

Putting Up Roadblocks On The Path to Diabetic Kidney Disease



Evan David Rosen, M.D., Ph.D.

Assistant Professor of Medicine, Harvard Medical School

One of the most feared complications of diabetes is end-stage renal (kidney) disease (ESRD). This condition, which requires either dialysis or kidney transplantation, is reached in about 10% of patients with type 2 diabetes and in 20% of type 1 diabetics. Type 2 diabetes still accounts for the majority of cases of ESRD, given the fact that it is so much more common than type 1 diabetes. And with type 2-diabetes on the rise in the United States, the numbers for ESRD have gone up proportionately. Last year alone, 90,000 Americans developed ESRD.

ESRD doesn't just appear out of the blue, however. The first stage of diabetic kidney disease occurs when small amounts of protein are excreted in the urine. The kidney normally acts as a filter to prevent proteins in the blood from spilling into the urine - in diabetes the filter becomes damaged and protein leaks through. Up to 60% of diabetics will have such extra protein in their urine at some point in their lives. In some of these patients, the amount of protein that leaks through the filter gets larger and larger, and eventually a series of pathological changes occur that lead to wholesale kidney failure. Once this occurs, there is very little that can be done other than dialysis or transplantation.

Given this unpleasant state of affairs, efforts have been directed at preventing the earliest form of kidney disease from appearing, or at least halting the progression from small amounts of protein spilling to larger quantities. The single most important factor appears to be good sugar control, which is one of the major reasons why doctors are always on their diabetic patients' cases to get them to reduce their blood glucose levels. Other factors can help as well, such as reducing blood pressure and quitting smoking.

There is also a group of medications that can help. These drugs are called ACE inhibitors, because they inhibit a protein called Angiotensin Converting Enzyme. ACE inhibitors are often prescribed for hypertension, but they appear to have benefits that have nothing to do with blood pressure. Commonly prescribed ACE inhibitors include captopril (CapotenTM), lisinopril (ZestrilTM or PrinivilTM), enalapril (VasotecTM), and ramipril (AltaceTM). Studies performed several years ago showed that ACE inhibitors prevent the onset and progression of early diabetic kidney disease in type 1 diabetes. Several smaller studies also suggested that ACE inhibitors were similarly useful in type 2 diabetes, and certainly the majority of diabetes specialists have used ACE

inhibitors liberally in such patients.

Now, three papers have appeared back to back to back in the latest issue of the *New England Journal of Medicine*, looking at the use of drugs called angiotensin II receptor antagonists, or ATII blockers, in type 2 diabetes. The most common ATII blockers on the market include irbesartan (Avapro™), valsartan (Diovan™), and losartan (Cozaar™). These drugs work in a similar way to ACE inhibitors, so it comes as not much of a surprise that they prevent the progression of diabetic kidney disease. Still, it's nice to get confirmation of this assumption in three separate large trials. Furthermore, two of the studies looked specifically at patients with moderate amounts of protein in their urine, and showed a 16-23% reduction in the development of ESRD and death.

This is all to the good, of course. I just think it's important to mention a few things that may help you if you're a patient with type 2 diabetes, or a physician taking care of such patients. First, I believe strongly that ACE inhibitors are the first option in the prevention of diabetic nephropathy, for both type 1 and type 2 diabetes. They have been around longer than ATII blockers, we know them better, and frankly, they are at least half as expensive. This last fact, coupled with the fact that ACE inhibitors will soon be off patent and will thus be even cheaper, is why these drug company funded studies were performed only with ATII blockers and did not include ACE inhibitors. It is true that in about 5-20% of people, ACE inhibitors can cause a benign (albeit annoying) cough. It is my practice to use ATII blockers only in those patients who develop such a cough on ACE inhibitors. Second, patients with diabetes who also develop high blood pressure (an extremely common combination) should be treated with an ACE inhibitor (or ATII blocker if a cough develops) before trying other blood pressure medications. This is to give the double benefit of blood pressure reduction and protection from diabetic kidney disease in one pill.

It pains me to think of all the patients I have seen in consultation who have early diabetic kidney disease and who are taking several expensive pills for hypertension that do not include an ACE inhibitor. Finally, neither ACE inhibitors nor ATII blockers are a substitute for good sugar control. It is important that patients are not left with the impression that these drugs totally eliminate the risk of diabetic kidney disease. The most important factor is still maintaining a near normal glucose level. Furthermore, neither ACE inhibitors nor ATII blockers protect against other complications of diabetes like retinopathy (eye disease) and neuropathy (nerve damage) - only good glucose control can prevent these conditions.

References:

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Written by Evan D. Rosen, M.D., Ph.D.

Content created 9/26/01

Content last reviewed September 26, 2001