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Study Suggests Antioxidants Inhibit Exercise-induced Insulin Sensitivity

Another study trashing antioxidants – this time vitamins C and E – was published recently in *Proceedings of the National Academy of Sciences USA*.[1] It was a small, double-blind, placebo-controlled study of 40 healthy young men put on an exercise program of 85 minutes five days a week for four weeks. Half the group got antioxidants in the form of 500 mg vitamin C twice daily and 400 IU d-alpha-tocopherol (one isomer of vitamin E) once daily; the other 20 got identical placebos. The upshot of the study was that markers of insulin sensitivity were increased significantly in the group that did not take the antioxidant, but not in the group who took the antioxidant. From this the authors concluded, as the title indicates, that "Antioxidants prevent health-promoting effects of physical exercise in humans."

To draw such a sweeping conclusion based on a small, narrowly-selected population (only healthy young men) seems somewhat reckless. In addition, it suggests all antioxidants – not just vitamins C and E – have such an effect. To quote Dr. Rob Childs, nutritional biochemist for the Cervelo Pro Cycling Test Team, who was interviewed by the online publication NutraIngredients:[2]

"Firstly, the study only investigated the effects of two free radical scavengers in a highly complex system involving hundreds of antioxidant compounds. This makes it inappropriate to extrapolate the study findings to other antioxidants. Secondly, the potential advantages provided by antioxidant supplementation for attenuating muscle soreness and structural damage, while enhancing muscle recovery and performance, were not assessed."

As usually occurs with studies examining the effects of vitamin E, only the alpha-tocopherol isomer was used, while it has been demonstrated that the other tocopherols have different but perhaps equally important functions. For instance, it is known that both delta- and alpha-tocopherols improve insulin sensitivity,[3] while gamma-tocopherol has been shown to block experimentally-induced pancreatic beta-cell destruction – the initiating factor in type 1 diabetes.[4]

While the study design does not seem particularly flawed, the results fly in the face of literally hundreds of studies either implicating oxidative stress in the pathogenesis of insulin resistance and diabetes or pointing to the effectiveness of antioxidants to improve insulin resistance. By their own admission, the authors suggest their results are a departure

from what has been found in previous studies. They also note the oxidative stress induced by exercise occurred in short bursts, as opposed to chronic oxidative stress that is more commonly experienced.

A few examples of studies that either demonstrate oxidative stress is a cause of (not a benefit for) insulin resistance or show the benefit of antioxidant supplementation for insulin resistance follow.

Several large studies have demonstrated that oxidative stress decreases insulin sensitivity and contributes to diabetes. Some of these studies are considerably larger than the small study in question. For instance, in the famous Framingham Offspring Study, in a group of 2,002 non-diabetic individuals, oxidative stress *was* associated with insulin resistance in individuals at risk for diabetes.[5] Another large study of 2,285 men and 2,019 women found dietary antioxidants – alpha-, gamma- and delta-tocopherols in particular – were associated with a significantly decreased risk for developing diabetes.[6]

In one study, 24 hypertensive individuals who took 600 mg vitamin E daily experienced significantly improved insulin sensitivity and increased glutathione levels.[3] In another placebo-controlled trial of 48 normal or overweight adults, those taking an antioxidant supplement (800 IU vitamin E, 500 mg vitamin C, 10 mg beta-carotene) for eight weeks demonstrated improved insulin sensitivity, increased adiponectin (one of the measures of insulin sensitivity used in the study in question – increased by exercise but not when antioxidants were included), improved endothelial function, and decreased markers of oxidative stress in the blood.[7]

In addition, elevated blood sugar and the oxidative stress that results is a major contributing factor for complications of diabetes. Whole books could be written on the benefits of antioxidants for prevention and treatment of diabetic complications.

Summary of key factors:

- Small study; narrow population (only young, healthy men)
- Examined short-term oxidative stress as opposed to long-term oxidative stress, which is more common in the real world
- Makes sweeping generalities implying such an effect would occur in all populations, including those at risk for developing insulin resistance, and with all antioxidants
- Flies in the face of hundreds of articles that have demonstrated a positive correlation between insulin resistance and oxidative stress
- Contradicted by many studies demonstrating the benefits of antioxidants for insulin resistance, including vitamin E

References

1. Ristow M, Zarse K, Oberbach A, et al. Antioxidants prevent health-promoting effects of physical exercise in humans. *Proc Natl Acad Sci U S A* 2009 May 11 [Epub ahead of print]
2. http://www.nutraingredients-usa.com/content/view/print/246799 [Accessed May 15, 2009]
3. Barbagallo M, Dominguez IJ, Tagliamonte MR, et al. Effects of vitamin E and glutathione on glucose metabolism: role of magnesium. *Hypertension* 1999;34:1002-1006.
4. Sjoholm A, Berggren PO, Cooney RV. gamma-Tocopherol partially protects insulin-secreting cells against functional inhibition by nitric oxide. *Biochem Biophys Res Commun* 2000;277:334-340.
5. Meigs JB, Larson MG, Fox CS, et al. Association of oxidative stress, insulin resistance, and diabetes risk phenotypes: the Framingham Offspring Study. *Diabetes Care* 2007;30:2529-2535.
6. Montonen J, Knekt P, Jarvinen R, Reunanen A. Dietary antioxidant intake and risk of type 2 diabetes. *Diabetes Care* 2004;27:362-366.
7. Vincent HK, Bourguignon CM, Weltman AL, et al. Effects of antioxidant supplementation on insulin sensitivity, endothelial adhesion molecules, and oxidative stress in normal-weight and overweight young adults. *Metabolism* 2009;58:254-262.

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