

# Farmakoterapija stomatološkog bolesnika starije dobi

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## Sažetak

*Mnogi čimbenici mogu mijenjati reakciju starijih ljudi na lijek. Razlozi tomu mogu biti fiziološke promjene kao rezultat promjena u sastavu organizma i radu organa. Veći dio tih promjena posljedica su normalna procesa starenja. One mogu promijeniti farmakokinetiku i farmakodinamiku lijeka.*

*Patološke promjene, koje su češće u starijih, također mogu utjecati na učinak lijeka. Stariji ljudi boluju od većeg broja bolesti nego mladi ljudi. Mnogobrojne bolesti mogu biti razlogom polipragmazije. Uporabom većeg broja lijekova povećava se opasnost od neželjenih učinaka lijekova ili interakcija među njima.*

*Daljnji važan razlog pogrešaka terapije u starijih i pojave neželjenih učinaka lijekova smatra se da je posljedica loše provedbe terapije samog bolesnika, koji ne poštuje upute svojega terapeuta.*

*Terapeut mora osigurati prikladnu terapiju u starijih osoba, prilagoditi dozu mogućim promjenama organizma koje su posljedica starenja i koje mogu utjecati na farmakokinetiku, izbjegavati istodobnu uporabu većeg broja lijekova kad god je to moguće vodeći računa o mogućim interakcijama i nuspojavama.*

**Ključne riječi:** *lijekovi u starosti, terapija starije osobe*

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## Uvod

Udio starijih ljudi u svjetskoj populaciji raste brže no ikad. U budućnosti stariji će ljudi postati veći dio svjetskog stanovništva.

Starijim ljudima obično se smatraju oni iznad 65 godina. To nije idealno, jer često postoje ne srazmjeri između biološke i kalendarske dobi. Zato bi trebalo nastojati odrediti biološku dob, kad god je to moguće.

U SAD je 1950. godine 8% pučanstva bilo u dobi iznad 60 godina, 1980. taj je dio iznosio 11%,

a 2030. očekuje se rast do 18% (1). U Hrvatskoj je 1981. bilo 10,8% stanovništva u dobi 65 godina i više, a 2000. se očekuje 11,4% (2).

Stariji ljudi upotrebljavaju mnogo lijekova. Od svih lijekova koji se daju odraslima stariji uzimaju 22 do 30%. Farmakoterapija starijih ljudi razlikuje se od one za ostale odrasle ljude (3,4,5,6).

Budući da se starenjem postupno mijenja kinetika lijekova i učinci koje oni izazivaju, povećavaju se individualne razlike u količinama lijekova potrebnim kako bi se postigao određeni terapijski učinak.

Zbog toga se starijim bolesnicima uvijek treba prilagoditi dozu lijeka (7).

Reakciju na lijek određuje količina lijeka koja stigne do mjesta njegova djelovanja i brzina kojom se to događa, osjetljivost i/ili broj receptora, te vrijeme za koje se lijek zadrži u tijelu. Ti čimbenici su određeni farmakokinetikom (apsorpcija, distribucija, biotransformacija i ekskrecija) i farmakodinamikom lijeka (brojem receptora i njihovom osjetljivošću) (8,9,10). Farmakokinetika i farmakodinamika mijenjaju se starenjem.

### Farmakokinetičke promjene

Farmakokinetičke promjene posljedica su promjena u sastavu i funkciji organa koje nastaju starenjem.

**A p s o r p c i j a .** Promjene u gastrointestinalnom sustavu mogu promijeniti apsorpciju peroralno uzetog lijeka (11). Razlog tomu može biti povećan pH u želucu, usporeno pražnjenje želuca (12), smanjen gastrointestinalni motilitet, smanjena površina i smanjen splahnlični protok krvi (13).

**D i s t r i b u c i j a .** Raspodjela lijeka mijenja se u starosti zbog smanjene tjelesne težine, serumskih albumina, ukupne količine tjelesne vode i povećana postotka masti. To može uzrokovati smanjen volumen raspodjele hidrosolubilnih lijekova, povećan volumen raspodjele liposolubilnih lijekova ili povećanu količinu slobodnog lijeka u krvi.

**B i o t r a n s f o r m a c i j a .** Lijekovi se mogu usporeno biotransformirati zbog smanjenja jetre smanjenoga protoka krvi kroz nju. Aktivnost jetrenih enzima, poput citokrom P450, smanjena je jer im je i metabolizam lijekova reduciran, no procesi konjugacije metabolita razmjerno su dobro sačuvani.

