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Editorial

Undertreatment of dyslipidemia: from the Arabian Gulf to the USA. Time to solve this problem!

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Abstract

Undertreatment of dyslipideamia is a universal problem and reduces the efficasy of hypolipidaemic drugs to reduce cardiovascular event rates. The means to face this problem are available and should be utilized to optimize dyslipidaemia control and clinical outcomes.

The current issue of *Current Medical Research and Opinion* includes the results of the CEPHEUS Study in the Arabian Gulf on lipid target achievement among high and highest cardiovascular disease (CVD) risk patients[1]. This study evaluated the treatment efficacy of dyslipidemia in 5275 subjects from six Arab Gulf States (Bahrain, the Kingdom of Saudi Arabia, Kuwait, Oman, Qatar and the United Arab Emirates) at high or highest CVD risk according to current guidelines[1]. Low density lipoprotein cholesterol (LDL-C) target (<70 mg/dl; 1.8 mmol/L) was achieved in 25%, non-HDL-C in 36% and apolipoprotein B (ApoB) in 38% of the highest risk patients compared with achievements of targets in LDL-C (<100 mg/dl; 2.5 mmol/L) of 46%, non-HDL-C 58% and ApoB 51% in the high risk group[1]. In patients with triglycerides (TGs) ≥200 mg/dl (≥2.2 mmol/L), LDL-C target was achieved in 16% and ApoB in 15% of patients in the highest risk group compared with achieving LDL-C in 32% and ApoB 22% targets in the high risk cohort[1]. These data suggest that a large proportion of high and highest CVD risk dyslipidemic patients in the Arabian Gulf States on lipid-lowering drugs are not at recommended lipid targets and that a substantial residual risk of CVD (RRCVD) remains[1].

This is not the first paper reporting undertreatment of dyslipidemia worldwide. However, there are practically no data about the Arabian Gulf States. These states have a problem with familial hypercholesterolemia (FH)[2,3], metabolic syndrome and diabetes[4,5]. These two conditions, among others, increase CVD risk and there is an absolute necessity to effectively treat all CVD risk factors, among which is dyslipidemia.

Similar data are reported by the CEPHEUS South Africa Study[6], the CEPHEUS Pan-Asia Study[7], the CEPHEUS Centralized Pan-European Study[8] and other European Countries[9] as well as the OLYMPIC and the metabolic syndrome Greece ($n = 10{,}000$) studies[10,11], a study from the UK ($n = 117{,}840$)[12] and a study from the US National Health and Nutrition Examination Survey[13]. The recent Euroaspire IV[14] included high risk individuals (coronary patients) from 26 countries[14]. Among high risk patients 39% had a total cholesterol value >180 mg/dl (4.5 mmol/L), 42% an LDL-C value >100 mg/dl (2.5 mmol/L), and 85% an LDL-C value >70 mg/dl (1.8 mmol/L)[14].

In Greece 95% of post-infarction patients were on statins but only 34% were at LDL-C target >70 mg/dl (1.8 mmol/L)[14].

The fact that undertreatment of hypercholesterolemia is a universal phenomenon/problem is evident from the above evidence. It is high time to solve, at least in part, this problem.

The effort started during the 90 s. Greg Fonarow from the UCLA with the Cardiac Hospital Atherosclerosis Management Program (CHAMP) focused on initiation of all guideline-based treatments for secondary CVD following an acute cardiac event[15]. He educated hospital staff (interns, residents, nurses) at practically no cost and in the discharge form a phrase for each risk factor was added. Did the patient reach the guideline suggested target? If not why? This reminded interns to persuade patients if they had any objections or to titrate the dose of statin (as far as dyslipidemia was concerned) if that had not been done. The result was impressive. Aspirin use at discharge increased from 68 to 92% ($p<0.01$), beta-blocker use from 12 to 62% ($p<0.01$) and angiotensin enzyme (ACE) inhibitor use from 6 to 58% ($p<0.01$). Statin use increased from 6 to 86% ($p<0.01$) resulting in an increase in achieving a LDL-C <100 mg/dl (6 vs 58%, $p<0.001$)[15]. The clinical outcome was more impressive. Post-CHAMP patient groups (1994–1995) had half the incidence of recurrent CVD events during the next year compared with the pre-CHAMP period (1992–1993)[15].

We carried out similar studies, performing four best practice 1 year studies. The concept was to persuade physicians to establish why patients are not on target and remind them to attempt to achieve these targets. In these studies, one for dyslipidemia[16], one for diabetes[17], one for arterial hypertension[18], and one for multiple CVD risk factors[19], the effort succeeded. The dyslipidemia study[16] showed a doubling in patients achieving the LDL-C target and an estimated reduction in CVD risk within 1 year: 45% for the Framingham equation and 63% for the PROCAM equation[16]. The other studies produced similar results[17–19]. Given that the simultaneous and multifactorial treatment of all CVD risk factors provides maximum protection it is very important to target all CVD risk factors. Nevertheless, there is considerable room for improvement and progress towards evidence-based clinical practice[20].

