SAMe-TT_2R_2 Score: Useful in All Patients With Nonvalvular Atrial Fibrillation? Response

Puntuación SAMe-TT_2R_2: ¿es útil en todos los pacientes con fibrilación auricular no valvular? Respuesta

To the Editor,

We appreciate the comments of Escobar et al[1] regarding our article.[1] The introduction of alternatives to vitamin K antagonists (VKA) has demonstrated the importance of the early identification of patients who are most likely to exhibit poor International Normalized Ratio (INR) control.

The SAMe-TT_2R_2 score has been proposed as a predictor of poor anticoagulation control.[2] Although it has been validated in a number of populations of patients with atrial fibrillation, this score could still be improved, as the *C*-statistic reported in these studies is low (0.55-0.6).[3] Moreover, our results indicate that it is less useful in patients in unstable situations, such as recent decompensated heart failure.[1]

Factors such as a history of bleeding, multidrug therapy, and eating habits appear to show promise in terms of improving the predictive capacity of new scores that will better distinguish those patients who are less suitable to receive VKA.[3] Other factors—such as abuse of alcohol or other drugs, chronic kidney disease, cancer, mental disorders,[4] and even the experience of the physician adjusting the VKA dose—have also been shown to be capable of predicting an inadequate percentage of time in therapeutic range.[5]

However, although new scoring systems will probably enhance our capacity to predict poor INR control, they should not involve a degree of complexity that would limit their use in routine clinical practice, unless they offer a significant improvement.

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About Bradycardia and Secondary Heart Failure Induced by Ivabradine in a Patient With HIV

A propósito de bradicardia e insuficiencia cardiaca secundaria a ivabradina en paciente con VIH

To the Editor,

We read with great interest the article on bradycardia in a human immunodeficiency virus (HIV) patient treated with ivabradine, published by Romero-León et al[1] in *Revista Española de Cardiología*. As the authors propose, there seems to be an obvious need to integrate our knowledge about the interactions associated with drugs used in cardiology with those administered in other diseases. That said, we wish to stress several important points.

- The patient also took carvedilol, which she tolerated well. What would have happened without the combined effect of ivabradine is unknown.
- According to the directions for use, ivabradine is expressly contraindicated when inhibitors of cytochrome P450 3A4 (CYP3A4), the cytochrome that metabolizes this agent, are employed. In general, ritonavir and, to a lesser extent, atazanavir are important CYP3A4 inhibitors. However, there are genetic polymorphisms[2] that result in the development of numerous variants and responses, ranging from subclinical to manifest, such as that reported here.
- Presently, pharmacogenetic aspects[3] are not usually considered prior to using a treatment. However, it may be an option to take into account in the future, considering the *a priori* complexity of patients such as the woman described by Romero-León et al. An example that should serve is that the United States Food and Drug Administration (FDA) has included this information in the directions for use of these drugs since 2007.
- Something comparable occurs with eplerenone which, in addition, would increase the risk of hyperkalemia,[4] in light of its effects and the fact that the patient was also being treated with angiotensin-converting enzyme inhibitors. This could also interfere with cardiac impulse generation and conduction in cases similar to that described.
- Given that emtricitabine and tenofovir are excreted mainly by the kidneys, their coadministration with medications that reduce renal function or compete for active tubular secretion (aspirin in this case) is contraindicated.

For the above reasons, this case is highly interesting, not only because of the clinically relevant interaction of the aforementioned antiretroviral agents with ivabradine and eplerenone (in both cases, due to CYP3A4 inhibition), but also because of the adjuvant role with carvedilol and, indirectly, with aspirin (due to competition for active tubular secretion). With respect to statin therapy, not administered in this patient, but often necessary in heart