**E k s k r e c i j a .** Izlučivanje lijekova osobito ubregom, također se smanjuje starenjem. Klirens mnogih lijekova u starosti je manji. Funkcija bubrega slabi i u starosti iznosi 50% one u mlade odrasle osobe. Poluvrijeme eliminacije lijekova povećava se kao posljedica većeg volumena raspodjele liposolubilnih lijekova) i/ili smanjenja renalnog i metaboličkog klirensa (14). [Postupni porast  $t_{1/2}$  u plazmi anksiolitika diazepamom tijekom života je primjer za to (15)].

### Farmakodinamičke promjene

Važan čimbenik koji utječe na učinak lijeka u starosti jesu promjene njegove farmakodinamike. Razlozi farmakodinamičkih promjena u reaktivnosti na lijek, koje nastaju starenjem, mogu biti posljedica: promjena u broju receptora, promjena u afinitetu lijeka za njih ili promjena u odgovoru na vezu lijek-receptor. Učinak lijeka postignut jednakom koncentracijom lijeka u plazmi može biti različit kod mlade i starije osobe.

Lijekovi koji djeluju u središnjem živčanom sustavu mogu izazivati kod starijih jači učinak od onog koji bi se očekivao prema njihovoj koncentraciji u plazmi. Primjerice, sedativi i hipnotici mogu izazvati izraženiju mamurnost u starijih ljudi. Ti lijekovi mogu češće deprimirati i respiraciju zbog redukcije vitalnoga kapaciteta pluća i slabijega disanja starijih ljudi.

Odgovor na  $\beta$ -adrenergične agoniste i antagoniste čini se da je također slabiji u starijih ljudi (16). Vjeruje se da je tome razlog smanjeni broj receptora. I osjetljivost baroreceptora je smanjena u starosti, te se kao posljedica toga može razviti ortostatska hipotenzija pri uzimanju lijekova za sniženje krvnog tlaka.

Fiziološke promjene i gubitak homeostatskih mehanizama mogu imati za posljedicu povećanu osjetljivost na neželjene učinke lijekova poput hipotenzije kod psihotropnih lijekova, ili krvarenja pri terapiji antikoagulansima, čak i u slučajevima kada je doza pravilno prilagođena farmakokinetičkim promjenama nastalim starenjem.

Patološke promjene mogu često utjecati na metabolizam lijekova u starijih ljudi. Oni boluju od većeg broja bolesti nego mladi ljudi. Neke su bolesti degenerativne, a neke posljedica samog procesa starenja. Među starijim ljudima češće su razne bolesti srca, arteroskleroza, artritis, dijabetes, osteoporoza, razne gastrointestinalne bolesti, slabljenje imunostava (s povećanom sklonosti infekcijama), senzorna oštećenja, te mišićno-koštana oštećenja. Utvrđeno je da 80% starijih ljudi ima bar jednu kroničnu bolest. Studija Wilsona i sur. (17) na 200 gerijatrijskih bolesnika pokazala je da je pri hospitalizaciji 78% pacijenata imalo bar četiri bolesti. Logična posljedica takve multiple patologije jest **polipragmazija**, a s njom i neželjenii učinci terapije i klinički znatne interakcije lijekova.

U studiji Caranasosa i sur. (18) od 6000 hospitalizacija 50% bolesti bilo je uzrokovano lijekovima među bolesnicima u dobi od 50 do 80 godina. Jedna trećina tih bolesti bila je povezana s osam lijekova: aspirinom, digoksinom, varfarinom, hidroklorotiazidom, prednizonom, vinkristinom, noretindronom i furosemidom.

Neželjeni učinci lijekova u bolesnika starije dobi često su posljedica činjenice da ti ljudi teže razumijevaju načine uzimanja lijekova. Potencijalno ozbiljne pogreške u liječenju (ne uzimanje lijekova, uzimanje lijekova koje nije ordinirao liječnik ili stomatolog, greške doziranja, nepravilni razmaci među dozama) posljedica su nerazumijevanja i slabog pamćenja, oslabljenog vida i sluha, financijskih ograničenja, nemogućnosti suradnje s okolinom, samozanemarivanja i dr. Pogreške terapeuta mogu također kod starijih ljudi biti razlogom polipragmazije i neželjenih učinaka lijekova (19, 20).

### Neželjeni učinci i interakcije

Neželjeni učinci najčešće prate terapiju: artritis, kongestivnih srčanih pogrešaka, dijabetesa, hipertenzije, hipertrofije prostate, urinarne i respiratorne infekcije.

