cases with atrial
fibrilllation and ventricular tachycardia (Ahmed, 2003). The increased risk of digoxin toxicity in old patients is primarily attributed to reduced renal excretion (Hanratty et al., 2000).

Many elderly patients are on long-term therapy with diuretics. Because of a decrease in total body water with advancing age, an equal volume of fluid loss in young and old patients represents more severe dehydration in the elderly. Combined with the decrease in thirst, fluid intake, and cardiovascular reflexes, hypovolemia may contribute to deficits in hemoperfusion of vital organs (Vestal, 1997; Turnheim, 1998). In addition, the risk of patients over 65 years of age, especially when they are female, to develop hypokalemia, hyponatremia, and prerenal azotemia under treatment with thiazides in combination with loop diuretics is markedly higher than in younger patients (Hörl, 2002; Howes, 2002).

Diuretic therapy in the elderly is also complicated by the fact that the site of action of both loop and thiazide diuretics is the luminal cell membrane of the renal tubule. The intensity of the diuretic effect of these compounds is therefore not primarily related to their concentration in plasma but to that in the lumen of the tubule. The reduction of the renal clearance of loop and thiazide diuretics in the elderly results in higher plasma levels and systemic toxicity, whereas the diuretic and natriuretic effect is decreased (Oberbauer et al., 1995; Mühlberg et al., 2001).

The sensitivity of elderly patients to the anticoagulant effect of coumarines is higher than in younger individuals, the risk of bleeding is increased (Hylek, 2001; Russmann et al., 1997). The concentration-response relation of heparin, on the other hand, was shown not to change (Turnheim, 1998).

The age-related decrease in glucose tolerance appears to be a consequence of reduced insulin secretion and insulin sensitivity (insulin resistance), even when adjusted for increased obesity and physical inactivity that are usually associated with old age (Müller et al., 1996; Ikegami et al., 1997). Because of an age-dependent impairment of glucose counterregulation, advanced age is a risk factor for hypoglycemia caused by sulfonylureas (Turnheim, 1998).

The cell density of the bone marrow decreases and cell proliferation is diminished in the elderly, stimulation by growth factors is reduced. Hence, patients of this age group are particularly sensitive to the adverse effects of antineer drugs. The hematological toxicity of these compounds is increased as are the adverse effects on the gastrointestinal tract, the heart, and the nervous system (Vestal, 1997; Turnheim, 1998). The properties of a number of individual cytostatic drugs in elderly individuals have been described elsewhere (Skirvin and Lichtman, 2002).

The frequency of adverse effects of non-steroidal anti-inflammatory drugs (NSAID) on the gastrointestinal tract and the kidney increases with age, 3–4% of elderly patients treated with NSAID experience bleeding from the intestine compared with about 1% in younger subjects (AGS Panel, 1998; Wolfe et al., 1999). The recently developed selective inhibitors of cyclooxygenase-2 (COX-2) have analgesic and anti-inflammatory properties comparable to the classical non-selective NSAID, but gastrointestinal complications are half as frequent (Bombardier, 2002). The prevalence and severity of renal side effects observed with the classical NSAID and the COX-2 inhibitors are equal (Harris, 2002). The American Geriatrics Society has endorsed the use of COX-2 inhibitors for management of persistent pain in older persons (Editorial, 2002).

The central nervous system is a particularly vulnerable drug target in the elderly. Between the age of 20 and 80 years, brain weight is reduced by 20% and neuronal loss has been reported for several brain regions. The gray matter decreases continuously in volume with age, the white matter remains relatively unchanged. Most importantly, the number of synapses decreases (Katzman, 1995). The age-related reduction in dopamine content and receptor abundance predisposes to an increased frequency and severity of extrapyramidal symptoms in response to dopaminergic blockade by neuroleptics and metoclopramide. A high incidence of tardive dyskinesia, akathisia, and Parkinson syndrome is observed in geriatric patients on long-term antipsychotic therapy. The reduction in acetylcholine content, on the other hand, renders old individuals more susceptible to cognitive impairment and other anticholinergic effects of neuroleptics and tricyclic antidepressants (Kompoliti and Goetz, 1998; Turnheim, 1998).

The prevalence for pain increases with advancing age. When poorly controlled, pain may lead to depression and reduces the activities of daily living. Pain management in the aged should follow the WHO three-step scheme using non-opiod analgesics, weak and strong opioids in sequential order with tricyclic antidepressants and antiepileptics as adjuvants (Davis and Srivastava, 2003). Care has to be exercised with opioids as the response to conventional doses may be increased in the elderly, frequently there is oversedation, respiratory depression, and a reduction of protective reflexes (Turnheim, 1998).

