Stručni rad

# Perindopril — značajan doprinos liječenju arterijske hipertenzije i kardiovaskularnih bolesti

Professional article

# Perindopril — a landmark in hypertension and cardiovascular disease management

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***SAŽETAK:*** *Arterijska hipertenzija predstavlja glavni čimbenik rizika za kardiovaskularne i cerebrovaskularne bolesti. Ova je bolest izrazito rasprostranjena u cijelom svijetu i zahvaća polovicu osoba starijih od 60 godina. Inhibitori angiotenzin konvertirajućeg enzima (ACE) su zlatni standard u liječenju hipertenzije. Međutim, postoje važne razlike među dostupnim ACE inhibitorima. Perindopril se ističe po specifičnim svojstvima, kao što su dugo djelovanje, 24-satna kontrola arterijskog tlaka, visoka lipofilnost i visoki ACE afinitet tkiva. Nadalje, kliničke studije koje istražuju učinke perindoprila na morbiditet i mortalitet dokazale su korisnost u liječenju tijekom cijelog kontinuuma kardiovaskularnih bolesti. Kako je neprikladno liječenje jedan od najvažnijih razloga za nedostatnu kontrolu arterijskog tlaka, visoka učinkovitost i sigurnost Perineva® (Krkin perindopril) i njegova dostupnost u različitim oblicima doziranja, jakostima i kombinacijama fiksnih doza mogla bi olakšati zbrinjavanje arterijske hipertenzije i poboljšati suradljivost hrvatskih pacijenata.*

***KLJUČNE RIJEČI:*** *perindopril, arterijska hipertenzija, kardiovaskularne bolesti, učinkovitost, sigurnost.*

***SUMMARY:*** *Hypertension is a major cardiovascular and cerebrovascular risk factor and is highly prevalent throughout the world, affecting 50% of people over 60 years of age. Angiotensin-converting enzyme (ACE) inhibitors are the gold standard in the treatment of hypertension. However, there exist important differences among the available ACE inhibitors. Perindopril is distinguished based on specific characteristics, such as long duration of action, 24-hour blood pressure control, high lipophilicity, and high tissue ACE affinity. Moreover, clinical studies investigating the effects of perindopril on morbidity and mortality have provided evidence of its benefits along cardiovascular disease continuum. Since inappropriate treatment was one of the most important reasons for the inadequate blood pressure control, the high efficacy and safety of Perineva® (Krka's perindopril) and its availability in a variety of dosage forms, strengths and fixed-dose combinations might facilitate the management of hypertension and improve compliance among the Croatian patients.*

***KEYWORDS:*** *perindopril, hypertension, cardiovascular disease, efficacy, safety.*

***CITATION:*** *Kardio list. 2011;6(3-4):56-60.*

Arterijska hipertenzija (AH) predstavlja vodeći kardiovaskularni i cerebrovaskularni čimbenik rizika i čestu bolest diljem svijeta koja pogađa polovicu osoba starijih od 60 godina[1]. Unatoč činjenice da se liječenje kontinuirano poboljšava, samo jedna trećina liječenih pacijenata ima normalne vrijednosti arterijskog tlaka (AT)[1,2].

Inhibitori angiotenzin konvertirajućeg enzima (ACE) su za liječenje AH i zatajivanja srca predstavljeni prije nekoliko desetljeća. Danas, ne samo da su priznati kao najutjecajniji lijekovi u kardiovaskularnoj terapiji, već također postoje veoma pouzdani podaci o njihovom profilu tolerancije[2,3]. Iako su ACE inhibitori zlatni standard u liječenju AH, trebalo bi napomenuti da postoje važne razlike među dostupnim ACE inhibitorima. Perindopril je za liječenje AH prvi puta na tržište pušten u Francuskoj 1987 godine[3]. Idućih godina je na temelju novih istraživanja i kliničkih studija ovaj lijek odobren za nove indikacije, uključujući zatajivanje srca[4] i stabilnu koronarnu bolest srca[5]. Zbog njegovog opsežnog popisa indikacija tijekom cijelog kardiovaskularnog kontinuuma (**Slika 1**) perindopril je postao iznimno popularan u cijelom svijetu[3].

