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Intravenous Vitamin C Protects Against Metabolic Syndrome and Activates Nrf2

by Nina Mikirova, PhD

(OMNS, Feb 1, 2017) Vitamin C is essential for life in humans, as the capacity to synthesize it has been lost in the course of our evolution. Besides its antioxidant properties and its role in collagen synthesis, vitamin C has been shown to boost the immune system, to markedly lower blood histamine concentrations, and to have antiviral activity. Large epidemiological studies have shown that intake of vitamin C and other antioxidants can protect against hypertension and the symptoms of diabetes mellitus (such as diabetic retinopathy), and can increase high-density lipoprotein (HDL) cholesterol (thought to be protective), and enhance endothelial function.

When vitamin C is infused intravenously at doses of 10,000 milligrams or higher, it can reach 100 times the level in the blood achievable with oral vitamin C. At this very high level, it shows cytotoxicity against some types of cancer cells. Our laboratory wanted to know whether intravenous vitamin C (IVC, 15,000 mg) would alleviate inflammation and metabolic syndrome. If this study showed positive results, this would potentially benefit millions of people world-wide with chronic inflammatory disease.[1]

Metabolic syndrome

Metabolic syndrome or "adiposity" is a chronic accumulation of body fat. Metabolic syndrome is one of the major public health challenges worldwide that is characterized by:

- Increased fat around the waist
- Elevated blood triglycerides
- Decreased HDL cholesterol
- Elevated fasting glucose
- Elevated blood pressure

These symptoms are associated with chronic diseases such as respiratory and cardiovascular disease, type two diabetes, fatty liver, visceral adiposis, and cancer, which all increase mortality.

Excess fat is associated with chronic low-grade inflammation. Over time this fatty tissue can release signals to the rest of the body that accelerate inflammation. This in large part explains the development of obesity-related disease. Excess fat can also cause insulin resistance and hyperglycemia. It can also trigger atherosclerosis, dyslipidemia (high blood fat levels), high blood pressure, blood clots, and ischemic stroke.

Oxidative stress caused by metabolic syndrome may also play a role in cancer development, as it causes epigenetic changes in gene expression that can promote the development of cancer.

Inflammatory cytokine signals

We wanted to understand the effects of IVC on the expression of cytokines (messenger molecules) involved in inflammation and the immune response, and to determine if IVC helps to reduce inflammation and stimulate the immune response at a genomic level.

IVC treatments increased the ascorbic acid level and the ratio of reduced to oxidized ascorbic acid in blood. This ratio was decreased in participants with a high level of inflammation in subjects with metabolic syndrome, which may be explained by their increased level of oxidative stress.[2] Therefore, the higher the ratio of reduced to oxidized ascorbic acid, the better for treatment. In this regard, vitamin C was considered as a "healing factor" by Irwin Stone.

Inflammation score

Our study showed that after IVC treatment, the "inflammation score," defined by the level of inflammatory and anti-inflammatory cytokines, was decreased. IVC treatment evidently modulated immunological genes in blood cells, suggesting potential benefits in regulating inflammation and redox potential. Several other markers of inflammation and anti-inflammation associated with metabolic syndrome were improved, which indicated a decreased risk for chronic disease.

This finding is very important because it proved that IVC treatment of metabolic syndrome and low-grade inflammation resulted in a lower "inflammation score," which is thought to protect against many types of chronic disease.

Nrf2 regulates antioxidants

Our laboratory analyzed the expression after IVC treatment of one of the factors responsible for the enzymes and proteins involved in the stress response.[1]

This was *nuclear respiratory factor 2* (Nrf2), a transcription factor that regulates the expression of several enzymes that synthesize antioxidants and detoxifying molecules.[1,3] In addition, Nrf2 enhances the expression of genes involved in cell energy production and maintenance, which are essential for health and longevity.[4] Nrf2 signaling is essential for detoxification of reactive metabolites and reactive oxygen species (ROS). This factor also helps cells to get rid of toxins. The products of Nrf2 signaling enhance protection against molecular damage. Our study showed that after IVC treatment, genes coding for Nrf2 and several other important signaling molecules were up-regulated.[1] This activation of Nrf2, by IVC treatment can protect against age-related degenerative diseases and cancer,

Aging causes a decline in levels of Nrf2 that promotes oxidative damage. This mechanism is involved in many aged-related diseases, such as Parkinson's, Alzheimer's, and Huntington's diseases, and animal models of atherosclerosis.[5-9]

In many disease states, oxidative and/or inflammatory stress has a crucial role. Degenerative and immunological disorders, including atherosclerosis, inflammatory bowel disease, diabetes, rheumatoid arthritis, HIV/AIDS, neurological disorders, sepsis, and many others, affect more than 45 million people worldwide. Though these diseases appear to be very different, the Nrf2 pathway plays an important role in many of them.

Nrf2 is able to prevent disease by suppressing oxidative stress, so interventions that activate Nrf2 would promote longevity, healthy aging and lower cancer incidence. Recent medical research has shown that Nrf2-activating strategies - which can include drugs, foods, dietary supplements, and exercise - can prevent a wide variety of diseases.[10]

Activation of Nrf2 can protect against acute insults to the lung, kidney, brain, liver, eye and heart that are caused by diverse factors including chemical toxins. Nrf2 activation can help to prevent chronic diseases such as diabetes and obesity, and several neurodegenerative diseases. Nrf2 activity improves atherosclerosis, liver inflammation, and fibrosis associated with obesity in a mouse model. It also is known to be important in rheumatoid arthritis. Oxidative stress is significantly involved in cartilage degradation in arthritis; and the presence of a functional Nrf2 gene is essential for maintaining and rebuilding new cartilage.

In summary, the activation of the Nrf2 pathway has been widely accepted as a promising anti-inflammatory treatment for many diseases including cancer.

Conclusion

Our study demonstrated that high dose vitamin C can protect against inflammation in subjects with metabolic syndrome. Our results suggest that the activation of transcription factor Nrf2 by IVC treatment can induce protection against age-related degenerative diseases and cancer.

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