

Arterijska hipertenzija u osoba starije životne dobi

Hypertension in the elderly

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SAŽETAK: Arterijska hipertenzija (AH) u starijih osoba predstavlja veliki javnozdravstveni problem zbog visoke prevalencije i trenda starenja svjetske populacije. Najčešće se radi o izoliranoj sistoličkoj hipertenziji (90% bolesnika iznad 70 godina) te se kod osoba starije životne dobi kao najbitniji čimbenici rizika izdvajaju vrijednosti tlaka pulsa i sistoličkog tlaka. Patofiziološki u podlozi su brojne strukturne (gubitak elastičnosti velikih krvnih žila, smanjena rastezljivost, porast brzine pulsno vala) i funkcionalne (endotelna disfunkcija, smanjena osjetljivost beta receptora, smanjena funkcija baroreceptora, osjetljivost na sol) promjene. Liječenje AH u starijih do sada je bilo veliki izazov jer nije bilo dovoljno studija koje su se bavile tom populacijom, što se promijenilo objavom rezultata studije HYVET. Ova je studija uključila najstarije bolesnike (iznad 80 godina) te je dokazala kako sniženje vrijednosti arterijskog tlaka za 15/6 mmHg dovodi do značajno manje opće smrtnosti (21%), kardiovaskularne smrtnosti (23%), incidencije moždanog udara (30%) i srčanog zatajivanja (64%). Kao lijek prvog izbora u starijoj populaciji izdvojili bismo tiazidski diuretik, a budući ti pacijenti većinom zahtijevaju višestruku terapiju izdvojili bismo blokatore kalcijevih kanala ili ACE inhibitore. Naravno i komorbiditeti određuju osnovnu ili dodatnu terapiju.

KLJUČNE RIJEČI: arterijska hipertenzija, starije osobe, diuretici.

Uvod i epidemiologija

Svjetska populacija stari, a prevalencija arterijske hipertenzije (AH) raste s dobi. U Europi je 1960. god. 15% populacije bilo starije od 60 godina, a 2005. god. ta se brojka povisila na 22%. Pretpostavlja se kako će do 2050. god. 27% europske populacije biti starije od 65 godina. Teško je točno definirati stariju životnu dob, ali za potrebe ovog članka uzet ćemo tradicionalnu demografsku definiciju iznad 65 godina. Unutar te populacije postoje subpopulacije s klinički bitnim razlikama pa tako razlikujemo "mlade stare" (65-74 godine), "starije stare" (75-84 godina) i "najstarije stare" (iznad 85 godina). Arterijska hipertenzija predstavlja vrlo čestu bolest (oko jedne milijarde ljudi diljem svijeta) čija je važnost još i veća jer je jedan od najčešćih promjenjivih čimbenika rizika povezanih uz druge kardiovaskularne bolesti (ateroskleroza, moždani udar, infarkt miokarda, srčano zatajivanje). Klinička dijagnoza AH postavlja se s više od tri ambulantna mjerenja

SUMMARY: Hypertension in the elderly is a major public health problem due to high prevalence and the world population ageing trend. The majority of elderly patients suffer from isolated systolic hypertension (90% of patients over 70 years of age). Furthermore, pulse pressure and systolic pressure are the most important risk factors in the elderly persons. Pathophysiologically, there is a great number of structural (loss of elasticity of large blood vessels, decreased elasticity, increased pulse wave velocity) and functional (endothelial dysfunction, decreased sensitivity of beta receptors, decreased baroreceptor function, sensitivity to salt) changes in the background. Treatment of hypertension in the elderly has so far been a big challenge, because there were not enough studies that have dealt with this population. Now this has changed after the results of the HYVET study have been published. This study included the oldest patients (above 80 years of age) and has proven that lowering pressure by 15/6 mmHg, leads to significantly lower overall mortality (21%), cardiovascular mortality (23%), incidence of stroke (30%) and heart failure (64%). We emphasize thiazide diuretic as the first choice drug in the elderly population, and since these patients usually require multiple treatment, we emphasize calcium channel blockers or ACE inhibitors. Comorbidities, naturally, determine the basic or additional therapy.

