KIDNEY FAILURE AND DIALYSIS

The kidney (renal) system controls the crucial urinary function of the body. It is responsible for filtering the blood and disposing of waste products, toxins and excess fluid in the form of urine. It also maintains water balance and regulates various chemical levels and blood pressure. If the kidneys cannot do their job, waste products and toxins accumulate in the blood. This affects other organ systems, often producing neurological symptoms and circulatory problems. Any sort of acute (sudden) or chronic (gradual/prolonged) illnesses can interfere with kidney function and lead to long-term disease. Kidney disease may shorten life expectancy.

Acute kidney failure can be triggered by all sorts of conditions. For example, a massive hemorrhage, heart attack or overwhelming infection (sepsis) can severely and suddenly restrict blood flow, quickly injuring the sensitive kidney tissues. The most common medical conditions leading to chronic renal failure are hardening of the arteries (atherosclerosis), high blood pressure and diabetes. These long-term diseases damage the circulation involved with the kidneys. Serious damage is also caused by organic and inorganic toxins, such as poisonous mushrooms, solvents, wood alcohol, antifreeze and heavy metals, either inhaled or ingested. There are many other causes of kidney failure, including chronic toxic exposure, inherited kidney diseases, vascular diseases and autoimmune disease.

Because kidney disease and renal failure are often triggered by other disorders it is important to identify the initial or potential cause. Diabetics must carefully control their sugar levels. Hypertensive patients must keep blood pressure down and all of us need to eliminate ongoing exposure to toxins. Some drugs can help manage chemical imbalances, circulatory problems and accumulation of waste products. Proper nutrition and dietary management are particularly important, and reduced protein intake is often advised in cases of renal failure.

If these measures do not sufficiently limit renal failure, a kidney transplant may be necessary. A less traumatic but very intrusive alternative is dialysis – the use of artificial devices to perform the kidney's functions. Two types of dialysis are commonly used today – hemodialysis and peritoneal dialysis.

Like chemical and radiation therapy for cancer patients, these procedures are life-saving but exact a heavy toll on the body's antioxidant defenses.

HEMODIALYSIS

In hemodialysis, blood is shunted out of the body to a mechanical filtering device, cleansed, chemically balanced, and shunted back into the person's circulatory system. The procedure is repeated several times a week. Each session takes several hours, during which the patient is physically attached to the machine.

PERITONEAL DIALYSIS

Peritoneal dialysis cleans blood without removing it from the body by using the peritoneal membrane (inner lining of the abdomen) as a filter. This membrane has many of the characteristics of the kidney's filtering system. Once a plastic tube has been implanted in the abdominal wall, patients usually carry out the procedure for themselves. A special dialysis solution (dialysate) is passed through the tube and into the abdomen. Waste material from the blood filters through the small vessels of the peritoneal membrane and is trapped by the fluid. After a few hours, the dialysate is drained and discarded. This procedure may be repeated several times a day.

GSH AND RENAL FAILURE

One cause of renal toxicity and kidney failure is exposure to heavy metals such as mercury, cadmium and lead. The body detoxifies these substances principally through GSH-related enzymes. Glutathione molecules bind themselves to these metals by the process of chelation, after which they are easily and safely removed from the body. The cells of the kidney are protected by high levels of GSH. In treatment for severe mercury toxicity, tests in laboratory trials and with kidney patients show that adding NAC (a GSH-enhancing drug) to the dialysate helps chelate inorganic mercury and remove it from the solution.

Acute renal failure occurs most commonly when the kidneys suffer inadequate blood flow (ischemia). Laboratory studies at the University of Texas and elsewhere have shown that damage suffered during ischemic renal failure is lessened by the infusion of NAC. This appears to result from an improved supply of antioxidants to the tissue, the detoxification of noxious metabolites like nitric oxide, or both.

Many pharmaceutical drugs have been implicated in kidney failure. Such common medications as ibuprofen, acetaminophen and even vitamin D put a high demand on the kidneys, and can damage them. Many of the anti-cancer agents used in chemotherapy do the same. Cyclosporin – an immuno-suppressant used after organ transplantation and in certain kidney diseases such as the nephrotic syndrome – can also damage the kidneys. Research indicates that elevated antioxidant defenses help protect the body from cyclosporin toxicity.

A rarer cause of kidney failure is polycystic kidney disease – the growth of cysts within the kidneys, eventually impairing their function. Experiments were carried out to artificially lower GSH levels with the drug BSO. This led to worsening of the disease and suggests that the presence of GSH plays a protective role.

The most common cause of poor blood flow is atherosclerosis – the build-up of plaque and other blockages in blood vessels. While GSH detoxifies pharmaceutical drugs and heavy metals, and fights such threats as polycystic kidney disease, it also fights plaque formation by inhibiting lipid peroxidation.

GSH AND DIALYSIS

Renal failure patients suffer from a profound imbalance of oxidants and antioxidants that grows worse as the kidney fails – and dialysis only compounds the problem. In spite of their life-saving action, peritoneal dialysis and especially hemodialysis worsen this aspect of kidney malfunction by increasing oxidative stress levels. Because dialysis is not optional for these patients, its side-effects must be addressed.

Some researchers think that dialysis damages the anti-oxidant system and leads to a dramatic fall in levels of the GSH enzymes that protect us from lipid peroxidation. The result is long-term complications such as accelerated atherosclerosis. In fact, cardiovascular disease is the major cause of morbidity and mortality in patients with end-stage renal failure. There is plenty of evidence to show that antioxidant support might benefit these patients. A strong link between kidney function and glutathione availability has been identified. This has led some scientists to suggest that glutathione peroxidase levels may prove to be a yardstick of kidney function.

