

Comment on: Tikhonenko et al. (2010) Remodeling of Retinal Fatty Acids in an Animal Model of Diabetes: A Decrease in Long-Chain Polyunsaturated Fatty Acids Is Associated with a Decrease in Fatty Acid Elongases Elovl2 and Elovl4. *Diabetes*;59:219–227

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Tikhonenko et al. (1) recently reported that diabetes-induced changes in retinal fatty acid metabolism lead to a significant decrease in retinal n-3 polyunsaturated fatty acids (PUFAs), especially docosahexaenoic acid (DHA). They proposed that these changes in fatty acid compositions may be related to the chronic inflammation that occurs in the diabetic retina.

Even though they admitted it was possible that high levels of reactive oxygen species (ROS) cause the degradation of the highly oxidation-prone DHA molecule, Tikhonenko et al. concluded that altered fatty acid metabolism was responsible for such retina-specific fatty acid changes.

Recently, we reported that hard exudates in the human diabetic retina, which are believed to develop as a result of extravasation of plasma lipids, have lower levels of DHA and eicosapentaenoic acid than plasma lipids (2). This fact implies that oxidation-prone PUFAs, including DHA, in hard exudates may be more readily degraded (peroxidized) by high levels of ROS. We thus proposed that these alterations of the fatty acid composition may be another pathophysiological explanation for the existing chronic inflammatory conditions in the diabetic retina. Both the reduction of anti-inflammatory effects caused by the decrement of long-chain PUFAs and the accumulation of lipid peroxidation products from degraded PUFA, which have a chemotactic effect on inflammatory cells (macrophages) and are directly toxic to capillary or retina tissues, may be

other possible proinflammatory mechanisms in the diabetic retina (3).

Even with recent studies of the potential cardioprotective effects of n-3 PUFA, whether PUFA supplements could be beneficial for diabetic patients is still controversial. Theoretically, increased proportions of oxidation-prone PUFA in lipids may be related to enhanced susceptibility to oxidative stress, especially under hyperglycemic conditions, which promote localized oxidative stress in tissues vulnerable to diabetic damage. Vascular damage and related vascular leakage of plasma contents are an important pathological mechanism of diabetic retinopathy, and accumulated substances in the extracellular space are known to be highly liable to oxidative damage. Thus, modification of dietary intake of n-3 PUFA in patients with diabetic retinopathy should be evaluated with caution, keeping in mind the potential risks for peroxidation of the accumulated PUFA in the diabetic retina (4).

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REFERENCES

1. Tikhonenko M, Lydic TA, Wang Y, Chen W, Opreanu M, Sochacki A, McSorley KM, Renis RL, Kern T, Jump DB, Reid GE, Busik JV. Remodeling of retinal fatty acids in an animal model of diabetes: a decrease in long-chain polyunsaturated fatty acids is associated with a decrease in fatty acid elongases Elovl2 and Elovl4. *Diabetes* 2010;59:219–227
2. Byeon SH, Chung H, Kwon OW. Polyunsaturated fatty acid composition of surgically removed hard exudates in diabetic macular edema. *Ophthalmic Surg Lasers Imaging*. 9 March 2010 [Epub ahead of print]
3. Lyons TJ, Li W, Wells-Knecht MC, Jokl R. Toxicity of mildly modified low-density lipoproteins to cultured retinal capillary endothelial cells and pericytes. *Diabetes* 1994;43:1090–1095
4. Song JH, Fujimoto K, Miyazawa T. Polyunsaturated (n-3) fatty acids susceptible to peroxidation are increased in plasma and tissue lipids of rats fed docosahexaenoic acid-containing oils. *J Nutr* 2000;130:3028–3033

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