KEYWORDS: hypertension, elderly persons, diuretics.

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Introduction and epidemiology

The world population is growing old, while the prevalence of arterial hypertension rises with age. 15% of the population was over 60 years of age in 1960 in Europe, while in 2005 this figure rose to 22%. It is assumed that 27% of the European population will be over 65 years of age by the year 2050. It is difficult to define old age precisely, but for the purpose of this article we shall consider the traditional demographic definition for old age over 65. Within this population there are subpopulations showing clinically important differences, so we distinguish between "younger old" (65-74 years of age), "older old" (75-84 years of age) and "oldest old" (over 85 years of age). Hypertension is very a common disease (about 1 billion people in the world suffer from it). Its importance is even greater as it is one of the most common variable risk factors associated with other cardiovascular diseases (atherosclerosis, stroke, myocardial infarction,

povišenog arterijskog tlaka (AT) iznad 140/90 mmHg, no kod određenih entiteta ciljne vrijednosti AT su i niže (130/90 mmHg za dijabetes, kroničnu bubrežnu bolest, koronarnu bolest srca, perifernu arterijsku bolest te čak i 120/80 za disfunkciju lijeve klijetke). Bitno je izmjeriti AT u stajanju te se ta vrijednost uzima kao dijagnostička (moguće je sniženje vrijednosti AT za do 30%, odnosno više od 20 mmHg). U Europi, prema podacima za 2003. god., prevalencija AH iznosi 44% (najviše u Njemačkoj 55%). U SAD prevalencija AH godine 2004. iznosila je 27% (jednaka za muškarce i žene iznad 18 godina), a rasla je s dobi, pa je tako većina starijih imala razvijenu bolest. Prema NHANES podacima iz 2009. god. prevalencija AH u muškaraca veća je u mladim od 55 godina, a kod žena u starijih od 55 godina. U dobi od 45-54 godina prevalencija je 35% u oba spola, a u dobi od 75 godina i više 65% muškaraca i 75% žena ima AH. Prema Framinghamskoj studiji hipertenzivni bolesnici dva do tri puta češće razvijaju koronarnu bolest srca (uključivo anginu pectoris, akutni infarkt miokarda i iznenadnu srčanu smrt), tri puta češće razvijaju moždani udar, a 3,5 puta češće srčano popuštanje. Pacijenti s dijabetesom imaju 1,5 do 2 puta viši rizik od pojave AH, a ova bolest je, uz dijabetes, najčešći razlog kronične bubrežne bolesti danas. Oko 90-95% bolesnika ima esencijalnu hipertenziju, a 5-10% sekundarnu hipertenziju (najčešće renovaskularnu hipertenziju i primarni hiperaldosteronizam). Iako je u starijoj populaciji svjesnost o vlastitoj bolesti veća te se osobe starije životne dobi bolje pridržavaju terapijskih uputa nego pacijenti srednjih godina, postizanje željenih vrijednosti AT izrazito je teško, posebice u populaciji iznad 85 godina. Terapija u starijoj životnoj dobi do sada je bila izazov jer je većina studija imala gornju granicu dobi kao ulazni kriterij te rezultati nisu bili prezentirani u korelaciji s dobi. To se promijenilo sa studijom HYVET (*The Hypertension in the Very Elderly Trial*) koja je provedena na populaciji iznad 80 godina.

