

Other forms of dietary intervention

Date written: July 2004
Final submission: July 2004
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GUIDELINES

A carbohydrate-restricted, low-iron-available, polyphenol-enriched (CR-LIPE) diet may slow the progression of diabetic nephropathy. (Level II evidence; one small randomised controlled trial (RCT); clinically relevant outcome; large effect)

Background

Animal models of chronic kidney disease (CKD) have suggested possible renoprotective roles for carbohydrate restriction, augmentation of polyphenol intake and restriction of dietary iron. Caloric restriction (principally achieved by carbohydrate restriction) has been shown in animal models to prevent renal failure progression independently of dietary protein intake (Tapp 1989). Polyphenols inhibit the digestion and absorption of protein, energy and iron, and significantly prolong renal survival in experimental models of glomerulosclerosis (Yokozawa 1996). Finally, iron has been identified as an important factor in the progression of experimental nephropathy after the inciting injury was removed (Alfrey 1994). The objective of this guideline was to assess the potential effectiveness of any of these dietary interventions on renal failure progression.

Search strategy

Databases searched: Medline (1999 to November Week 2, 2003). MeSH terms for kidney diseases were combined with MeSH terms and text words for dietary restriction, CR-LIPE and iron. The results were then combined with the Cochrane highly sensitive search strategy for randomised controlled trials and MeSH terms and text words for identifying meta-analyses and systematic reviews. The Cochrane Renal Group Specialised Register of Randomised Controlled Trials was also searched for relevant trials not indexed by Medline.

Date of search: 16 December 2003.

What is the evidence?

1. There is one RCT.
2. Facchini and Saylor (2003) conducted a prospective, open-label, randomised controlled trial of a low-iron-available, polyphenol-enriched, 50% carbohydrate

restricted (CR-LIPE) diet vs a standard, protein-restricted (0.8 g/kg/day) diet in 191 type 2 diabetic patients with various degrees of chronic renal disease (CKD) (GFR 15–75 mL/min) or proteinuria (350–12000 mg/day). Over a mean follow-up period of 3.9 ± 1.8 years, serum creatinine concentration doubled in 19 (21%) patients on CR-LIPE compared with 31 (39%) patients on the control diet ($p < 0.01$). Renal death occurred in 18 (20%) patients on CR-LIPE and 31 (39%) of controls ($p < 0.01$). The observed differences between the groups were independent of follow-up interval, sex, mean arterial blood pressure, glycated haemoglobin, initial renal dysfunction and angiotensin system inhibition. Drop-out rates were low in each group (CR-LIPE 9%, controls 13%). Dietary compliance was not assessed, but serum ferritin concentration did fall significantly in the CR-LIPE group (from 301 ± 162 to 36 ± 31 $\mu\text{g/L}$), while it was unchanged in control subjects. Despite the development of iron deficiency in a number of subjects in the CR-LIPE group, haemoglobin levels did not fall (141 ± 21 vs 140 ± 20 g/L). Body weight and serum albumin concentration also did not fall in the CR-LIPE patients. The principal limitations of the study were: (a) its small size (potentially limiting the generalisability of these findings); (b) the lack of monitoring of dietary compliance; and, (c) the uncertainty regarding adequate concealment of randomisation allocation.

Summary of the evidence

One small RCT has demonstrated that a CR-LIPE diet is markedly more effective at retarding the progression of diabetic nephropathy than standard dietary protein restriction. These findings should be considered preliminary.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

UK Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: No recommendation.

British Dietetic Association Renal Nutrition Group: No recommendation

European Dialysis and Transplant Nurses Association - European Renal Care Association: No recommendation.

European Society of Parenteral and Enteral Nutrition: No recommendation.

Implementation and audit

No recommendation.

Suggestions for future research

A large, multi-centre, RCT of CR-LIPE diet in patients with diabetic and non-diabetic renal failure is recommended.

