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NEPHROLOGY - EDITORIAL

Statin use in patients with chronic kidney disease stages 2–4: targeting beyond improved mortality rates

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The well-designed study by Neves et al. [1] showed that statin and/or vitamin D non-use were independent risk factors of mortality ($p = 0.005$) in their cohort of patients ($n = 95$) with chronic kidney disease (CKD) stages 4 and 5 (mean estimated glomerular filtration rate [eGFR] = 16.1 ml/min/1.73 m^2). After a mean follow-up of 24.1 ± 9.8 months, all patients receiving both statins and vitamin D were alive (18 of 18 patients; 100%). In contrast, only 24 of the 43 patients (56.4%) receiving neither a statin nor vitamin D were alive at the end of the study [1].

Statin use in patients with CKD offers several advantages besides improving mortality rates. Cardiovascular disease (CVD) is the leading cause of death in patients with stages 4 and 5 CKD [2, 3]. Mortality from CVD in this population is approximately 10 to 20 times higher than in the general population [4]. In an analysis of the Pravastatin Pooling Project [5], a subject-level database combining the results from 3 randomized trials of the effects of pravastatin 40 mg/day vs. placebo, the benefit induced by statin use on CVD risk in 19,700 participants with mild/moderate CKD was determined. The 3 randomized studies included in this analysis were the following: the Cholesterol and Recurrent Events (CARE) trial [6], the Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) study [7] and the West of Scotland Coronary Prevention Study (WOSCOPS) [8]. Of the 19,700 total participants in these studies, 12,333 (62.6%) had mild CKD, as defined by an estimated glomerular filtration rate (eGFR) of 60 to 89.9 ml/min/1.73 m^2 and 4,491 (22.8%) had moderate CKD as defined by an eGFR of 30 to 59.9 ml/min/1.73 m^2. Pravastatin significantly reduced the adjusted incidence of the primary outcome of coronary mortality, non-fatal myocardial infarction and coronary revascularization (hazard ratio [HR], 0.77; 95% confidence interval [CI] 0.68–0.86) and the expanded outcome (cardiovascular mortality, non-fatal myocardial infarction, coronary revascularization or stroke; HR, 0.79; 95% CI 0.71–0.88) in people with moderate CKD [5]. Thus, the effects of statin use in patients with CKD not only include reduction of mortality rates, but also a decrease in CVD events (non-fatal myocardial infarction, stroke and revascularization episodes).

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Neves et al. [1] correctly mention that in the German Diabetes and Dialysis (Die Deutsche Diabetes Dialyse Studie; 4D) study [9], death from all causes was similar in the atorvastatin and the placebo groups (297 vs. 320 patients, or 48 vs. 50%, respectively; RR 0.93, 95% CI 0.79–1.08; $p = 0.33$). However, atorvastatin therapy resulted in a significant reduction of all cardiac events combined compared with placebo (205 vs. 246 events, or 33 vs. 39%, respectively; RR 0.82, 95% CI 0.68–0.99; $p = 0.03$). There was also a trend toward a smaller percentage of deaths from cardiac causes (121 vs. 149 deaths, or 20 vs. 23%, respectively; RR 0.81, 95% CI 0.64–1.03; $p = 0.08$) [9]. These results should not be viewed as non-significant.

Patients with nephrotic syndrome in CKD stages 1 through 4 have both an increased production and a decreased catabolism of low-density lipoprotein (LDL) cholesterol, resulting in increased total and LDL-cholesterol levels [10]. Hypertriglyceridemia may also occur, probably due to a reduction in apolipoprotein C-II activity and the presence of a lipoprotein lipase inhibitor, causing decreased activity of lipoprotein lipase and thus decreased catabolism of triglycerides [10]. In contrast, patients with non-nephrotic CKD stages 2 through 4 tend to have normal LDL-cholesterol levels, decreased HDL-cholesterol levels and elevated triglycerides; these alterations are probably due to the above-mentioned reduced lipoprotein lipase activity [10]. As a result, an increase in the LDL/HDL ratio occurs, which, together with elevated lipoprotein (a) levels, contribute to the atherosclerotic complications of these patients [11]. Thus, patients with CKD also have moderate/advanced atherosclerosis in other arterial beds, such as the carotids [12, 13] and/or the heart [14].

Among other studies, the GREek Atorvastatin and Coronary heart disease Evaluation (GREACE) trial showed that renal and ischemic heart disease may progress in parallel and therefore, statins may be beneficial to both organs [15–17]. Several studies have demonstrated that statins improve renal function [18–20]; thus, their use in patients with CKD is virtually mandatory so as to reduce CKD progression and renal function decline rates.

Statin use in patients with CKD is coupled with several beneficial actions. Although mortality rates are an important issue, they should not be the only criterion determining whether patients with CKD merit being on routine statin use or not. All patients with CKD should receive statins to reduce the decline of their kidney function and improve their CVD risk.

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