Patofiziologija

Porast prevalencije AH s dobi proizlazi iz strukturnih i funkcionalnih promjena arterija koje prate proces starenja. Velike krvne žile, poput aorte, gube elastičnost, smanjuje im se rastezljivost, prvenstveno zbog strukturnih promjena medije (stres frakture elastina uz pojačanu razgradnju, pojačano odlaganje kolagena i kalcija) što rezultira povećanjem promjera krvne žile. Na krutost arterija utječu i vazoaktivni medijatori iz endotela kao endotelin 1. Pojačana krutost arterija pojačava brzinu pulsog vala što uzrokuje raniji povrat reflektiranih valova s periferije do proksimalne aorte gdje se udružuju s anterogradnim valovima te uzrokuju kasni porast sistoličkog AT (augmentacijski indeks) što dodatno oštećuje endotel. Taj kasni porast sistoličkog AT dodatno pojačava *afterload* na već i tako opterećen miokard te može uzrokovati ili pogoršati koronarnu bolest srca (povećava potrebu miokarda za kisikom, povećava hipertrofiju lijeve klijetke, smanjuje rano dijastoličko punjenje). Uslijed smanjenog stvaranja dušikova oksida (endotelna disfunkcija) dolazi do slabije dilatacije arterija tijekom pojačanog protoka što također povisuje sistolički AT. Zbog svega navedenog tijekom godina dolazi do postupnog ali konstantnog porasta sistoličkog AT. Dijastolički AT doseže svoj maksimum oko 60. godine života i nakon toga se smanjuje što se povezuje s oslabljenom sposobnosti krutih velikih arterija i aorte da se prošire u sistoli i kontrahiraju u dijastoli i time povećaju dijastolički AT (zbog smanjenog dijastoličkog AT može doći do smanjenja koronarne perfuzije). Zbog porasta sistoličkog i sniženja dijastoličkog tlaka tijekom starenja dolazi do pora-

heart failure). Clinical diagnosis of hypertension is made with more than 3 outpatient measurements of elevated blood pressure (BP) above 140/90 mmHg, but with certain subjects, the target BP values were lower (130/90 mmHg for diabetes, chronic renal disease, coronary artery disease, peripheral artery disease, and even 120/80 for left ventricular dysfunction). It is important to measure the BP in the standing position, and this value is considered to be a diagnostic value (BP may be lowered by 30%, or more than 20 mmHg). According to the 2003 data, the prevalence of hypertension is rounded at 44% in Europe (most in Germany at 55%). In the U.S., the prevalence was 27% in 2004 (the same for men and women over 18 years of age), and it rose with age, so the majority of elderly persons had a developed hypertension. According to 2009 NHANES data, the prevalence of hypertension was higher in men under 55 years of age and in women over 55 years of age. At the age from 45 to 54, the prevalence was 35% in both genders, while at the age of 75 and over that age, 65% of men and 75% of women suffer from hypertension. According to the Framingham Heart study, patients suffering from hypertension develop coronary heart disease 2 to 3 times more often (angina pectoris, acute myocardial infarction, sudden cardiac death), they develop stroke three times more often and heart failure 3.5 times more often. Patients with diabetes have 1.5 to 2 times greater risk of developing hypertension, and along with diabetes, it is the most common cause of chronic kidney disease today. Approximately 90-95% of patients have essential hypertension, while 5-10% have secondary hypertension (most frequently, renovascular hypertension and primary hyperaldosteronism). Although the elderly population is better aware of their disease and they better adhere to treatment instructions than middle-aged patients, it is extremely difficult to achieve the desired BP values, especially in the population over 85. Therapy in elderly age has so far been a challenge, because most studies had an upper age limit as input criteria and the results were not presented in correlation with age. This changed with the HYVET study which was conducted on the population over 80 years of age that will be addressed later.

Pathophysiology

The rise in the prevalence of hypertension with age derives from the structural and functional changes to the arteries that occur simultaneously with an aging process. Large blood vessels like the aorta lose elasticity, primarily due to structural changes in the media (stress of elastin fracture accompanied by an increased degradation, increased collagen and calcium deposition), resulting in an increased diameter of blood vessels. The arterial stiffness is affected by vasoactive mediators from the endothelium as the endothelin 1. Increased arterial stiffness accelerates the pulse wave velocity which causes an early return of reflected waves from the periphery to the proximal aorta where they merge with anterograde waves that cause delayed elevation of systolic BP (augmentation index), thus further damaging the endothelium. The late elevation of systolic BP additionally increases the afterload on the already loaded myocardium and can cause or exacerbate coronary artery disease (increases the need of the myocardium for oxygen, increases left ventricular hypertrophy, reduces early diastolic filling). Reduced formation of nitric oxide (endothelial dysfunction) causes reduced dilation of the arteries during increased flow, which also elevates systolic BP. Due to the above specified facts, a gradual but constant elevation of systolic BP occurs over years. Diastolic BP culminates at the age of 60 only to be lowered afterwards, which is associated with

