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Ramipril u liječenju visokorizičnih kardiovaskularnih bolesnika

Ramipril in the treatment of high-risk cardiovascular patients

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SAŽETAK: Čimbenike rizika čine stanja ili navike koje povećavaju rizik nastanka bolesti. Čimbenici rizika, poput arterijske hipertenzije, pušenja, povišene vrijednosti kolesterola i dijabetesa, značajno doprinose razvoju kardiovaskularnih bolesti koje su vodeći uzrok smrtnosti i pobola u industrijaliziranim zemljama. Inhibitori angiotenzin konvertirajućeg enzima smanjuju rizik od kardiovaskularnih događaja kod pacijenata sa svim razinama rizika. Brojne kliničke studije su već dokazale učinkovitost i sigurnost ramiprila u liječenju hipertenzije. Rezultati studije HOPE su već ukazali na jasne vaskularne i metaboličke prednosti terapije ramiprila. Ove prednosti su dosljedne bez obzira na prisutne čimbenike rizika bolesnika ili primjenu dodatnih liječenja. Kliničke studije Krkinog ramiprila su potvrdile njegovu učinkovitost u postizanju ciljnih razina arterijskog tlaka i ukazale na dodatne koristi kod visokorizičnih bolesnika.

KLJUČNE RIJEČI: arterijska hipertenzija, čimbenici rizika, ramipril.

SUMMARY: Risk factors are conditions or habits that increase the risk of developing a disease. Risk factors such as hypertension, smoking, high cholesterol and diabetes contribute significantly to the development of cardiovascular diseases. Cardiovascular diseases are the major cause of mortality and morbidity in industrialised countries. Angiotensin-converting enzyme inhibitors reduce the risk of cardiovascular events in patients at all levels of risk. Numerous clinical studies have already proved the efficacy and safety of ramipril in hypertension treatment. The results of the HOPE study also demonstrated clear vascular and metabolic benefits of ramipril therapy. These benefits were consistent regardless of the patients' risk factors or additional treatments. Clinical studies with Krka's ramipril confirmed its efficacy in achieving target blood pressure levels and demonstrated its various additional benefits in high-risk patients.

KEYWORDS: hypertension, risk factors, ramipril.

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Čimbenici rizika kao što su arterijska hipertenzija (AH), pušenje, povišena vrijednost kolesterola i dijabetes značajno doprinose razvoju kardiovaskularnih bolesti koje su vodeći uzrok smrtnosti i pobola u industrijaliziranim zemljama, usprkos napretku postignutom u prevenciji i liječenju. Zdravstveni problem se širi na zemlje u razvoju i tako postaje svjetska zdravstvena prijetnja[1]. U posljednjih nekoliko godina uloženi su značajni napori u smanjenju globalnog kardiovaskularnog rizika koji zahtjeva evaluaciju i liječenje višestrukih čimbenika rizika. Iako ne možemo utjecati na nepromjenjive čimbenike rizika (npr. dob, spol ili rasa), možemo uspješno kontrolirati i smanjiti one promjenjive (npr. AH, pušenje, povišen kolesterol i dijabetes).

Procjenjuje se da je rizik od koronarne bolesti srca visok ili vrlo visok u više od 50% bolesnika koji boluju od AH. Rizik se čini podcijenjen u kliničkoj praksi, poglavito kod pacijenata s najvišim rizikom. Velike kliničke studije s uporabom inhibitora angiotenzin konvertirajućeg enzima (ACE inhibitori) su dokazale da ovi lijekovi smanjuju rizik od kardiovasku-

Risk factors such as hypertension, smoking, high cholesterol and diabetes contribute significantly to the development of cardiovascular diseases, which are the major cause of mortality and morbidity in industrialised countries, despite advances in prevention and treatment. This health problem is spreading to developing countries and is thus becoming a worldwide health threat[1]. In the past several years, significant efforts have been made in the management of global cardiovascular risk, which requires evaluation and treatment of multiple risk factors. Although we cannot change non-modifiable factors (e.g. age, gender, or race), we can successfully control and reduce modifiable risk factors (e. g. hypertension, smoking, high cholesterol and diabetes).

It is estimated that the risk of coronary heart disease is high or very high in more than 50% of hypertensive patients. The risk appears to be underestimated in clinical practice, especially in those patients at the highest risk. Major clinical studies with angiotensin-converting enzyme inhibitors (ACEIs) have shown that these drugs reduce the risk of cardiovascu-

larnih događaja kod bolesnika neovisno o razini rizika s najvećim dobrobitom kod visokorizičnih bolesnika[1].

