What Should We Do About Proteinuria?

One of the most confusing issues primary care practitioners currently face is the appropriate medical management of proteinuria—an increasingly common condition. We used to think of proteinuria as something that related only to the kidneys. As such, only practitioners whose focus was on renal function (or dysfunction) paid much attention to proteinuria. In recent years, however, we have come to understand that the condition potentially has much larger implications. As a result, we are all obligated to pay more attention to proteinuria—but what exactly should we do about it?

Let’s first review what we know with reasonable certainty about proteinuria. We know that the presence of increased amounts of protein in the urine—either as microalbuminuria (best defined as a urinary albumin/creatinine ratio between 30 and 300 mg/g in a spot urine) or as frank proteinuria (an albumin/creatinine ratio of greater than 300 mg/g in a spot urine)—is an abnormal and undesirable condition. The presence of proteinuria basically means that there are holes in the endothelial cells that are critical to maintaining the structural integrity of blood vessel walls. And vascular endothelial dysfunction is essentially a marker for systemic dysfunction of the entire endothelial infrastructure throughout the body. Proteinuria, therefore, becomes a “poor man’s” biopsy of the endothelial system, which is not otherwise amenable to sampling.

Given that major vascular events (such as myocardial infarction and stroke) are strongly associated with endothelial dysfunction, it comes as no surprise that proteinuria is a risk factor for these vascular catastrophes. And we know only too well that endothelial dysfunction can be accelerated by such cardiovascular risk factors as diabetes, dyslipidemia, smoking, obesity, and hypertension. But is proteinuria simply a marker (or consequence) of vascular disease or is it an actual cause or contributor? Answering this elusive question would have very important implications for the more practical issue of whether and when aggressive treatment of proteinuria—along with other established cardiovascular risk factors—is warranted.

Unfortunately, the prospective data addressing this question are very limited at this time. Two of the most helpful studies are the Irbesartan in Diabetic Nephropathy Trial and the Reduction of Endpoints in Non-Insulin-Dependent Diabetes Mellitus (NIDDM) with the Angiotensin II Antagonist Losartan (RENAAL) Study. Both studies unequivocally demonstrated that aggressive treatment of proteinuria with angiotensin II receptor blockers markedly reduced the frequency of negative renal outcomes in people with type 2 diabetes. This reduction was clearly above and beyond the reduction in renal risk associated with blood pressure lowering. When it comes to the question of cardiovascular risk reduction, though, the results are harder to interpret. There were definite trends in the direction of fewer cardiovascular events, but these trends did not achieve statistical significance. It’s important to note that neither study was adequately powered to demonstrate significant cardiovascular risk reductions.

It seems, therefore, that while the renal benefits of aggressive proteinuria management are clear, we can’t yet come to a definitive conclusion about the possible cardiovascular benefits. Until we know more, however, it seems prudent to make reasonable efforts to reduce proteinuria whenever we encounter it by emphasizing the use of drugs that block the renin-angiotensin-aldosterone system.

Author disclosures
The author reports no actual or potential conflicts of interest with regard to this editorial.

Disclaimer
The opinions expressed herein are those of the author and do not necessarily reflect those of Federal Practitioner, Quadrant HealthCom Inc., the U.S. government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.

REFERENCES