Perindopril je dugodjelujući, lipofilni ACE inhibitor s visokim ACE afinitetom tkiva koji se primjenjuje jednom dnevno. Poboljšanje ravnoteže angiotenzina II s bradikininom ostvareno perindoprilom donosi niz blagotvornih učinaka na kardiovaskularni sustav, uključujući antihiperten-

Hypertension is a major cardiovascular and cerebrovascular risk factor and is highly prevalent throughout the world, affecting 50% of people over 60 years of age[1]. Despite the fact that there are constantly improving treatments available, only one third of patients who are treated have a normalisation of blood pressure (BP)[1,2].

Angiotensin-converting enzyme (ACE) inhibitors were introduced a few decades ago for the treatment of hypertension and heart failure. Today, they are not only recognised as having the broadest impact of any medicine in cardiovascular therapy, they also benefit from very solid data on their tolerability profile[2,3]. Even though ACE inhibitors are the gold standard in the treatment of hypertension, it should be noted that there exist important differences among the available ACE inhibitors. Perindopril was first introduced to the market in France in 1987 for the treatment of hypertension[3]. In the following years, it was approved, on the basis of new findings and clinical studies, for new indications, including heart failure[4] and stable coronary heart disease[5]. Because of its extensive range of indications in all stages of the cardiovascular disease continuum (**Figure 1**) perindopril has become extremely popular all over the world[3].

Perindopril is a long-acting, once-daily lipophilic ACE inhibitor with high tissue ACE affinity. Improvement in the angiotensin II-bradykinin balance achieved by perindopril has a number of beneficial effects on the cardiovascular system, including antihypertensive and antiatherosclerotic

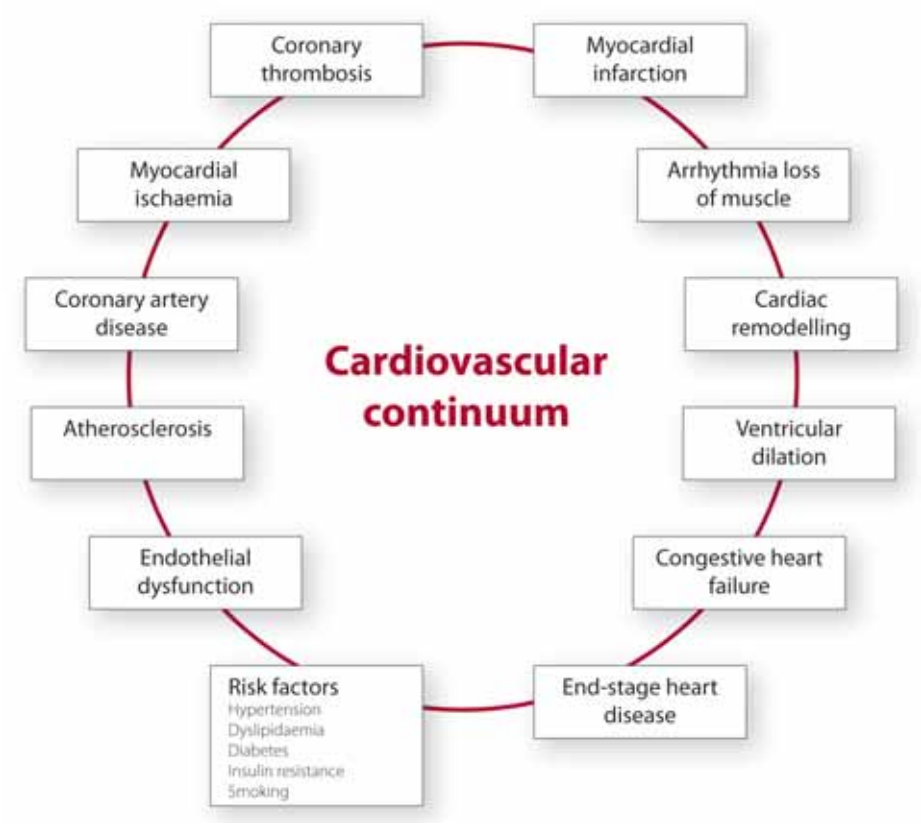


**Figure 1.** *Clinical studies (literature 3 and 6) investigating the effects of perindopril on morbidity and mortality have provided evidence of benefits along cardiovascular disease continuum.*

zivni i antiaterosklerotski učinak[3]. Velike morbiditetne/mortalitetne kliničke studije, kao što su EUROPA i PROGRESS, pokazale su da antihipertenzivno liječenje perindoprilom smanjuje i sprječava kardiovaskularne bolesti kod niza pacijenata s vaskularnim bolestima. Stoga, ishodi ovih i drugih kliničkih studija uz snižavanje vrijednosti AT podržavaju i koncept zaštitnog kardiovaskularnog učinka ACE inhibicije perindoprilom[3,5,7].

