

Angiotensin blockade for diabetes: Monitor microalbuminuria?

EVIDENCE-BASED ANSWER

No studies address whether continued screening for microalbuminuria once a patient is taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-2 receptor blocker (ARB) improves outcomes. Indirect evidence and expert

opinion suggest that it may be beneficial to continue microalbuminuria surveillance to assess response to therapy and monitor disease progression (strength of recommendation: **C**, based on expert opinion).

CLINICAL COMMENTARY

It is unclear whether microalbuminuria tests in these cases is money well spent

At the residency where I teach, clinicians routinely try to get to the evidence behind the expert opinions, and faculty are discouraged from giving off the cuff or experiential answers. When asked whether to monitor microalbuminuria for patients with diabetes receiving ACE inhibitors or ARBs, it is frustrating to discover that no direct evidence supports the experts' advice.

The screening test for urine microalbuminuria at our hospital costs \$90. Since most patients with diabetes are being treated with ACE inhibitors or ARBs, it would be nice to know that the money for the testing is well spent. Unfortunately, in this instance, we can only continue to practice the "standard of care" and hope for future research to definitively answer this question.

Chris Vincent, MD
Swedish Family Medicine Residency,
University of Washington, Seattle

Evidence summary

Our comprehensive literature search found no studies that provide direct evidence for or against continuing to monitor microalbuminuria among patients with diabetes already on ACE inhibitor or ARB therapy. We reviewed and included indirect evidence and expert opinion to answer this clinical question.

Diabetes mellitus is the leading cause of end-stage renal disease in the

Western world.¹ The prevalence of diabetic nephropathy continues to rise along with the rapidly rising prevalence of obesity and diabetes, with 40% of patients with diabetes at risk of developing nephropathy. One study that followed 5097 patients with type 2 diabetes over a median of 10.4 years found that 2% of patients progressed from normal levels of urinary protein to microalbuminuria; 2.8% changed

John Muench, MD, MPH,
Carol Blenning, MD
Department of Family Medicine,
Oregon Health and Science
University, Portland
Dolores Zegar Judkins, MLS
Oregon Health and Science
University, Portland

FAST TRACK

Experts call for microalbuminuria surveillance to assess response to therapy, but no evidence supports this

from microalbuminuria to macroalbuminuria (urine albumin >300 mg in a 24-hour period); and 2.3% progressed to chronic renal disease (creatinine ≥ 2 mg/dL) from macroalbuminuria per year.² Chronic renal disease is more likely to occur in those patients whose hypertension or hyperglycemia is poorly controlled.

For patients with diabetes who develop microalbuminuria, the evidence is good for starting ACE inhibitors or ARBs for renal protection.^{3,4} The American Diabetes Association (ADA) also recommends that patients with diabetes and hypertension and those aged >55 years with other cardiovascular risk factors (history of cardiovascular disease, dyslipidemia, or tobacco use) be started on ACE inhibitors or ARBs.¹ There is also good evidence that screening for microalbuminuria can identify those who might benefit from treatments that delay the onset of nephropathy.⁵

Recent studies have raised the possibility of further benefit in prevention and treatment of diabetic nephropathy by maximizing doses of ACE inhibitors or ARBs, and even from the dual blockade attained from using both. For example, during a 2-year trial—in which 590 patients with diabetes and microalbuminuria were randomized to receive placebo, 150 mg irbesartan, or 300 mg irbesartan—14.9% of the placebo group, 9.7% of the 150-mg group, and only 5.2% of the 300-mg group progressed to overt nephropathy.⁶ In very small randomized trial of 20 patients with type 2 diabetes, adding 16 mg of candesartan to the maximal dose of an ACE inhibitor decreased albuminuria an additional 28%.⁷

Experts argue that it may benefit patients to continue regular surveillance for the presence or progression of microalbuminuria even if they are al-

ready taking an ACE inhibitor or ARB so that therapy can be maximized.^{1,8} However, no direct evidence supports this recommendation.

Recommendations from others

The ADA suggests that clinicians perform a test each year for microalbuminuria among patients with type 1 diabetes of ≥ 5 years duration, and in all patients with type 2 diabetes at diagnosis and during pregnancy. They also recommend continued surveillance of proteinuria to assess both response to therapy and progression of disease.¹

The National Kidney Foundation recommends continued surveillance of microalbuminuria to assess progression of chronic kidney disease and response to therapy.⁸

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes—2006. *Diabetes Care* 2006; 29:S4–S42.
2. Adler AI, Stevens RJ, Manley SE. Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Intl* 2003; 63:225–232.
3. Sferra L, Kelsberg G. Do ACE inhibitors prevent nephropathy in type 2 diabetes without proteinuria? *J Fam Pract* 2004; 53:68–69.
4. Foreman BH, Chambliss ML. Are ARBs or ACE inhibitors preferred for nephropathy in diabetes? *J Fam Pract* 2004; 53:241–242.
5. Hale WA, Nashelsky J. Does microalbuminuria screening in diabetes prevent complications? *J Fam Pract* 2003; 52:229–230.
6. Parving HH, Lehnert H, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med* 2001; 345:870–878.
7. Rossing K, Jacobsen P, et al. Renoprotective effects of adding angiotensin II receptor blocker to maximal recommended doses of ACE inhibitor in diabetic nephropathy: a randomized double-blind crossover trial. *Diabetes Care* 2003; 26:2268–2274.
8. Eknayan G, Hostetter T, Bakris GL, et al. Proteinuria and Other Markers of Chronic Kidney Disease: A Position Statement of the National Kidney Foundation (NKF) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). *Am J Kidney Dis* 2003; 42:617–622.