sta tlaka pulsa (razlika između sistoličkog i dijastoličkog tlaka). Tlak pulsa predstavlja mjeru stupnja krutosti arterija povezanu s dobi te se pokazao kao važan predskazatelj koronarne bolesti srca (ako je viši od 63mmHg u osoba starijih od 59 godina). Povišen tlak pulsa oštećuje intimu i elastične elemente stijenke krvnih žila, ubrzava aterosklerozu, povećava mogućnost tromboze i rupture aterosklerotskog plaka. U skladu s navedenim, većina (65% pacijenata iznad 60 godina, 90% pacijenata iznad 70 godina) starijih hipertoničara boluje od izolirane sistoličke hipertenzije (ISH), dok se kod ostalih radi o sistoličko-dijastoličkoj hipertenziji. Prevalencija ISH veća je kod žena. Zanimljivo je napomenuti da se ranije smatralo kako je porast sistoličkog AT u starosti neophodan odgovor organizma da bi se održala perfuzija odnosno fiziološki proces starenja, a dijastolički je tlak smatran ključnim za razvoj komplikacija. Dijastolički AT najjači je pretkazatelj kardiovaskularnog rizika za bolesnike mlađe od 50 godina, no u starijih pokazuje bimodalnu povezanost, pa je tako pojačan rizik podjednak za vrijednosti iznad 90mmHg i ispod 70 mmHg. Prema rezultatima HOT studije idealan dijastolički tlak je 82,6 mmHg i daljnje smanjenje nije pokazalo korist. U pacijenata između 50 i 59 godina sva tri indeksa AT (sistolički, dijastolički i tlak pulsa) bili su podjednako dobri predskazatelji, no nakon 60. godine života vrijednost sistoličkog i tlaka pulsa postaju najznačajniji prediktori kardiovaskularnog rizika (sistolički AT za cerebrovaskularne komplikacije, kronično bubrežno zatajenje te vrijednost sistoličkog i tlaka pulsa za stenozu karotidnih arterija).

Zbog smanjenja osjetljivosti beta receptora dolazi do pojačanog lučenja noradrenalina, a zbog nefroangioskleroze do smanjenog lučenja renina i posljedično aldosterona te stariji bolesnici imaju povećan rizik hiperkalijemije. U starosti također dolazi do smanjenja funkcije baroreceptora te porasta venske insuficijencije što povisuje mogućnost ortostatske hipotenzije, sinkope i padova. No, kod starijih također može doći i do ortostatske hipertenzije što je najvjerojatnije povezano s pojačanom alfa adrenergičnom aktivnosti.

Osjetljivost na sol, tipična za starije i adipoznije populacije, karakterizirana je porastom AT kao odgovorom na pozitivan balans soli. Kapacitet bubrega za pojačano izlučivanje natrija smanjuje se s dobi što, zadržavanjem natrija i vode, pridonosi porastu sistoličkog AT. No, osjetljivost na sol u starijih povezana je i sa smanjenjem stvaranja natriuretskih agensa (prostaglandin E2, dopamin).

Na kraju je patofiziološki bitno i spomenuti, kao i kod hipertoničara svih dobi, važnost stila života (tjelesna aktivnost, pušenje, alkohol, prehrana, sol).

Dijagnostika

Kao i kod ostalih bolesnika s AT dijagnoza se postavlja uz barem tri mjerenja povišenog AT izmjerena u barem dva posjeta liječniku. Dijagnozu bi trebalo upotpuniti 24-satnim kontinuiranim mjerenjem AT, procjenom oštećenja ciljnih organa i promjenjivih kardiovaskularnih čimbenika rizika (pušenje, hiperlipidemija, alkohol).