Krka je svoj perindopril uvela 2005. godine kao prvi generički perindopril dostupan na tržištu središnje Europe. Trenutno je dostupan u mnogim europskim zemljama te je postao najpropisivaniji generički perindopril u Europi[8]. Učinkovitost i sigurnost Krkinog perindoprila je već ranije dokazana u studijama sigurnosti i učinkovitosti nakon odobrenja, kao i vlastitim kliničkim studijama[9-11].

U Sloveniji je provedena studija koja potvrđuje učinkovitost i sigurnost Krkinog perindoprila u liječenju blage do umjerene AH. U studiji su sudjelovala 2.664 pacijenta, prosječne dobi 61,5 ± 12,7 godina. Statistički značajna redukcija i sistoličkog i dijastoličkog AT je postignuta nakon 3 mjeseca terapije. U prosjeku, sistolički AT je smanjen za 26 mmHg (15,4%), a dijastolički AT za 12 mmHg (12,2%). Statistički značajne redukcije AT su također uočene u osoba starije životne dobi (**Slika 2, Slika 3**)[9]. Ukupna klinička učinkovitost Krkinog perindoprila je procijenjena kao odlična, vrlo dobra ili dobra kod gotovo 90% pacijenata. Lijek su pacijenti dobro podnosili bez obzira na njihovu dob, pošto su tijekom studije nastupile samo blage i prolazne nuspojave. Rezultat ove studije jasno pokazuje da je ovo učinkovit i siguran antihipertenzivni lijek[9].

effects[3]. Large morbidity-mortality clinical studies, such as EUROPA and PROGRESS, have shown that antihypertensive treatment with perindopril reduces and prevents cardiovascular disease in a wide range of patients with vascular diseases. Thus, the outcomes of these and other clinical studies support the concept of cardiovascular protective effects of ACE inhibition with perindopril beyond BP lowering[3,5,7].

Krka introduced its perindopril in 2005 as the first generic perindopril available on Central European markets. It is currently available in many European countries and has become the most prescribed generic perindopril in Europe[8]. The efficacy and safety of Krka's perindopril were proven in post-authorisation safety and efficacy studies as well as in own clinical studies[9-11].

A study assessing the efficacy and safety of Krka's perindopril in the treatment of mild to moderate hypertension was conducted in Slovenia. The study comprised 2664 patients, the average age was 61.5 ± 12.7 years. A statistically significant reduction in both systolic and diastolic BP was achieved after 3 months of treatment. On average, systolic BP was reduced by 26 mmHg (15.4%) and diastolic BP by 12 mmHg (12.2%). Statistically significant reductions were also seen in a population of elderly patients (**Figure 2, Figure 3**)[9]. The overall clinical efficacy of Krka's perindopril was evaluated as excellent, very good or good in almost 90% of the patients. It was well tolerated by the patients regardless of their age, as in the course of the study only mild and transient adverse reactions occurred. The results of the study clearly demonstrate that is an effective and safe antihypertensive medicine[9].

