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Review

The effect of statins on microalbuminuria, proteinuria, progression of kidney function, and all-cause mortality in patients with non-end stage chronic kidney disease: A meta-analysis

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ABSTRACT

Conclusive evidence regarding the effect of statins on non-end stage chronic kidney disease (CKD) has not been reported previously. This meta-analysis evaluated the association between statins and microalbuminuria, proteinuria, progression, and all-cause mortality in patients with non-end stage CKD. Databases (e.g., PubMed, Embase and the Cochrane Library) were searched for randomized controlled trials (RCTs) with data on statins, microalbuminuria, proteinuria, renal health endpoints, and all-cause mortality patients with non-end stage CKD to perform this meta-analysis. The mean difference (MD) of the urine albumin excretion ratios (UAER), 24-h urine protein excretion, and risk ratios (RR) of all-cause mortality and renal health endpoints were calculated, and the results are presented with 95% confidence intervals (CI). A total of 23 RCTs with 39,419 participants were selected. The analysis demonstrated that statins statistically reduced UAER to 26.73 μg/min [95%CI (−51.04, −2.43), $Z = 2.16$, $P < 0.05$], 24-h urine protein excretion to 682.68 mg [95%CI (−886.72, −478.63), $Z = 6.56$, $P < 0.01$] and decreased all-cause mortality [RR = 0.78, 95%CI (0.72, 0.84), $Z = 6.08$, $P < 0.01$]. However, the analysis results did not indicate that statins reduced the events of renal health endpoints [RR = 0.96, 95%CI (0.91,1.01), $Z = 1.40$, $P > 0.05$]. In summary, our study indicates that statins statistically reduced microalbuminuria, proteinuria, and clinical deaths, but statins did not effectively slow the clinical progression of non-end stage CKD.

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1. Introduction

Statins are increasingly used in the treatment of chronic kidney disease (CKD), and numerous clinical trials and meta-analyses demonstrated a potential renal effect of statins [1–5]. However, the effects of statins on microalbuminuria, proteinuria, progression of kidney function and all-cause mortality in non-end stage CKD patients were not reported.

The research outcomes of statins on microalbuminuria are inconsistent. Statins pharmacologically improve microalbuminuria levels in multiple ways, such as podocyte protection, prevention of tubulointerstitial injury, and improvement of endothelial dysfunction [6–8]. However, the use of large dose statins may raise microalbuminuria because of reduced protein trafficking across proximal tubular cells [9,10]. Conclusions from different clinical studies of statins on proteinuria also differ. For example, the recent outcome of the PLANET I study [11] stated that atorvastatin reduced proteinuria, but rosuvastatin did not exhibit this effect. We performed this meta-analysis to address whether statins improved the microalbuminuria or proteinuria levels in non-end stage CKD.

The relationship between statins and CKD progression has not been clarified. For example, the SHARP study [12] and ALLHAT study [13] reported that statins exhibit little or no effect on CKD progression. However, the 4S study [14] reached the opposite conclusion. We assessed whether statins affected CKD progression. We adopted the renal health endpoint as an index to evaluate the clinical progression of CKD. This concept was first discussed in the 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From The Panel Members Appointed To The Eighth Joint National Committee (JNC8) [15].

Finally, whether statins reduced all-cause mortality in non-end stage CKD is inconclusive, and this meta-analysis also investigated this effect.

2. Methods

2.1. Criteria for eligible studies

2.1.1. Types of studies

Randomized controlled trials (RCTs) or quasi-RCTs were included.

2.1.2. Types of participants

2.1.2.1. Inclusion criteria. Patients with chronic kidney injury were enrolled in our study.

2.1.2.2. Exclusion criteria. Patients with end stage renal disease (ESRD) on dialysis, kidney transplant recipients, and patients with acute kidney injury were excluded.

2.1.3. Type of interventions

Studies comparing statins and non-statin treatment were considered eligible for the meta-analysis. Patients in these studies were divided into a control group and a statin group. Patients in the control group were treated with placebo or conventional therapy without statins, and patients in the statin group were treated with statins only or received comprehensive treatment with statins.

2.1.4. Outcome measurements

2.1.4.1. End of treatment microalbuminuria. Microalbuminuria was defined as follows: urine albumin between 30 mg and 300 mg/d, urinary albumin-to-creatinine ratio (UACR) of 30 ~ 300 mg/g, or a urinary albumin excretion ratio (UAER) of 20 ~ 200 μg/min [16].

2.1.4.2. End of treatment proteinuria. Proteinuria was defined as a 24-h baseline urine protein excretion level higher than 300 mg.

2.1.4.3. Events of renal health endpoints. Events of renal health endpoints referred to kidney failure resulting in dialysis or transplantation, a doubling of creatinine level or a halving of glomerular filtration rate (GFR) [15].

2.1.4.4. All-cause mortality. All-cause mortality was refered as a ratio of total number of deaths caused by various reasons and the average population of the same period, it is used to evaluate the risk of death from illness and injury in a certain period of time.

2.2. Study selection, data extraction and quality assessment

2.2.1. Study selection

Electronic databases (e.g., PubMed, Embase and the Cochrane Library) were searched for eligible studies. The last search date was May 5, 2015. We used three search themes for PubMed: statins, CKD and ESRD. The search strategy was developed using MeSH terms