Kratko priopćenje | Short communication

# Što još možemo učiniti u liječenju pacijenata s hiperlipidemijom?

# What more can we do when treating patients with hyperlipidemia?

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***SAŽETAK:*** *Klinička praksa pokazuje da svega polovica pacijenata u sekundarnoj prevenciji dosegne ciljnu vrijednost LDL kolesterola što ukazuje na problem neadekvatne kontrole LDL. U jednoj od najnovijih studija s Krkinim atorvastatinom (Atoris®), procijenjeno je dostizanje ciljnih razina lipida i to je uspoređeno s rezultatima prethodnih godina. Rezultati su pokazali da liječenje atorvastatinom statistički značajno i sigurno snižava razine ukupnog kolesterola, LDL i triglicerida kod različitih skupina pacijenata, uključujući i osobe starije životne dobi. Usporedba sa studijom provedenom 2007. je pokazala da je tada prosječno svega 50% pacijenata postiglo ciljne razine LDL uz prosječnu dozu atorvastatina od 19,5 mg. U najnovijoj studiji iz 2009. godine, ciljne razine LDL postiglo je 71% pacijenata uz prosječnu dozu od 26,9 mg atorvastatina dnevno.*

***KLJUČNE RIJEČI:*** *atorvastatin, hiperlipidemija, stariji pacijenti.*

***ABSTRACT:*** *Clinical practice shows that only about half of the patients in secondary prevention reach their target LDL cholesterol levels, which points to the problem of inadequate LDL control. In one of the latest studies with Krka's atorvastatin (Atoris®), achieving target lipid levels was evaluated and compared with the results of the previous years. Evaluation of results showed that treatment with atorvastatin statistically significantly and safely reduced total cholesterol, LDL cholesterol and triglyceride levels in different groups of patients, including the elderly. Comparison with the study conducted in 2007 showed that at that time there were on average only 50% of patients who achieved LDL target levels and the average dose of atorvastatin was 19.5 mg, while in the latest study conducted in 2009, there were 71% of patients who achieved the LDL cholesterol target levels and the average dose was 26.9 mg of atorvastatin per day.*

***KEYWORDS:*** *atorvastatin, hyperlipidemia, elderly patients.*

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Hiperlipidemija predstavlja jedan od glavnih čimbenika rizika za kardiovaskularne bolesti (KVB) — glavnog uzročnika smrti u razvijenim zemljama[1]. Europske smjernice sugeriraju da je glavni cilj liječenja hiperlipidemije razina LDL kolesterola koja bi se, uz promjenu načina života, trebala primarno reducirati terapijom statinima. Štoviše, europske smjernice daju točne ciljne vrijednosti koje bi se trebale postići u liječenju pacijenata s hiperlipidemijom[2]. Cilj liječenja i načini njegovog ostvarenja su jasno definirani. No, što pokazuje klinička praksa? Prema rezultatima studije EUROASPIRE III, koja je uključivala 22 europske zemlje, samo otprilike polovica pacijenata u sekundarnoj prevenciji koronarne bolesti srca (KBS) dosegne svoj ciljni LDL što ukazuje na problem neadekvatne kontrole LDL u svakodnevnoj bolničkoj praksi[3]. Ovo je jedna od važnih činjenica koju ističu i Krkine studije[4-6].

U jednoj od najnovijih studija s Krkinim atorvastatinom, evaluirano je i uspoređeno postizanje ciljnih razina lipida s rezultatima prethodnih godina. Studija je uključivala široki raspon pacijenata te su obavljene dodatne podanalize na zasebnim skupinama pacijenata, uključujući starije od 65 godina, one s KBS, zatajivanjem srca, cerebrovaskularnim bolestima, dijabetesom te pacijenata s perifernom arterijskom bolesti[4]. Studija se sastojala od 3 posjete: prva pri uključivanju u studiju, druga nakon jednog mjeseca liječenja (nije bila obvezna), a treća posjeta 4 do 6 mjeseci nakon uključivanja u studiju.

Od 1.162 pacijenata, u statističku analizu je uključeno njih 1.124 (51% muškaraca, 49% žena) — 56% je uključeno u primarnoj prevenciji, a 38% u sekundarnoj preven-

Hyperlipidemia is one of the major risk factors for cardiovascular disease (CVD) — a major cause of death in developed countries[1]. European guidelines suggest that the main treatment target of hyperlipidemia is the LDL cholesterol level which should be, in addition to lifestyle changes, reduced primarily by statin treatment. What is more, the European guidelines give us exact target values which should be achieved when treating patients with hyperlipidemia[2]. The goal of treatment and the means to achieve it are clearly defined. But what does the clinical practice show? According to the EUROASPIRE III study, which included 22 European countries, only about half of the patients in secondary prevention of coronary heart disease (CHD) reach their LDL target levels, which points to the problem of inadequate LDL in every-day clinical practice[3]. This is one of the important highlights of Krka's own clinical studies as well.

