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Association of Baseline Use of Niacin with Progression of Chronic Kidney Disease in over 3 Million U.S. Veterans

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Background: It has been suggested that dyslipidemia can contribute to deterioration of kidney function. Niacin has been used to manage elevated triglycerides and low HDL levels. We hypothesize that niacin also reduces the progression of renal function decline in a cohort of U.S. Veterans.

Methods: In a cohort of 3.3 million U.S. Veterans with normal baseline eGFR in 2005-2006 we examined the association of baseline use of niacin with slopes of eGFR over median follow up of 7.7 years (6.0, 8.4). The referent group was patients who never used niacin throughout the cohort period. Associations were examined in crude and adjusted logistic regression models (for slopes <-5ml/min/1.73m^2/year), with adjustments for demographics, comorbidities, HDL, triglycerides, total cholesterol, and use of statins.

Results: Patients were 60±14 years old, 6% female, 17% African-American, and 23% diabetic with a mean baseline eGFR 84±15 mL/min/1.73m^2. In the total cohort, 9.3% of patients had a rapid kidney function decline with an eGFR slope of <-5 mL/min/1.73m^2/year. In logistic regression models after adjustment for case-mix covariates including BMI and cardiovascular and other comorbidities, baseline use of niacin was associated with lower odds of rapid kidney function. Associations remained significant after further adjustments for HDL, triglycerides total cholesterol, and use of statins.

"*Across all models of adjustment,* ***patients who took niacin had an 11% decreased risk of death***," said Elani Streja, PhD, from the University of California, Irvine Medical Center in Orange.

The study results were presented here at Kidney Week 2014.

These results are in contrast with those seen in the AIM-HIGH and HPS-2 THRIVE studies. A meta-analysis of those studies found a 10% increased risk for all-cause mortality (risk ratio, 1.10; 95% confidence interval, 1.00 - 1.20). In addition, there were increased risks for serious adverse effects with niacin.

Niacin has been shown to decrease reactive oxygen species, inflammation, hypertriglyceridemia, **hyperphosphatemia**, and endothelial dysfunction — **all factors associated with a decline in eGFR**. However, it is not clear whether niacin can actually slow the decline in eGFR.

In their observational study, Dr Streja and colleagues compared 119,891 US Department of Veterans Affairs (VA) patients who were prescribed niacin in 2005 and 2006 with 3,233,579 VA patients who were never prescribed niacin.

A decline in eGFR was defined as an annual decrease of more than 5 mL/min per 1.73 m^2.

At baseline, all patients had normal eGFR. However, niacin patients had a **higher** [**BMI**] body mass index than non-niacin patients (31 vs 29 kg/m^2), **lower** [**HDL**] high-density-lipoprotein cholesterol levels (39 vs 46 mg/dL), **higher triglyceride** levels (214 vs 148 mg/dL), and more use of ACE inhibitors, angiotensin receptor blockers, and statins.

Niacin patients were also older than non-niacin patients (63 vs 60 years), were less likely to be black (9% vs 18%), and **had more hypertension, diabetes, atherosclerotic cardiovascular disease, and congestive heart failure**.

Women made up just 8% of each group, which is not surprising given that this was an older VA population.

Over a median **follow up of 7.7 years**, a **decline in eGFR was less common in niacin than in non-niacin patients** (***odds ratio, 0.88***) after adjustment for demographic, laboratory, and clinical variables, comorbidities, and the use of ACE inhibitors, angiotensin receptor blockers, and statins.

The strengths of this study include its large sample, which consisted of a nationally representative contemporary cohort, and its long follow-up period, Dr Streja said.
Limitations include the lack of data on niacin prescriptions outside the VA system, previous niacin exposure at baseline, patient adherence to niacin, and lipid levels prior to niacin prescription, as well as the observational nature of the study. In addition, the low number of women in the study makes it difficult to generalize the findings to women.

Hard-to-Believe Results

The usual process is to start with retrospective studies and, when they are positive, do prospective randomized controlled clinical trials, said session moderator Ron Gansevoort, MD, from the University Medical Center Groningen in the Netherlands.
"*This is, of course, the other way around*," he told *Medscape Medical News*. "*We've got already two randomized controlled clinical trials that showed the serious side-effect profile of niacin and even increased mortality. Now we get a retrospective study showing benefit, and it's difficult to believe that it might be true*," he explained.
"*It would have been better to look at duration of use and cumulative daily dosage*," Dr Gansevoort said. That could possibly have shown a trend in benefits, he said, "but these data are unfortunately lacking at the moment."
Dr Streja said it might be possible to do such analyses from the study data.
Dr Gansevoort pointed out that another limitation of the study could be an indication bias, as in any retrospective study; this does not occur in prospective randomized controlled clinical trials.

