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LDL-C Response to Portfolio Foods Containing High Levels of Phytosterols, Whole Food Fiber, and Alpha-Linoleic Acid in Statin Reluctant Patients: Impact of CYP7A1-rs3808607 and APOE Isoforms

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Abstract:

INTRODUCTION: Up to 20% of outpatients receiving HMG-CoA reductase inhibitors (statins) experience treatment reluctance on the basis of side effects, leaving a large population at increased risk of CVD. We hypothesized that a practical food-based approach can be utilized to lower LDL-C in statin reluctant patients and that the lipid response can be predicted based upon CYP7A1-rs3808607 (CYP7A1) and APOE genetic isoforms.

METHODS: This was a multicenter, randomized, double-blind, free-living cross-over study composed of 2 phases of 4 wk each, separated by a 4 wk washout. Participants (n=54) received an assortment of individually packaged, shelf stable snacks along with printed instructions to ingest 2 servings of the foods per day as a substitute for similar items they were eating already. No other dietary or behavior adjustments were requested. Treatment products supplied at least 1800 mg alpha-linoleic acid (ALA), 5 g of fiber and 1g of phytosterols per serving. Control products were calorie-matched like items drawn from the general grocery marketplace. Lipid parameters were measured and averaged over 2 d at baseline and at 4 wk of each phase. Ingestion of study foods was confirmed by C18:3n3 serum level assessment. Single nucleotide polymorphisms and APOE isoform were assessed by Taqman genotyping assay.

RESULTS: As compared to control, LDL-C decreased 8.8% in the treatment arm ($p < 0.0001$, range -37.6% to +20.5%) and total cholesterol fell 5.1% ($p < 0.004$). No significant change was seen in HDL-C, TG or fasting glucose levels. LDL-C was reduced by diet in CYP7A1 T/T homozygotes ($-0.3924 + 0.1271 \text{ mmol/l}$, $p = 0.0033$) and APOE4 carriers ($-0.3808 + 0.098 \text{ mmol/l}$, $p = 0.0003$).

CONCLUSIONS: Significant LDL-C reductions can be affected through a simple food intervention supplying high levels of phytosterols, fiber and ALA. CYP7A1 and APOE isoforms influence the variability in LDL-C response and can help identify individual patients especially appropriate for a food-based LDL-C lowering approach. Given the large number of patients unable/unwilling to take statins, our findings have significant impact for management of this challenging population.



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Author Disclosure Information:

S.L. Kopecky: Other Research Support; Modest; Step One Foods. **E. Klodas:** Ownership Interest; Significant; Step One Foods. **S. Alias:** None. **J. Bauman:** None. **S. Jew:** None. **P.J. Jones:** Other Research Support; Modest; Step One Foods. Other Research Support; Significant; Manitoba Agri Health Research Network.

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