Degree of Anticoagulation Control in Patients With Atrial Fibrillation in Spain: Need to Minimize Biases and Contextualize Results

Grado de control de la anticoagulación en pacientes con fibrilación auricular en España: necesidad de minimizar sesgos y contextualizar resultados

To the Editor,

We have read with interest the PAULA,[1] ANFAGAL,[2] and CALIFA[3] studies, published in *Revista Española de Cardiología*, on the degree of control of oral anticoagulant therapy in patients with nonvalvular atrial fibrillation. These 3 observational studies have used clinical practice results to advance our understanding of these drugs. We would like to make some clarifications that we believe to be important when reading and interpreting the results and therefore the conclusions.

With the exception of the ANFAGAL study,[2] the studies show a risk of sample selection bias due to the selection of the researchers (freely) and the patients (consecutive). In our view, random sampling is feasible, even that of patients, by taking advantage of the availability in the Spanish health care system of the database of medications financed by the system. It is also surprising that the primary endpoint, the time in therapeutic range, has been calculated in the PAULA study,[1] in contrast to the other 2 studies,[2,3] by including unstable international normalized ratio (INR) results, instead of the maintenance period established by the current recommendations,[4] which may pose a risk of information bias.

The results obtained show that the percentages of time in therapeutic range (69.0%[1] and 63.8%[3]) were similar to (or even better than) those found in other countries, such as Germany (68.1%)[5] and the United Kingdom (63.1%).[6] In the CHRONOS-TAO study,[7] the results were also calculated according to an "adjusted range" INR of 1.8 to 3.2, explained by the possible margin of error of the coagulometer (± 0.2). Thus, the percentage of patients with "good control" varied between 83.5% and 94.1%, according to the cutoff of the time in therapeutic range. We believe that the results could also have been obtained using this adjusted range, because small deviations from the therapeutic range (2-3) do not warrant treatment modification in clinical practice.

Regarding factors associated with suboptimal control, the PAULA study[1] raised the possibility of a priori identification of those patients who will have suboptimal control with vitamin K antagonists, so that they can be treated with direct oral anticoagulants. First, some causes of "poor control" can be minimized by specific interventions (eg, improvements in dietary habits, professional training, development of computerized records, self-monitoring). Second, some important confounders were not controlled, such as therapeutic adherence, an especially relevant factor because Spanish guidelines specify that adequate therapeutic adherence must be verified before switching from a vitamin K antagonist to direct oral anticoagulants.[4] Another important factor is the geographical area. Indeed, the ANFAGAL study[2] found statistically significant differences in the time in therapeutic range according to the health care area. Finally, each study identified distinct factors associated with suboptimal control. This variability, together with the discrepancies found in the literature, as described by the CALIFA study,[3] undermine the reliability of the results.

Therefore, we consider that caution is required when interpreting the results obtained on the degree of control of oral anticoagulation in Spain and the factors related to suboptimal control. We also believe that subjective descriptions such as "patients with poor control" should be avoided, or that their meaning should at least be qualified, as such descriptors could be excessive.

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