

A low-cost salt substitute reduces blood pressure in high-risk individuals

Decreasing dietary salt intake is potentially a low-cost means of reducing the burden of blood-pressure-related disease. A recent paper reports on the blood pressure effects of using a salt substitute in rural Chinese individuals at high risk for vascular disease.

In a randomized double-blind trial, 608 individuals were provided with either normal salt (100% NaCl) or commercially available salt substitute (65% NaCl, 25% KCl, 10% MgSO₄) to cover all household uses. Over the 12-month follow-up period, systolic blood pressure (equivalent at baseline) was a mean of 3.7 mmHg lower in the salt-substitute group than in the normal-salt group ($P < 0.001$). The magnitude of this reduction seemed to increase with time ($P = 0.001$; maximal difference: 5.4 mmHg at 12 months). No differences in diastolic blood pressure were observed between the two groups at any time. First morning urine sodium concentrations were similar in the two groups at 6 and 12 months, but urine potassium concentrations were significantly higher in the salt-substitute group at both time points (by 6.8 mmol/l and 7.2 mmol/l, respectively). No incidences of severe hyperkalemia were recorded, and the rates of serious adverse events were similar in the two groups.

The study group concluded that salt substitution resulted in a sustained cost-effective clinically relevant reduction in systolic blood pressure. Salt substitution might be appropriate for high-risk individuals in developing countries, where the majority of dietary salt intake does not come from processed foods.

Original article The China Salt Substitute Study Collaborative Group (2007) Salt substitution: a low-cost strategy for blood pressure control among rural Chinese: a randomized, controlled trial. *J Hypertens* 25: 2011–2018

Restoring nightly blood pressure dip by altering timing of antihypertensive therapy in CKD

Individuals whose blood pressure does not drop by at least 10% at night ('nondippers') are at increased risk of cardiovascular morbidity and mortality. Nondipping status is common

among patients with chronic kidney disease (CKD) and is associated with an increased risk of end-stage renal disease. Minutolo *et al.* investigated whether altering the timing of administration of antihypertensive drugs can restore the normal circadian rhythm of blood pressure in CKD patients.

The study enrolled 32 outpatients with CKD who had an estimated glomerular filtration rate $< 90 \text{ ml/min/1.73 m}^2$, nondipper status (night:day ratio of mean ambulatory blood pressure [ABP] > 0.9) and a mean ABP of $< 135/85 \text{ mmHg}$. Patients' antihypertensive treatment regimens were modified by a shift in the dosing of one antihypertensive drug (not a diuretic) from the morning to the evening.

After 8 weeks of the modified treatment regimen, 28 of 32 patients (87.5%) had achieved dipping status. The average night:day ratio of ABP decreased significantly from baseline to 8 weeks after the drug shift (from 0.95 ± 0.04 to 0.87 ± 0.04 ; $P < 0.001$). Mean systolic and mean diastolic office blood pressures in the morning also dropped markedly over 8 weeks ($P = 0.02$ for both parameters). Mean urinary protein excretion decreased significantly from $271 \pm 284 \text{ mg/day}$ at baseline to $182 \pm 225 \text{ mg/day}$ 8 weeks after the drug shift ($P < 0.001$). The mean number of antihypertensive drugs taken per patient during the study was 2.4 ± 1.4 . No relationship was found between the number or type of drugs administered and the change in blood pressure following the drug shift.

Original article Minutolo R *et al.* (2007) Changing the timing of antihypertensive therapy to reduce nocturnal blood pressure in CKD: an 8-week uncontrolled trial. *Am J Kidney Dis* 50: 908–917

Coenzyme Q₁₀ deficiency with renal involvement: a newly characterized disorder

Primary coenzyme Q₁₀ (CoQ₁₀, or ubiquinone) is vital for mitochondrial energy production. Deficiency of this enzyme normally manifests as neurological and muscular symptoms. Diomedi-Camassei and colleagues describe the first four cases of primary CoQ₁₀ deficiency with renal involvement, linking the disorder to novel mutations of the COQ2 gene that encodes the para-hydroxybenzoate–polyprenyltransferase enzyme of the CoQ₁₀ synthesis pathway.