Najčešće propisivani lijekovi za bolesnike starije dobi jesu:

- lijekovi za kardiovaskularni sustav (kardiotonici, diuretici, antihipertenzivi)
- psihotropni lijekovi
- analgetici.

Među lijekovima uzetih automedikacijom najčešći su:

- analgetici (Aspirin)
- laksativi
- antacidi
- vitamini (multivitaminski pripravci, vitamini E i C i vitamini s mineralima).

Najčešći neželjeni učinci lijekova u bolesnika starije dobi (često posljedica polipragmazije) jesu:

- kardiotoksičnost digitalisa uz diuretike, koji potiču lučenje kalija;
- peptički ulkus uz kortikosteroide i NES analgetike;
- respiratorna depresija pri uporabi opioidnih analgetika;
- stupor, konfuzija ili ekscitacija pri uporabi sedativa i anksiolitika.

Čestoća neželjenih učinaka raste eksponencijalno s brojem uzetih lijekova.

**POZOR!** Ljudi stariji od 80 godina netolerantni su za **neuroleptike** (koji im se daju zbog konfuznih stanja) i **diuretike** (koje uzimaju zbog otoka zglobova) koji izazivaju promjene u ravnoteži elektrolita i mogu biti uzrokom polukomatoznih stanja (21)!

Neki lijekovi mogu prouzročiti vrlo ozbiljne neželjene učinke i doze tih lijekova treba smanjiti (Tablica 1) ili ih treba izbjegavati u liječenju starijih ljudi (Tablica 2).

Kod starijih ljudi smanjen je protok slinje i pufer-ski sustav slinje (22, 23). Uz to kao neželjeni učinak terapije i jedna od posljedica polipragmazije kojom se može susresti stomatolog jest **kserostomija**.

Tablica 1. Popis nekih lijekova koji se u smanjenoj dozi propisuju starijim osobama

Table 1. Reduced dosages for some drugs in the elderly

Lijek	Drug	Moguće posljedice pri primjeni uobičajene doze	Possible consequence of non-reduced doses
aminoglikozidi	Aminoglycosides	nefrotoksičnost	nephrotoxicity
benzodiazepini	Benzodiazepines	pojačana depresija SŽS	extended depression of CNS
digoksin	Digoxin	toksičnost digoksina	digoxin toxicity
haloperidol	Haloperidol	ekstrapiramidni simptomi	extrapyramidal disorders
levodopa	Levodopa	hipotenzija	arterial hypotension
metoklopramid	Metoclopramid	mentalna konfuzija	mental confusion
petidin	Pethidine	depresija disanja	respiratory depression
tiroksin	Thyroxine	infarkt miokarda	myocardial infarction
vitamin D	Vitamin D	nefrotoksičnost	nephrotoxicity

Tablica 2. Neki lijekovi koje ne bi trebalo propisivati starijim osobama

Table 2. The drugs that should be avoided in elderly

Lijek	Drug	Neželjeni učinak	Adverse reaction
fenilbutazon	Phenilbutazone	aplastična anemija	aplastic anaemia
gvanetidin	Guanethidine	ortostatska hipertenzija	orthostatic hypotension
karbenoksolon	Carbenoxolone	retencija tekućine, zatajivanje srca	fluid retention, cardiac failure
klorpropamid	Chlorpropamide	hipoglikemija	hypoglycaemia
klortalidon	Chlorthalidone	produžena diureza	prolongation of diuresis
nitrofurantoin	Nitrofurantoin	periferna neuropatija	peripheral neuropathy
pentazocin	Pentazocine	konfuzija	confusion

Tablica 3. Lijekovi koji uzrokuju kserostomiju

Table 3. Some drugs that cause xerostomia

antikolinergici	anticholinergic
antihistaminici	antihistamines
antidepresivi	antidepressants
benzodiazepini	benzodiazepines
antipsihotici	antipsychotics
diuretici	diuretics

Antimuskarinski učinak često prati uporabu mnogih lijekova bolesnicima starije životne dobi. U Tablici 3 navedeni su lijekovi koji mogu izazvati kserostomiju. Starijim ljudima kserostomija može pravi niz problema. U osoba s mobilnim protetskim nadomjesticima suha usta mogu smanjiti retenciju proteza, izazvati poteškoće govora ili potaknuti pacijenta da ne nosi protezu. Oštećenja izazvana trenjem i pad intraoralnog pH (zbog nedostatnog vlaženja slinom i manjka puferskih sustava) stvaraju predispoziciju u bolesnika za infekcije kandidom te ubrzani nastanak karijesa.

