# Lipid-lowering therapies and achievement of LDL-cholesterol targets

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In the present issue of *Archives of Medical Science*, Mark *et al*. [1] report the results of a survey conducted last year in Hungary. This consisted of 1,626 adult patients with high cardiovascular (CV) risk, due to unstable angina (23%), peripheral artery disease (17%), previous myocardial infarction (34%), stroke (30%) or transient ischemic attack (17%). The main aim of the study was to assess the achievement of low density lipoprotein cholesterol (LDL-C) target levels, and to compare it with previous data from surveys performed by the same authors. The LDL-C target value in the present study was 2.6 mmol/l (100 mg/dl), in line with the recommendation of the Hungarian Cardiovascular Consensus Conference (2010) [2]; using this LDL-C target, the authors reported a 43.3% achievement rate. Furthermore, they noticed that the goal achievement rate was higher in patients followed by specialists ($n$ = 1,152) vs. those followed by general practitioners ($n$ = 474) (45% vs. 40%, respectively), but this difference did not reach significance [1].

The overall achievement rate was poor despite the high CV risk; this is a common problem in Europe and especially in Central and Eastern European countries [3]. As recently discussed [4], although the quality of lipid-lowering treatments has improved, in many European countries therapeutic inertia and a lack of sufficient knowledge regarding the best management of patients with lipid disorders remains an important problem [4, 5]. In addition, there is insufficient collaboration between specialists and primary care physicians [3-5]. We discuss potential problems of adherence to therapy in 3 different categories: patient-, prescriber- and drug-related factors.

Regarding patient-related factors, it is important to highlight the potential role of side effects and polypharmacy; indeed, patients at high CV risk usually need several drugs (e.g. anti-hypertensive, anti-diabetic and anti-platelet drugs). This was also true for the patients included in the Mark *et al.* study [1], where 46% had diabetes and 88% hypertension. Other patient-related factors include patient participation and understanding why the treatment is needed (awareness). This is linked to attendance and optimal frequency of follow-up visits [4-6].

Prescriber-related factors include the knowledge of LDL-C guideline targets, which have become more difficult to achieve over the years: this is a universal phenomenon that persisted during the decade 2000 to 2010

[7]. There have been prospective attempts to improve this situation, but mainly focused on the time after the acute event; in contrast, there have only been a few attempts to improve adherence in secondary cardiovascular disease (CVD) prevention drugs away from the acute event, taking into account "real word data" [8]. In the Greek atorvastatin on coronary heart disease evaluation (GREACE) [9], patients with established coronary artery disease (CAD) were randomised either to "structured care" (atorvastatin titrated from 10 to 80 mg/day in order to achieve an LDL-C target of 2.6 mmol/l, 100 mg/dl; $n$ = 800) or to "usual" medical care ($n$ = 800). Patients were followed for a mean of 3 years and there was an effort to keep the "structured care" group of patients on statins; this resulted in the achievement of the LDL-C goal in 95% of patients. Other prescriber-related factors include the training and the cost limitations (generic drugs, government funding, insurance etc.) [9].

Another crucial issue is the role of specialist vs. non-specialist in the treatment of lipid disorders. It has recently been highlighted that therapeutic inertia [4], lack of (or insufficient) knowledge and mistakes by physicians (especially general practitioners) are reasons why they do not use high doses of statins and very often decrease the doses of statins in patients who receive them after hospitalization or consultation with specialists. This is also true for the study of Mark *et al*. [1], where achievement rate was higher in patients followed by specialists than general practitioners. In addition, in this latter study [1], the authors stratified their high risk patients according to the new dyslipidaemia guidelines of the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) [10]; as a result of this, 83% of their patients belonged to the very-high risk category with an LDL-C target value of 1.80 mmol/l 70 mg/dl). Only 11% of the very-high risk patients ollowed by general practitioners achieved this stricter LDL-C target [1]. This again supports the concept of therapeutic inertia, as well as the need of specialized professionals (physician and nurse services).

Further, drug-related factors may potentially interfere with adherence to therapy. Combination therapy is often necessary in subjects with high or very-high CV risk (usually with atherogenic dyslipidemia) but it may not be used as a result of a number of potential issues, including lack of knowledge, high cost of therapy, lack of evidence and decreased adherence due to polypharmacy [11]. Combination formulations may result in greater adherence, and there is already experience with successful results with combination therapy for lipid disorders [12, 13]. It should also be highlighted that lipid-lowering treatments have additional benefits, such as on kidney function, non-alcoholic fatty liver disease (NAFLD) and thrombosis [14]. This may be counteracted by statin-related increased new onset of diabetes [15], but it is important that the CV and mortality benefits of statin therapy significantly exceed the diabetes hazard, even in patients at high risk of developing diabetes [16-18].

Finally, there is currently a strong debate whether we should treat patients on the basis of their plasma lipid levels or on the basis of their risk [19]. Most international guidelines as well as several expert panels have confirmed that LDL-C represents the primary or even the only target of therapy [5, 10, 13]. Yet, increasing evidence suggests abandoning the paradigm of treating dyslipidemic patients to LDL-C targets only and moving away to a more tailored treatment approach. In this context, atherogenic dyslipidemia and its associated risk would become a target of tailored therapy. Indeed, increasing evidence suggests that the "quality" of plasma lipids (e.g. small, dense LDL and dysfunctional high density lipoprotein [13, 20, 21]). In conclusion, we should not treat the cholesterol, but the risk!

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