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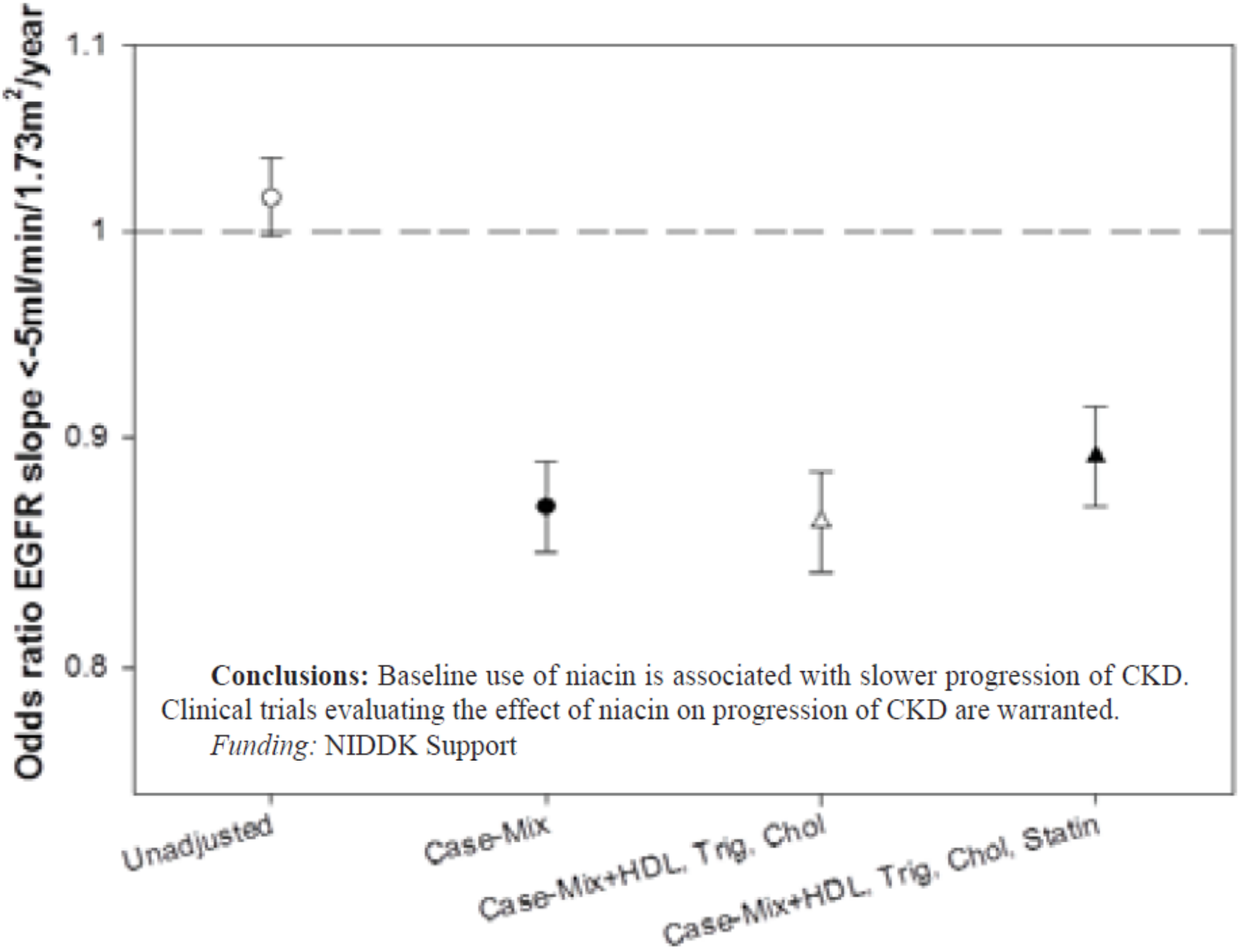

Conclusions: Baseline use of niacin is associated with slower progression of CKD. Clinical trials evaluating the effect of niacin on progression of CKD are warranted.

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