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### **Hypertension, Insulin Resistance, Oxidative Stress: What Can I Do?**

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In recent Your Life Your Health articles we have discussed hypertension, oxidative stress and insulin resistance. Quickly, let's review:

1. Many people are at risk for high blood pressure (hypertension) because of abnormalities in the cells which line their arteries. Those cells are called endothelium and that abnormality is called "endothelium dysfunction."
2. Oxidative stress is the result of many harmful substances affecting the body such as the products of fat cells, tobacco smoke, diabetes, trans fats in the diet, elevated cholesterol, inactivity and many other environmental conditions and destructive behaviors. Oxidative stress causes endothelial dysfunction.
3. Insulin resistance is the condition where your liver, muscles and other parts of your body do not respond properly to insulin. The normal response to insulin is the movement of glucose (sugar) from the blood into muscle cells and the decrease of glucose production by the liver. When the response to insulin is not normal, the body makes more insulin, resulting in elevated insulin levels called "hyperinsulinism."
4. Insulin resistance and hyperinsulinism forces the beta cells in the pancreas – these are the cells which produce insulin – to work overtime. When the beta cells are overworked they become fatigued, at which time a condition called pre-diabetes will develop. When the beta cells are exhausted – unable to produce enough insulin – diabetes type 2 results.

We already know that exercise, losing weight and stopping smoking will improve oxidative stress and insulin resistance. And, it is possible to measure oxidative stress with blood tests. The tests are not inexpensive and they are not paid for by insurance. Also, it is possible to measure insulin resistance by using a formula which SETMA has built into its computer system called HOMA-IR. As the insulin resistance improves, a change in the results from this formula demonstrates that improvement.

Now, to the point of all of this. The question is, and it has not been totally answered definitively, does insulin resistance cause hypertension and will treatment of insulin resistance improve blood pressure? There have been many efforts to answer this question. We will examine one of them.

A paper entitled "Prevention of Hypertension Insulin Resistance and Oxidative Stress by Alpha-Lipoic Acid," was published in the journal *Hypertension* in 2002. The aim of the study was to investigate whether a dietary supplementation of alpha lipoic acid could prevent:

- blood pressure elevation,

- insulin resistance, and
- the increase in aorta superoxide anion production (one of the measures of oxidative stress)

The investigators fed sugar water to rats. Now, before there are any jokes about which class or category of humans would correlate with the rats, remember, this is exactly what we do to our children and to ourselves. When our children are hungry after school we feed them sugar water in the form of non-nutrient beverages such as cokes and other sugar-filled drinks, which have no nutrient value. Would it alarm you to know that drinking one coke a day will double your risk of developing diabetes? It should. Would it alarm you if you knew that one coke has a higher glycemic load – the measure of the effect a food has on your blood sugar level and on your insulin production – than an entire meal should have? It should.

In this experiment, the rats, like humans who drink “sugar water” by whatever name, had increases in their blood pressure, insulin resistance and in oxidative stress. There were positive relationships between the occurrences of:

- Oxidative stress and increase in blood pressure
- Insulin resistance and increase in blood pressure
- Insulin resistance and oxidative stress

These findings demonstrate that high-glucose feeding rapidly caused hypertension and insulin resistance, both of which were associated with oxidative stress.

This study showed that alpha lipoic acid – a natural occurring substance in your body and an important supplement which we recommend to our patients -- added to the feed of one group of rats, had an antihypertensive action and also prevented insulin resistance. This appears to be associated with alpha lipoic acid’s antioxidative properties because it prevented the increase in oxidative stress.

Lipoic acid supplementation in the diet had the following effects on rats with chronic glucose feeding:

- The insulin levels were lowered slightly
- The blood glucose was significantly decreased
- The development of insulin resistance was prevented by the alpha lipoic acid.

### **Diabetes, Hypertension and Heart Disease**

Diabetes is recognized as an important cardiovascular risk factor. In fact, diabetes is called a cardiovascular risk equivalent because it contributes as great a risk of heart disease as does high blood pressure, high cholesterol and smoking. Many people will feel relief in that they do not have diabetes. Is that sense of security well founded? Probably not, particularly when you know that a sedentary life style – an inactive

lifestyle, a lifestyle without exercise, a life style where you do not take 10,000 steps a day – is a greater risk factor for the development of congestive heart failure than is diabetes.

