

Antihypertensive drugs for CVD

To the Editor:

I enjoyed reading the article by Wexler and Feldman¹ concerning which antihypertensive drugs to choose for patients with cardiovascular disease. I thought their recommendations for treatment of heart failure, coronary artery disease, and stroke were rational and well supported by the literature. However, they did not fully address the major issues that face clinicians regarding the persistent gaps between the identification, awareness, treatment, and control rates for hypertension in our country.²

I was cited as a proponent of an individualized approach to treatment, as opposed to using the more formulaic approach advocated by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).³ Not mentioned in their article is my rationale behind this position: the continuous, graded relationship between blood pressure and cardiovascular events.⁴ Unfortunately, threshold-based considerations for treatment do not provide a broad enough perspective; many patients require earlier and more intensive strategies to control blood pressure sufficiently to prevent cardiovascular events.

Healthcare providers need to recognize that choice of appropriate blood pressure goals for individual patients should be predicated on cardiovascular risk rather than on hitting a given threshold. An individualized approach should be thoughtfully considered in each patient based on global cardiovascular risk, which encompasses an understanding of family history; comorbid conditions such as dyslipidemia, dia-

betes, and obesity; and lifestyle factors such as smoking, dietary, and exercise habits.

Better strategies needed for compliance

As I consider what has changed in the past 10 years in blood pressure-lowering therapeutics, I am struck by 3 key factors that increase the gap between treatment and control rates:

- Greater focus on controlling systolic blood pressure, in large part driven by the Framingham Heart Study indicating that after age 60 years cardiovascular events are better predicted by systolic than diastolic blood pressure⁵
- Recognition that in many patients—particularly those with cardiovascular disease, kidney disease, or diabetes—lower systolic blood pressure goals may be preferable⁶⁻⁸
- The fact that increasing numbers of our patients are overweight, sedentary, and have unhealthy eating patterns that limit the efficacy of antihypertensive medications.^{9,10}

As a result, patients are less likely to get to goal with 1 medication. More often than not, patients require anywhere from 2 to 4 medications to control systolic blood pressure. Of added concern is that patients often require multiple medications for other medical problems. Thus, healthcare providers and patients may be less willing to accept more than 1 medication to treat only high blood pressure. This creates substantial “therapeutic inertia” on both the provider and patient sides of treatment planning.¹¹

Consequently, improved strategies for overcoming therapeutic inertia are needed, in particular renewed educational efforts as to the importance of achieving lower blood pressure goals, which does make a

difference in decreasing the likelihood of cardiovascular events. Moreover, there needs to be greater awareness among providers of strategies to simplify the therapeutic approach.

One option is to consider using more robust fixed-dose combinations to provide better blood pressure control without increasing the number of pills patients must take. I often illustrate to patients the overall effectiveness rate of antihypertensive medications: we generally need at least 1 drug for each 10-mm Hg systolic blood pressure reduction. Consequently, a patient with systolic blood pressure 30 mm Hg above goal will often require 3 medications. Optimally, a fixed-dose combination containing 2 medications that lower blood pressure by different and complementary mechanisms should close at least 20 mm Hg of that gap, in addition to critical dietary changes such as limiting salt intake. The advantage of well-tolerated medicines in simple fixed-dose formulations to facilitate blood pressure control is evident in several clinical trials.¹²

Options for targeting renin-angiotensin blockade

Another important point brought out in the Wexler and Feldman review is that patients at risk for cardiovascular disease often benefit from the use of drugs that block the renin-angiotensin system or the sympathetic nervous system as part of an effective blood pressure-lowering regimen.¹³ This is true for patients with a history of heart failure, coronary artery disease, or stroke. Personally, I feel that each patient needs careful and cautious individualization in this regard. I am struck by the consistency of data showing that targeting the renin-angiotensin system as part of a successful blood pressure-lowering regimen provides incremental benefit for reducing the risk of cardiovascular events. These agents should be dosed in the top range approved for controlling blood pressure, as most clinical trials indicate that the higher dosing range is often associated with the greatest cardiovascular risk reduction.¹⁴

Another question is how best to facilitate blood-pressure lowering in patients taking a renin-angiotensin system blocker. As I examine the literature, it is evident that thiazide diuretics or calcium channel blockers provide the most robust means for enhancing blood pressure reduction in conjunction with a renin-angiotensin system blocker because of their complementary mechanisms of action. For example, thiazide diuretics lower blood pressure by reducing volume, which may activate the renin-angiotensin system as a compensatory mechanism and in turn raise blood pressure; a renin-angiotensin system blocker counteracts this effect and provides additive blood pressure control.¹⁵ Which combinations are associated with the greatest opportunity to reduce cardiovascular events is unknown, but fortunately the subject of ongoing clinical trials. In the meantime, it is fair to say that these 2 classes of drugs should be considered as important adjuncts to renin-angiotensin system blockade as part of an overall blood pressure-lowering strategy. The efficacy and tolerability of such combinations are well established.