Brojnim kliničkim studijama je već dokazana učinkovitost i sigurnost ramiprila kod liječenja AH u različitim skupinama bolesnika, uključujući one s visokim rizikom od kardiovaskularnih događaja. Studija *Heart Outcomes Prevention Evaluation Study* (HOPE) je pokazala rezultate 4,5 godišnjeg praćenja liječenja primjenom 10 mg ramiprila dnevno kod visokorizičnih kardiovaskularnih bolesnika (bolesnici s dokazanom ishemijskom bolešću srca, moždanim udarom, perifernom arterijskom bolešću ili dijabetesom povezanih barem s jednim od sljedećih faktora: AH, povišeni kolesterol, pušenje ili mikroalbuminurija[2]. Studija je uključila više od 9.000 bolesnika. Tijekom praćenja ispitanika liječenih ramiprilom relativni rizik od nefatalnog infarkta miokarda je smanjen za 23%, fatalnog infarkta miokarda i neočekivane smrti za 16%, nove i posebice pogoršavajuće angine za 12% i učestalost postupaka koronarne revaskularizacije za 18%. Korisno djelovanje ramiprila na nastanak infarkta miokarda je uočeno kod onih koji uzimaju ili ne uzimaju antitrombocitnu terapiju, hipolipemike, i/ili beta blokatore ukazujući da su učinci bili neovisni od spomenutih lijekova, ali i dodatno postignuti uz ove lijekove[2]. Ova studija je produžena na dodatno razdoblje od 2,6 godine radi ocjenjivanja dugoročnih učinaka ramiprila na primarne ciljeve. Tijekom daljnjeg praćenja onih kod kojih na kraju HOPE studije nije bilo zabilježenih događaja, postojao je trend u smjeru daljnjeg smanjenja velikih kardiovaskularnih događaja. Tijekom proširenog praćenja kod bolesnika kod kojih se nije razvio dijabetes na kraju HOPE studije je zabilježeno daljnje smanjenje rizika od dijabetesa u grupi s ramiprilom (33% smanjenja) u odnosu na placebo[3]. Tijekom cjelokupnog razdoblja studije (7,2 godine) zabilježeno je 31% smanjenje novonastalog dijabetesa kod bolesnika u skupini na ramiprilu u odnosu na placebo (**Tabela 1**)[3].

lar events in patients at all levels of risk, with the greatest benefits seen in those at highest risk[1].

Numerous clinical studies have already proved the efficacy and safety of ramipril in hypertension treatment in different groups of patients, including those at high risk for cardiovascular events. *The Heart Outcomes Prevention Evaluation Study* (HOPE) showed the results of 4.5 years follow-up treatment with 10 mg of ramipril daily of high risk cardiovascular patients (patients with documented ischemic heart disease, non-debilitating stroke, peripheral arterial disease or diabetes associated with at least 1 of the following factors: hypertension, high cholesterol, smoking, or microalbuminuria[2]. The study included over 9,000 patients. During the follow-up in patients treated with ramipril the relative risk of non-fatal myocardial infarction was reduced by 23%, of fatal myocardial infarction and unexpected death by 16%, of new and, particularly, worsening angina by 12% and the rate of coronary revascularisation procedures by 18%. The beneficial impact of ramipril on the occurrence of myocardial infarction was observed in those taking or not taking antiplatelet agents, lipid lowering agents, and/or beta-blockers, indicating that the effects were independent and additive to those drugs[2]. This study was then extended for another 2.6 years to evaluate long-term effects of ramipril on primary results. During the extended follow-up in those who were event-free at the end of the HOPE study, there was a trend toward a further reduction in major cardiovascular events. During the extension, in those patients who had not developed diabetes by the end of the HOPE study, there was a significant further reduction in the risk of diabetes in the ramipril group (33% reduction) when compared to the placebo group[3]. During the entire study period (7.2 years), there was a 31% reduction in new diagnoses of diabetes in patients in the ramipril group vs placebo (**Table 1**)[3].

OUTCOME	RELATIVE RISK REDUCTION
Myocardial infarction, stroke, cardiovascular death	17%
Myocardial infarction	19%
Stroke	21%
Cardiovascular death	14%
Revascularisation	16%
New diagnosis of diabetes	31%

Table 1. Outcomes of the HOPE study for the entire study period (7.2 years).