Liječenje

Brojne su studije dokazale kako snižavanje vrijednosti AT prema urednim vrijednostima ima povoljne učinke. SHEP (Systolic Hypertension in the Elderly Program) studija je dokazala kako aktivno liječenje ISH klortalidonom, s atenololom ili reserpinom ili bez njih, bitno smanjuje incidenciju

impaired ability of stiff large arteries and aorta to expand in the systole and contract in the diastole thereby elevating diastolic pressure (lowered diastolic BP may cause reduced coronary perfusion). During the aging process, a high systolic and a low diastolic BP lead to elevated pulse pressure (difference between systolic and diastolic pressure). Pulse pressure is a measure of age-related arterial stiffness degree and has proven to be an important predictor of coronary heart disease (if it exceeds 63 mmHg in patients over 59 years of age). Elevated pulse pressure impairs the intima and elastic elements of the blood vessel walls, accelerates atherosclerosis, increases the possibility of thrombosis and atherosclerotic plaque rupture. Accordingly, the majority of elderly hypertensive patients suffer from isolated systolic hypertension-ISH (65% of patients over 60 years of age, 90% of patients over 70 years) while the other patients suffer from systolic-diastolic hypertension. ISH prevalence is greater in women. It is worth noting that in the past the elevation of the systolic BP in elderly persons was a necessary body response for the purpose of maintaining perfusion or physiological aging process, while the diastolic pressure was considered crucial for the development of complications. Diastolic BP is the most important cardiovascular risk predictor for patients under 50 years of age, but in the elderly persons it shows bimodal connection, so the increased risk is the same for the values over 90 mmHg and under 70 mmHg. According to the results of HOT study, the ideal diastolic BP is 82.6 mmHg and a further reduction did not show any benefit. In patients aged from 50 to 59, all three BP indices (systolic, diastolic, pulse pressure) were equally good predictors, but after the age of 60, systolic and pulse pressure become the most important predictors of cardiovascular risk (systolic BP for cerebrovascular complications, chronic renal failure, systolic and pulse pressure for carotid artery stenosis).

Reduced sensitivity of beta receptors causes higher secretion of noradrenaline, while nephroangiosclerosis causes reduced secretion of renin and consequently aldosterone, so elderly patients are at higher risk of developing hyperkalemia. Elderly persons also have reduced baroreceptor function and elevated venous insufficiency, which increases the possibility of orthostatic hypotension, syncope and falls. But the elderly persons may also suffer from orthostatic hypertension, which is probably associated with increased alpha adrenergic activity.

The sensitivity to salt, typical for the elderly people and more adipose population is characterized by elevation of BP as a response to a positive salt balance. The capacity of the kidney to enhance secretion of sodium is reduced with age, which, by retaining sodium and water contributes to elevation of systolic BP. However, the sensitivity to salt in the elderly persons is associated with decreased formation of natriuretic agents (prostaglandin E2, dopamine).

Finally from the pathophysiological perspective, the importance of lifestyle (physical activity, smoking, alcohol, diet, salt) is also worth noting for hypertensive patients of all ages.

Diagnostics

As in any other patients with hypertension, the diagnosis is made at least after 3 measurements of elevated BP measured at least during 2 ambulatory visits. The diagnosis should be complemented by continuous measurement of BP, assessment of target organ impairment and variable cardiovascular risk factors (smoking, hyperlipidemia, alcohol).

moždanog udara (37% ishemijskog i 54% hemoragijskog). The Systolic Hypertension in Europe (Syst-Eur) studija (srednja dob 70,2 godine) zaustavljena je nakon dvije godine kada je dokazano kako kontrola AT uz nitrendipin i po potrebi enalapril i HCTZ smanjuje incidenciju moždanog udara za 42% u odnosu na placebo. Studija je također dokazala koliko je bitno što ranije započeti liječenje.

