Statini u prevenciji srčanožilnih bolesti – činjenice i predrasude

Statins in the Prevention of Cardiovascular Diseases: Facts and Prejudices

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SAŽETAK: Unatoč brojnim dokazima o neposrednoj učinkovitosti statina u snizivanju ukupnog i LDL kolesterola te dugoročnih učinaka u primarnoj i sekundarnoj prevenciji srčanožilnih bolesti, još uvijek se u svakodnevnoj praksi susrećemo s različitim predrasudama vezanima za neželjene učinke liječenja i eventualnu štetnost statina ne samo bolesnika nego i nekih liječnika. Osnovni mehanizam djelovanja statina inhibicija je enzima hidroksi-metil-glutaril koenzima A reduktaze (HMG CoA), enzima koji je ključan u sintezi kolesterola. Drugi potencijalni mehanizmi njihove učinkovitosti jesu stabilizacija aterosklerotskoga plaka, smanjenje endotelne disfunkcije, upalnih te protrombotskih intravaskularnih procesa. Nuspojave liječenja statinima većinom su blage s učestalošću na razini placeba i najčešće ne zahtijevaju prekid liječenja. Treba istaknuti da uvijek treba poticati bolesnike na aktivni, nesedentarni način života, odnosno redovitu tjelesnu aktivnost, zbog njezinih jasnih pozitivnih učinaka u prevenciji te u liječenju dislipidemije i srčanožilnih bolesti.

SUMMARY: In spite of ample evidence supporting the direct effectiveness of statins in the reduction of total and low-density lipoprotein (LDL) cholesterol and long-term effects in primary and secondary prevention of cardiovascular diseases, in everyday practice we are still faced with various prejudices against the undesired effects of treatment and the possible adverse effects of statins, not only among patients, but among some physicians as well. The basic mechanism of action of statins is inhibiting 3-hydroxymethyl-3-methylglutaryl coenzyme A reductase (HMG-CoA), a key enzyme in cholesterol synthesis. Their other potential mechanisms are stabilization of atherosclerotic plaque and reduction of endothelial dysfunction, as well as inflammatory and post-thrombotic intravascular processes. The side effects of treatment with statins are generally mild, with a frequency comparable to placebo, and usually do not require the termination of treatment. It is necessary to emphasize that patients must always be encouraged to adopt an active, non-sedentary lifestyle that includes regular physical activity, due to its clear positive effects in the prevention and treatment of dyslipidemia and cardiovascular diseases.

KLJUČNE RIJEČI: statini, dislipidemija, kardiovaskularna prevencija.

KEYWORDS: statins, dyslipidemia, cardiovascular prevention.

CITATION: Cardiol Croat. 2016;11(1-2):81–86. | **DOI:** http://dx.doi.org/10.15836/ccar2016.81

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RECEIVED:
February 1, 2016

ACCEPTED:
February 13, 2016

Uvod

Lijekovi za snizivanje kolesterola, tzv. statini, nezaobilazni su temelj i učestalo se propisuju u kliničkoj praksi za prevenciju i liječenje srčanožilnih bolesti[1,2]. Unatoč brojnim dokazima o neposrednoj učinkovitosti statina u snizivanju ukupnog i LDL kolesterola te dugoročnih učinaka u primarnoj i sekundarnoj prevenciji srčanožilnih bolesti[3-6], još uvijek se u svakodnevnoj praksi susrećemo s različitim predrasudama vezanima za neželjene učinke liječenja i eventualnu štetnost statina, ne samo kod bolesnika nego i kod nekih liječnika.

Introduction

Medication for cholesterol reduction, also known as statins, are the foundation of the prevention and treatment of cardiovascular diseases and are frequently prescribed in clinical practice[1,2]. In spite of ample evidence supporting the direct effectiveness of statins in the reduction of total and low-density lipoprotein (LDL) cholesterol and long-term effects in primary and secondary prevention of cardiovascular diseases[3-6], in everyday practice we are still faced with various prejudices against the undesired effects of treatment and the possible