The association of diabetes and hypertension increases the degree of cardiovascular risk, so recent therapeutic guidelines recommend to lower blood pressure of hypertensive diabetic patients to levels below those recommended for other hypertensive patients.

Indeed, the Hypertension Optimal Treatment Study revealed that lowering diastolic blood pressure in patients with diabetes to 80 mm Hg decreases the risk of major cardiovascular events and cardiovascular mortality compared with lowering the diastolic blood pressure to 90 mm Hg, as recommended for nondiabetic hypertensive patients.

### **The enhanced risks of cardiovascular disease associated with diabetes may be due to an increase in oxidative stress**

Without getting too technical, this increase in oxidative stress can come from two sources:

1. Excessive production of reactive oxygen species, the highly reactive substances which are harmful to the body
2. Reduced antioxidant reserve.

The reality is that normal bodily functions always produce these reactive oxygen species. In fact, they have a positive function in the body when they are kept in balance. They become harmful when they are made in abundance due to illness, pollution, obesity, inactivity, smoking, etc. And, they become harmful when those reactive oxygen species which are made during normal body metabolism are not inactivated by a system of reactions involving anti-oxidants – naturally occurring substances which are used by the body to disarm the toxic reactive oxygen species.

### **Alpha Lipoic acid is one of the substances which is used by the body to combat oxidative stress**

Many experiments have suggested that increased reactive oxygen species production may be involved in the development and complications of diabetes and hypertension. And treatment with alpha lipoic acid has been reported to lower blood pressure in spontaneously hypertensive rats. In type 2 diabetics, alpha lipoic acid treatment has been found to improve insulin sensitivity.

### **Blood Pressure and Body Weight**

In this experiment, the chronic administration of glucose in drinking water resulted in a progressive increase in systolic arterial pressure, which reached an average of 166 mm Hg after 3 weeks. The supplementation with alpha lipoic acid prevented the rise in

systolic blood pressure. The final body weights between the treated and the non-treated rats were similar.

### **Plasma Glucose and Insulin Concentrations**

The effects of chronic glucose feeding and alpha lipoic acid supplemented diet on plasma glucose and insulin levels showed that the plasma insulin levels were improved. More impressive was the improvement in the plasma glucose levels in the alpha lipoic acid treated rats. Finally, the development of insulin resistance, as reflected by a higher HOMA-IR was prevented by the alpha lipoic acid diet in the glucose-fed rats.

### **Antioxidant Reserve**

The antioxidant reserve is a measure of the activity of glutathione in the body. Glutathione is the most important body defense against oxidative stress. Unfortunately, humans can't take glutathione supplements because humans cannot absorb them. However, humans can increase their glutathione levels by taking substances which are used by the body to produce glutathione. (For more information on glutathione see Your Life Your Health at [www.jameslholly.com](http://www.jameslholly.com))

In the article which we are presently reviewing the chronic administration of glucose induced a significant decrease of 16% in the activity of glutathione in plasma. Alpha lipoic acid supplement to the diet prevented the decrease in glutathione in the glucose-treated rats.

### **The major findings of the present study are as follows:**

- chronic glucose feeding for 3 weeks resulted in diabetes as reflected by an increase in both blood glucose and insulin levels
- chronic administration of glucose was associated with a progressive increase in systolic arterial pressure, with an increase in oxidative stress and with a decrease antioxidant defense against oxidative stress.
- supplementation with alpha lipoic acid in the diet of chronically glucose-fed rats prevented the rise in blood pressure, the increase in oxidative stress and the decrease in antioxidant defense against oxidative stress.
- significant correlations were found between the level of blood pressure and the degree of oxidative stress and insulin resistance.

### **Conclusion**

There is instruction for us in this experiment:

1. Feeding yourself or your children with glucose will harm health. This is done by excessive feeding with high glycemic foods and/or beverages.

2. Antioxidants are important to your health. Most of these should be obtained in a diet balanced with fruits and vegetables, but they can be obtained through some nutritional supplements.
3. If you have high blood pressure, take your medicine, lose weight, decrease the glycemic index and the glycemic load of the food you eat and increase your activity.
4. While this experiment does not prove that taking lipoic acid will improve blood pressure, oxidative stress, insulin resistance and health in humans, it is highly suggestive. Taking R-Lipoic Acid 100 mg twice a day will benefit your health. And, if you have diabetes, and particularly if you have diabetic neuropathy – numbness or pain in the feet – taking a larger dose can be beneficial to your health.

Remember, it is your life and it is your health.