Rezultati studije HOPE su već ukazali na jasne vaskularne i metaboličke prednosti liječenja primjenom ramiprila. Koristi su bile prisutne bez obzira na čimbenike rizika ili dodatna liječenja[3].

Provedeno je nekoliko kliničkih studija s Krkinom ramiprilom sa ciljem ocjene njegovog učinka i sigurnosti kod visokorizičnih kardiovaskularnih bolesnika. Tako su provedene tri studije u različitim skupinama bolesnika visokog rizika: hiper-

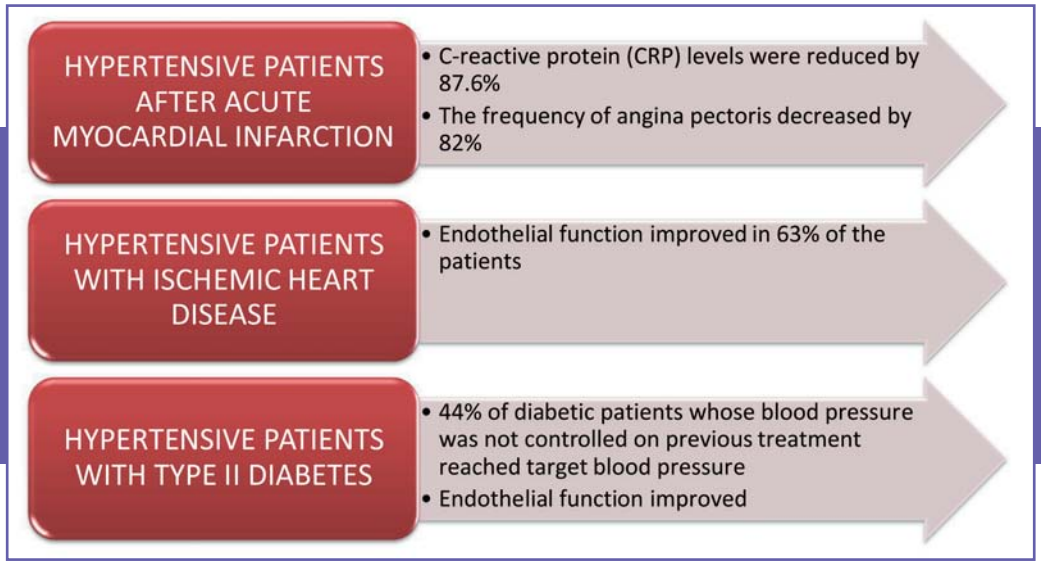
The results of the HOPE study demonstrated clear vascular and metabolic benefits of ramipril therapy. These benefits were consistent regardless of the patients' risk factors or additional treatments[3].

Several clinical studies were also performed with Krka's ramipril, with the objective to evaluate its efficacy and safety in high-risk cardiovascular patients. Three studies were performed in different groups of patients at high risk: hyper-

tenzivni bolesnici nakon akutnog infarkta miokarda, hipertenzivni bolesnici s ishemijskom bolešću srca i hipertenzivni bolesnici s dijabetesom tipa II. Sve studije su potvrdile Krkin ramipril kod postizanja ciljnih razina arterijskog tlaka i ukazale na različite pridružene dobrobiti u visokorizičnih bolesnika (**Tabela 2**)[4-8].

tensive patients after acute myocardial infarction, hypertensive patients with ischemic heart disease, and hypertensive patients with type II diabetes. All studies confirmed Krka's ramipril efficacy in achieving target blood pressure levels and demonstrated different additional benefits in high risk patients (**Table 2**)[4-8].

Table 2.
Clinical experience with Krka's ramipril inhigh risk patients.



Krkin ramipril je dostupan kao monoterapija (Ampril®) te u obliku dviju kombinacija fiksnih doza (Ampril®HL ili Ampril®HD)[9]. Različite jačine i pakiranja osiguravaju da liječenje visokorizičnih skupina bolesnika bude prilagođeno pojedinačnim potrebama bolesnika.

Krka's ramipril is available as a mono substance (Ampril®) and in the form of two fixed-dose combinations (Ampril®HL or Ampril®HD)[9]. Various strengths and package sizes ensure that treatment of high risk patient groups can also be tailored to the individual patient needs.

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