Therapy of Membranous Nephropathy: Use of Low-Protein Diet

To the Editor:

We have read with interest the editorial of Dr. Lee A. Hebert, “Therapy of Membranous Nephropathy: What To Do After the (Meta) Analyses” (1). Dr. Hebert stated in his editorial that the Modification of Diet in Renal Disease (MDRD) Study has shown that in patients with proteinuria higher than 1 g/day, reducing the dietary protein intake to about 0.75 g/kg of ideal body weight per day significantly slows GFR loss compared with a dietary protein intake of approximately 1.1 gm/kg per day. He references the New England Journal of Medicine article of Klahr et al. (2).

We do not believe that Dr. Hebert’s conclusions are consistent with what Klahr et al. published. Dr. Klahr et al. found that patients in the low blood pressure group, who had more pronounced proteinuria (proteinuria higher than 1 g/24 h) at baseline, had a significant slower rate of decline in the GFR. There is no evidence that we can find in Dr. Klahr’s article that low protein intake alone affects the renal function of patients with proteinuria higher than 1 g/24 h.

We think that the MDRD Study failed to convincingly show that a low-protein diet alone can significantly slow the progression of renal disease: “No significant benefits of these interventions were demonstrated at the end of follow-up in either study group, when patients with diverse renal diseases were considered together.” This statement from the authors seems to get lost in the nephrology community amid our zealous search to find further interventional measures to prevent progressive renal failure. We are not sure at this time that we can recommend a low-protein diet to our patients on the basis of the results of the MDRD Study published in the New England Journal of Medicine in March of last year.

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REFERENCES


Response:

In Study 1 of the Modification of Diet in Renal Disease (MDRD) Study (patients with various forms of renal disease and baseline GFR of 25 to 55 mL/min per 1.73 m² body surface area), the terminal GFR slope (measured from the fourth month of follow-up in the MDRD Study and projected to 3 yr of follow-up) was 28% less in the low-protein group compared with the usual protein group (P = 0.009). The GFR projected to 3 yr of follow-up was also numerically higher in the low-protein group compared with the usual protein group. However, this difference in GFR did not achieve statistical significance (P = 0.30). On this basis, our primary results article concluded that the benefit of the low-protein diet was not proved (1). However, many of us involved in the MDRD Study feel that the terminal slope (as defined above) is a more relevant measure of the effectiveness of the dietary and blood pressure interventions of the MDRD Study than is the overall GFR slope (from baseline to 3 yr of follow-up). The rationale is that a recent analysis of the MDRD data provides clear evidence that the acute decrease in GFR (baseline to 4 months of follow-up) that was seen in the Study A patients assigned to the low blood pressure group or the low dietary protein group is hemodynamic in origin (2). Thus, it is the GFR slope after this acute hemodynamic change in GFR that probably represents the true progression of renal disease (structural damage to the kidney). As discussed above, this slope is significantly less steep in those assigned to the low-protein group compared with those in the usual protein group. This potential benefit of the low-protein diet was independent of baseline protein. I incorrectly stated that this benefit was seen only in those with proteinuria exceeding 1 g/day.

Another line of evidence that the low-protein diet is beneficial is that the patients assigned to the low-protein group showed significantly smaller increases in proteinuria with time compared with those assigned to the usual protein group. Because proteinuria appears to be a pathogenic event in the progression of renal disease (3), the ability of the low-protein diet to delay the onset of heavy proteinuria is another reason to suggest that a low-protein diet is of benefit to patients with progressive forms of renal disease.

Finally, a recent analysis of the MDRD patients 10 months after the completion of the study showed that GFR was higher (+2.34 mL/min; P = 0.11) in those assigned to the low-protein group compared with the usual protein group. Also, the relative risk for death or renal failure in the low-protein group was less (0.62; P = 0.056) than that in the usual protein group (4). There was no evidence from the MDRD Study that the low-protein diet caused harm (1).

On the basis of the above evidence, it appears prudent clinically, if not statistically, to encourage patients with progressive forms of renal disease to follow a diet that is moderately restricted in protein.