Mehanizam djelovanja

Osnovni mehanizam djelovanja statina jest inhibicija enzima hidroksi-metil-glutaril koenzima A reduktaze (HMG CoA), enzima koji je ključan u sintezi kolesterola u svim tjelesnim stanicama, poglavito hepatocitima. Time se smanjuje endogena sinteza ukupnog i LDL kolesterola i njihova koncentracija u krvi[1]. Glavni predstavnici skupine i u Hrvatskoj se najčešće uporabljuju atorvastatin (10 – 80 mg), simvastatin (20 – 80 mg), rosuvastatin (5 – 40 mg) i fluvastatin (40 – 80 mg). Načelno, rosuvastatin je najpotentniji u snizivanju LDL kolesterola uzimajući u obzir maksimalne doze pojedinih predstavnika skupine, odnosno, rosuvastatin i atorvastatin učinkovitiji su od simvastatina i osobito fluvastatina u snizivanju LDL kolesterola[7-9]. Ukupno gledajući, statini imaju minimalni učinak na povećanje koncentracije HDL kolesterola, u prosjeku do 5 %. Simvastatin i rosuvastatin učinkovitiji su u povećanju koncentracije HDL kolesterola s obzirom na atorvastatin[8,10,11]. Atorvastatin i rosuvastatin najučinkovitiji su u snizivanju koncentracije triglicerida, a njihov je učinak ovisan o dozi i incijalnoj koncentraciji triglicerida[8,12,13].

S obzirom na činjenicu da se kolesterol u tijelu sintetizira u velikoj mjeri u ranojutarnjim satima, preporučuje se propisivanje uzimanja statina s kratkim poluživotom (simvastatin < 5 sati, fluvastatin < 3 sata) uvečer. Nasuprot tomu, statine s dužim poluživotom (atorvastatin 14 sati, rosuvastatin 19 sati) može se propisivati u bilo koje doba dana[14].

Pleiotropni učinci statina

Nasuprot neposrednom mehanizmu djelovanja u obliku snizivanja ukupnog i LDLkolesterola, mehanizmi kojima statini dovode do dugoročnih učinaka u smanjenju srčanožilnog morbiditeta i mortaliteta nisu dokraja razjašnjeni. Regresija ateroskeroze zapažena je tek u maloga broja bolesnika, a klinička učinkovitost statina opisana je i u kraćem razdoblju od šest mjeseci njihove primjene[15], mnogo prije nego je moguće očekivati eventualnu znatniju regresiju aterosklerotskih promjena. Osim neposrednog učinka na razinu ukupnog i LDL kolesterola, drugi potencijalni mehanizmi njihove učinkovitosti, tzv. pleiotropni učinci, stabilizacija su aterosklerotskoga plaka, smanjenje endotelne disfunkcije, upalnih te protrombotskih intravaskularnih procesa[16-18].

Primarna prevencija srčanožilnih bolesti

Brojne studije sa statinima provedene su na populaciji pacijenata bez dokazane srčanožilne bolesti u posljednjim dvama ili više desetljeća. Većina njih pokazala je smanjenje ukupnog i srčanožilnog mortaliteta u skupini koja je uzimala statin s obzirom na placebo, a neke su čak i prekinute prije planiranog završetka zbog zabilježene značajne koristi u skupini pacijenata liječenih statinom[19-21]. Provedene metaanalize „statinskih" studija u primarnoj prevenciji srčanožilnih bolesti također su pokazale smanjenje ukupnog mortaliteta u osoba liječenih statinima, ali u bitno manjem opsegu s obzirom na rezultate pojedinih studija uzimajući u obzir smanjenje apsolutnog rizika[3,4].

U primarnoj prevenciji srčanožilnih bolesti, danas se rutinski uporabljuju tablice za procjenu globalnog rizika za razvoj srčanožilnih bolesti i svakom se potencijalnom bolesniku pristupa individualno. Na temelju 12 europskih kohortnih stu-

adverse effects of statins, not only among patients, but some physicians as well.

Mechanism of action

The basic mechanism of action of statins is inhibiting 3-hydroxymethyl-3-methylglutaryl coenzyme A reductase (HMG-CoA), a key enzyme in cholesterol synthesis in all bodily cells, especially hepatocytes. This leads to a reduction in the endogenous synthesis of total cholesterol and LDL cholesterol, and to the reduction of their concentration in the blood[1]. The main representatives of the group that are most frequently used in Croatia are atorvastatin (10-80 mg), simvastatin (20-80 mg), rosuvastatin (5-40 mg), and fluvastatin (40-80 mg). Generally, rosuvastatin is the strongest for the reduction of LDL cholesterol when the maximum doses for individual representatives of the group are taken into account. In other words, rosuvastatin and atorvastatin are more effective than simvastatin and especially fluvastatin when it comes to the reduction of LDL cholesterol[7-9]. All in all, statins have a minimal effect on the increase of the concentration of HDL cholesterol, up to 5% on average. Simvastatin and rosuvastatin are more effective in increasing the concentration of high-density lipoprotein (HDL) cholesterol than atorvastatin[8,10,11]. Atorvastatin and rosuvastatin are the most effective in the reduction of the concentration of triglycerides, and their effect is dependent on the dose and initial concentration of triglycerides[8,12,13].

