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Retrospective Study

Statin escape phenomenon: Fact or fiction?

The aim of this study was to provide additional data on the possible statin escape phenomenon based on the experience of a lipid clinic and elucidate potential risk factors.

This was a retrospective (from 1999 to 2013) observational study including dyslipidemic adults followed-up for ≥3 years in the Outpatient Lipid Clinic of the University Hospital of Ioannina in Greece. A complete assessment of serum lipid profile along with cardiovascular risk factors and concomitant treatment was available.

Demographic characteristics as well as various clinical and laboratory data were recorded at the baseline visit, at 6 months and the most recent visit. These included: a) age, gender, and smoking status, b) body mass index (BMI) and waist circumference, c) fasting glucose levels and glycated hemoglobin (HbA1c), d) blood pressure (BP), e) estimated glomerular filtration rated (MDRD - eGFR), and f) a complete fasting lipid profile, including total cholesterol (TCHOL), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), LDL-C and non-high density lipoprotein cholesterol (non-HDL-C). Blood samples were collected in the morning into sterile Vacutainer-SST II advance tubes (Becton–Dickinson, Plymouth, UK) after overnight fasting for at least 8–12 h. The tubes were refrigerated immediately after collection, were centrifuged at 4 ^{o}C within 40 min of blood sampling, and then were analyzed within 2 h. Serum concentrations of TCHOL were determined enzymatically on an Olympus AU600 Clinical Chemistry Analyzer (Olympus Diagnostica, Hamburg, Germany). HDL-C was determined by a direct assay (Olympus Diagnostica, Hamburg, Germany). LDL-C was

calculated using the Friedewald formula [TCHOL – (TG/5 + HDL-C)], provided that TG levels were <400 mg/dL (4.5 mmol/L). Serum Apo-A-I, Apo-B, Apo-E and Lp(a) levels were measured with a Behring Nephelometer BN100 and with reagents from Dade Behring GmbH analyzer (Liederbach, Germany). The diagnosis of metabolic syndrome was based on the presence of at least 3 of the following criteria: a) fasting glucose ≥100 mg/dL (5.55 mmol/L), b) BMI ≥30 kg/m^2 or waist ≥102 cm for male subjects and BMI ≥27 kg/m2 or waist ≥88 for female subjects, c) fasting TG levels ≥ 150 mg/dL (1.7 mmol/L), d) systolic BP ≥130 mmHg and/or diastolic BP ≥85 mmHg and e) HDL-C <40 (1 mmol/L) and <50 mg/dL (1.3 mmol/L) for male and female subjects, respectively. The diagnosis of established diabetes was made a) when fasting glucose levels were ≥126 mg/dL (6.99 mmol/L) in 2 separate measurements prior to the baseline visit, b) when glucose levels were ≥200 mg/dL (11.1 mmol/L) 2 hours following an oral glucose tolerance test with 75 gr of glucose at the baseline visit, or c) when the individuals were already on antidiabetic therapy.

The evaluation of adherence to medication was based on the Hellenic national e-prescription web database. Subjects were classified according to their compliance with treatment as good or poor compliers if they refill ≥ or <80% of their expected prescriptions over time, respectively. We excluded those individuals meeting one of the following criteria: use of statin therapy at baseline visit, discontinuation of statin treatment at most recent visit, change in statin treatment during follow-up and poor compliance to treatment. Statin escape phenomenon was defined as an increase in subject LDL-C levels at the most recent visit by >10% compared with the value at 6 months following initiation of statin therapy.

Due to the small number of the eligible participants, we were not able to identify potential predictors for the statin-escape phenomenon or establish an association between statin escape and incidence of cardiovascular disease. Nevertheless, our study confirms the limited bibliography reporting on statin escape phenomenon and its quite

high prevalence. Thus, further investigation on the underlying pathophysiology of the statin escape phenomenon and its potential clinical ramifications is required.

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