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Letters to the Editor

Are There Gaps in the Evidence on the Treatment of Mild Hypertension in Patients With Low Cardiovascular Risk?

¿Existen lagunas en la evidencia vinculada al tratamiento de la hipertensión leve de bajo riesgo cardiovascular?

To the Editor,

I read with great interest the articles on the new European guidelines for the management of arterial hypertension.[1,2] One of the changes with respect to the previous guidelines is that the recommendation to start drug treatment in patients with grade 1 hypertension (140-159/90-99 mmHg) and low to moderate cardiovascular (CV) risk after a reasonable period of lifestyle measures has been upgraded from a class IIa level B recommendation to a class I level A recommendation.[1,2] This change would appear to indicate that there is ample evidence from randomized controlled trials (RCTs) or meta-analyses to support this recommendation and that the medical community agrees that antihypertensive drug treatment is beneficial, useful, and effective in this setting.[1]

Drug therapy for grade 1 hypertension in patients with a low CV risk profile is one of the most controversial topics in the area of cardiovascular prevention.[3] The aim of this article was to briefly address the question of whether there are still gaps in the evidence on the treatment of mild hypertension in this subgroup of patients.[4]

Apart from the general biases associated with RCTs,[3] studies analyzing low CV risk and mild hypertension typically use different definitions of what constitutes low risk.[3] If we consider the CV risk categories established in the European hypertension guidelines,[1] then representative studies of low CV risk should include individuals with a less than 1% risk of a fatal cardiovascular event over a 10-year period.[1] Likewise, studies of moderate and high CV risk should include samples with a 10-year risk of $\geq$ 1% to $<$ 5% and $\geq$ 5% to $<$ 10%, respectively. One of the criticisms of using CV mortality as a marker of CV risk is that the relationship of major CV events to CV mortality varies with risk and age.[3] This bias, however, is minimized in studies of patients with a mean age younger than 60 years and a 10-year CV mortality risk of less than 1%. Because age has such a strong influence in the CV risk continuum,[3] several prediction models automatically classify mildly hypertensive men aged 55 years or older and women aged 60 years or older in at least the moderate CV risk category, even in the absence of concomitant risk factors.[3] This would appear to particularly apply to regions with a higher-risk population for CV disease.

Under the above premises, let us now consider the 3 meta-analyses and the RCT forming the basis of the new evidence level for the recommendation to treat grade I hypertension in patients with low CV risk.[1] Mean patient age was 63.5 years in the meta-analysis by Sunstrom et al.[5] and 63.0 in that by Brunstrom et al.[6] and the respective 10-year CV mortality risks were 6.2% and 8.5%. Tomopoulos et al.,[7] by contrast, reported a 10-year mortality risk of 4.5%.

In the HOPE-3 (Heart Outcomes Prevention Evaluation) trial, the patients had a mean age of 65.7 years and a 10-year CV mortality risk of 4.8%.[8]

Despite the scant evidence on how to manage grade 1 hypertension in patients with low CV risk,[1–3] the European guidelines also recommend antihypertensive treatment in this population[1] due to the linear relationship observed between blood pressure and CV events in several cohort studies with a B level of evidence.[1–3]

Finally, there are 4 additional issues that need highlighting: *a*) treatment of mild hypertension in patients with low CV risk should be individualized, as these patients are not a homogeneous group; *b*) delayed initiation of drug treatment can put patients at risk because of poor adherence and obstacles impeding the implementation of healthy lifestyle changes and because of the increased risk of a CV event occurring during this period[3]; *c*) the recommendation to allow a reasonable period for the implementation of lifestyle measures is not supported by direct evidence from RCTs or meta-analyses[3]; and *d*) studies of hypertension in patients with low CV risk should exclude hypertensive patients with asymptomatic organ damage, diabetes mellitus, markedly elevated risk factors, and established CV or renal disease.[1] These patients have not been excluded in any of the studied performed to date.

In conclusion, it would appear that there are still gaps in the evidence on the treatment of mild hypertension in patients with low CV risk. The recommendation to start antihypertensive drug treatment in these patients is a class B recommendation. Cardiovascular mortality and age are useful variables for identifying suitable studies of mildly hypertensive patients with low CV risk.

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Are There Gaps in the Evidence on the Treatment of Mild Hypertension in Patients With Low Cardiovascular Risk? Response

¿Existen lagunas en la evidencia vinculada al tratamiento de la hipertensión leve de bajo riesgo cardiovascular? Respuesta

To the Editor,

We thank Alberto Morales-Salinas for his interest in our article[1] on the new European guidelines for hypertension.[2] We fully agree that the scientific evidence on most of the aspects concerning grade 1 hypertension and low cardiovascular risk is scarce and that this situation will probably continue because prospective placebo-controlled studies are unlikely to be performed to evaluate the effects of treatment on mid- and long-term morbidity and mortality in this type of patient. This lack of evidence affects and will continue to affect both lifestyle-related interventions and antihypertensive drug therapy. Thus, we have no other option but to continue basing our therapeutic decisions on the limited evidence available and to apply it on an individualized basis to our patients according to their clinical characteristics, a fact mentioned by Morales-Salinas and emphasized by the European guidelines.

In these times of precision, personalized, and preventive medicine, treatment initiation at early stages of the hypertensive process is the most logical approach, given that an intervention delay permits progression of hypertension and is associated with residual risk after blood pressure normalization. For patients with grade 1 hypertension and low cardiovascular risk, the recommended strategy is to lower blood pressure through lifestyle changes for a period of up to 6 months. This approach is advised because these patients' values are very close to normal, although more than half are overweight and have a sedentary lifestyle, and because modest weight loss via a better diet and regular physical exercise can normalize blood pressure. Nonetheless, the intervention must also be personalized according to the socioeconomic characteristics of the population.

The European guidelines aim to be a general rule based on the best available evidence from controlled clinical trials and their meta-analyses. Because the patients included in these studies are often dissimilar to those seen in the clinic, we should individualize the guidelines by weighing up the pros and cons of our decisions with the patient. However, the responsibility for clinical decisions always lies with the physician treating the patient.

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