Diabetes and Hypertension: Not the final chapter

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Many good chapters have been written on diabetes and hypertension. We know that diabetes is one of the major risk factors for morbidity and mortality in victims of coronary heart disease, cerebrovascular disease, and peripheral vascular disease. Because multiple risk factors for macrovascular disease are frequently found in diabetic individuals, the prevalence of these macrovascular complications is increased 2–4 times in diabetic populations.

Thus, a good point to remember is that, in the care of diabetes, we must focus not only on normalizing blood glucose, but also, among other things, on preventing or treating hypertension, hyperlipidemia, obesity, and smoking—the risk factors for macrovascular disease.

Let's zoom in on hypertension. In 1980, 128 papers were written on diabetes and hypertension; in 1990, 307; and in the first 6 mo of this year, 177. This is a prodigious pool of knowledge. However, because this knowledge is still evolving, and the final chapter will not be written for some time, a certain degree of confusion about what we know, and impatience for what we still do not know, is natural.

We know that the prevalence of hypertension in diabetic patients is ~1.5–2 times greater than in an appropriately matched nondiabetic population, and that coexisting hypertension and diabetes act as additive risk factors to accelerate vascular complications. Unfortunately, no randomized clinical trial has tested the hypothesis that lowering blood pressure will reduce the risk of cardiovascular disease in diabetes. However, by inference from the several large randomized clinical trials on people without diabetes, aggressive treatment of hypertension among diabetic patients is recommended. Therefore, the source of our confusion is not whether we should treat hypertension in diabetes, but rather how to treat it.

The final report of the working group on hypertension in diabetes published in 1987 (1) recommended the following as first-line therapy for hypertensive subjects with diabetes: diuretics, β-blockers, ACE inhibitors, CCBs, and α-blockers. This is an extraordinarily long list of drugs to choose from and undoubtedly a source of confusion. Since the "final report" was published, a myriad of papers have proposed that we narrow the first-line therapy for hypertensive patients with diabetes to ACE inhibitors, CCBs, and α-blockers. In this issue, Moser and Ross (p. 542–47) attempt to rescue diuretics and β-blockers with the cogent arguments that these are the only classes of drugs shown thus far to reduce morbidity and mortality in nondiabetic, hypertensive subjects in long-term clinical trials. But what about in diabetic patients? So far, there have been no clinical trials. Furthermore, what about comparing diuretics or β-blockers with the newer ACE inhibitors or CCBs in diabetic patients and in nondiabetic subjects? Again, there are no clinical trials. Thus, we are left with a high degree of uncertainty, because we cannot answer these major questions with scientific facts.

Moser and Ross reviewed in great detail the negative effects of thiazide diuretics and β-blockers on lipid and carbohydrate metabolism and insulin resistance. A similar review on ACE inhibitors, CCBs, and α-blockers will be much shorter because, instead of possessing such negative metabolic effects, they have some that are beneficial—as summarized in a recent commentary by Brouhard (2).

What Moser and Ross provide is a good reminder that the negative metabolic effect of thiazides are dose-dependent and negligible at low dosage and, furthermore, that the elevation in serum cholesterol that occurs early in thiazide therapy disappears in long-term follow-up. For β-blockers, the negative metabolic effects are as clear as are its protective effects on the recurrence of coronary artery disease events in patients with ischemic heart disease.

Therefore, until the final chapter is written, it is prudent to initiate pharmacological treatment for hypertension among diabetic patients with ACE inhibitors, CCBs, or α-blockers. If thiazide diuretics are effective at low dosage, they are also an appropriate initial therapy. Similarly, for patients who have had a recent myocardial infarction, or those with exertional angina, cardioselective

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ACE, ANGIOTENSIN CONVERTING ENZYME; CCB, CALCIUM CHANNEL BLOCKERS.

β-blockers also are an excellent choice for initial therapy.

In a disease with multiple risk factors, it is imperative that the treatment of one factor does not worsen others. This is particularly true for diabetic patients, because long-term therapeutic trials for hypertension are not available, so the end result cannot be predicted from theoretical considerations. Therefore, we must continue to await the final chapter on this important subject. Until then, let's ask our patients about quality of life and frequently monitor them for any potential complications of the therapy we prescribe.

References

1. Working Group on Hypertension in Diabetes: Statement on hypertension in diabetes mellitus: final report. *Arch Int Med* 147:830–42, 1987
2. Brouhard B: Antihypertensive therapy for patients with diabetes mellitus. *Diabetes Care* 15:918–21, 1992