



Ostalo

Other

## Arterijska hipertenzija u starijih bolesnika — trebamo li liječiti?

## Arterial hypertension in elderly patients — do we need to treat them?

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**V**išestruki klinički i temeljni pokusi ističu arterijsku hipertenziju (AH) kao veliki nezavisni rizični čimbenik kardiovaskularnog morbiditeta i mortaliteta čije liječenje predstavlja temelj prevencije i uvelike poboljšava ishode i kvalitetu života bolesnika. Međutim, pitanje liječenja AH u starijih bolesnika (>80 godina) predstavlja kontroverzu više desetaka godina sa čuvenom paradigmom iz još dalekih pedesetih godina 20. stoljeća da je normalni arterijski tlak (AT) “100+dob bolesnika”. Shodno ovoj jednostavnoj formuli, normalni sistolički AT u 75-godišnjeg bolesnika iznosio bi 175 mmHg unatoč činjenici, kako pokazuju epidemiološke studije, da ovi bolesnici imaju četiri puta povišen ukupni kardiovaskularni rizik. Starija populacija bolesnika u istraživanju AH nekako je uvijek ostajala

**M**ultiple clinical and basic trials show that arterial hypertension is a major independent risk factor of cardiovascular morbidity and mortality, the treatment of which is the basis for prevention and greatly improves the outcome and quality of a patient's life. However, the issue concerning the treatment of hypertension in elderly patients (>80 years of age) has been controversial for several dozens of years with the famous paradigm dating back to the fifties of the 20th century that normal blood pressure (BP) is “100+patient's age”. According to this simple formula, normal systolic BP in 75-year old patient would be 175 mmHg despite the fact as the epidemiological studies show, that these patients are four times more exposed to total cardiovascular risk. Elderly population of pa-



po strani: najčešće su bile ispitivane manje grupe bolesnika (često je dob bila i razlogom isključenja iz studije), u kliničkim pokusima uvijek je isticana važnost regulacije dijastoličkog AT, unatoč činjenici da kod starijih bolesnika rastu vrijednosti sistoličkog AT dok su one dijastoličkog često nepromijenjene ili u nekim slučajevima s vremenom čak i niže. Unatrag nekoliko godina kliničke studije ukazuju da je povećana vrijednost tlaka pulsa (razlika sistoličkog i dijastoličkog tlaka) direktno povezana sa neželjenim kardiovaskularnim ishodima odnosno da bi liječenje sistoličke hipertenzije (a ne samo dijastoličke, kako se mislilo unatrag 20 godina) moglo imati povoljan učinak na bolesnike starije životne dobi.

Sva ova pitanja i dileme oko antihipertenzivne terapije kod starijih bolesnika s AH bile su razlogom provođenja HYVET studije (*Hypertension in the Very Elderly Trial*) čiji su rezultati objavljeni 2008. godine u časopisu *New England Journal of Medicine*. HYVET je kao osnovno postavio naizgled banalno pitanje: da li je antihipertenzivna terapija učinkovita kod osoba starijih od 80 godina? Ispitivanje je provedeno u 13 zemalja, a uključilo je 3.845 bolesnika starijih od 80 godina čiji je dijastolički tlak bio niži od 109 mmHg dok su sistoličke vrijednosti prilikom uključivanja u studiju iznosile 160-199 mmHg (sjedeći) ili >140 mmHg u stajaćem položaju. Bolesnici su potom bili randomizirani na placebo ili indapamid 1,5 mg (sustained release). Ukoliko se nije uspjela postići ciljna vrijednost AT od 150/80 mmHg i niže, ispitanicima u aktivnoj skupini dodao se ACE inhibitor perindopril (2-4 mg), dok bi se u placebo skupini dodalo više placeba. Praćenje bolesnika trajalo je ukupno oko 4 godine. Nakon dvije godine u aktivnoj grupi sistolički tlak je bio za 29,5 mmHg niži od ishodišnjeg, dok je sniženje u placebo grupi iznosilo oko 14,5 mmHg. Napominjemo da se terapija dobro podnosila te da nuspojave praktički nisu ni zabilježene. Rezultati same studije ukazivali su na značajnu redukciju fatalnih moždanih udara (čak 39%,  $P=0,045$ ) što je bio i primarni cilj istraživanja i zatajenja srca za čak 64% ( $P<0,001$ ). Ukupni mortalitet bio je snižen za oko 21% ( $P=0,55$ ). Rezultati studije HYVET jasno sugeriraju da snižavanje vrijednosti AT u osoba starijih od 80 godina, što se uspješno postiže kombinacijom indapamida i perindoprila, značajno smanjuje morbiditet i mortalitet, a samim tim i produžuje očekivano trajanje života. HYVET studija snažno je odjeknula i u medicinskoj javnosti, a potvrda kvalitete ispitivanja stigla je u svibnju 2009. godine kada je studija proglašena ispitivanjem godine 2008. prema izboru *Society for Clinical Trials* i *American Heart Association*.

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## Literature

1. Beckett NS, Peters R, Fletcher AE, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008;358:1887-98.

tients in hypertension research has always been marginalized. The smallest patients' groups have frequently been tested (the age has also been the reason for excluding them from the study), in clinical trials the importance of diastolic BP regulation has always been emphasized despite the fact that in elderly patients systolic BP values rise, while diastolic BP values usually remain unchanged or are even lower in some cases. Several years ago, the clinical studies indicate that higher pulse pressure value (the difference between the systolic and diastolic pressure) is directly related with undesired cardiovascular outcomes or rather that the systolic hypertension treatment (not only of diastolic, as it was thought some 20 years ago) could have a positive effect on elderly patients.

All such questions and dilemmas concerning antihypertensive therapy with elderly patients with AH were the reason for conducting HYVET study (*Hypertension in the Very Elderly Trial*) the findings of which were published in 2008 in *New England Journal of Medicine*. HYVET seems to have asked a simple question: Is the antihypertensive therapy an efficient therapy with people over 80 years of age? The study was conducted in 13 countries and included some 3,845 patients over 80 years of age whose diastolic BP was lower than 190 mmHg, while the systolic BP values at the time of including in the study amounted to 160-199 mmHg (when sitting) or >140 mmHg when standing. The patients would be randomized to placebo or indapamide 1.5 mg (sustained release). If the target value of BP of 150/80 mmHg and lower is not achieved, ACE inhibitor perindopril (2-4 mg) was added to the respondents in the active group, while in the placebo group some more placebo would be added. The follow-up of patients lasted for around 4 years. After two years in the active group, the systolic BP was lower by 29.5 than what it was previously, while the reduction in the placebo group amounted to 14.5 mmHg. We mention that the therapy was well tolerated and side effects were practically not recorded. The findings of the study indicated a significant reduction of fatal strokes (even 39%,  $P=0.045$ ) which was the primary goal of research and heart failure by even 64% ( $P<0.001$ ). Total mortality has been lowered by around 21% ( $P=0.55$ ). The findings of the study HYVET clearly suggest the reduction of BP values in persons over 80, which is successfully achieved by a combination of indapamide and perindopril, greatly reducing morbidity and mortality and consequently extending the life expectancy. HYVET study strongly echoed in the medical public and the quality assurance of study was publicized in May 2009 when the study was declared a questionnaire of the year 2008 according to selection by *Society for Clinical Trials* and *the American Heart Association*.