Natural Medicine and Kidney Disease

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Nephrotic Syndrome Family Wellness Day

NephCure Kidney International

Disclosure

- Dr. Henderson is a naturopathic doctor licensed in the state of CT.
- Botanical medicine is in the scope of practice for naturopathic doctors.
- I have been an FSGS patient since 1993.
- Names of referenced studies are in green and available on PubMed. PubMed index numbers listed.
- I have no financial interest in any of the items discussed in this presentation.

Topic for today:

Focus on the treatment goal of reducing proteinuria/kidney inflammation in glomerular disease.

What natural substances show evidence of improving glomerular disease.

- Not covering how to improve kidney filtration, although many items that improve proteinuria do support kidney filtration.
- Not how to support a patient on dialysis.
- Not how to support a patient with a kidney transplant. Always assume an herb is contraindicated post-transplant until proven otherwise.
- No specific patient recommendations today, just awareness of research in field.

Perception of what is good for the kidneys vs. reality of what is beneficial

- Kidney herbs usually geared toward UTI or kidney stones, not helping nephrotic syndrome. No known benefit to cranberry for nephrotic syndrome.
- “Kidney cleanses” are a popular catch-all for kidney disease that don’t do anything for proteinuria.
- Herbs that may actually help nephrotic syndrome are often not well known, and if they are known may be commonly associated with something other than kidney function.

Herbal diuretics-- do the kidneys really need to be cleansed?

- Often sold in health food stores often as detox teas. These include uva ursi, juniper, buchu, goldenrod, dandelion, parsley.
- Diuretics push the kidneys to work harder. They don't "build the kidneys" or do anything to protect kidney tissue from the damage of chronic kidney disease.
- Usually these herbs are high in potassium, which can be dangerous with advanced kidney disease.

What actually impacts the course of nephrotic syndrome?

- Medicinal mushrooms
- The role of sleep/ melatonin in kidney health
- The role of thyroid health
- Individual herbs that show promise with reducing proteinuria
- Use of enzymes as anti-inflammatory agent

What is the source in nature of the compounds in many prescription medications used to treat glomerular disease?

- Many of these medications use to treat kidney disease like Cyclosporine and Mycophenolate, actually originally came from mushrooms.
- There is a long history of use of medicinal mushrooms in Asia for kidney ailments.
- The Cordyceps mushroom and reishi mushrooms have been studied for use with kidney disease.
- New information on the mushroom Antrodia camphorata.

Cordyceps mushroom

- Very long history of use in Traditional Chinese Medicine for kidney disease.
- Source in nature of the prescription medication Cyclosporine, which was a breakthrough medication.
- In an animal model shows less fibrosis and sclerosis of the kidney.
- Improvements in serum creatinine and BUN
- Reduced proteinuria

[Effect of Cordyceps sinensis powder on renal oxidative stress and mitochondria functions in 5/6 nephrectomized rats]. PMID 26043568

Cordyceps mushrooms has been researched to help:

- IgA nephropathy
- Membranous glomerulonephritis
- Diabetic nephropathy
- Lupus nephritis
- Kidney transplant health

Reishi mushroom (Ganoderma lucidum) studied with FSGS

- All FSGS patients taking reishi mushrooms in this study experienced a significant reduction in proteinuria.
- Efficacy of reishi attributed to both immune modulation and effect on endothelial tissue (lining of the membrane). Reishi makes the kidney less permeable, to help proteinuria and helps stop erosion of outer membrane of the nephron (the podocyte).
- Ganoderma lucidum suppresses endothelial cell cytotoxicity and proteinuria in persistent proteinuric focal segmental glomerulosclerosis (FSGS) nephrosis. PMID: 15567896

Further study of reishi mushrooms

- Unique compounds, Lingzhiols, isolated from reishi mushrooms, inhibit the phosphorylation in rat renal proximal tubular cells and decrease inflammation in mesangium of the glomerulus. Lingzhiols, unprecedented rotary door-shaped meroterpenoids as potent and selective inhibitors of p-Smad3 from Ganoderma lucidum. PMID: 24128039
- Varying components of reishi mushrooms may have different roles in modifying the immune response. Reishi mushrooms inhibited oxidative damage and apoptosis (cell death) in cultured kidney cells. Ganoderma extract prevents albumin-induced oxidative damage and chemokines synthesis in cultured human proximal tubular epithelial cells.