To test this hypothesis, elderly patients undergoing continuous peritoneal dialysis were studied to determine two things – nutritional status and oxidative stress levels. The former was measured by their ability to absorb and process certain nutrients, especially serum albumin and iron. Test results were well below normal. As for antioxidant defenses, glutathione peroxidase levels were even lower. It is clear that the ability of kidney patients to fight oxidation is profoundly and progressively compromised. Oxidative stress left unchallenged leads to untold damage.

To get a clearer picture of the process, the cells of the peritoneal membrane of peritoneal dialysis patients were examined. Researchers found that when the patients were exposed to the life-saving dialysate fluid, GSH levels fell significantly. To counteract this decline, OTZ (a pharmaceutical precursor of GSH) was added to the dialysate fluid. This helped restore GSH to protective levels in these tissues.

The link between GSH status and oxidative stress in dialysis patients is not only widely accepted, it is also considered highly significant. In patients with renal failure oxidative stress damages the circulating red blood cells (erythrocytes) causing low hemoglobin levels (anemia). This damage is normally kept to a minimum by glutathione – the principal antioxidant in this struggle. GSH acts on the surface of the wall of the red blood cell to preserve its integrity. Since hemodialysis causes significant oxidative changes and damages red blood cells, it is important that patients undergoing this procedure maintain high GSH levels. Drugs like NAC and OTZ effectively raise glutathione levels and improve the ability of patients to fight oxidative stress, but there are also safer, dietary ways to raise GSH levels.

Many dialysis patients are treated for their anemia (shortage of red blood cells) with erythropoietin. This drug is intended to stimulate the production of red blood cells, but provides an additional benefit. It turns out that younger cells have higher levels of GSH and are thus more resistant to lipid peroxidation and cell-wall breakdown. Studies have shown that antioxidants given to patients on erythropoietin may enhance the effectiveness

of the drug, making it possible to lower dosage. This was demonstrated by giving patients intravenous GSH during dialysis sessions.

Another important study of hemodialysis patients was conducted by C. Costagliola's team in Italy. In this double-blind study some patients were given intravenous GSH while others received placebo. To test for anemia, doctors measured red blood cell, hemoglobin and hematocrit levels – all known to fall in dialysis patients. Those receiving GSH maintained higher levels than those on placebo. Their levels of oxidative stress also fell. Similar but separate Italian studies led by M. Usberti also resulted in lower levels of anemia. These findings show that elevated GSH levels help manage the anemia to which dialysis patients are particularly prone.

CASE STUDY

Since poor antioxidant and detoxification defenses are implicated in kidney disease and the complications of dialysis, there is reason to believe that GSH supplementation may help individuals like George, a 62-year-old former country and western singer.

George had struggled with diabetes for over thirty years. Following only moderate success controlling his sugar levels, he developed progressive kidney failure and subsequent anemia. In a few short years he went from an active, gregarious entertainer to a listless, sofa-ridden recluse. His energy level and concentration deteriorated more and more and the local hospital clinic inn Hawaii where he lived was obliged to monitor his condition closely. His levels of biliary urea nitrogen (BUN) and creatinine crept higher and higher – signs of diminishing kidney function – and his red blood cell (hemoglobin) value continued to fall. His physician placed him on a waiting list to undergo preparation for dialysis.

After hearing about GSH, George started taking 20 grams per day of a whey protein isolate high in GSH precursors. Within three weeks his BUN and creatinine levels started to fall – a sign of improving kidney function. After a further three weeks his hemoglobin climbed by one full gram per deciliter (g/dL) of blood and he was again singing at his friends' parties. His wife was uncomfortable about his exposure to alcohol and cigarettes but three months later his renal function tests and hemoglobin levels had improved so much his physician put plans for dialysis on hold.

PROTEIN INTAKE AND RENAL FAILURE

Diseased kidneys already have trouble clearing away breakdown products, many of which come from the digestion of dietary protein. Large quantities of protein leave high levels of urea-nitrogen in the blood, a condition called uremia that leads to further health problems. Therefore, protein intake is restricted and carefully monitored. Renal failure patients are encouraged to eat plenty of carbohydrates, but protein is an important nutrient and cannot be avoided. Since kidney failure patients often can consume it only in limited quantities, its quality is of great importance.

A measure of food protein quality is biological value (BV). It rates the usefulness and quantity of biochemicals made available to the body by a particular food protein. BV

especially reflects the proportion of essential to non-essential amino acids. We must have a continuous supply of essential amino acids in our diet. We need non-essential amino acids too, but don't necessarily have to eat them – our body can manufacture them fro the essential ones. For dialysis patients, proteins rich in essential amino acids are preferable because of their higher biological value. Some patients undergoing dialysis become protein deficient (hypoalbuminemic). For them, the quality of dietary protein is even more important.

The natural protein with the highest biological value is whey protein, which is ideal for kidney patients. Also, the amino acids found in some whey proteins are GSH precursors (building blocks). Their presence depends principally on how the whey protein is prepared and stored.

CONCLUSION

GSH plays important roles in the prevention and treatment of renal failure, the anemia that often accompanies kidney failure and dialysis, and the cardiovascular complications of kidney disease. The use of GSH-modifying agents is a promising treatment for both short and long-term complications of kidney failure. GSH acts simultaneously as a detoxifier and as an antioxidant, preventing lipid peroxidation. Because some whey proteins contain additional nutritional benefits and act as glutathione precursors, they are a useful compliment to traditional therapy.

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