They propose that inherited mutations in *COQ2* cause a primary glomerular disease—“*COQ2* nephropathy”—characterized by renal lesions of varying severity and proliferation of dysmorphic mitochondria, but not necessarily neurological manifestations.

Patients were between 6 months and 2 years of age when studied. They had presented with isolated nephrotic syndrome, steroid-resistant nephrotic syndrome (associated with progressive encephalomyopathy in one case) or neonatal renal failure. Genetic analyses detected a homozygous c437G>A mutation, two homozygous c890A>G mutations (harbored by a sibling pair, who had previously been reported), and a combined heterozygous mutation (c590G>A and c683A>G). Electron microscopy of renal tissue from all four patients revealed increased numbers of abnormal mitochondria in glomerular cells, particularly podocytes. Biochemical analysis of skeletal muscle and renal cortex showed decreased activity of respiratory chain complexes II and III and low levels of CoQ₁₀. *COQ2* mutations were absent from the 500 control DNA samples analyzed, and from four patients with CoQ₁₀ deficiency but no renal involvement.

Early identification of *COQ2* nephropathy could, say the authors, enable prompt initiation of ubiquinone supplementation.

Original article Diomedì-Camassei F *et al.* (2007) *COQ2* nephropathy: a newly described inherited mitochondriopathy with primary renal involvement. *J Am Soc Nephrol* 18: 2773–2780

New treatment algorithms for idiopathic glomerular disease

The calcineurin inhibitor ciclosporin is known to be an effective treatment for idiopathic glomerular disease associated with the nephrotic syndrome (INS); however, cohesive guidelines for the use of this agent in patients with INS are lacking.

An international panel of experts has evaluated the merit of clinical data on the use of ciclosporin in the three most common histological variants of INS—minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) and membranous nephropathy. The algorithms for adults and children that they have developed—which include guidance on

who, when and how to treat, plus treatment goals and recommendations for follow-up—have been published in *Kidney International*.

Cattran *et al.* based their guidelines on the following findings. Ciclosporin successfully induced remission of proteinuria in approximately 80% of steroid-sensitive cases of MCD. Ciclosporin also induced remission and preserved long-term renal function in steroid-dependent and steroid-resistant MCD and in steroid-resistant FSGS. The response rate in FSGS was lower than in MCD, however, and the authors recommend that ciclosporin therapy should continue for at least 12 months in patients with FSGS. Ciclosporin also lowered proteinuria in 70–80% of patients with steroid-resistant membranous nephropathy but, similarly, long-term therapy of at least 1 year was required. Although ciclosporin is generally safe, clinicians need to be vigilant to the risk of nephrotoxicity and should monitor renal function carefully during therapy.

Original article Cattran DC *et al.* (2007) Cyclosporin in idiopathic glomerular disease associated with the nephrotic syndrome: workshop recommendations. *Kidney Int* [doi:10.1038/sj.ki.5002553]

Tacrolimus effective in steroid-dependent minimal change nephrotic syndrome

A recent study found that a 24-week course of oral tacrolimus (along with tapering doses of prednisone) might be an effective alternative to ciclosporin in Chinese adults with steroid-dependent minimal change disease, and might induce remission more quickly than ciclosporin.

The study enrolled 26 Chinese adults with biopsy-proven minimal change disease, steroid-dependent nephrotic syndrome, and a serum creatinine level <133 μmol/l (1.5 mg/dl). Patients were self-assigned to at least 24 weeks of oral tacrolimus ($n=12$; target trough level 4–8 ng/ml) or intravenous ciclosporin ($n=14$; 750 mg/m² body surface area once every 4 weeks). All patients also received oral prednisone 0.5 mg/kg/day, tapered to cessation after complete remission (i.e. normalization of proteinuria).

One patient in each group discontinued therapy before completing 24 weeks because of severe drug-related adverse effects