  PMID: 16434408

Antroquinonol, an extract from the mushroom Antrodia camphorata

- Unique mushroom that grows on camphor tree in Taiwan
- Shows promise to treat FSGS in an animal model
- Reduced proteinuria, podocyte injury, kidney inflammation and fibrosis.

- Antroquinonol reduces oxidative stress by enhancing the Nrf2 signaling pathway and inhibits inflammation and sclerosis in focal segmental glomerulosclerosis mice.
- PMID: 21376112

Kidney disease connection to insomnia

- Kidney patients tend to be “night owls” and have irregular or late sleep cycle.
- Connection with insomnia noted in Traditional Chinese Medicine (TCM)
- Large population study found those who sleep less than 5 hours are more likely to develop proteinuria.
- Self-reported sleep duration and prediction of proteinuria: a retrospective cohort study. PMID 22019276

Kidney patients may have low levels of the sleep hormone melatonin

- Melatonin is a peptide hormone made from albumin.
- Albumin is the protein leaking out in the urine.
- Melatonin peaks between 10 p.m. and 12 midnight. Difficult to test blood levels but often inferred with sleep trouble.
- We make less melatonin with age.

Why is sleep so important to the kidneys?

- The kidneys are built to respond to the sleep hormone.
- Melatonin receptors are found in many different organs of the body including the kidneys, suggesting the sleep is restorative on many levels.
- A Review of Melatonin, Its Receptors and Drugs
- PMID: 27551178

Use of melatonin improved proteinuria in animal model

- Effects of melatonin attributed to anti-oxidant properties and immune modulation.
- Melatonin ameliorates oxidative stress, inflammation, proteinuria, and progression of renal damage in rats with renal mass reduction. PMID: 18077597
- Melatonin has been characterized as an immune stimulant but also helps reduce inflammation/ help autoimmune conditions.
- Melatonin: Buffering the Immune System PMID: 23609496

Why do kidney patients feels so cold?

- Chronically low body temperature is common with nephrotic syndrome.
- Traditional Chinese Medicine (TCM) characterizes nephrotic syndrome as internal cold and dampness.
- Dysfunction of the thyroid is often observed with nephrotic syndrome.
- Particularly important to address in growing children, as the thyroid is involved with growth and development.

Changes in thyroid status with kidney patients is well established.

- Changes in the Thyroid Hormone Profiles in Children with Nephrotic Syndrome.
  https://www.ncbi.nlm.nih.gov/pubmed/30304897

- Auto-immune Thyroiditis in an Infant Masquerading as Congenital Nephrotic Syndrome. https://www.ncbi.nlm.nih.gov/pubmed/30128632

- Nephrotic Syndrome Increases the Need for Levothyroxine Replacement in Patients with Hypothyroidism.
  https://www.ncbi.nlm.nih.gov/pubmed/28208903

- Hypothyroidism and Nephrotic Syndrome: Why, When and How to Treat.
  https://www.ncbi.nlm.nih.gov/pubmed/28176633

Why does nephrotic syndrome effect the level of thyroid hormones?

- Active thyroid hormones may be lost in the urine along with albumin.
- Thyroid hormone is made from albumin, the protein leaking out.
- Low T3 and or T4 is common. A test that only looks at TSH does not include fT3 (free T3) and fT4 (free T4).

Benefit of addressing a low thyroid with nephrotic syndrome.

