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Introduction

The functional tissue of the kidneys is delicate and can be damaged not only by disease, but also by drugs, especially anti-cancer chemotherapy (notoriously the platinum compounds) as well as some immunosuppressant and antibiotic agents. Some herbal ingredients are also documented as nephrotoxic.

Medically, laboratory values of creatinine in a blood sample are used to check kidney function; supranormal creatinine values reflect impaired kidney function due to damage to the renal tissue. Short term, recovery of levels can occur if the cause is rapidly rectified, but persistently elevated creatinine is considered indicative of lasting mechanical damage and does not usually return the previous normal range.

Stinging nettle *seed* is not at all known outside the herbalist community. Trained herbalists regularly work with hundreds of herbal remedies, the majority of which lack mainstream scientific or clinical data. Restoration of kidney function due to mechanical damage is traditionally not considered possible, either by either conventional or herbal medicine. The following case reports show normalization of elevated creatine levels using nettle seed as the primary herbal remedy.

Employing beneficial herb-drug interactions is a consistent theme of my practice that is well illustrated by incorporating nettle seed into renal-protective protocols for cancer patients undergoing chemotherapy with platinum drugs. Monitoring creatinine before during and after platinum chemotherapy has consistently demonstrated the value of this approach, often to the surprise of the oncologists involved.

Urtica semen reduces serum creatinine levels.

Introduction

Urtica dioica L. and *Urtica urens* L., (stinging nettles) have a long history of use in folkloric and science based herbal medicine. Traditionally used as a nutritive and "blood cleanser" or alterative agent, a substantial pharmacological and clinical literature supports its use for arthritic and allergic conditions (leaf/herb) and improving urological symptoms of benign prostatic hyperplasia (root). The available literature is based on either the aerial parts (folia/herba), or the root (radix). The root is monographed by WHO, ESCOP and Commission E, and the herb/leaf is monographed

by ESCOP and Commission E.1-4 However none of these, or other pharmacopoeial sources identify the seed (semen) as a medicinally distinct plant part.

The literature on constituents or pharmacology of nettle seeds is sparse. An HPLC analysis of the lipid fraction indicates the presence of a high proportion of unsaturated fatty acids, especially palmitic, and a small amount of omega-3 unsaturated fatty acids.⁵ Of interest is the presence of a lectin in the seeds of *U. pilulifera*, a Turkish stinging nettle.⁶ A lectin from the roots of *U. dioica* known as *Urtica dioica* agglutinin (UDA) is known as a novel T-Cell mitogen with superantigenic properties.⁷ UDA has an unique pattern of T-cell activation and cytokine induction which has led to its use as a probe in investigations of superantigen activity.⁸

Whether the seeds of *U. dioica* also contain a lectin with UDA superantigenic properties is unknown due to the absence of research.

The clinical use of nettle seed extracts for treatment of renal dysfunction represents a novel indication for the herb, first suggested by North American herbalist David Winston and to date unsupported by published reports.⁹ The following two cases involve the use of nettle seed extracts in patients with serious renal challenges, and utilize serum creatinine laboratory values data to serially monitor the effects of the extract.

Serum Creatinine

Serum creatinine is commonly measured as an index of glomerular function. Broadly speaking serum creatinine varies inversely with the glomerular filtration rate (GFR), other things being equal. A number of non-renal factors may affect creatinine levels, ranging from heavy dietary meat ingestion, medications including glucocorticoids and cimetidine, and muscle mass decrease in chronic illness. There is also a small but variable degree of proximal tubule secretion of creatinine, which declines as GFR decreases and which may confound interpretations of creatinine values. In cases where renal function and GFR require more accurate evaluation, inulin, or radionuclide labelled molecules such as ¹²⁵I-iothalamate are used. Nonetheless, creatinine remains a simple single measure test of nephron function. Units of measurement vary in laboratory reports, upper limits for of normal serum concentration in men are 1.2mg/dL (conventional units), or 110 micromol/L (SI units). Values for women are ~85% men's values.

Case one – Integrative Oncology Patient:

Status post nephrectomy.

A previously healthy 51 year old male, who had been diagnosed with aggressive leiomyosarcoma with liver metastases in 1994 at age 43. Following the diagnosis, he had debulking surgery including a radical right nephrectomy, right hepatectomy and adrenalectomy. Since that time he had been pursuing various treatment approaches for his cancer. He received radiofrequency ablation of hepatic lesions, assay driven chemotherapy, local hypothermia, and various immunotherapies, culminating in two stem cell transplants. He had successfully controlled his situation with these approaches for eight years, and initially consulted our practice because of his interest in botanical therapies for cancer.