Another method, also very effective and complementary to those discussed above is 'Pay per Performance'. The results of the Dyslipidaemia International Study (DYSIS) were reported at the European Society of Cardiology (ESC) congress and published[21,22]. DYSIS compared LDL-C target achievement in two West European Countries: the UK, with an incentive-driven reimbursement system, and Germany, with a budget-restrictive (white list) healthcare system. Overall, 79.8% of UK patients achieved the LDL-C target of <100 mg/dL (median: 82 mg/dL), compared with 42.0% of patients in Germany (median: 111 mg/dL), despite the higher use of ezetimibe in the German population (11.3 vs 3%)[21,22]. Dyslipidemic patients in the UK were more likely to be treated with potent statins whereas German doctors were more confined with insurance restrictions than UK physicians (e.g. atorvastatin was not included in the white list of drugs in Germany, because of its price[21,22]). Thus, lipid (mainly LDL-C) targets were more likely to be achieved in clinical practice with a pay-for-performance system than in Germany with the budget-restrictive system[21,22]. The UK healthcare system makes physicians participate in a clinical audit, and these results are used to assess the quality of care provided. There are no specific quality-improvement strategies in Germany, where generic simvastatin is the main statin[21,22]. A total of 85% of German patients were treated with simvastatin (mean dose 27 mg/d) compared with 66% of UK patients (mean simvastatin dose 37 mg/d), while nearly 25% of UK patients were treated with atorvastatin (mean dose 34 mg/d) vs just 4% of Germans who received this higher-potency statin[21,22]. Furthermore, the German population had a higher baseline incidence of CVD, cerebrovascular disease, peripheral arterial disease and diabetes mellitus, more secondary prevention patients that need to achieve even lower LDL-C targets[21,22]. Similar results were reported by a pharmacist-based pay-for-performance project in the UK[23]. This paradigm shows that reviewing GP data and financially rewarding the attainment of target treatment for LDL-C and other CVD risk factors, as in the UK, a country with financial restrictions, might in the long run cost even less than a budget-restrictive system, seen in Germany, a wealthier country. If you take into consideration the lives saved and improved quality of life, then a pay-for-performance policy is medically, humanely, and probably financially more beneficial than a budget-restrictive choice.

A considerable effort was also made in the US: the American College of Cardiology Guidelines Applied in Practice (GAP)[24,25] was an attempt in this direction. In 2007 the real-time GAP implementation correlated with more frequent use of in-hospital post-myocardial infarction treatment[25]. Among others, statin use increased from 66 to 81% ($p<0.0001$)[25]. Real-time GAP implementation was associated with fewer re-hospitalizations for CVD (19.8 vs 25.2%, $p=0.001$), myocardial infarction (3.5 vs 5.4%, $p=0.0243$) and combined death/CVD/myocardial infarction (9.5 vs 13.9%, $p=0.0009$) during the 6 months after discharge[25]. The above suggest that a pilot program started in the state of Michigan US by the American College of Cardiology and adopted by hospitals led to a higher use of evidence-based therapies and correspondingly better outcomes than those associated with the initial GAP, or usual care[24,25].

The concept of ideal cardiovascular (CV) health, with emphasis on the prevention of CVD, was set by the American Heart Association (AHA) within its strategic goals for 2020[26]. This was designed to focus mainly on the promotion of a healthy lifestyle and multifactorial intervention by non-pharmacological and pharmacological means aiming at prevention or effective control of CVD risk factors[26]. Ideal CV health is defined as optimal levels for three CVD risk factors (blood pressure, fasting plasma glucose and total cholesterol) and four behaviors (body mass index, smoking, physical activity and healthy diet)[26]. These seven ideal CV metrics, called life's simple seven, are probably the best available measure of life-time CVD risk[27]. Recent studies have shown the levels of ideal CV health in the United States to be very low (1%) at a community level[28] and to be associated with CVD events, stroke and all cause mortality[28]. Within this effort the control of LDL-C is one of the main targets using physical activity, diet and hypolipidemic drugs alone or in combination[26]. In that context, the statin–ezetimibe combination may help patients reach new 'stricter' cholesterol goals[29].

Overall, there is a need for the state, universities, hospitals, scientific societies, general practitioners, and patients to achieve guideline-based lipid levels and substantially reduce CVD morbidity and mortality. It is high time to achieve this goal.

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