Zbog reduciranih homeostatskih mehanizama starijim bolesnicima treba oprezno primjenjivati sve lijekove koji mogu promijeniti **krvni tlak, frekvenciju srca ili tonus glatkih mišića**.

Stomatolog treba obratiti pozornost na moguću **ortostatsku hipotenziju** koja se u ljudi starije dobi češće javlja nego kod mladih. Stoga treba pacijenta upozoriti na postupno ustajanje sa zubarskog stolca.

Terapijske doze **lokalnih anestetika** koji se uobičajeno primjenjuju bolesnicima, stariji ljudi ne moraju dobro podnositi (24). Fiziološke promjene u starijih, koje utječu na farmakokinetiku lijekova, mogu utjecati na razinu lokalnog anestetika u organizmu. Poluvrijeme lidokaina raste u osoba starijih od 65 godina u usporedbi s njegovim poluvreme-

nom u mladih odraslih osoba (25). Stomatolog bi trebao svom bolesniku temeljem njegove tjelesne težine i mogućih starenjem izazvanih promjena jetara i bubrega izračunati dozu lokalnog anestetika, čime bi se povećale granice sigurnosti njegove uporabe.

### Zaključak

Stariji se bolesnici razlikuju od mladih odraslih ljudi u reakciji na lijekove (26,27). Uz to, na učinak lijeka u starijih utječu i istodobna uporaba većeg broja lijekova, patološka stanja i pogreške u uzimanju lijekova. Pravila kojih se treba stomatolog držati pri propisivanju lijekova starijim ljudima prema preporuci SZO (28) jesu:

1. Procijeniti je li uporaba lijeka prijeko potrebna! Je li dijagnoza točna i potpuna? Je li je lijek prijeko potreban? Postoji li bolja alternativa?
2. Ne propisati lijek ako nije prijeko potreban! Računati na moguće nuspojave i razmotriti moguću zamjenu.
3. Procijeniti dozu lijeka! Odgovara li mogućim promjenama fiziološkog stanja organizma? Posebno s pažnjom na funkciju bubrega i jetara!
4. Procijeniti oblik lijeka koji se želi upotrijebiti. Je li npr. tableta najprihvatljiviji oblik ili bi injekcija, čepić ili sirup bili bolji? Je li pakovanje lijeka prikladno za stariju osobu?
5. Procijeniti je li možda neki novi simptom posljedica neželjenog učinka lijeka ili prekida njegova uzimanja.
6. Uzeti potanku **anamnezu** vodeći računa o interakcijama s tvarima koje pacijent možda uzi-

- ma bez znanja terapeuta, poput raznih biljnih ili pomoćnih tvari, lijekova iz kućne apoteke ili lijekova dobivenih od prijatelja.
7. Koristiti se fiksnim kombinacijama samo kada su dobro proučene i kada mogu poboljšati toleranciju ili djelotvornost.
  8. Ako se u terapiju bolesnika uvodi neki novi lijek, treba procijeniti može li se neki lijek iz dotadašnje terapije ispustiti.
  9. Provjeriti provodi li bolesnik terapiju pravilno i redovito, brojeći npr. preostale tablete! Je li bolesnik (ili rodbina) dobro upućen u način provedbe terapije?
  10. Upamtiti - prestanak terapije jednako je važan kao i početak terapije!

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# Geriatric Dental Patients and Pharmacotherapy

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## Summary

*Many factors can change the response to drugs in the elderly. First there are physiological changes as a result of changes in the body composition and function of organs. Many of them are a consequence of the essentially normal aging process. They can lead to altered drug pharmacokinetics and pharmacodynamics. Second, pathological factors that can influence drug effects are commoner in the elderly. Increased drug usage contributes to more adverse reactions and drug-interactions. Poor patient compliance is assumed to be the third major source of drug therapy errors and consequently adverse drug reactions.*

*The physician must provide adequate management of drug therapy in the elderly, adjusting the dose to possible alterations of age-related pharmacokinetic changes and avoiding multiple medications whenever possible, bearing in mind the possibility of interactions and side effects.*

Key words: *drugs in the elderly, geriatric therapy*

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## REVIEW

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## Introduction

The proportion of the world's population represented by the elderly is increasing faster than ever. In the future elderly people will become a great part of the world's population.

The elderly are usually defined as those aged 65 years of age or older. This is not ideal, because discrepancies between biological age and calendar age are frequent. Biological age limit should be determined whenever possible.