In one of the latest studies with Krka's atorvastatin, achieving target lipid levels was evaluated and compared with the results of the previous years. The study included a wide range of patients and additional subanalyses were performed on separate groups, including patients of more than 65 years of age, patients with CHD, heart failure, cerebrovascular disease, diabetes, and patients with peripheral artery disease4. The study consisted of 3 visits: the first visit at inclusion, the second after one month of treatment (not obligatory), and the third visit 4 to 6 months after the inclusion.

Out of 1.162 patients, 1.124 were considered in the statistical analysis (51% male, 49% female) ? 56% were in-

ciji (nije bilo podataka za 6% pacijenata). U 29% pacijenata registriran je dijabetes, infarkt miokarda kod njih 13%, perkutana koronarna intervencija kod 7%, angina pektoris kod 7%, periferna arterijska bolest kod 7% i moždani udar kod 13%. Gotovo polovica pacijenata bila je starija od 65 godina (prosječna dob 62,7 ± 10,5). Više od 70% pacijenata nije bilo prethodno liječeno hipolipemicima. Pacijenti su primali atorvastatin (Atoris®) u dozama od 10 do 80 mg. U prosjeku su bili liječeni gotovo 5 mjeseci (147 dana). Na kraju studije, više od jedne trećine pacijenata bilo je liječeno s 40 ili više mg atorvastatina. Prosječna dnevna doza atorvastatina na završetku studije iznosila je 26,9 mg[4].

Glavni rezultati su predstavljeni u **tablici 1**, a značajke određenih skupina pacijenata i rezultati podanaliza predstavljeni su u **tablicama 2** i **3**. Liječenje atorvastatinom u svim dozama (također od 40 mg i više) je statistički značajno smanjilo ukupni kolesterol, razine LDL i triglicerida kod različitih skupina pacijenata, uključujući i osobe starije životne dobi i bilo je sigurno[4,5].

cluded in primary prevention and 38% in secondary prevention (there were no data for 6% of patients). Diabetes was reported in 29% of patients, myocardial infarction in 13%, percutaneous coronary intervention (PCI) in 7%, angina pectoris in 7%, peripheral artery disease in 7%, and stroke in 13%. Almost one half of the patients were at least 65 years of age (the average age of patients was 62.7 ± 10.5 years). Over 70% of the patients had not been treated with hypolipidemic drugs before. The patients were receiving atorvastatin (Atoris®) in doses from 10 mg to 80 mg. On average they were treated for almost 5 months (147 days). At the end of the study, more than one third of the patients were treated with 40 mg of atorvastatin or more. The average daily dose of atorvastatin at the end of the study was 26.9 mg[4].

The main results are presented in **Table 1**, and the characteristics of certain groups of included patients and the results of subanalyses of their data are presented in **Tables 2** and **3**. Treatment with atorvastatin statistically significantly and safely reduced total cholesterol, LDL and triglyceride levels in different groups of patients, including the elderly, in all doses, also 40 mg and more[4,5].

***Table 1.*** *Lipid levels measured at each visit of the study.*

| Visit (duration of treatment) | Total cholesterol (mmol/l) | LDL cholesterol (mmol/l) | Triglycerides (mmol/l) |
|---|---|---|---|
| **1** (t = 0 months) | 6.61 | 4.06 | 2.46 |
| **2** (t = 1 month) | 5.09 (-23.1%) | 2.84 (-27.2%) | 1.87 (-16.8%) |
| **3** (t = 4 to 6 months) | 4.60 (-29.4%) | 2.50 (-35.2%) | 1.63 (-22.7%) |

*The percentages in the brackets represent the relative reduction compared to the lipid level measured at the first visit. The reduction of total cholesterol, LDL cholesterol and triglycerides was statistically significant in all three groups (p<0.0001). HDL cholesterol increase was in all three groups statistically non-significant (2.3% at the second visit and 3.3% at the third visit compared to the first visit)[4].*

***Table 2.*** *The relative lipid changes at the last visit (after 6 months of treatment) in different groups of patients (the results of the subanalyses).*

| Group (number of patients) | Total cholesterol | LDL cholesterol | Triglycerides |
|---|---|---|---|
| Patients at least 65 years of age (n=534) | -28.7% | -35.0% | -23.3% |
| Patients with coronary heart disease (n=246) | -28.6% | -35.2% | -23.5% |
| Patients with heart failure (n=66) | -27.8% | -27.6% | -22.5% |
| Patients with cerebrovascular disease (n=126) | -30.2% | -35.5% | -25.1% |
| Patients with diabetes (n=321) | -29.7% | -34.6% | -26.1% |
| Patients with peripheral artery disease (n=74) | -30.7% | -38.6% | -23.2% |

