Correspondence

Letter by Weingärtner et al Regarding Article, “Combined Effects of Ezetimibe and Phytosterols on Cholesterol Metabolism: A Randomized, Controlled Feeding Study in Humans”

To the Editor:

Lin et al1 present an interesting study in which they tested the hypothesis that combining ezetimibe and phytosterols is more effective than ezetimibe treatment alone in reducing serum cholesterol. In a randomized, double-blind, placebo-controlled, triple-crossover study, they found that combining ezetimibe with phytosterols is more effective in reducing cholesterol levels than ezetimibe alone, and they concluded that it is important to determine whether this combined treatment approach would provide better clinical outcome.

Our research group has previously assessed the effect of combining lipid lowering with ezetimibe and phytosterols in comparison to ezetimibe, phytosterols, and Western-type diet alone in apoE−/− mice.2 In this experimental model, we found a result similar to Lin et al in their clinical study: Combining ezetimibe with phytosterols was more effective in cholesterol lowering than ezetimibe alone. However, the data showed that plasma plant sterol concentrations strongly correlated with increased atherosclerotic lesion formation, suggesting that plant sterols per se are atherogenic. Indeed, Lin et al achieved the reduction of serum cholesterol levels by phytosterols at the expense of increased plant sterol serum concentrations (campesterol-to-cholesterol and stigmasterol-to-cholesterol). On the basis of malignant atherosclerosis in patients with the inherited disease phytosterolemia, the association of the genetic regulation of serum phytosterol levels with the risk of coronary artery disease and several epidemiological studies that have shown a correlation between increased plant sterol plasma levels and cardiovascular risk,2–4 these results raise the serious question of safety of plant sterols in the management of hypercholesterolemia.5

In the presence of safety concerns and the complete absence of any evidence for a positive clinical effect of plant sterols, low-density lipoprotein lowering alone cannot justify a treatment recommendation. For both phytosterols and ezetimibe, studies evaluating hard clinical end points are missing. For ezetimibe, they are on the way (IMPROVE IT), but for a diet supplementation with phytosterols they are not planned.3 Without such studies, the effectiveness and safety of inhibitors of cholesterol absorption remains unknown.

Disclosures

The University of the Saarland received minor unrestricted research grants from MSD and Raisio Nutrition Ltd.

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References

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_Circulation_. 2012;125:e456
doi: 10.1161/CIRCULATIONAHA.111.060806

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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