Future efforts

The real focus for the future, therefore, may be identifying the optimal regimen-based pharmacotherapy for reducing the likelihood of cardiovascular events. Based on examination of the clinical literature and my quarter-century of experience in clinical practice, I advocate an individualized approach to choosing not only appropriate blood pressure goals for individual patients, but also making careful and well-planned decisions about an optimal medical regimen. This takes into account how much blood pressure reduction is required and, of course, concomitant cardiovascular conditions. The majority of patients who have or are at risk for cardiovascular disease will need therapy that targets the renin-angiotensin system as part of a successful blood pressure-lowering regimen. Optimally, a robust fixed-dose combination therapy approach should be considered. The more effective and simpler the

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Blood pressure goals for patients should be based on individual cardiovascular risks, not on hitting a particular threshold

regimen, the more likely the patient is to stay on treatment.

Future clinical efforts should be dedicated to improving education and overcoming therapeutic inertia among both healthcare providers and patients alike. Improving adherence to any hypertensive regimen is crucial over the long term in order to achieve the lower blood pressure goals that are consistently associated with lessened risk for cardiovascular events.

I salute Drs Wexler and Feldman for their well-organized review, but at the same time this perspective needs to be broadened to consider regimen-based approaches to achieving appropriate blood pressure goals for individual patients.

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The authors respond:

We are in agreement with Dr Weir that it is incumbent upon physicians to overcome the “therapeutic inertia” so prevalent in the treatment of hypertension.¹¹ We further agree that in the ideal setting, individualization of patient treatment would be preferred. Guidelines (such as JNC-7³) should be utilized as a mechanism to support the clinician’s thought process when attempting to determine the correct medical therapy for each patient, not supplant it.

Our primary objective of this review was risk attenuation. In our opinion, a clinician should take into account the specifics of each patient in developing a health care plan that best suits that patient. As such, there should be only a limited number of discrepancies between an individualized care-plan and “the guidelines.” As Dr Weir pointed out, risk reduction is graduated and we seek to maximize medical therapy for each patient. However, given the poor state of blood pressure control in the United States, we have previously opined that clinicians must first recognize the importance of blood pressure control and that it may require aggressive medical therapy with multiple medica-

tions, before it is possible to implement treatment on an individual basis.¹

In 2002, 89.7% of all patients screened or treated for hypertension were evaluated in a primary care office.¹⁶ In a national survey of primary care physicians, 41% were not familiar with or had not heard of the JNC recommendations.¹⁷ Before we can expect patient individualization, we must first improve physician understanding of the disease itself. Once clinicians have begun to close the gap on the number of untreated or undertreated patients, we can move to the next level of an individualized care plan.

Therefore, in the year 2006, while recognizing they are less than perfect we still support the recommendations promulgated by JNC-7.³ Although not individualized, sometimes artificial “goals” may not be a bad surrogate of the future ideal. The theory that there is a gradation of risk attenuation supports the notion that some medical therapy may be better than none at all. The JNC-7 guidelines are unlikely to be deleterious to any patient, and may help with drug selection, provide gross generalities for blood pressure management, or prompt a clinician to refer a patient to a specialist if they are uncomfortable with an inability to reach “the goal.” Best individualized therapy or a “guideline” is the difference between healthcare policy versus the best patient care. Phrased in colloquial terms: what is best for the nation vs what is best for your specific patient. Neither is incorrect; but 2 different perspectives of the same issue that should complement one another.

Considering the continued poor control of hypertension in the United States, we believe that focusing on blood pressure goals will provide the greatest impact on morbidity and mortality in the near term. In the long term, we concur with Dr Weir that individualization of therapy is the ultimate goal.

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Before we can expect to individualize treatments, we must first improve physician understanding of the disease itself

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