The potential for adverse reactions is also increased with antiepileptic drugs, more atypical effects such as intellectual deficits are observed in geriatric patients. The hematological toxicity of these agents is increased in old age as well. In addition, the cardiac symptoms caused for example by intravenous administration of carbamazepine and phenytoin may be life-threatening in the elderly, whereas they are usually irrelevant in young adults. The dosage of phenytoin is generally complicated because of the non-linear pharmacokinetic behavior of this anticonvulsant (Bachmann and Bello, 1999). It is advised to reduce the initial dose of antiepileptic drugs by 50% in geriatric patients. Plasma concentrations required for young adults may be toxic for the elderly, hence the dosage should be primarily adjusted by clinical symptoms, not by target plasma levels established for therapeutic drug monitoring in young individuals (Willmore, 1995; Hetzel, 1997; Tallis et al., 2002).
Age-dependent changes in the GABA<sub>A</sub>-benzodiazepine receptor complex were shown not only in number but also in subunit composition. Possibly these alterations are responsible for the high sensitivity of elderly patients to benzodiazepines, for instance midazolam (Klotz, 1998). Not only is sedation accentuated, but in addition there may be confusion, ataxia, and immobility. Benzodiazepines may cause impairment of short-term memory and contribute to subtle cognitive disturbances in the aged. Many elderly are dependent on benzodiazepines, withdrawal symptoms include tremor, agitation, insomnia, and seizures. Should treatment with these agents be absolutely necessary, short-acting benzodiazepines such as triazolam and oxazepam are to be preferred (Kompoliti and Goetz, 1998). Meprobamate is highly addictive, it should not be used in old individuals (Beers, 1997).

The prescription of psychotropic drugs is disproportionately high in the elderly and frequently inappropriate. This problem appears to be especially acute in nursing homes. Intellectual functions are not only diminished by benzodiazepines but also by antidepressants, neuroleptics, and anticonvulsants. Frequently neuroleptics are given for non-psychotic behavioral and psychological symptoms (Ruths et al., 2001).

As mentioned above, the antimuscarinic effects of tricyclic antidepressants are augmented in older individuals, this patient group may react with symptoms such as agitation, confusion, impairment of attention and memory, and ultimately delirium. Selective serotonin reuptake inhibitors (SSRI) do not have significant anticholinergic effects, hence these drugs should be the first-choice antidepressants in the elderly (Kompoliti and Goetz, 1998; Turnheim, 1998).

Other drugs with antimuscarinic activity are phenothiazines and butyrophenones, histamine H<sub>1</sub>-receptor antagonists, and conventional M-cholinocceptor antagonists such as atropine.

In addition, the antidepressants amitriptylin, imipramin, and maprotilin and the neuroleptics thioridazine, droperidol, and haloperidol may have adverse cardiac effects, causing prolongation of the QT-interval in the electrocardiogram and possibly life-threatening ventricular tachyarrhythmias (‘torsade de points’). Old age, bradycardia, heart failure, and multiple drug use are risk factors for these effects (De Ponti et al., 2002). SSRI antidepressants and the newer atypical neuroleptics risperidone, quetiapine, olanzapine, and clozapine have no or only a negligible effect on the QT-interval.

In short, the uncritical use of sedative drugs appears to be an important cause for the increase in morbidity in old age. Some of these compounds may give rise to global cognitive deficits, motor incoordination and gait irregularities as well as cardiac arrhythmias. Consequently, the incidence of falls and injuries is increased both in community-dwelling older persons and those living in long-term care-facilities (Leipzig et al., 1999; Ensrud et Ensurd et al., 2002). Although there are some uncertainties concerning the association between drug use, illnesses, and falls (Agostini and Tinetti, 2002), clearly the use of CNS-active medication in the elderly should be curtailed as much as possible.

4. Antiaging or longevity medicine

Throughout the industrialized countries, the marketing of ‘antiaging’ remedies is a multi-million dollar business that claims to slow, stop, or even reverse the aging process. But in spite of considerable hype to the contrary, there is no scientifically valid evidence that anti aging drugs presently on the market (DHEA, growth hormone, melatonin, fish oil, St Johns wort, procain, ginsend, ginko biloba, etc) can increase longevity (Platt, 1990; Turnheim, 1995; Olshansky et al., 2002). In some cases these products may even be harmful (US General Accounting Office, 2001) and those selling them often misrepresent the science upon which the antiaging claim is based. Nevertheless, experiments with laboratory animals indicate that it may be possible to alter the rate of aging or the maximal life expectancy, and legitimate research is under way to develop drugs that have this effect. Of interest is the observation that life is prolonged in mice and rats with caloric restriction, presumably in part by delaying the occurrence of age-related diseases (Masoro, 2000). Other strategies that may increase life expectancy include interventions that reduce oxidative stress, hormone and cell replacement therapies (including stem cells), telomerase activation, or other genetic manipulations (Butler et al., 2002). The clinical studies concerning the effects of anti oxidants on aging have been inconclusive, whereas the adverse effects of these agents are sizable (Dröge, 2002).