- Kidney disease can effect the thyroid, but the thyroid may also effect the kidney.
- In this study, thyroid replacement in nephrotic syndrome patients with low thyroid hormones, helped bring about remission from nephrotic syndrome.
- Thyroid hormone replacement for nephrotic syndrome patients with euthyroid sick syndrome: a meta-analysis. PMID: 25154407

Treatment for nephrotic syndrome

- Usually starts with prednisone
- An ACE inhibitor (blood pressure medication) is often used
- Stronger immune suppressants, many of which started as transplant therapy, are often used.
- Goal is to reduce proteinuria and prevent scarring of the kidney (permanent damage).

There are 2 main branches of the immune system. Autoimmune conditions are usually associated with a dominance of 1 type of immunity.

Cell-mediated immunity

- Minimal Change
- FSGS

Antibody immunity

- IgA nephropathy
- Membranous glomerulonephritis
- Membranoproliferative glomerulonephritis

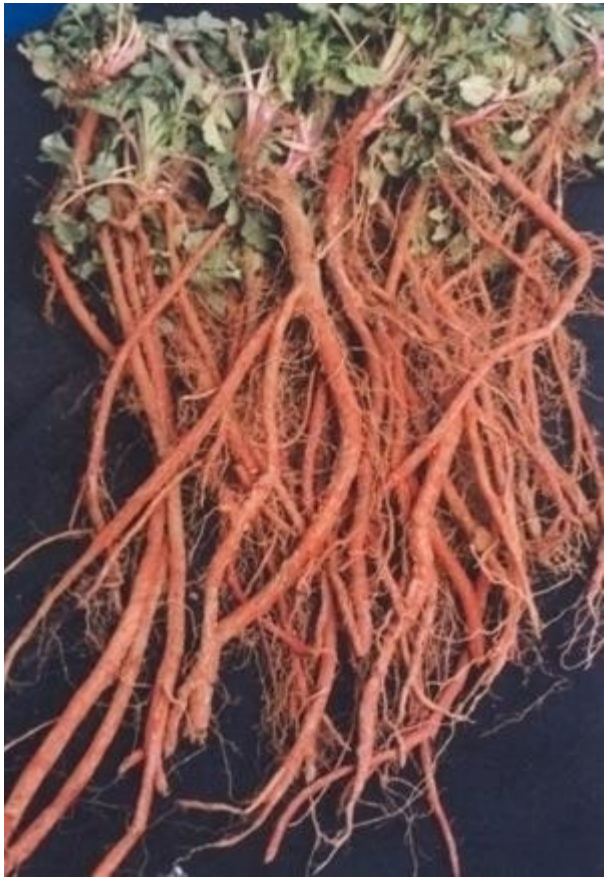
Immune suppressants lower interleukin 2 (Il-2) which turns on cell-mediated immunity.

- Interleukin 2 (Il-2) is a messenger that turns on cell-mediated immunity.
- Many natural agents also lower Il-2.

<u>The natural agents that lower Il-2 include:</u>

- Cordyceps mushroom
- Salvia miltiorrhiza
- Ginkgo Biloba
- Curcumin
- Garlic
- Rutin

Salvia miltiorrhiza



- Salvia Miltiorrhiza, also called Dan shen or Chinese red sage.
- Considered an herb for the heart in Traditional Chinese Medicine. Has been studied for cardiac support.
- Reduced proteinuria and creatinine in an animal model.
- Renoprotective effect of Tanshinone IIA, an active component of Salvia miltiorrhiza, on rats with chronic kidney disease.

  PMID 21043035

Ginkgo biloba for nephrotic syndrome

- Commonly used herb, very high in antioxidants.
- Well-studied for a wide variety of applications.
- Can be useful for the kidneys at all stages of kidney disease.
- Appears to help nephrotic syndrome through a variety of mechanisms.
- Blood thinner

Ginkgo biloba to reduce capillary permeability.

- The kidney is one of the most highly vascular areas of the body.
- The leaking of protein is associated with increased leaking of capillaries in the kidney.
- Ginkgo biloba reduced proteinuria by reducing capillary permeability. Effect comparable to steroids. Vascular hyperpermeability in nephrotic edema. PMID: 10867533

Ginkgo also appears to alter the immune response associated with nephrotic syndrome.