In 1950 the elderly represented 8% of the population in the USA in 1980 11% and by 2030 it is predicted that this percentage will have grown to 18 % (1). In 1981 the elderly represented 10.8% of the population in Croatia and by 2000 this percentage will have grown to 11.4% (2).

The elderly take a considerable number of medications, which represents 22 to 30% of all medications for the general adult population. The use of drugs in the elderly differs from younger adults (3, 4,5,6).

As adults age drug kinetics gradually changeds and the result is an increase in the individual variability of doses required for a given effect. For this reason dose adjustment must always be done in elderly patients (7).

Response to a drug is ultimately determined by the amount that reaches the receptors, the speed at which it reaches them, the sensitivity and/or number of receptors and the duration of the drug's sojourn in the body.

These factors are in turn affected by pharmacokinetic processes (the absorption, distribution, bio-

transformation and excretion of the drug) (8,9,10) and pharmacodynamic factors (principally the number of available receptors and their receptivity to a particular drug).

The pharmacokinetic and pharmacodynamic change with old age.

### Pharmacokinetic changes

Pharmacokinetic changes result from changes in body composition and the function of organs.

**Absorption.** Changes in the gastrointestinal tract could have an impact on the absorption of drugs (11) taken by orally. These changes include an increase in gastric pH, a reduced rate of gastric emptying (12), a decrease in gastrointestinal motility and surface area and a decrease in splanchnic blood flow (13).

**Distribution.** The reduction in lean body mass, serum albumin and total body water as well as the increase in percentage of body fat result in changes in distribution of drugs depending on their lipid solubility and protein binding.

**Biotransformation.** Hepatic blood flow and the function of some of the drug metabolizing enzymes are also reduced in the elderly. The activities of cytochrome P-450 enzymes are reduced, but conjugation mechanisms are relatively well maintained.

**Excretion.** The renal excretory system is also affected by age. The clearance of many drugs is reduced in the elderly. Renal function declines at a variable rate to about 50% of that in the young adult.

The elimination half life of drugs is increased as a consequence of the larger apparent volume of distribution (of lipid soluble drugs) and/or reduction of renal or metabolic clearance (14).

[The steadily increasing plasma  $t_{1/2}$  of the anxiolytic drug, *diazepam* is an example of this (15)].

### Pharmacodynamic changes

Changes in pharmacodynamics are an important factor in the elderly. The possibilities of pharmacodynamic alterations in drug reactivity with aging are: a change in the number of receptors, a change

in their affinity for the drug or a change in tissue responsiveness to drug-receptor binding.

The same plasma concentration of a drug can cause a different effect in young and old subjects.

Drugs that act on the central nervous system seem to produce an exaggerated response in relation to that one expected from the plasma concentration, and sedatives and hypnotics may have a pronounced hangover effect. These drugs are also more likely to depress respiration, because vital capacity and maximum breathing capacity are lessened in the elderly.

Response to  $\beta$ -adrenoceptor agonists and antagonists appears to be partly blunted in old age (16). It is believed that this is due to a reduction in the number of receptors.

Baroreceptor sensitivity is reduced, leading to potential for orthostatic hypotension with drugs that reduce blood pressure.

Physiologic changes and loss of homeostatic resilience can result in increased susceptibility to the unwanted effects of drugs, such as hypotension from psychotropic medication and hemorrhage from anticoagulation, even when the dosage is appropriately adjusted to account for age-related pharmacokinetic changes.

Pathological factors that can influence drug metabolism are commoner in the elderly. These individuals have more illnesses than younger people, some of which are degenerative and others are the consequence of essentially normal processes of aging. Among the elderly there is an increased incidence of all forms of heart disease, atherosclerosis, arthritides, diabetes, osteoporosis, gastrointestinal problems, decreased immune response (leading to increased sensitivity to infection) and various sensory and musculoskeletal disorders.

It has been estimated that 80% of the elderly have at least one chronic disease. A clinical study by Willson et al (17) of 200 geriatric hospital admissions showed that 78% suffered from at least four major diseases.

A logical consequence of these multiple pathological factors is polypharmacy and with it adverse drug reactions and drug interactions.

In an extended study by Caranasos et al (18) in over 6000 hospital admissions 50% of illnesses that were clearly drug induced occurred in patients aged

from 50 to 80 years. One third of these drug-induced illnesses were traceable to eight drugs: aspirin, digoxin, warfarin, hydrochlorothiazide, prednisone, vincristine, norethindrone and furosemide.