DHEA (dehydroepiandrosterone) levels are reduced in many elderly individuals, prompting its substitution. However, advantageous effects of this key hormone in the world of antiaging medicine await confirmation, whereas an increased risk for hormone-dependent tumors cannot be excluded (Jockenhövel et al., 2001). In addition, problems that arise from the use of DHEA stem from the fact that this compounds is considered a food additive in the USA, not a drug, hence neither the DHEA content nor the risk-benefit relation are controlled (Meier, 2004). The production of growth hormone, which has anabolic actions on muscle and bone, is also markedly diminished after the age of 60. The effects of growth hormone are mediated in part by insulin-like growth factor 1, IGF-1, which may have tumor-promoting properties. Further, growth hormone is an insulin-antagonistic agent and causes fluid retention as well as acromegaly. The clinical efficacy of growth hormone in the anti-aging indication and the relation of desirable to adverse effects has not been shown in controlled studies (Jockenhövel et al., 2001; Strasburger et al., 2002). A particular non sense is the marketing of oral formulations of growth hormone (Vance, 2003).
An increase in life expectancy beyond that seen in the past century will require insights into the mechanism of the aging process which could provide the basis for its pharmacological manipulation. So far, no such progress is in sight (Holden, 2002).

5. Conclusions

Persons aged 65 or older are particularly susceptible to adverse drug reactions because of multimorbidity, the high number of medications used by this population, and age-associated changes in pharmacokinetic and pharmacodynamic properties. As much as one fifth of all hospital admissions of older subjects are attributed to adverse drug effects that are often unrecognized by these patients (Mannesse et al., 2000). Changes in patient medical status over time can cause long-term drug therapy to become unsafe or ineffective.

Certain drugs are rarely if ever indicated for the elderly because safer and/or more effective alternatives exist. Beers (1997) published a list of ‘inappropriate medications’ which should be avoided in old individuals, including amitriptylin, chlor Diazepoxide, disopyramide, doxepin, meprobamate, α-methylidopa, pentazocine, propanthelin, belladonna alkaloids, and ticlopidine. Between 3 and 25% of prescriptions to elderly persons were classified as inappropriate (Spore et al., 1997; Sloane et al., 2002). Selection of medication is an important factor influencing the likelihood of adverse drug events.

Because of these uncertainties, advanced age is frequently considered to be an unpredictable risk factor for drug treatment, consequently the elderly may be denied adequate pharmacotherapy (Editorial, 1993; Turnheim, 1998).

The drug doses that are usually prescribed for younger adults may be too high for old individuals. In addition, it is important to recognize the heterogeneity of drug response in the elderly. Therefore, there are no simple rules for prescribing that may apply to the entire elderly population. Rather, the dose has to be determined individually considering particularly the reduction in body weight and renal elimination in a given patient. Pharmacokinetic guidelines may be used to calculate doses that result in drug serum levels in the aged equivalent to younger adults. But this procedure neglects changes in sensitivity to drugs. Hence, starting from a smaller initial dose than used in younger adults (for example 50%) the dose should be titrated to a clearly defined therapeutic response. It would be convenient to use therapeutic drug monitoring to adjust dosage in old-age patients. However, robust drug serum concentration-effect relations for the elderly are lacking and therapeutic target concentrations are not well established for this age group. As a matter of fact, it may be difficult if not impossible to define such target concentrations for the elderly because of the marked inter individual variation in this segment of the population.

The need for pharmacotherapy has to be evaluated very restrictively in geriatric patients, the number of drugs administered simultaneously should be reduced as much as possible. The list of medications should be reviewed critically and periodically, i.e. drugs no longer needed should be discontinued. Only basic diseases should be treated, not epiphenomena. Hence, therapeutic priorities must be identified. The age-dependent pharmacological properties of the drugs prescribed for the elderly should be clear to the physician. A once or twice daily drug administration is optimal. This goal may be reached using drug preparations with retarded release or fixed drug combinations.

It has to be realized that drugs may worsen the course of chronic diseases. For instance, in patients with compensated insufficiency of the heart β-adrenergic blockers, calcium-channel blockers, and disopyramide may cause manifest cardiac failure; in patients with peripheral vascular disease β-adrenergic blockers can precipitate claudication; NSAID, aminoglycoside antibiotics, and intra vascular X-ray contrast media may aggravate kidney damage; the use of antimuscarinic agents can result in glaucoma, constipation, or urinary retention. Drugs that impair cognitive functions may cause social isolation and withdrawal. Adverse drug effects have to be considered when symptoms such as dehydration, postural hypotension, dementia or excitation, confusion, syncope and falls occur, especially when diuretic, antihypertensive, and psychotropic drugs are administered to elderly patients.

References