Kao što je već istaknuto, udio pacijenata koji su postigli ciljne razine LDL kolesterola je jedna od važnih činjenica koju ističe i Krkina vlastita klinička studija sa statinima. Ona omogućava usporedbu učinkovitosti liječenja kod različitih skupina pacijenata, kao i procjenu poboljšanja u liječenju tijekom godina. Stoga smo usporedili rezultate studije provedene 2009. god. s rezultatima jedne od kliničkih studija koja je s Krkinim atorvastatinom provedena dvije

As already pointed out, the percentage of patients achieving LDL cholesterol target levels is one of the important highlights of Krka's own clinical studies with statins. It allows us to compare the efficacy of the treatment among different groups of patients, as well as evaluate the improvements in the treatment through the years. Therefore, we compared the results of this study conducted in 2009 with the results of one of the clinical studies which was

***Table 3.*** *Average dose of atorvastatin, average duration of treatment, percentage of patients reaching LDL cholesterol target levels after 4 to 6 months of treatment and the number of patients with adverse events (the results of subanalyses).*

| Group of patients | Average dose at the last visit (mg/day) | Average duration of the treatment (days) | Percentage of patients reaching LDL cholesterol target levels | Number of patients with adverse events related to the treatment |
|---|---|---|---|---|
| Patients at least 65 years of age | 27.7 | 147.3 | 70 | 12 |
| Patients with coronary heart disease | 33.3 | 148.8 | 66 | 1 |
| Patients with heart failure | 34.5 | 142.2 | 68 | 1 |
| Patients with cerebrovascular disease | 35.5 | 149.3 | 65 | 3 |
| Patients with diabetes | 29.5 | 144.7 | 72 | 3 |
| Patients with peripheral artery disease | 32.7 | 155.7 | 71 | 2 |

The LDL cholesterol target level for patients in primary prevention was 3 mmol/l, and for patients in secondary prevention it was 2.5 mmol/l.

godine ranije. Usporedba rezultata je pokazala očigledno poboljšanje. 2007. god. je u prosjeku bilo svega 50% pacijenata koji su postigli ciljne razine LDL, a prosječna doza atorvastatina iznosila 19,5 mg dnevno. 2009. god. je 71% pacijenata postiglo ciljne razine uz prosječnu dozu od 26,9 mg atorvastatina dnevno (procjena ukupnih rezultata svih skupina pacijenata uključenih u svaku studiju)[4,6].

Rezultati studije su također potvrdili da je liječenje atorvastatinom sigurno. Devedeset i osam posto pacijenata nije imalo nikakve nuspojave. Većina nuspojava je bila blaga ili umjerena. Najčešće nuspojave su bile bolovi u mišićima i svrbež[4].

Možemo zaključiti da je posljednja studija potvrdila učinkovitost i sigurnost liječenja atorvastatinom kod širokog spektra pacijenata, uključujući starije, u svim dozama, uključujući 40 mg ili više. Usporedba ovih rezultata s rezultatima studije Krkinog atorvastatina iz prethodnih godina je pokazala trend boljem praćenju razina LDL te time prema boljem smanjenju kardiovaskularnog rizika. Kao što pokazuju rezultati, još uvijek postoji prostor za daljnja poboljšanja.

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conducted with Krka's atorvastatin two years earlier. The comparison of the results showed an obvious improvement. In 2007 there were on average only 50% of patients who achieved LDL cholesterol target levels and the average dose was 19.5 mg of atorvastatin per day, while in 2009, there were 71% of patients who achieved the LDL cholesterol target levels and the average dose was 26.9 mg of atorvastatin per day (evaluation of the total results in all groups of patients included in each study)[4,6].

The results of the study also confirmed that treatment with atorvastatin was safe. Ninety-eight percent of the patients did not experience any adverse events. Most of the adverse events were mild or moderate. The most common adverse events were muscle aches and itching4.

We can conclude that with the latest study, the efficacy and safety of atorvastatin treatment were confirmed in a wide range of patients, including the elderly, and for all doses, including 40 mg and more. Comparison of these results with the results of studies with Krka's atorvastatin from the previous years shows a trend towards keeping a better track of patients' LDL cholesterol levels, and hence towards better cardiovascular risk reduction. There is still room for further improvement, as shown by the results.

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