Since cholesterol synthesizes in the body takes place mostly in the early hours of the morning, one should prescribe that statins with a short half-life (simvastatin <5 hours, fluvastatin <3 hours) be taken in the evening. On the other hand, statins with a longer half-life (atorvastatin 14 hours, rosuvastatin 19 hours) can be prescribed for any time of day[14].

Pleiotropic effects of statins

Unlike the direct mechanisms of action that reduce total and LDL cholesterol, mechanisms that allow statins to cause long-term reduction of cardiovascular morbidity and mortality have yet to be fully explained. Atherosclerosis regression has been found only in a small number of patients, and the clinical effectiveness of statins has been described for a time period shorter than six months[15], which is too short to expect a significant regression of atherosclerosis. Apart from the direct effect on the level of total and LDL cholesterol, other potential mechanisms of action, also known as pleiotropic effects, include stabilization of atherosclerotic plaque and reduction of endothelial dysfunction, as well as inflammatory and post-thrombotic intravascular processes[16-18].

Primary prevention of cardiovascular diseases

Numerous studies on statins have been carried out on patients without confirmed cardiovascular diseases in the last two decades or more. Most studies found showed a reduction in total and cardiovascular mortality in the group that received a statin compared with placebo, and some were even cancelled before completion due to notable improvement in the group of patients treated with a statin[19-21]. Meta-analyses of "statin" studies in the primary prevention of cardiovascu-

dija uveden je SCORE (prema engl. *Systemic COronary Risk Evaluation*) sustav, čime je omogućena procjena desetogodišnjega srčanožilnog rizika, i to posebno za europske regije visokog (sjeverna Europa i tranzicijske zemlje) i niskog (južnoeuropske ili mediteranske zemlje) rizika[22]. Hrvatska pripada zemljama visokog rizika!

Preporučene vrijednosti LDL kolesterola u primarnoj prevenciji srčanožilnih bolesti:

- bolesnici s umjerenim rizikom (SCORE >1 do 5 %); < 3,0 mmol/l
- visoki rizik za razvoj srčanožilnih bolesti (SCORE ≥ 5 do < 10 %): LDL kolesterol < 2,5 mmol/L[1].

Sekundarna prevencija srčanožilnih bolesti

U bolesnika s dokazanom srčanožilnom bolesti rizik od razvoja srčanog infarkta, moždanog udara ili nagle smrti vrlo je visok. Stoga je nužno te bolesnike u najvećoj mogućoj mjeri zaštititi od takvih neželjenih događaja. Metaanalize velikih „statinskih" studija u sekundarnoj prevenciji nedvojbeno su pokazale smanjenje smrtnosti u bolesnika liječenih statinima[5,6].

U bolesnika s akutnim koronarnim sindromom, preporuka je započeti liječenje u akutnoj fazi bolesti visokim dozama statina, u pravilu, atorvastatinom u dozi od 80 mg[2]. Doza se nakon nekoliko mjeseci prilagođuje izmjerenim vrijednostima LDL kolesterola.

Preporučene vrijednosti LDL kolesterola u sekundarnoj prevenciji srčanožilnih bolesti, odnosno za bolesnike s dokazanom koronarnom, karotidnom ili značajnom aterosklerotskom bolesti perifernih arterija, aneurizmom abdominalne aorte, kroničnom bubrežnom insuficijencijom, šećernom bolesti tipa 2 ili vrlo visokim rizikom za razvoj srčanožilne bolesti (ukupni SCORE > 10 %,): LDL kolesterol < 1,8 mmol/L ili ga je potrebno sniziti za najmanje 50% od izmjerenih vrijednosti prije početka liječenja.

Važno je istaknuti da aktualne smjernice za liječenje dislipidemije navode da praktično svi bolesnici sa šećernom bolesti, zbog već opisanoga izraženog rizičnog profila, trebaju imati u farmakološkoj terapiji statin, neovisno o razini LDL kolesterola[1].

Bez obzira na to u kojoj se fazi prevencije ili razvijene srčanožilne bolesti pojedini bolesnik nalazi, osim terapije statinom, uvijek ih treba poticati na aktivni, nesedentarni način života, odnosno, redovitu tjelesnu aktivnost zbog jasnih pozitivnih učinaka na lipidni profil[23,24] te time i dugoročne ishode liječenja.

