Resistant Hypertension. What Is the Best Approach?

To the Editor:

Recently, Rodilla et al[1] published a study on the use of spironolactone versus doxazosin in patients with refractory arterial hypertension. To this end, the authors carried out a retrospective comparative study of 181 patients with resistant arterial hypertension to whom they administered spironolactone or doxazosin. The results of the study showed that blood pressure (BP) fell by 28/12 mm Hg in those treated with spironolactone, compared with 16/7 mm Hg with doxazosin; the drop was significantly larger with spironolactone. Thirty-nine percent of the patients who were treated with spironolactone and 23% of those treated with doxazosin (P=.02) reached their BP control goals. In the logistic regression analysis, diabetes was a predictor of poor BP control.

Resistant arterial hypertension is more prevalent than is believed. It is frequently under-diagnosed, and as a result, it is not always treated properly. Although the question of what is the best drug to use in each clinical situation has been the subject of many debates, given that the majority of hypertensive patients need at least 2 anti-hypertension drugs to reach their BP goals, this debate is probably irrelevant at present. Indeed, when we analyse the mean number of anti-hypertensive drugs used in clinical studies, we find that that number is about 3, and furthermore, most studies fail to reach the desired arterial pressure results.[2] Consequently, the question is not, perhaps, what anti-hypertensive drug to use, but rather, what are the best combinations for each patient; and if the BP continues to be high, what drug or drugs should be added.

Despite not being a randomised clinical trial, given the lack of sufficient data regarding how patients with refractory arterial hypertension should be treated,[3] Rodilla et al's results shed some light on the subject. However, we must take some considerations into account. Firstly, except for mentioning the presence of diabetes and metabolic syndrome, the authors reveal no data regarding the prevalence of ischaemic cardiopathy or heart failure, to name a pair of relevant diseases in which arterial hypertension has a significant role. Thus, the use of spironolactone has been associated with better prognosis in patients with heart failure,[4] while it has been pointed out that treatment with doxazosin has been related with a higher incidence of heart failure, although it seems that this is not the case when it is used in conjunction with a renin-angiotensin system inhibitor and a diuretic.[5] It is also possible that the addition of doxazosin to a renin-angiotensin inhibitor is associated with beneficial effects in diabetic patients.[6] Although BP decreases observed in the study by Rodilla et al are significant, somewhat more pronounced than with spironolactone, which in theory should point to a better prognosis, it would be interesting to know if this effect is accompanied by a parallel decrease in cardiovascular morbidity and mortality. We should not forget the results of the ONTARGET[7] and TRANSCEND[8] studies, in which despite the fact that all patients presented a high cardiovascular risk and about 69% in the ONTARGET study and 76% in the TRANSCEND study were hypertensive, a pronounced decrease in BP was not associated with the expected clinical benefits.

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Response

To the Editor:

The comments raised by Barrios et al are interesting and reveal the importance of treating uncontrolled arterial hypertension and refractory arterial hypertension (RAH). With respect to the population under study, 25 (14%) of the 181 patients had a history of stable ischaemic cardiopathy (in all cases the ischaemic event had taken place more than 6 months previously); 12 were in the group receiving spironolactone (14%), and 13 were receiving doxazosin (14%) (differences are not significant). This history of ischaemic cardiopathy was not included in later multiple regression analysis. Patients with a history of heart failure had been excluded from the analysis according to the "c" criterion (suffering from a systemic disease that could interfere in the evaluation of the evolving changes in arterial pressure), since the evaluation of the change in arterial pressure was the most measureable parameter in the study. It must be emphasised that, out of a potential population of 687 patients with poorly controlled RAH, we only analysed the response of 181 patients (26%) in the end.[1]

The results of the ONTARGET and TRANSCEND studies have been very important for clinical practice, but as Barrios et al correctly point out, not all of the patients were hypertensive and the mean value for clinical arterial pressure at the beginning of the study, before receiving telmisartan or ramipril, was 141/82 mm Hg. We will have to wait for the definitive analysis and the publication of the cardiovascular complications relating to changes in arterial pressure in order to really know how much they were decreased in these studies. It is possible that the drop in arterial pressure was very beneficial in patients with uncontrolled high arterial pressure, and that the most significant side effects presented in patients with normal or low arterial pressure, given that all of them were treated equally (controlling arterial pressure was not the primary goal in these studies).

It is evident that a randomised clinical trial is the only method for evaluating the effectiveness of 2 treatment alternatives; however, the lack of conclusive evidence and the difficulty of carrying out this type of study are well-known in the case of RAH.[2] Furthermore, patients with RAH frequently suffer from side effects that oblige them to change treatments,[3] which also makes such an evaluation more difficult. While we gather more evidence, reducing arterial pressure, regardless of the method that is used, will probably be the best treatment for preventing complications, for which reason evaluating data such as that in our study can be useful in clinical practice.

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