- Ginkgo reduces fibrosis of the kidney by inhibiting mTOR signaling.
- The prescription medication Rapamune is an immune suppressant that also inhibits mTOR.
- Ethanolic Ginkgo biloba leaf extract prevents renal fibrosis through Akt/mTOR signaling in diabetic nephropathy. PMID: 26547529

Ginkgo also helps the high cholesterol associated with nephrotic syndrome.

- When the kidneys spill protein, the liver responds by producing cholesterol.
- Reducing proteinuria will reduce the high cholesterol.
- A cholesterol lowering agent often used while proteinuria is being managed.
- Ginkgo can reduce this very high cholesterol. [Therapeutic effect of Ginkgo biloba leaf extract on hypercholestrolemia in children with nephrotic syndrome]. PMID: 17545089

Curcumin

- Animal model showed less sclerosis of the kidney.
- Curcumin reduced inflammatory compounds, IgG and complement activation.
- Curcumin alleviates immune-complex-mediated glomerulonephritis in factor-H-deficient mice. PMID: 23347386

Garlic

- In an animal study of nephrotic syndrome, garlic did not reduce proteinuria or the number of glomeruli damaged, but the area of glomerulus damaged was smaller.
- Garlic also helped with cholesterol. Garlic ameliorates hyperlipidemia in chronic aminonucleoside nephrosis. PMID: 11055549

Rutin

- Bioflavonoid (co-factor of vitamin C) found in foods– buckwheat, apple (skins), figs and rooibos tea.
- Chemically similar to quercetin, a well-known antioxidant/ anti-inflammatory agent.
- Rutin may reduce creatinine, BUN and proteinuria. Also helps reduce sclerosis and tubular injuries to the kidney.
- Rutin ameliorates renal fibrosis and proteinuria in 5/6-nephrectomized rats by anti-oxidation and inhibiting activation of TGFβ1-smad signaling.

  PMID 26191162

Rehmannia glutinosa

Rehmannia glutinosa has a long history of use in China. Considered one of the 50 fundamental herbs in Traditional Chinese Medicine.

Rehmannia reduced proteinuria in an animal model. Reduced fibrosis and sclerosis noted. It also helped serum creatinine and blood pressure.

Rehmannia glutinosa ameliorates the progressive renal failure induced by 5/6 nephrectomy.

PMID 19146934

Brazilian red propolis

Brazilian red propolis is a specific bee product. In an animal model Brazilian red propolis showed significant reduction of:

- hypertension
- proteinuria
- serum creatinine
- glomerulosclerosis
- renal macrophage infiltration
- oxidative stress.

Brazilian red propolis attenuates hypertension and renal damage in 5/6 renal ablation model.

PMID 25607548

The herb Polygoni Multiflori, more commonly known as Fo-Ti, was found to be useful against FSGS in an animal model.

- Traditional herb of longevity in China, most often used for alopecia in the West.
- Extract of this herb suppressed proteinuria, protected against podocyte damage, reduced renal fibrotic gene expressions, and alleviated the severity of glomerulosclerosis.
- The natural compound 2,3,5,4'-tetrahydroxystilbene-2-O-β-d glucoside protects against adriamycin-induced nephropathy through activating the Nrf2-Keap1 antioxidant pathway. PMID: 29064158

Enzymes as anti-inflammatory agent

- Use of bromelain, an enzyme in capsule form, derived from pineapple, popular anti-inflammatory agent in natural medicine.
- Wobenzyme, a specific enzyme product, studied found to inhibit sclerosis of the kidney.
- [Fibronectin content in the urine of patients with chronic glomerulonephritis as a test for the efficiency of treatment]. PMID: 11393035

Conclusion

- Use of natural agents for nephrotic syndrome is an emerging area of research.
- Many natural agents show promise in reducing kidney inflammation and proteinuria
- Potential to slow sclerosis of the kidney and disease progression.