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Atherosclerosis newsletter

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Statins are cholesterol-lowering drugs indicated in the treatment of hypercholesterolemia for the prevention of atherosclerotic cardiovascular disease. Although since the early '90s many randomized controlled trials with roughly 100'000 person-years of follow-up have been conducted, there are still open questions on efficacy and safety in special patients' groups. Another area of uncertainty is the degree of adherence to this ideally life-long therapy. These topics are addressed by articles published in the two November issues of *Atherosclerosis*.

Statin initiation and all-cause mortality in incident statin-naïve dialysis patients

Chronic kidney disease (CKD) is a major burden of global healthcare. Patients who have end-stage kidney disease (ESKD) and are on dialysis have a much higher mortality rate compared with the general population. Registry studies indicated that cardiovascular disease (CVD) is an independent risk factor for and the leading cause of death in dialysis patients. Kim et al. explored the association between statin initiation after starting dialysis and all-cause mortality in statin-naïve ESKD patients.

Nationwide data of incident dialysis patients from 2010 to 2017 in South Korea were analyzed. Patients who had previous cardiovascular events or were administered statins before dialysis were excluded. The study group included dialysis patients receiving statins within 1 year after dialysis initiation. The control group was organized after propensity-score matching with age, sex, time of dialysis initiation, and underlying diabetes mellitus and hypertension. The main outcomes were all-cause mortality and major cardiovascular events.

1596 patients who started statin treatment and 1:1 matched statin-nonusers were included in the study. During the 9438 person-year follow-up, 468 deaths and 264 major adverse cardiovascular events (MACEs) occurred. Statin initiation was associated with a reduced risk of all-cause mortality but not with MACE incidence. The risk ratio of mortality is lower when statins are prescribed at the dosage recommended by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines.

Statin initiation was associated with lower risk of all-cause mortality in statin-naïve ESKD patients. Further prospective studies are warranted to validate the association of statin initiation with mortality in incident dialysis cases.

This article is further discussed in a critical editorial.

A systematic review and meta-analysis on the effects of statins on pregnancy outcomes

Due to their undisputed efficacy and their good safety profile, statins are widely prescribed drugs. Statins are contraindicated in pregnancy, due to their potential teratogenicity. However, data are still inconsistent and some even suggest a potential benefit of statin use against pregnancy complications. Vahedian-Azimi et al. aimed to investigate the effects of statins on pregnancy outcomes, including stillbirth, fetal abortion, and preterm delivery, through a systematic review of the literature and a meta-analysis of the available clinical studies.

A literature search was performed through PubMed, Scopus, and Web of Science up to May 2020. Data were extracted from 18 clinical studies. Random effect meta-analyses were conducted using the restricted maximum likelihood method. The common effect sizes were calculated as odds ratios (ORs) and their 95% confidence interval (CI) for each main outcome.

Nine studies were included in the meta-analysis. There was no significant association between statin therapy and stillbirth. While statin exposure was significantly associated with increased rates of spontaneous abortion, it was non-significantly associated with increased rates of induced abortion and elective abortion. A non-significant numerically reduced rate of preterm delivery was observed in statin users.

Statin therapy was not associated with stillbirth or induced and elective abortion rates. Significant increase after statin therapy was observed for spontaneous abortion. These results need to be confirmed and validated in future studies.

The relationship between directly measured statin adherence, self-reported adherence measures and cholesterol levels in patients with coronary heart disease

Despite extensive evidence proving the beneficial effect of statins on clinical outcomes, with low rates of side-effects, poor adherence is common. Insufficient statin therapy is associated with an increased risk of major adverse cardiovascular events and a graded, inverse association between statin adherence and mortality has been shown for patients with established cardiovascular disease (CVD). Accordingly, reduced adherence is a major barrier to address to achieve successful prevention of CVD. Kristiansen et al. aimed to determine the relationship between statin adherence measured directly, and by self-report measures and serum cholesterol levels.

Patients prescribed atorvastatin participated in a cross-sectional study 2–36 months after a coronary event. Self-reported adherence included statin adherence the past week, the 8-item Morisky medication adherence scale (MMAS-8), and the Gehi et al. adherence question. Atorvastatin was measured directly in spot blood plasma by a novel liquid chromatography tandem mass-spectrometry

method discriminating adherence (0–1 doses omitted) and reduced adherence (≥2 doses omitted). Participants were unaware of the atorvastatin analyses at study participation.

Mean age was 63 years and 8% had reduced atorvastatin adherence according to the direct method. In patients classified with reduced adherence by the direct method, 40% reported reduced statin adherence, 32% reported reduced adherence with the MMAS-8 and 22% with the Gehi question. Among those adherent by the direct method, 96% also reported high statin adherence, 95% reported high adherence on the MMAS-8 while 94% reported high adherence on the Gehi question. Cohen's kappa agreement score with the direct method was 0.4 for self-reported statin adherence, 0.3 for the Gehi question and 0.2 for the MMAS-8. Adherence determined by the direct method, self-reported statin adherence over previous week, and the Gehi question was inversely related to LDL-cholesterol levels.

Plasma-statin measurements reveal reduced adherence with higher sensitivity than self-report measures, relate to cholesterol levels, and may prove to be a useful tool to improve lipid management.