

SAME-TT₂R₂ Score: Useful in All Patients With Nonvalvular Atrial Fibrillation? Response



Puntuación SAME-TT₂R₂: ¿es útil en todos los pacientes con fibrilación auricular no valvular? Respuesta

To the Editor,

We appreciate the comments of Escobar et al¹ 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-TT₂R₂ 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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REFERENCES

- Andreu-Cayuelas JM, Puche CM, Caro-Martínez C, Flores-Blanco PJ, Valdés M, Manzano-Fernández S. La puntuación SAME-TT₂R₂ no predice el tiempo en rango terapéutico tras un ingreso por insuficiencia cardíaca aguda en pacientes con fibrilación auricular. *Rev Esp Cardiol*. 2016;69:453–4.
- Apostolakis S, Sullivan RM, Olshansky B, Lip GY. Factors affecting quality of anticoagulation control amongst atrial fibrillation patients on warfarin: the SAME-TT₂R₂ score. *Chest*. 2013;144:1555–63.
- Lobos-Bejarano JM, Barrios-Alonso V, Polo-García J, Escobar-Cervantes C, Vargas-Ortega D, Marín-Montañés N, et al. Evaluation of SAME-TT₂R₂ score and other clinical factors influencing the quality of anticoagulation therapy in non-valvular atrial fibrillation: a nationwide study in Spain. *Curr Med Res Opin*. 2016. Available at: <http://dx.doi.org/10.1185/03007995.2016.1164676> [Epub ahead of print].
- Rose AJ, Hylek EM, Ozonoff A, Ash AS, Reisman JI, Berlowitz DR. Patient characteristics associated with oral anticoagulation control: results of the Veterans Affairs Study to Improve Anticoagulation (VARIA). *J Thromb Haemost*. 2010;8:2182–91.
- Dlott JS, George RA, Huang X, Odeh M, Kaufman HW, Ansell J, et al. National assessment of warfarin anticoagulation therapy for stroke prevention in atrial fibrillation. *Circulation*. 2014;129:1407–14.

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



A propósito de bradicardia e insuficiencia cardíaca 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 al¹ 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 polymorphisms² that result in the development of numerous variants and responses, ranging from subclinical to manifest, such as that reported here.

- Presently, pharmacogenetic aspects³ 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

disease, all of them except for fluvastatin, pitavastatin, and rosuvastatin, interact with anti-HIV drugs (via CYP).

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REFERENCES

1. Romero-León JM, Gálvez-Contreras MC, Díez-García LF. Bradicardia sintomática e insuficiencia cardíaca precipitadas por ivabradina a una paciente que recibe

tratamiento antirretroviral. Rev Esp Cardiol. 2016. <http://dx.doi.org/10.1016/j.rec.2016.02.005>

2. López Aspiroz E, Cabrera Figueroa SE, Iglesias Gómez A, Valverde Merino MP, Domínguez-Gil Hurlé A. CYP3A4 polymorphism and lopinavir toxicity in an HIV-infected pregnant woman. Clin Drug Investig. 2015;35:61–6.
3. Humma LM, Terra SG. Pharmacogenetics and cardiovascular disease: impact on drug response and applications to disease management. Am J Health Syst Pharm. 2002;59:1241–52.
4. Crespo-Leiro MG, Segovia-Cubero J, González-Costello J, Bayes-Genis A, López-Fernández S, Roig E, et al. Adecuación en España a las recomendaciones terapéuticas de la guía de la ESC sobre insuficiencia cardíaca: ESC Heart Failure Long-term Registry. Rev Esp Cardiol. 2015;68:785–93.

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



A propósito de bradicardia e insuficiencia cardíaca secundaria a ivabradina en paciente con VIH. Respuesta

To the Editor,

We thank Morales-Martínez de Tejada for his considerations regarding our letter,¹ and would like to add the following comments. The episode of ivabradine intoxication occurred when the patient was receiving carvedilol, which may have further complicated the situation. The temporal relationship between ivabradine exposure and its discontinuation was clear, and this drug is contraindicated in all patients with human immunodeficiency virus (HIV) infection who are taking protease inhibitors, with or without carvedilol.

As eplerenone is mainly metabolized by CYP3A4,² it should not be administered in combination with potent inhibitors or potent inducers of this enzyme. Our patient had begun to receive the drug 2 years earlier, after an acute myocardial infarction and, as her left ventricular ejection fraction remains low, she continues to take it. In follow-up visits prior to and after the aforementioned episode, she was always found to have normal serum potassium concentrations. Eventually, the decision was made to simplify her antiretroviral therapy and the viral protease inhibitors were discontinued. As Dr. Morales-Martínez de Tejada points out, emtricitabine and tenofovir are mainly eliminated by the kidneys, and caution should be exercised when they are administered together with medications, such as aspirin, which are removed by active tubular secretion. However, the combined use of these drugs is not formally contraindicated.³

Finally, pharmacogenetic studies may have a number of applications in the treatment of cardiovascular diseases and could

provide solutions to these problems. However, we still have much to learn about their usefulness before incorporating them as a regular part of clinical decision-making.⁴ Meanwhile, we should be on the alert for possible interactions among the drugs we prescribe to our patients and study them conscientiously.

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REFERENCES

1. Romero-León JM, Gálvez-Contreras MC, Díez-García LF. Bradicardia sintomática e insuficiencia cardíaca precipitadas por ivabradina a una paciente que recibe tratamiento antirretroviral. Rev Esp Cardiol. 2016;69:529–30.
2. Dhillon S. Eplerenone: a review of its use in patients with chronic systolic heart failure and mild symptoms. Drugs. 2013;73:1451–62.
3. Interactions with NRTIs. [accessed 14 Apr 2016]. Available at: <http://www.hiv-druginteractions.org>.
4. Humma LM, Terra SG. Pharmacogenetics and cardiovascular disease: impact on drug response and applications to disease management. Am J Health Syst Pharm. 2002;59:1241–52.

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Systemic Thrombolysis for High-risk Pulmonary Embolism Versus Percutaneous Transcatheter Treatment



Trombolisis sistémica de la embolia pulmonar de alto riesgo frente al tratamiento percutáneo

To the Editor,

Systemic thrombolysis for primary reperfusion therapy is the treatment of choice for patients with high-risk pulmonary embolism (PE) (ie, those with shock or hypotension). If

thrombolysis is contraindicated or has failed, surgical embolectomy or percutaneous catheter-directed treatment is recommended. However, when systemic thrombolytic therapy is contraindicated, local administration is also contraindicated, in which case transcatheter procedures should be used without local thrombolysis.¹ Sánchez-Recalde et al² presented a series of 8 PE patients treated at their hospital. Seven patients underwent percutaneous treatment, of whom 4 also received local catheter-administered alteplase, although this approach is contraindicated for thrombolysis. According to the recommendations of the clinical guidelines, traumatic brain injury is an absolute contraindication and thus alteplase should not have been used. The