Nuspojave liječenja statinima

Nuspojave liječenja statinima relativno su rijetke i blage, često su na razini placeba i ne zahtijevaju prekid liječenja.

GASTROINTESTINALNE NUSPOJAVE

Rijetke su blaže gastrointestinalne tegobe kao mučnina, abdominalni grčevi, proljevi ili konstipacija.

OŠTEĆENJE JETRE

Često među bolesnicima, ali i nekim liječnicima, postoje neopravdani strah i otpor od njihove primjene jer „oštećuju" jetru. Nepovoljni učinci na funkciju jetre i porast koncentracije jetrenih enzima uz terapiju statinom na razini su placeba, odnosno učestalost je oko 1 %[25-27]. Ako i dođe do blažeg poralar diseases also showed total mortality reduction among patients treated with statins, but to a much lesser extent when compared with the results of individual studies, and when taking into account absolute risk reduction[3,4].

In primary prevention of cardiovascular diseases, Tables for global risk assessment for the development of cardiovascular diseases are now routinely used, and each patient is treated individually. The SCORE (Systemic COronary Risk Evaluation) system was introduced on the basis of 12 European cohort studies, which enabled the assessment of a 10-year cardiovascular risk separately for European regions with high risk (northern Europe and transitional countries) and low risk (countries from southern Europe or Mediterranean countries)[22]. Croatia is among the high-risk countries!

The recommended values of LDL cholesterol in primary prevention of cardiovascular diseases are as follows:

- Patients with moderate risk (SCORE >1 to 5%); < 3,0 mmol/L;
- High risk of developing cardiovascular diseases (SCORE ≥5% to <10%); LDL cholesterol <2.5 mmol/L[1].

Secondary prevention of cardiovascular diseases

In patients with a confirmed cardiovascular disease, the risk of heart attack, stroke, or sudden death is very high. Therefore, it is necessary to protect patients from such undesired events as much as possible. The meta-analyses of large "statin" studies in secondary prevention have clearly shown a mortality reduction in patients treated with statins[5,6]. When it comes to patients with acute coronary syndromes, it is recommended to begin treatment in the acute phase of the disease using higher doses of statins, and as a rule atorvastatin at a dose of 80 mg[2] should be used. After several months, the dose is adjusted to the measured values of LDL cholesterol.

The recommended values of LDL cholesterol in secondary prevention of cardiovascular diseases, or for patients with a confirmed coronary, carotid, or significant atherosclerotic disease of the peripheral arteries, aneurysm of the abdominal aorta, chronic kidney disease, diabetes type 2, or very high risk for developing a cardiovascular disease (total SCORE >10%) are: LDL cholesterol < 1.8 mmol/L, or reduced by at least 50% of measured values before treatment.

It should be noted that current guidelines for dyslipidemia treatment state that practically all patients with diabetes should include statins in their medication treatment irrespective of LDL cholesterol levels, due to the risk profile described above.

Regardless of the phase of prevention the patient may be in the progression of a cardiovascular disease, apart from the treatment with statin, the patient should always be encouraged to adopt an active, non-sedentary lifestyle, i.e. regular physical activity, due to its clear positive effects on the lipid profile[23,24] and, therefore, the long-term outcomes of the treatment.

Side effects of statin treatment

The side effects of statin treatment are relatively rare and mild, frequently on the level of placebo, and do not require the termination of treatment.

sta transaminaza, to, u pravilu, nije znak hepatotoksičnosti, nego indukcije enzima u hepatocitima. Danas se smatra da je potrebno odrediti koncentraciju transaminaza u krvi prije početka terapije statinom te da nakon početka liječenja nisu potrebne njihove rutinske kontrole, nego ih treba određivati samo na kliničku indikaciju. Tek porast koncentracije transaminaza (alanin aminotransferaze – ALT) u krvi veći od trostruke gornje granice normalnih vrijednosti indikacija je za prekid terapije, odnosno smanjenje doze ili promjenu statina[28].