It emerged that the patient's serum creatinine had been persistently elevated since his nephrectomy. Serum laboratory values were regularly monitored as part of his standing order blood work. Although there was a degree of variation in his "normal" readings, the values were always significantly above the accepted upper normal level of

The trial administration coincided with a sharp fall in serum creatinine, and but following the end of the trial period, there was a slight increase again. A second period of administration of nettle seed extract commenced on 12/23/02. Serum levels dropped again. The total period of administration of the extract was eight weeks, over two one month courses. Serum creatinine

values remained stable at a lower mean for several months following the second administration. (mean 120 micromol/L).

Case Two – Lupus patient – Status post renal graft.

A 24 year old female status renal allograft, presenting in 1998 with vaginal candidiasis, irritable bowel, multiple dermatopathies, dysglycemia, seasonal allergies, pruritis and CIN II cervical dysplasia. Following a history of three progressively severe episodes of lupus related uremia culminating in renal failure, she was recipient of renal allograft from maternal donor in 1995. Immunosuppression initially was maintained by prednisone, cyclosporine and azothioprine. Family history was notable for Raynaud's, SLE, diabetes and lung cancer. Over the first two years, the patient was treated successfully with numerous botanical prescriptions and supplements, leading to resolution of cervical dysplasia, candidiasis, allergies, digestive and skin issues. She was also prescribed a general renal protective protocol(Sig 5ml t.i.d. with Omega -3 Oils (Max EPA) 6gms q.d see Protocol 1) to ameliorate the nephrotoxic effects of cyclosporine. Serial laboratory tests included serum creatinine and BUN, and U/A with microscopy, together with serum cyclosporine levels.

Protocol One – Renal Protection Rx

Ginkgo biloba FE 30 ml

Silybum marianum FE 30 ml

Salvia multiorhizza 1:2 30 ml

Panax ginseng 1:3 10 ml

In 2000, her previously "high normal" creatinine level of 1.2mg/dL began a persistent climb culminating in a very rapid rise in May 2000 to peak at a level of 2.0mg/dL. Needle biopsy confirmed an acute graft rejection, and immunosuppression was intensified by the transplant physicians, including high dose prednisone pulse. A second biopsy revealed persistent mononucleocyte infiltration and tacrolimus (Prograf™) was added to the immunosuppressive regime, this time resulting in reversal of acute rejection, survival of the graft and a reduction of the elevated serum creatinine. After stabilization, immunosuppression was changed to prednisone, MMF (Cellcept™) and tacrolimus (Prograf™). The prednisone was tapered, during which time licorice root support for the withdrawal from steroids was added. Creatinine levels however remained consistently elevated at 1.6 mg/dL, and she was advised by the transplant team that this was her "new normal" level of renal function. Commencing September 12th, nettle seed extract, in combination with extract of couchgrass (*Agropyron repens*) rhizome (3:1 *Urtica:Agropyron*) was prescribed at a dose of 5 ml t.i.d. and the serum creatinine levels began to decline. The formula was replaced by nettle seed monotherapy on October 28th and administration continued for three month period. Creatinine levels renormalized at 1.2 mg/dL. (Chart 2)

Discussion

This two case series suggests a potential beneficial effect of nettle seed extracts on compromised glomerular function as measured by serum creatinine levels. Elevated serum creatinine levels only appear when significant glomerular function has been lost. In both cases a long-term reduction in previously sustained elevated levels was achieved that extended well beyond the period of administration of the extract. Two biopsies were performed on the renal graft patient that demonstrated significant histopathology, and the acute graft versus host rejection was reversed with immuno-suppressive drugs, not herbs. However in terms of herbal therapeutics there appear to be grounds for considering nettle seed as a possible functional renal "trophorestorative", since in both patients lower creatinine levels were regained in following administration of the herbal extract.

Herbal treatment of serious kidney conditions is controversial. The lack of remedies in the traditional materia medica to directly address loss of glomerular function has led some authors

to take a pessimistic view of the benefits of herbal treatment of renal dysfunction.¹⁰ Others, confronted by the clinical reality of patients with renal grafts, have taken a more considered view of the possibilities presented by botanicals for renal protection and support.¹¹ While caution is warranted in all cases of kidney disease, it is possible that nettle seed may fill a much needed gap in the materia medica of the genitourinary system as a renal trophorestorative. It would also appear that there is potential for integrative medical management of such cases. Given the high cost of dialysis, the use of *Urtica semen* extracts as a possible agent to restore glomerular function should be further investigated.

Postscript 2004

Both patients were impressed with the effects of the *Urtica semen*. Both continued to do well with apparently stable renal function unaided by continued herbal support. The nephrectomy patient recently experienced an increase in creatinine levels following major surgical procedure. The allograft patient continues to pursue an active career in performing arts in the Pacific Northwest.

Nettle seed extract

The extract of nettle seed used in the above case series was a standard tincture 1:5, 30% EtOH, supplied by Herbalist & Alchemist Inc. 51 S Wandling Avenue, Washington, NJ. 07882-3537.

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