References

Alfrey AC. Role of iron and oxygen radicals in the progression of chronic renal failure. *Am J Kidney Dis* 1994; 23: 183–7.

Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. *Diabetes* 2003; 52: 1204–9.

Tapp DC, Wortham WG, Addison JF et al. Food restriction retards body growth and prevents end-stage renal pathology in remnant kidneys of rats regardless of protein intake. *Lab Invest* 1989; 60:184-95.

Yokozawa T, Chung HY, He LQ et al. Effectiveness of green tannin on rats with chronic renal failure. *Biosci. Biotech Biochem.* 1996; 60: 1000–5.

Appendices

Table 1 Characteristics of included studies

| Study ID (author, year) | N | Study Design | Setting | Participants | Intervention (experimental group) | Intervention (control group) | Follow up (months) | Comments |
|-------------------------|-----|---|--|---|---|--|--------------------|----------|
| Facchini et al, 2003 | 191 | Prospective randomised controlled Trial | Nephrology clinics (multicentre trial) | Patients with Type 2 diabetes with various degrees of renal failure and proteinuria | Carbohydrate-restricted, low iron-available, polyphenol-enriched diet (CR-LIPE) N = 100 | Conventional standard protein-restricted diet N = 91 | 8–64 | |
| | | | | | | | | |

Table 2 Quality of randomised trials

| Study ID (author, year) | Method of allocation concealment | Blinding | | | Intention-to-treat analysis | Loss to follow up |
|-------------------------|----------------------------------|----------------|-----------------|---------------------|-----------------------------|-------------------|
| | | (participants) | (investigators) | (outcome assessors) | | |
| Facchini et al, 2003 | Central | No | No | No | Yes | 21/191 (11%) |
| | | | | | | |

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Table 3 Results for continuous outcomes

| Study ID (author, year) | Outcomes | Intervention group (mean [SD]) | Control group (mean [SD]) | Difference in means [95% CI] |
|-------------------------|-----------------------------|--------------------------------|---------------------------|------------------------------|
| Facchini et al, 2003 | Weight (kg) at follow up | 76 (14) | 78 (14) | -2.00 (95%CI:-0.37, -0.09) |
| | Albumin (g/L) at follow up | 41 (6) | 41 (7) | 0.00 (95%CI:-2.04, 2.04) |
| | Hb (g/L) at follow up | 140 (20) | 140 (26) | 0.00 (95%CI:-7.31, 7.31) |
| | TC (mmol/L) at follow up | 5.8 (1.4) | 5.5 (1.5) | 0.30 (95%CI:-0.15, 0.75) |
| | LDL-C (mmol/L) at follow up | 3.68 (1.01) | 3.47 (1.99) | 0.21 (95%CI:-0.30, 0.72) |
| | HDL-C (mmol/L) at follow up | 1.22 (0.50) | 0.92 (0.41) | 0.30 (95%CI:0.16, 0.44) |
| | TC/HDLC at follow up | 4.7 (0.7) | 5.8 (1.1) | -1.10 (95%CI:-1.39, -0.81) |

Hb = haemoglobin; TC = total cholesterol; LDL-C = LDL cholesterol; HDL-C = HDL cholesterol

Table 4 Results for dichotomous outcomes

| Study ID (author, year) | Outcomes | Intervention group (number of patients with events/number of patients exposed) | Control group (number of patients with events/number of patients not exposed) | Relative risk (RR) [95% CI] | Risk difference (RD) [95% CI] |
|-------------------------|------------------------------------|--|---|-----------------------------|-------------------------------|
| Facchini et al, 2003 | Renal replacement therapy or death | 18 /100 | 31/91 | 0.53 (95%CI: 0.32, 0.88) | -0.16 (95%CI:-0.28, -0.04) |
| | Doubling of serum Cr | 19/91 | 31/71 | 0.48 (95%CI: 0.30, 0.77) | -0.23 (95%CI: -0.37, -0.09) |