

Yet more hypertension guidelines: what do they add?

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There is certainly no shortage of well-meaning advice for clinicians treating hypertension. Already this year three major organizations have published guidelines: The International Society of Hypertension in Blacks (ISHIB) [1], the Joint National Committee on the Prevention, Detection and Treatment of High Blood Pressure (JNC 7) [2], and the European Society of Hypertension/European Society of Cardiology (ESH/ESC) [3].

Now, in this issue of the *Journal of Hypertension*, two other organizations have joined the fray: the World Health Organization/International Society of Hypertension (WHO/ISH) [4], and the International Forum for Hypertension control and prevention in Africa (IFHA) [5]. This latter set of recommendations, which focuses on sub-Saharan Africa, clearly serves a unique ethnic and economic constituency and appears to be very relevant. But first, it is worth examining the WHO/ISH document and determining what new contributions it might offer.

Who will the WHO/ISH guidelines serve?

The writers of these guidelines are quick to offer a reason for their effort. Based on a WHO survey in 167 countries [6], over one-half of the countries lacked any formal hypertension guidelines and a large proportion of healthcare professionals were not adequately trained to treat hypertension. In addition, drugs for treating hypertension were not affordable in about one-quarter of all countries, and in some areas drugs and necessary clinical facilities were not available at all.

In view of this daunting challenge, it is not easy to fully understand the thrust of the WHO/ISH guidelines. Instead of focusing primarily on ideas and recommendations that could be helpful for those large parts of the

world that are severely lacking in hypertension care, this document seems to substantially overlap the JNC [2] and ESH [3] recommendations that are aimed primarily at North America and Europe. What is also remarkable about the WHO/ISH guidelines is that, despite their commonality with the JNC, the ESH and other recent major reports, they do not really acknowledge or even reference these other guidelines.

Figuring risk

Hypertension rarely exists as a solitary abnormality. More typically it is part of a syndrome of metabolic and cardiovascular abnormalities that appear to follow familial patterns [7]. Because such common concomitant conditions as dyslipidemias or glucose intolerance exaggerate the likelihood of cardiovascular events in hypertensive patients, it makes sense to evaluate overall cardiovascular risk in deciding how aggressively to manage high blood pressure. Interestingly, however, there is not full agreement on this approach. The ESH/ESC [3] guidelines endorse the concept of risk stratification; in contrast, the JNC [2] guidelines have largely abandoned this approach and base their treatment recommendations primarily on blood pressure levels.

The WHO/ISH guidelines [4] basically follow the ESH/ESC [3] strategy and call for fairly comprehensive risk factor assessment. Although this certainly reflects good medical practice, it is still rather surprising that they did not choose to follow the more simple and less expensive JNC strategy. For the many patients in those parts of the world where every penny counts, the WHO/ISH authors might have provided a better service had they devised a more bare-bones alternative.

Selecting blood pressure targets

Most recent guidelines have agreed on a two-level approach to setting treatment goals. For most hypertensive patients, blood pressure should be reduced (by lifestyle modifications, drugs, or both) to < 140/90 mmHg. For patients who have diabetes or evidence for kidney disease, the target should be < 130/80 mmHg.

To its credit, the WHO/ISH writing group has gently but provocatively questioned the 140/90 mmHg suggestion. They point out that these "... recommendations are not based on robust clinical data". They also point out that at least one major hypertension outcomes study [8] found little benefit in reducing systolic blood pressure below 150 mmHg. Accordingly, the WHO/ISH guidelines suggest that, in situations where resources are limited, using this higher target level of 150 mmHg is an acceptable fallback position. They go even one step further and suggest that when antihypertensive drugs are scarce or unaffordable it might be reasonable to delay treatment in patients with stage 1 hypertension (140–159/90–99 mmHg) unless other risk factors, if known, dictate otherwise. This praiseworthy approach is virtually identical to that recommended by the ESH/ESC [3], which was also sensitive to situations of limited resources.

The issue of lifestyle changes

There is little doubt that appropriate lifestyle modifications can help reduce blood pressure. Weight loss, exercise [9], reduction of alcohol consumption [10] and the use of diets with reduced sodium content and augmented with fresh fruit and vegetables [11] have all been shown to be effective. In poverty-stricken societies these strategies, however, are not always relevant; and the dietary approaches may not even be affordable. In practice, these measures (which also have been advocated and described in detail in the JNC [2] and ESH/ESC [3] guidelines) are chiefly of value in more prosperous communities, but even there their success (away from the structure of organized clinical trials) is debatable. Perhaps the one recommendation of the WHO/ISH guidelines that might be most helpful in poorer areas concerns trying to influence the policies of governmental agencies and food manufacturers in the hope of reducing sodium consumption across these communities.

