Are we getting to lipid targets in real life?

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In this issue of *Archives of Medical Science* a Hungarian group reports on lipid goal achievement in 12,317 high risk patients [1]. This analysis considers the treatment of dyslipidemia between 2004 and 2008 and also compares the performance of general practitioners (GPs) and specialists (9,508 and 2,809 patients, respectively). During this period the percentage of patients "on target" for low density lipoprotein-cholesterol (LDL-C) increased from 14% to 32% and 20% to 43% when treated by GPs and specialists, respectively. In contrast, there was no significant improvement in high density lipoprotein-cholesterol (HDL-C) or triglyceride (TG) levels. The conclusion was that "more attention needs to be paid to changing treatment of patients to achieve target levels". This includes an increased use of combination therapy.

The authors [1] attribute the improvement in lipid management between 2004 and 2008 to the application of up-to-date consensus recommendations. More specifically, information was provided to physicians via journals, scientific meetings and country-level coordinators.

We previously conducted 4 pilot best-practice implementation enhancement programmes aimed at improving risk factor control [2-5]. Physicians from Hospitals or Health Centres recruited patients with metabolic syndrome (MetS) (628 patients, the SAGE-METS [Standardized arrangement for a guideline driven treatment of the metabolic syndrome] study) [2], diabetes mellitus (DM) (578 patients, the INDEED [Initiative for a new Diabetes therapeutic approach in a Mediterranean country] study) [3], hypertension (697 patients, the IMPULSION [Implementation of guidelines for the management of arterial hypertension] study) [4] or dyslipidemia (1127 patients, the IMPROVE-dyslipidemia [Implementation of strategy for the management of overt dyslipidemia] study) [5].

Participating physicians attended educational programmes related to current guidelines for MetS, DM, hypertension, dyslipidemia, overt cardiovascular disease (CVD), obesity and nutrition [2-5]. The physicians were motivated to participate as part of their continuing medical education program. Patients were also motivated by supplying them with a brochure that included instructions to help them achieve treatment goals.

The prevalence of dyslipidemia was reduced from 79 to 24% in the SAGE-METS study [2], from 76 to 12% in the INDEED study [3], from 59.7 to 53.6% in the IMPULSION study [4] and from 100 to 21% in the IMPROVE-dyslipidemia study [5]. The greatest reduction in LDL-C levels (31.6%) was observed in patients with dyslipidemia (IMPROVE-dyslipidemia study) [5]. Triglyceride levels were significantly reduced in all patient populations (p from < 0.002 to < 0.0001 for all comparisons). High density lipoprotein-cholesterol levels increased in all studies (p < 0.0001) except for the IMPULSION study where the rise was not significant.

All these studies [1-5] highlight the importance of continuous education of medical practitioners. Mark *et al.* [1] reported a higher percentage of patients achieving LDL-C targets when treated by specialists compared with those followed up by GPs (43% vs. 32%, respectively; p < 0.0001 by our calculations). In our studies [2-5] the performance of specialists and GPs was not compared.

Mark *et al.* [1] suggested that the high percentage of Hungarian patients on a statin may be at least partly attributed to available generic agents which are more affordable. The impact of this effect is likely to increase as more statins (and other lipid-lowering drugs) become generic. These authors [1] also specified that the use of combination therapy (e.g. statin plus ezetimibe) contributed to better goal achievement. This interpretation is in agreement with community-based studies that showed a significantly improved outcome in lipid targets following the addition of ezetimibe to a statin [6, 7]. Overall, a meta-analysis (n = 5,039) concluded that ezetimibe co-administration with a statin provides significant additional lipid-lowering effect (a further 23.6% reduction in LDL-C levels; p < 0.0001), allowing more patients to achieve LDL-C target values [8]. Similar results were obtained in another recent meta-analysis [9]. Higher doses of statins represent another therapeutic option, although this may be associated with an increased risk of adverse effects [10].

Although reduction of LDL-C remains the primary goal for lipid-lowering interventions, other targets (e.g. HDL-C and TG) may also be important [11-13]. In this context, non-HDL-C has also been proposed as a marker of residual CVD risk [14, 15]. Another potential therapeutic goal would be apolipoprotein (apo) A and B levels or their ratio [14, 16-18]. The advantage when using non-HDL-C, apo A and/or apo B is that these markers can be measured in the nonfasting state [14, 16, 17]. However, there is no definitive evidence showing that raising HDL-C levels in patients on statins will result in a significant reduction in vascular events [19, 20]. Similarly, it is not absolutely clear if TG levels (fasting or non-fasting) are independent predictors of vascular risk [17, 21-24]; however TG, besides LDL-C and C-reactive protein (CRP), seems to be predictors of cardiovascular events especially in patients with acute coronary syndromes [12, 25].

The role of "over the counter (OTC)" statins [26, 27] in achieving LDL-C goals is controversial [28-30]. Limitation of OTC statins include the fact that many countries have not approved this process, the dose allowed to be prescribed by the pharmacist is low (e.g. 10 mg simvastatin in the UK) and the cost has to be paid by the patient [26, 27].

Finally, we must deal with all vascular risk factors (e.g. hypertension, smoking, DM, obesity) and not just lipids [31, 32]. We should also keep in mind the increased CVD risk of certain populations (e.g. South Asians) and the possibility of different therapeutic targets in those patients [33, 34].

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