HYVET studija bavila se najstarijim bolesnicima (iznad 80 godina) s povišenim sistoličkim AT (iznad 160 mmHg) te se uspoređivalo liječenje indapamidom uz, po potrebi, dodatak perindoprilu i placebo. 3.845 pacijenata praćeno je 2 godine (studija je završena ranije zbog pozitivnih rezultata) te je u aktivno liječenoj skupini zabilježeno smanjenje vrijednosti AT u prosjeku za 15/6 mmHg, zatim 30% manja incidencija moždanog udara, 39% manja mogućnost smrti od moždanog udara, 64% manja incidencija srčanog zatajivanja, 23% manja mogućnost kardiovaskularne smrti, 21% manja mogućnost smrti od bilo kojeg razloga. Nedostaci HYVET studije bili su što nisu uključeni bolesnici s prvim stupnjem hipertenzije, što je razdoblje praćenja bio samo 2 godine te što nije određena optimalna vrijednost AT za redukciju kardiovaskularnih događaja. Podaci HYVET studije imaju veliku važnost za javno zdravstvo budući je populacija iznad 80 godina najbrže rastuća svjetska populacija. Kao i kod svih bolesnika s AH liječenje treba započeti s promjenom životnih navika. Štoviše, kod zdravih starijih bolesnika promjena životnih navika izrazito je bitna zbog sprječavanja pojave AH, a kod blažih oblika može biti i jedina terapija. Prestanak pušenja, smanjenje prekomjerne tjelesne mase, smanjenje stresa, smanjeni unos soli, pojačana tjelesna aktivnost, prestanak konzumacije alkohola, kontrola lipidnog statusa najbitnije su promjene koje mogu reducirati ili čak i isključiti antihipertenzivnu terapiju kod određenih bolesnika (svaka od navedenih promjena može smanjiti AT za 2 pa čak do 20 mmHg). Treba spomenuti dijetni režim DASH (*Dietary Approaches to Stop Hypertension*) — više voća i povrća, manje masti. Sve navedeno ne samo da smanjuje AT, nego smanjuje rizik od ostalih bolesti (ateroskleroza, dijabetes...) koje zajedno s AH uzrokuju oštećenje ciljnih organa. Kada promjena životnih navika nije dovoljna za postizanje željenih vrijednosti AT, potrebno je uključiti antihipertenzivni lijek u najnižoj dozi te ga potom prema potrebi postupno povisivati do maksimalne dozvoljene doze. U slučaju da jedan lijek nije dovoljan za zadovoljavajuću regulaciju tlaka potrebno je uvesti lijek iz druge skupine antihipertenziva, a po potrebi i daljnje lijekove. Tijazidski diuretici su preporučeni kao inicijalna terapija za starije — uzrokuju smanjenje intravaskularnog volumena, periferne vaskularne rezistencije i AT te se dosta dobro podnose. Potreban je oprez zbog moguće hipokalijemije, ortostatske hipotenzije, hiponatrijemije, hipomagnezije, hiperuricemije, intolerancije glukoze, pogoršanja bubrežne funkcije. Započinje se s dozom od 6,25 mg na dan koja se po potrebi postupno povisuje do 50mg (viša doza nema dokazan učinak, ali se povećava mogućnost nuspojava). Klortalidon je bolji od hidroklortalidazida zbog dužeg i 1,5-2 puta jačeg djelovanja, no veća je mogućnost metaboličkih nuspojava. Umjesto tijazida može se koristiti i indapamid te furosemid. U slučaju da diuretici nisu dovoljni ili da postoji dodatna indikacija koriste se lijekovi iz drugih antihipertenzivnih skupina ovisno o komorbiditetima. Blokatori kalcijevih kanala druga su skupina koja se preporuča u starijih zbog vrlo dobre podnošljivosti i brojnih povoljnih kardiovaskularnih efekata. Beta blokatori koriste se u slučaju koronarne bolesti srca, srčanog zatajivanja, srčanih aritmija, tremora, no treba napomenuti oprez zbog moguće indukcije dijabetesa. Budući se starenjem smanjuje količina angioten-

Treatment

Numerous studies have shown that lowering BP to normal values have beneficial effects. SHEP (Systolic Hypertension in the Elderly Program) study demonstrated that active treatment of ISH by chlorthalidone, atenolol or reserpine, or without them, significantly reduces the incidence of stroke (37% ischemic and 54% hemorrhagic stroke). Syst-Eur study (mean age 70.2) was interrupted after 2 years when it was proven that the control of BP with nitrendipine, enalapril when required and HCTZ reduces the incidence of stroke by 42% compared to placebo. The study also demonstrated how important it is to start the treatment as early as possible.

