Title

Serum Aclorein-Modified Apolipoprotein A-I is Significantly Increased in Patients With End Stage Renal Disease on Maintenance Hemodialysis

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Publication Date

2017

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Title: Abstract 16902: Serum Aclorein-Modified Apolipoprotein A-I is Significantly Increased in Patients With End Stage Renal Disease on Maintenance Hemodialysis.[Miscellaneous]

Source: Circulation. 136(Suppl_1) (Supplement 1):A16902, November 14, 2017.

Abstract: Introduction: End stage renal disease (ESRD) is associated with a significantly increased risk of cardiovascular and all-cause mortality. This is most likely due to a number of factors including systemic inflammation, oxidative stress, hypertension, altered high density lipoprotein (HDL) composition and function, among others. In this regard, there is mounting evidence that patients with ESRD have reduced HDL function including diminished cholesterol efflux activity and impaired reverse cholesterol transport (RCT). The mechanisms responsible for impaired cholesterol efflux activity in ESRD have not been fully elucidated. There is emerging evidence that acrolein modification of apolipoprotein A-I (apoA-I) impairs HDL-induced cholesterol efflux activity and RCT. Also, elevated serum level of acrolein is associated with decreased activity of HDL-associated antioxidant enzyme, paraoxnase (PON).

Hypothesis: We hypothesized that the concentration of serum acrolein-modified apoA-I is greater in patients with ESRD on maintenance hemodialysis (MHD) than in healthy controls (CTL).

Methods: Serum samples from 30 ESRD patients and 10 age- and gender-matched CTLs were used to measure acrolein-modified apoA-I adduct levels using a sandwich ELISA assay developed by our team. We ensured that only non-smokers were selected given that smoking can increase serum acrolein levels (confirmed via cotinine ELISA). We also checked other indices of HDL function including apoA-I level, PON activity and cholesterol ester transfer protein (CETP) activity.

Results: ESRD patients had 35% lower serum apoA-I level (ESRD: 116.7+/-28.7 mg/dl, CTL: 179.0+/-46.2 mg/dl, $p<0.001$), 45% lower PON activity (ESRD: 79.6+/-22.8 kU/L, CTL: 148.5+/-36.5 kU/L, $p<0.001$), and 120% higher CETP activity (ESRD: 33.8+/-10.7 pmol/[mu]l/h, CTL: 14.1+/-8.0 pmol/[mu]l/h, $p<0.001$). In addition, we found that the ESRD group showed a 60% increase in aclorein-modified apoA-I adduct level than CTL group ($p<0.05$).

Conclusions: Here for the first time we demonstrate that serum levels of acrolein-modified ApoA-I are significantly increased in patients with ESRD on MHD. Future studies will need to determine whether acrolein modification of apoA-I can be one of the causes of impaired HDL function in ESRD patients.