Patient compliance is assigned to be the major source of medication errors and therefore adverse drug reactions. Potentially serious medication errors (omitting medications, use of medications not prescribed by the physician or dentist, errors of dosage or timing) are the consequence of poor comprehension and memory, poor vision and hearing, financial restriction, inability to cope with the environment, self-neglect etc. A physician's inadequate management of drug therapy in the elderly can also be a reason for polypharmacy and adverse drug reactions (19, 20).

### Adverse drug reactions and drug-interactions

Adverse drug reactions are most commonly encountered in the treatment of arthritis, congestive heart failure, diabetes, hypertension, prostatic hypertrophy, urinary and respiratory tract infection.

The most commonly prescribed drugs for the elderly are:

- cardiovascular agents (cardiotonics, diuretics, antihypertensive drugs)
- psychotropic drugs
- analgesics.

The elderly also take a considerable number of self-administered drugs. The most popular are:

- analgesics
- laxatives
- antacides
- vitamins (vitamine C and E, multiple vitamins with or without minerals).

Common adverse drug reactions among the old (very often the consequence of polypharmacy) are:

- cardiotoxicity from digitalis brought about by the simultaneous use of potassium-depleting diuretics,
- peptic ulcers from corticosteroids and NES analgesics,
- respiratory depression due to opioid analgesics,
- stupor, confusion and even excitation due to sedatives and antianxiety drugs.

The incidence of adverse reactions increases exponentially with the number of drugs taken.

NOTE! The old (80+ years) are particularly intolerant of **neuroleptics** (given for confusion) and **diuretics** (given for ankle swelling that is postural and not due to heart failure) which cause adverse electrolyte changes and semicomatose conditions (21).

Some drugs can cause very serious adverse reactions and the doses of such therapeutics must be reduced (Table 1) or should not be used in the elderly (Table 2).

Elderly patients have a reduced salivary flow and low buffering capacity (22, 23). However, these problems may also be caused by taking of one or more drugs. In their work dentists can use acronyms **xerostomia**. Table 3 lists those drugs that may adversely affect the production of saliva. In the geriatric patient with a removable prosthesis, a dry mouth can impair denture retention, make speech difficult and reduce the patient's acceptance of the appliance. The relative lack of salivary lubrication and buffering predisposes the patient to candidal infection and rampant caries.

Because of the known loss in homeostatic competence, drugs that alter blood pressure, heart rate and smooth muscle tone should be used with caution in the elderly.

The elderly may not tolerate the dosage of **local anesthetics** that would be considered usual in healthy adults (24). Age-based physiologic changes in pharmacokinetic response in older individuals can affect local anesthetic drug levels. It has been shown that the half-life of lidocaine in persons over the age of 65 is increased over that in young adults (25). Calculating the dosage of local anesthetic, based on body weight and possible age-based changes in the liver or kidneys, can increase the margin of safety for these drugs.

The elderly are more susceptible to orthostatic hypotension than younger adults. Special attention is called for when they go from a reclining posture in a dental chair to a standing position.

### Conclusions

It is obvious that an elderly patient differs from a younger adult in ways that can potentially affect



response to drugs (26, 27). It is also well known that response to drugs in the elderly are confounded by multiple medications, pathologic states and compliance errors. Precautions appropriate to dentistry, according to regulations for prescribing drugs in the elderly from WHO (28) are listed below:

1. Think about the necessity of taking drugs. Is the diagnosis correct and complete? Is the drug really necessary? Is there a better alternative?
2. Do not prescribe drugs that are not useful. Think about possible side effects and consider alternatives.
3. Think about the dose. Is it appropriate for possible alterations in the patient(s) physiological state? Is it appropriate for the patient's renal and hepatic function at the time?
4. Think about drug formulation. Is a tablet the most appropriate form of drug or would an injection, a suppository or syrup be better? Is the drug suitably packaged for the elderly patient?
5. Assume if any new symptoms may be due to drug side effect or more rarely to drug withdrawal.
6. Take a careful drug history. Bear in mind the possibility of interaction with substance the patient may be taking without doctor's knowledge, such as herbal or other nonprescribed remedies, old drugs taken from home or drugs obtained from friends.
7. Use fixed-combinations of drugs only when they are logical and well studied and they either aid compliance or improve tolerance or efficacy.
8. When adding a new drug to the therapeutic regimen, check whether another can be withdrawn.
9. Try to check whether the patient's compliance is adequate, e.g. by counting remaining tablets.
10. Remember that stopping a drug is as important as starting it.