MIOPATIJA, MIONEKROZA, RABDOMIOLIZA

Razvoj miopatije povezane s liječenjem statinima rijetka je i potencijalno vrlo ozbiljna nuspojava. Pojava klinički značajne mionekroze tijekom liječenja statinom na razini je od 0,1 % liječenih bolesnika[29]. Patogenetski mehanizam nije dokraja razjašnjen. Spominje se učinak statina na sintezu koenzima Q10 ili ubiquinona koji ima važnu ulogu u procesima proizvodnje energije potrebne za normalnu mišićnu funkciju[30,31]. Klinički se očituje bolovima i slabošću različitih mišićnih skupina, često nalik na mijalgije tijekom gripe. Osim kliničkih simptoma, za dijagnozu značajne mionekroze potrebno je laboratorijski dokazati najmanje deseterostruki porast aktivnosti enzima kreatin-kinaze (CK). Najteži oblik bolesti jest rabdomioliza povezana s upotrebom statina koja je definirana kao mionekroza s mioglobinurijom ili razvojem akutnoga bubrežnog zatajenja[32]. Ovakve, najteže manifestacije bolesti najčešće se pojavljuju uz konkomitantnu terapiju nekim lijekovima poput ciklosporina, gemfibrozila, makrolidnih antibiotika, niacina, digoksina, varfarina itd.[33]. Osim toga, kao rizični čimbenik za razvoj statinske miopatije spominje se genetska predispozicija, neke neuromuskularne bolesti, hipotireoza, bubrežna insuficijencija i dr.[32,33]. Smatra se da su fluvastatin te pravastatin povezani s najmanjom učestalosti pojave miopatije[34].

U svakodnevnoj je praksi razumno pri uvođenju statina u terapiju odrediti aktivnost CK, dok je poslije tijekom liječenja nije nužno rutinski određivati, osim pri pojavi kliničkih simptoma kao što su slabost ili bolovi u mišićima.

POVIŠENJE RAZINE GLUKOZE U KRVI I RAZVOJ ŠEĆERNE BOLESTI TIPA 2

Izgledno je da statini mogu blago povećati rizik od razvoja šećerne bolesti tipa 2 ili pak imati nepovoljni utjecaj na regulaciju glikemije u bolesnika s već postojećom šećernom bolesti. Taj je rizik izraženiji u bolesnika liječenih visokim u usporedbi s umjerenim dozama statina[35]. Uzimajući u obzir rezultate velikih studija kojima je potvrđeno da liječenje statinima u bolesnika sa šećernom bolesti smanjuje rizik od neželjenih srčanožilnih događaja i smrtnog ishoda, ti, povoljni učinci nadmašuju zamijećeni blago povišeni rizik od njihova nepovoljnog utjecaja na metabolizam glukoze[36,37].

EREKTILNA DISFUNKCIJA I STATINI

Svjedoci smo da se pokatkad u svakodnevnom radu susrećemo s pacijentima liječenima nekim od statina koji se žale na pojavu erektilne disfunkcije koju čvrsto povezuju ili imaju otpor od daljnjeg uzimanja lijeka, odnosno samoincijativno prekidaju liječenje.

GASTROINTESTINAL SIDE EFFECTS

Mild gastrointestinal difficulties are rare, but come in the form of nausea, abdominal cramps, diarrhea, or constipation.

LIVER DAMAGE

Among numerous patients, but also among some physicians, there is an unjustified fear of and resistance to statins because they "damage" the liver. Unfavorable effects on liver function and an increase in the concentration of liver enzymes during statin treatment are on the level of placebo, which means that the rate is around 1%[25-27]. Even a mild increase in the number of transaminase enzymes is generally not a sign of hepatotoxicity, but of enzyme induction in hepatocytes. Today, it is believed necessary to determine the concentration of transaminase enzymes in the blood before beginning statin treatment, and that routine check-ups of transaminase enzymes are not required after beginning treatment and should be determined only by clinical indication. An increase in the concentration of transaminase enzymes (alanine aminotransferase – ALT) in blood higher than triple the upper limit of normal values is an indication that treatment should be stopped, the dosage lowered, or the statin changed[28].

MYOPATHY, MYONECROSIS, RHABDOMYOLYSIS

Development of myopathy connected to statin treatment is a rare and potentially very serious side effect. The incidence of clinically significant myonecrosis during statin treatment is 0.1% of treated patients[29]. The pathogenetic mechanism has yet to be fully explained. There is mention of the effect of statin on the synthesis of the coenzyme Q10 or ubiquinone, which has an important role in the production of energy required for normal muscle function[30,31]. Clinically, it manifests through pain and weakness of various muscle groups, and is often similar to myalgia caused by influenza. Apart from clinical symptoms, the diagnosis of significant myonecrosis requires laboratory proof of at least a ten-time increase in the activity of creatine kinase (CK) enzyme. The most severe form of the disease is rhabdomyolysis connected to statin use, defined as myonecrosis with myoglobinuria, or the development of acute kidney failure[32]. Such severe manifestations of the disease most commonly occur when there is a concomitant therapy of medicines such as cyclosporin, gemfibrozil, macrolide antibiotics, niacin, digoxin, warfarin, etc[33]. Genetic predisposition is also said to be a risk factor in the development of statin myopathy, as well as some neuromuscular diseases, hypothyroidism, kidney insufficiency, etc[32,33]. It is believed that fluvastatin and pravastatin are associated with the smallest incidence of myopathy[34].