Choosing the first drug

In some ways the WHO/ISH approach to this issue acknowledges the tough decisions that are required in poor communities. In such settings, the unfortunate fact is that the first antihypertensive drug is often the only one. In settings where cost is the over-riding concern, the WHO/ISH recommendation that low-dose thiazides be the first drug is not unreasonable. Certainly this would be good advice for most African countries

since diuretics are known to have strong blood pressure-lowering efficacy in black hypertensive patients [12] and so could be expected to provide protection against cardiovascular endpoints. Elderly patients also respond quite well to diuretics [12,13], again providing a useful opportunity to prescribe these inexpensive agents.

Unfortunately, instead of limiting themselves to this persuasive argument, the WHO/ISH group has got into less supportable recommendations. A large part of their report has thoughtfully reviewed the strengths and weaknesses of a number of recent clinical trials in hypertension that have measured the effects of the various antihypertensive drug classes on major clinical outcomes. But, having reached the not unreasonable conclusion that blood pressure reduction itself is a major factor in providing protection against events, they then acknowledge the heterogeneity of responses to the different drug classes. They note, for example, that diuretics or calcium channel blockers are particularly effective in black patients and the elderly [14], although (unaccountably, and at risk of compromising their argument) they fail to point out the converse; specifically, that such drugs as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers may be more efficacious in non-black patients.

The recommendation by WHO/ISH that low-dose thiazides be the universal drugs of choice for first-line therapy in all patients (unless compelling indications require alternatives) is unfortunate. By taking this stand they dilute the value of a recommendation that could be of substantial value in the large numbers of patients for whom diuretics, in fact, are an effective and affordable choice. Indeed, this recommendation underscores the challenge (perhaps even the impossibility) of having a single set of guidelines to advise the entire globe.

More about treatment

One of the innovative recommendations made earlier this year by the ISHIB [1], JNC 7 [2] and ESH/ESC [3] guidelines was that combination drug therapy could be used right from the beginning in patients whose pre-treatment blood pressures were substantially elevated (typically, stage 2 hypertension) or where target organ damage or other risk factors demand a more aggressive approach. This strategy should not only have the effect of enhancing efficacy, but should also help patients reach blood pressure goals more rapidly and with fewer visits to the clinician. On the face of it, this approach would be particularly desirable in communities that lack adequate numbers of healthcare professionals.

The WHO/ISH guidelines do not specifically make that recommendation, although they do acknowledge that more than one drug is often required for adequate control. While not recommending combinations for first-line treatment, the guidelines discuss the compliance and efficacy benefits of fixed dose drug combinations, particularly when they can be obtained inexpensively. Since the availability and cost of these products varies so greatly around the world, such generalized comments may not be particularly helpful. It might have been more useful to evaluate the circumstances in regions where the needs for these combination products are greatest and to make more specific recommendations about optimal strategies.

For many patients, of course, this situation becomes even more complex because concomitant medical conditions will often impact the selection of antihypertensive drugs. These so-called compelling indications include such conditions as heart failure, ischemic heart disease, history of stroke, renal involvement and diabetes. The WHO/ISH document describes these issues and the relevant drug choices quite thoroughly with recommendations similar to those made in the guidelines already published [2,3]. But, the WHO/ISH authors, recognizing that their real audience may have limited flexibility in adopting these recommendations, quickly focus on cost-effectiveness.

Cost-effectiveness of treatment

Therapeutic decisions based on this concept are most valid if it is possible to vary both the cost and the expectations of treatment. Unfortunately, for many hypertensive patients living under conditions of poverty, there is no flexibility in choosing therapy: they must use what is available and affordable. Important factors like compelling indications, side effects and even efficacy cannot always alter the hard realities of what can be done. Admirably, the WHO/ISH document does not shirk these realities and goes so far as to make the argument that thoughtful drug selection, even when the cost at first may seem painfully high, still makes economic sense when compared with the expense of hospitalizations or other major interventions for the serious consequences of inadequate management. For those parts of the world with good or acceptable healthcare systems, this thinking is self-evident; for others, it still remains a luxury.

In considering hypertension treatment in settings of highly limited resources, the WHO/ISH authors again have not ducked some of the unpleasant truths about hypertension treatment. They acknowledge, for example, that within 1 year of starting treatment only about one-half of all patients will still be taking their medica-

tions [15]. It is unfortunate that the diuretics, which are recommended widely in poorer communities because of their inexpensiveness, are the drugs least likely to achieve persistency among patients [16]. It would be easy to say that patients should be given every possible means of education, support and encouragement to comply with their treatment regimens, but individuals trained to provide this type of support are often a scarce commodity.

