LETTER

Reply to Harris et al.: Differential impacts of omega-3 fatty acids and their derivatives on blood pressure

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In our paper (1), we present the results of a carefully controlled study demonstrating that docosahexaenoic acid (DHA) activated large-conductance Ca^{2+}- and voltage-activated K^+ (BK) channels and lowered blood pressure when applied acutely. We showed that various omega-3 fatty acids, omega-6 fatty acids, and their derivatives had remarkably different effects on blood pressure and BK channels when acutely applied. We do not offer any specific recommendation or advice as to the use of omega-3 fatty acids for clinical situations or as nutritional supplements. However, we note that hypertension is a well-recognized mortality risk factor and many in the United States die from related complications. In caring for the critically ill, perfusion pressure of vital tissues is a key concern and any decrease in blood pressure may not be tolerated. Considerable attention has been paid to the role of omega-3 fatty acids and other "immunonutrients" for the general population and critically ill patients; however, studies have yielded very controversial results regarding their impact or outcome. As stated by Harris et al. (2), the metabolism of fatty acids is a complex issue. The results of our structure-activity experiments highlighted remarkably contrasting effects of various omega-3 fatty acids, omega-6 fatty acids, and their derivatives. In particular, the results presented in the article showed that the ethyl ester of DHA failed to stimulate BK channels and had no effect on blood pressure. This finding suggests that the impact of this and other derivatives (such as the glycerol-ester) administered either orally or parenterally requires rigorous testing in clinical studies. In addition, the physiological responses of healthy individuals and critically ill patients to various fatty acids may differ appreciably. Our results emphasized the importance of properly specifying exact molecules whenever omega-3 fatty acids and fish oil are discussed. We hope that our mechanistic results encompassing multiple levels of physiological organization, from whole animals down to a single defined kinetic transition of the BK channel protein, along with the information provided by those studies using human subjects, as well as the Letter by Harris et al., will be useful for other scientists and clinicians to draw their conclusions for their own applications.

1 Hoshi T, et al. (2013) Omega-3 fatty acids lower blood pressure by directly activating large-conductance Ca^{2+}-dependent K^+ channels. *Proc Natl Acad Sci USA* 110(12):4816–4821.

2 Harris WS, De Caterina R, Marik PE (2013) Docosahexaenoic acid ethyl esters ineffective? *Proc Natl Acad Sci USA* 110:E2259.

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The authors declare no conflict of interest.

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