HYVET study addressed the oldest patients (over 80 years of age) with elevated systolic BP (over 160 mm Hg) and compared the treatment with indapamide and perindopril and placebo supplements, if necessary. 3845 patients were followed-up for a 2 years' period (the study was completed earlier due to positive results). Lowering of BP by 15/6 mmHg on the average was recorded in the active treatment group, followed by 30% lower incidence of stroke, 39% lower incidence of death caused by stroke, 64 % lower incidence of heart failure, 23% lower incidence of cardiovascular death, 21% lower incidence of death from any cause. While the first disadvantage of the HYVET study was that 1st degree hypertension patients were not considered, the second disadvantage was that the follow-up period lasted for only 2 years and that the optimal BP for reduction of cardiovascular events was not determined. The HYVET study data are of a great importance for public health as the population over 80 is the fastest growing world population. As in all patients with hypertension, the treatment should begin simultaneously with changes to a lifestyle. Moreover, the change to lifestyle habits is extremely important for prevention of hypertension in healthy elderly patients and it can be the only therapy in some milder forms. Quitting smoking, losing excess weight, cutting down on stress, reduced salt intake, increasing physical activity, quitting drinking alcohol, lipid status control are the most important changes that may reduce or even eliminate antihypertensive therapy in certain patients (each of these changes can lower BP by 2 or even up to 20 mmHg). We should also mention the DASH diet regime (*Dietary Approaches to Stop Hypertension*) — more fruit and vegetables, less fat are to be eaten. All this does not only lower BP, but it reduces the risk from other diseases (atherosclerosis, diabetes ...), which along with hypertension impair target organs. When changes to lifestyle are not enough to achieve the desired BP values, then the lowest dose antihypertensive drug should be introduced, only to be gradually increased to the maximum allowable dose. In the event that a drug is not sufficient for adequate pressure regulation, it is necessary to introduce a drug from another group of antihypertensive agents, and other drugs if necessary. Thiazide diuretics are recommended as an initial therapy for elderly people, leading to a reduction in intravascular volume, peripheral vascular resistance and BP. They are quite well tolerated. Caution is required for potential hypokalemia, orthostatic hypotension, hyponatremia, hypomagnesemia, hyperuricemia, glucose intolerance, impairment of renal function. It begins with a dose of 6.25 mg per day that gradually increases up to 50mg (a higher dose has no proven effect, but the chance of occurrence of side effects is greater). Chlorthalidone is better than the hydrochlorothiazide due to its longer and 1.5 to 2 times stronger potency, but the possibility of metabolic side effects is higher. Indapamide and furosemide can be used instead of thiazides. If diuretics are insufficient or there is an additional indication,