Sub-Saharan Africa

The guidelines for treating hypertension in sub-Saharan Africa [5] represent a welcome effort to devise effective and affordable strategies in an area that often has limited health care resources. Indeed, it is sobering to confront some of the facts of life pointed out in the document: for example, some countries in the region only put a total of \$10 annually into the health care of each citizen. Routine tests like electrocardiograms, which are taken for granted in other parts of the world, simply are not available to many people in this region; and the use of such simple devices as electronic blood pressure monitors is limited by the unaffordability of batteries. The authors of these guidelines have not been daunted, however, and have published a broad set of recommendations. And, unlike the WHO/ISH publication, they note the existence of the JNC 7 [2] and ESH/ESC [3] guidelines and, in fact, borrow some key recommendations from them.

A community approach

It is clear that issues and hypertension management in sub-Saharan Africa is different from other parts of the world. One important fact is that coronary heart disease is less prevalent than elsewhere, but that outcomes like stroke, heart failure and renal failure are particularly common. Given the local circumstances, the guidelines cannot focus only on strategies for the care of individuals, but must take into account public policies. Primordial prevention depends on plans to enhance healthy behavior through education programs. This, of course, depends on the commitment of government agencies and other concerned organizations in Africa to provide advocacy and resources to create environments in which broad preventive and early intervention strategies have a chance to be successful. Even the fairly small reductions of blood pressure that can be produced by appropriate lifestyle modifications, including diet and exercise plans, can have an important clinical and economic impact in preventing hypertension. It is noteworthy that these guidelines are forceful in addressing themselves to these public health issues.

Traditional recommendations

Many of the recommendations follow those that have been part of the established guidelines [2,3]. It is

interesting, and just a little surprising, that the classification for blood pressure proposed by JNC 7 has been adopted. In particular, the concept of “pre-hypertension”, defined as blood pressures in the range 120–139/80–89 mmHg, is listed as a clinical entity. From a public health point of view, of course, making lifestyle suggestions for people in this range makes a great deal of sense. But to make such a diagnosis in an individual patient, which even in more affluent parts of the world is regarded as being of somewhat questionable value [3,17], seems rather ambitious when health care is so tightly constrained.

The writers of these sub-Saharan Africa guidelines faced a dilemma when deciding what to recommend for risk stratification in hypertensive patients. In settings where standard evaluations like blood tests, electrocardiograms and fundoscopies are not always available, there will be limitations on how to quantify total risk. It would have been perfectly justifiable whether these new guidelines had abandoned the more rigorous ESH/ESC [3] approach and instead used the new JNC 7 [2] strategy of basing decisions primarily on blood pressure itself. Like the other guidelines, the sub-Saharan Africa group endorses lifestyle modification, to the extent that they can be followed under difficult economic circumstances, and also uses the concept of compelling indications for drug selection. Again, while strongly desirable, this may not always be possible.

Practical treatment strategies

Unlike much of the material in the sub-Saharan Africa paper that is borrowed or modified from other guidelines, the figure detailing overall management strategy is a pragmatic attempt to find a useful compromise in setting blood pressure goals and appropriately uses logic similar to that in the ESH/ESC and WHO/ISH reports. For hypertensive patients regarded as having ‘low’ risk (presumably without other major risks factors), a period of 6–12 months of lifestyle strategies and monitoring is proposed before drug therapy is started. And, even then, drug therapy would only be started if blood pressure is at least 150/95 mmHg. Patients with ‘medium’ risk would get drug therapy if blood pressures exceed 140/90 mmHg, but even for these patients an initial 3–6 month delay is recommended to determine whether lifestyle changes can make a difference and obviate drug therapy.

Not surprisingly, the recommendation for initial drug therapy of hypertension is to use a thiazide diuretic. It is a very reasonable assumption that these agents will be efficacious in reducing blood pressure in African hypertension patients. There is one apparent inconsistency: having suggested that patients with compelling indications (if possible) get drugs appropriate to

their needs, they then recommend that all others—including diabetics—start treatment with a thiazide. In a setting where ACE inhibitors or angiotensin receptor blockers are not available or affordable, this strategy may be acceptable. But it would be desirable, if possible, to regard diabetes as a compelling indication and to treat it appropriately, even while recognizing that in most diabetics a diuretic will be added in any case to the primary drug (usually an angiotensin receptor blocker or ACE inhibitor) to achieve optimal blood pressure control. Now that some of the ACE inhibitors are generic it should be possible to make them available at reasonably affordable prices to those patients who need them. Overall, however, these African guidelines provide much useful advice for their region.

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