

Meta-analysis: Dietary protein restriction delays progression in renal disease

Pedrini MT, Levey AS, Lau J, Chalmers TC, Wang PH. *The effect of dietary protein restriction on the progression of diabetic and nondiabetic renal diseases: a meta-analysis.* *Ann Intern Med.* 1996 April 1;124:627-32.

Objective

To determine the efficacy of dietary protein restriction in delaying progression of chronic renal disease in patients with and without diabetes by using meta-analysis.

Data sources

Studies were identified by searching MEDLINE (1966 to 1994) and by reviewing the bibliographies of published review articles and studies.

Study selection

Studies were selected if they were published, randomized, controlled trials or cross-over studies of low-protein diet in patients with nondiabetic renal disease or insulin-dependent diabetes mellitus (IDDM). For studies of nondiabetic renal disease, follow-up had to be > 1 year and include data on the number of patients who developed renal failure or died. For the studies of IDDM, follow-up had to be

Commentary

End-stage renal disease is a source of frustration for nephrologists. Since the 1940s, low-protein diets have been prescribed to reduce uremic symptoms, and results from numerous recent studies, mostly uncontrolled, suggest that reducing protein intake can slow the so-called "natural" progression of renal disease toward end-stage renal failure. A meta-analysis is needed here because the treatment effect has not been clear-cut in individual trials to date (1). Pedrini and colleagues used a robust renal event that could be easily observed in all trials (i.e., "renal death"—death or the need to start dialysis or transplant a kidney). This outcome is unusual for nephrologists to use: They generally use serum creatinine level or glomerular filtration rate measurements for the follow-up of patients with renal disease. The apparently conflicting results from this meta-analysis and from the Modification of Diet

> 9 months in length and include data on the change in glomerular filtration rate or degree of albuminuria.

Data extraction

Extracted data included number of patients, length of follow-up, protein intake of the prescribed diet, and the level of renal function (glomerular filtration rate, creatinine clearance level, serum creatinine level, and urinary albumin excretion rate). The cause of renal failure in nondiabetic patients was not available. Data were extracted by 2 independent reviewers.

Main results

5 randomized controlled trials (a total of 1413 patients with nondiabetic renal disease) that tested a protein intake of 0.4 to 0.6 g/kg of body weight per day and 5 studies (a total of 108 patients with IDDM) that tested a protein intake of 0.5 to 0.85 g/kg of body weight per day met the selection criteria. The pooled results of the studies of nondiabetic renal disease showed a reduced risk for renal failure or death in patients who had a protein-restricted diet compared with those who had a usual protein diet (relative risk [RR] 0.67, 95% CI 0.50 to

0.89, $P = 0.007$). The pooled results of the studies of IDDM showed a reduced risk for progression in renal disease (a decline in glomerular filtration rate or creatinine clearance level or an increase in urinary albumin excretion rate) among patients who had a protein-restricted diet compared with those who had a usual diet (RR 0.56, CI 0.40 to 0.77, $P < 0.001$). The beneficial effects of protein restriction were unrelated to change in blood pressure or glycemic control.

Conclusion

Dietary protein restriction reduces the risk for renal failure or death in nondiabetic renal disease and improves nephropathy in insulin-dependent diabetes mellitus.

Source of funding: University of California, Irvine.*

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Abstract and Commentary also published in *ACP Journal Club*. 1996;125:18.

in Renal Disease (MDRD) study (2) may reflect the use of different outcome criteria. The trend for a beneficial effect of low-protein diets in slowing progression to renal failure, however, is apparent in this meta-analysis that uses the renal death outcome and is also reported for the decline in the glomerular filtration rate in the second part of the MDRD study (2). These data strongly suggest that low-protein diets should be recommended for nondiabetic patients with chronic renal failure.

The evidence for patients with insulin-dependent diabetes and chronic renal failure, however, is less robust. As emphasized by the authors, data were available for only a few patients, follow-up was shorter, and not all the trials were randomized. 2 important potentially confounding factors were identified—receiving angiotensin-converting enzyme (ACE) inhibitors and

glycemic control—but these were well balanced between the groups.

Precautions should be taken against diets becoming hypocaloric in these frail patients when protein intake is reduced. Research and funding should now focus on the potential benefits of pharmacologic agents (ACE inhibitors, calcium antagonists, or angiotensin II antagonists) to enhance the nephroprotection confirmed by low-protein diets.

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References

1. Fouque D, Laville M, Boissel JP, et al. *BMJ*. 1992;304:216-20.
2. Klahr S, Levey AS, Beck GJ, et al. *N Engl J Med*. 1994;330:877-84.