In everyday practice, it is reasonable to measure CK activity when introducing a statin into treatment, whereas later during treatment it is not necessary to routinely measure it except when there are clinical symptoms such as weakness or muscle pain.

INCREASE OF BLOOD GLUCOSE AND DEVELOPMENT OF DIABETES TYPE 2

It is possible that statins may cause a small increase in the risk of developing diabetes type 2 or have an adverse effect on glycemia regulation in patients who already have diabetes. That risk is more pronounced in patients treated with doses of statin that were high when compared with moderate

Literaturni podatci ne podupiru takvo stajalište, dapače, postoje studije koje navode smanjenje erektilne disfunkcije kao jednu od mogućih „nesrčanožilnih" koristi od liječenja statinima[38,39].

Crvena riža i dislipidemija

Pripravci crvene riže danas su vrlo popularni među laicima kao prirodni pripravci za snizivanje kolesterola u krvi i često su im pacijenti skloniji nego uzimati statine za regulaciju dislipidemije. Ti pripravci sadržavaju različite aktivne tvari, a za njezino povoljno djelovanje najvažniji su monakolini koji blokiraju sintezu kolesterola u jetri. Monakolin K iz crvene riže po svojoj kemijskoj građi identičan je lovastatinu, uz napomenu da mu je doza u pripravcima niža nego ona koja se uobičajeno primjenjuje u obliku lijeka[40]!

Zaključak

Na temelju sada već višedesetljetnog iskustva u njihovoj primjeni, čvrstih dobro dokumentiranih dokaza na golemom broju liječenih bolesnika širom svijeta, jasno je da su statini nezaobilazni lijekovi u liječenju dislipidemije, odnosno u prevenciji i liječenju srčanožilnih bolesti. Nuspojave liječenja statinima većinom su blage s učestalošću na razini placeba i najčešće ne zahtijevaju prekid liječenja. Nakraju, svakako treba istaknuti da uvijek treba poticati bolesnike na aktivni, nesedentarni način života, odnosno na redovitu tjelesnu aktivnost zbog njenih jasnih pozitivnih učinaka u prevenciji te u liječenju dislipidemije i srčanožilnih bolesti.

doses[35]. Taking into consideration the results of large studies that confirmed that statin treatment in patients with diabetes reduces risk of undesired cardiovascular effects and mortal outcomes, such favorable effects outweigh the mild increase in the risk of unfavorable effects on glucose metabolism[36,37].

ERECTILE DYSFUNCTION AND STATINS

In everyday work we sometimes receive patients treated with a statin who complain about erectile dysfunction and associate it with their treatment, resist taking the medicine, or cancel the treatment of their own volition.

Existing literature does not support such a view. On the contrary, there are studies that claim that a reduction in erectile dysfunction is one of possible "non-cardiovascular" benefits of statin treatment[38,39].

Red yeast rice and dyslipidemia

Remedies made of red yeast rice are nowadays very popular among laymen and used to reduce cholesterol in the blood, and patients are often more likely to take them instead of statins for dyslipidemia regulation. Such remedies contain various active substances, and the favorable effect of the rice comes from monacolins, which block cholesterol synthesis in the liver. Monacolin K, found in red yeast rice, is chemically identical to lovastatin, but its dosage in remedies is smaller than the one usually used in medication[40]!

Conclusion

Several decades of experience with the application of statins, as well as firm and well-documented evidence from a large number of patients treated worldwide, show that statins are an unavoidable medication in the treatment of dyslipidemia and the prevention and treatment of cardiovascular diseases. The side effects of statin treatment are usually mild, with incidence on the level of placebo, and commonly do not require the termination of treatment. In conclusion, it should certainly be noted that patients must always be encouraged to adopt an active, non-sedentary lifestyle, i.e. regular physical activity, due to its clear positive effects in the prevention and treatment of dyslipidemia and cardiovascular diseases.

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