zina, mislilo se kako ACE inhibitori neće biti jednako učinkoviti kao drugi antihipertenzivi, no mnoge su studije pokazale suprotno (HOPE, PROGRESS). Štoviše, poznati su dodatni pozitivni učinci ACE inhibitora u pacijenata s preoblijem infarktom miokarda, srčanim zatajivanjem sa sistoličkom disfunkcijom miokarda, dijabetičkom nefropatijom te nefroangiosklerozom. Dakle, ACE inhibitori idealna su terapija u starijih bolesnika koji uz AH imaju dijabetes ili srčano zatajivanje, međutim potreban je oprez zbog moguće hiperkalijemije te progresije zatajenja bubrega (posebno kod stenoze renalne arterije). Blokatori angiotenzinskih receptora (ARB) koriste se u pacijenata sa srčanim zatajivanjem ili dijabetesom obično kao alternativa ACE inhibitoru, a brojne su studije pokazale njihovu korist (LIFE, MOSES). Izravni inhibitor renina (aliskiren) može biti dobra zamjena za ACE inhibitor ili ARB, a prema jednoj je studiji pokazana bolja učinkovitost od ramiprila. U tijeku su dvije studije (AGELESS, APOLO) koje imaju velik broj starijih pacijenata te će njihovi rezultati pokazati koje je pravo mjesto aliskirena. Nespecifični vazodilatatori hidralazin i minoksidil zbog brojnih nuspojava nisu u prvoj liniji terapije, nego se koriste u kombinaciji s drugim antihipertenzivima kod rezistentnih hipertenzija. Preporučljive su fiksne kombinacije više grupa antihipertenziva jer se tako povećava efikasnost, smanjuju nuspojave te, što je najbitnije, povećava suradljivost pacijenata i kontinuirano uzimanje lijekova. Ukratko, u slučaju nekomplikirane AH potrebno je započeti terapiju tijazidskim diuretikom, ACE inhibitorom ili sartanom, blokatorom kalcijevih kanala, beta blokatorom. Ipak je potrebno naglasiti kako bi prema svim navedenim novijim studijama prvi izbor trebao biti tijazidski diuretik. Ukoliko je povišenje AT od normalnih vrijednosti veće od 20/10 mmHg, najvjerojatnije će biti potrebna dva antihipertenziva, pa tako većina starijih pacijenata treba više od dva lijeka u terapiji. Kod pacijenata s komorbiditetima treba voditi računa o tome koja je grupa antihipertenziva najpogodnija za navedenu bolest.

Zaključak

Aktivno liječenje AH starijih, najbrže rastuće dobne grupacije na svijetu, značajno je iz razloga što se rizik od nepovoljnih kardiovaskularnih događaja evidentno smanjuje, što su dokazale brojne kliničke studije.

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drugs from other antihypertensive groups are used depending on comorbidities. Calcium channel blockers are the second group drug that is recommended for elderly persons, because it is well tolerable and it shows a number of favorable cardiovascular effects. Beta blockers are used in a case of coronary artery disease, heart failure, cardiac arrhythmias, tremors, but caution is required for potential induction of diabetes. Since the amount of angiotensin is reduced with age, it was thought that ACE inhibitors would not be as effective as other antihypertensive drugs, but many studies have demonstrated the opposite (HOPE, PROGRESS). What is more, additional positive effects of ACE inhibitors in patients with a history of myocardial infarction, heart failure with systolic myocardial dysfunction, diabetic nephropathy and nephroangiosclerosis are well known. Thus, ACE inhibitors are an ideal therapy in elderly patients who along with hypertension suffer from diabetes or heart failure. However, caution is required for potential hyperkalemia and progression of renal failure (especially in case of renal artery stenosis). Angiotensin receptor blockers (ARB) are used in patients with heart failure or diabetes usually as an alternative to ACE inhibitors, while a great number of studies have demonstrated their benefit (LIFE, MOSES). The direct renin inhibitor (aliskiren) may be a good substitute for ACE inhibitor or ARB, and one study demonstrated an improved efficacy of ramipril. Two studies (AGELESS, APOLO) including a large number of elderly patients are in progress. Their results will show the importance of aliskiren. Non-specific vasodilators, hydralazine and minoxidil, are not the first-line therapy because of numerous side effects, but are used along with other antihypertensive agents in case of resistant hypertension. Fixed combinations of several antihypertensive drug groups are recommended, as efficiency is thus increased and side effects are reduced. Most importantly, patients are more cooperative and they take drugs on a continuous basis. In short, in case of uncomplicated hypertension, we should start the therapy by using thiazide diuretic, ACE inhibitor or ARB, calcium channel blocker and beta blocker. However, it is necessary to emphasize that thiazide diuretic should be the first choice drug according to all recent studies. If the BP is elevated by more than 20/10 mmHg compared to normal values, two antihypertensive drugs will probably be required, so the majority of elderly patients require more than two drugs in their therapy. In patients with comorbidities, we should take into account the group of antihypertensive drugs which is the most appropriate for that disease.

Conclusion

Active treatment of hypertension in elderly persons, which is the fastest growing age group in the world, is significant because the risk of adverse cardiovascular events has obviously been reduced, as evidenced by a number of clinical trials.