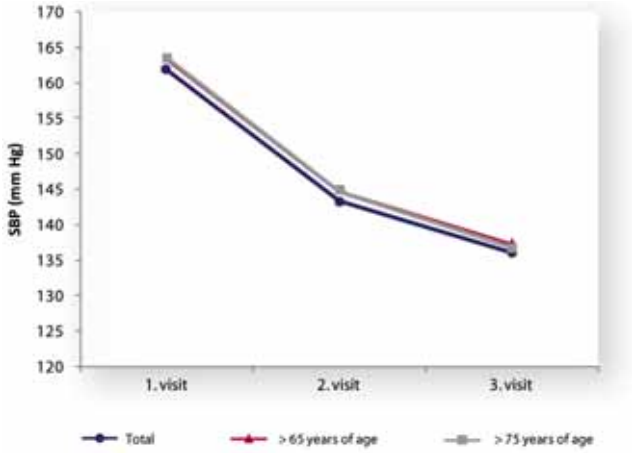


**Figure 2.** *Systolic blood pressure (SBP) values at individual visits in different subpopulations.*

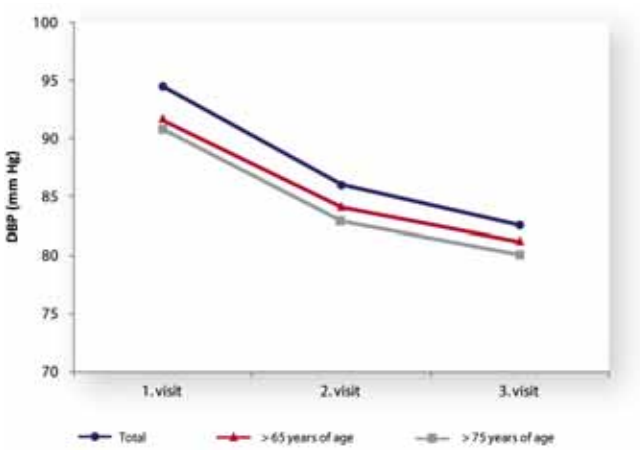


**Figure 3.** *Diastolic blood pressure (DBP) values at individual visits in different subpopulations.*

Ovaj lijek je također uključen u jednu od najvećih kliničkih studija Krkinih lijekova. Studija ATRACTIV je simulirala dobro poznatu studiju ASCOT, najveću ikad obavljenu europsku studiju iz područja AH[12]. Studija ATRACTIV, koja je procijenila učinkovitost složenog i modernog pristupa smanjenju kardiovaskularnog rizika u primarnoj zdravstvenoj zaštiti, provedena je u Republici Češkoj na više od 4.400 pacijenata. Poboljšano zbrinjavanje hipertoničara bilo je povezano sa značajnim smanjenjem prosječnog AT s 152,5/90,5 na 132,5/80,2 mmHg (**Slika 4**). Primjenjeni lijekovi tijekom studije su se dobro podnosili, a pojava nuspojava je bila minimalna[10,11].

This drug was also included in one of the largest non-interventional clinical studies with Krka's medicines. The ATRACTIV study simulated the well know ASCOT study which was the largest European study ever conducted in hypertension[12]. The ATRACTIV study, which assessed the efficacy of a complex and modern approach to cardiovascular risk reduction in primary health care, was conducted in more than 4400 patients in the Czech Republic. Improved management of hypertensive patients was associated with a significant decrease of average BP from 152.5/90.5 to 132.5/80.2 mmHg (**Figure 4**). Pharmacotherapy indicated during the study was well tolerated and the occurrence of adverse reactions was minimal[10,11].

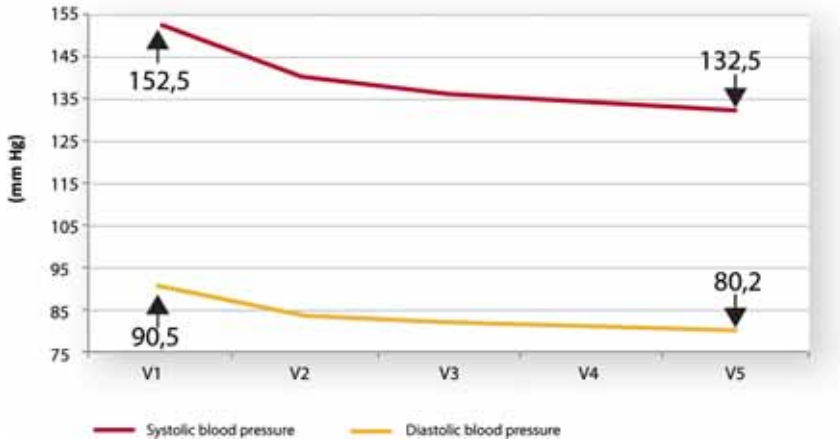


**Figure 4.** *Systolic blood pressure and diastolic blood pressure values at individual visits in the ATRACTIV study.*

Predstavljene studije su dale relevantne rezultate i važne informacije o učinkovitosti i sigurnosti Krkinog perindoprila (Perineva®; u Sloveniji pod tržišnim nazivom Prenessa®). Visoka učinkovitost i sigurnost ovog lijeka i njegova dostupnost u različitim oblicima doziranja, jakostima i kombinacijama fiksnih doza može olakšati liječenje AH i poboljšati suradljivost kod hrvatskih pacijenata.

Received: 28th Jan 2011

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The presented studies yielded relevant results and provided important information on the efficacy and safety of Krka's perindopril (Perineva®; in Slovenia marketed under the brand name Prenessa®). The high efficacy and safety of this drug and its availability in a variety of dosage forms, strengths and fixed-dose combinations might facilitate the management of hypertension and improve compliance among the Croatian patients.

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