

Correspondence

ACEIs and beta blockers as a risk factor for severe reactions to Hymenoptera venom, facts or fictions?

To the Editor:

The article by Francuzik et al,¹ “Phenotype and risk factors of venom-induced anaphylaxis: a case-control study of the European Anaphylaxis Registry,” recently published in the journal raises the controversial issue that angiotensin-converting enzyme inhibitors (ACEIs) and β -blockers may increase the risk of severe reactions to Hymenoptera venom. Such risk has been initially suggested by Stumpf et al² in 2006 by the results of a number of case reports, but was denied by others.^{3,4} The latest European Academy of Allergy and Clinical Immunology guidelines on venom immunotherapy (VIT) stated that the risk from ACEIs may have been overestimated because of the small populations, and that ACEI therapy may be continued during VIT, informing the patient about possible risk.⁵ Also, the recent document from European and US consensus groups confirmed that “there is minimal risk associated with beta-blockers and angiotensin-converting enzyme inhibitors during VIT.”⁶

Francuzik et al, by analyzing the data from 3612 patients with Hymenoptera venom-induced anaphylaxis, conclude that “Patients receiving beta-blockers or ACEIs had a higher risk of developing severe cardiovascular symptoms (including cardiac arrest).” Moreover, the authors write, “The role of cardiovascular medication cannot be isolated from the effect of concomitant cardiovascular conditions; therefore, we cannot state whether ACEIs and beta-blockers increase the severity of anaphylaxis.” Actually, the first part of the sentence about the effect of concomitant cardiovascular conditions addresses a pivotal aspect. Indeed, this study included cardiovascular disorders regardless of their type, although it is known that even if arterial hypertension and heart diseases are classified as cardiovascular disorders, the kind of disease evolution and the severity of events are different. In particular, in the recent guidelines from the European Society of Cardiology and the European Society of Hypertension, all aspects of arterial hypertension were covered, making clear the criteria to assess severity as well as cardiovascular risk.⁷ In addition, a range of heart diseases are not

associated with hypertension. In times of precision medicine, it is apparent that the conclusion by Francuzik et al about the high risk to develop severe cardiovascular symptoms in venom-allergic patients receiving β -blockers or ACEIs is too generic. It is likely that, because the data have been obtained through the European Anaphylaxis Registry, the authors may be able to clarify precisely for which cardiovascular indications patients were treated with ACEIs or β -blockers, therefore suggesting in which cases it is really necessary to discontinue the therapy. This would be a significant advance in understanding the actual role of ACEIs and β -blockers in severe reactions to Hymenoptera venom.

Cristoforo Incorvaia, MD^a

Stefano Pucci, MD^b

Oreste C. Febo, MD^a

From ^aCardiac/Pulmonary Rehabilitation, ASST Pini-CTO, Milan, and ^bthe Allergy Unit, General Hospital, Civitanova Marche, Italy. E-mail: cristoforo.incorvaia@gmail.com.

Disclosure of potential conflict of interest: C. Incorvaia is a scientific consultant for Stallergenes-Greer. The rest of the authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Francuzik W, Ruëff F, Bauer A, Bilò MB, Cardona V, Christoff G, et al. Phenotype and risk factors of venom-induced anaphylaxis: a case-control study of the European Anaphylaxis Registry [published online ahead of print June 22, 2020]. *J Allergy Clin Immunol*. <https://doi.org/10.1016/j.jaci.2020.06.008>.
2. Stumpf JL, Shehab N, Patel AC. Safety of angiotensin-converting enzyme inhibitors in patients with insect venom allergies. *Ann Pharmacother* 2006;40:699-703.
3. White KM, England RW. Safety of angiotensin-converting enzyme inhibitors while receiving venom immunotherapy. *Ann Allergy Asthma Immunol* 2008;101:426-30.
4. Stoevesandt J, Hain J, Stolze I, Kerston A, Trautmann A. Angiotensin-converting enzyme inhibitors do not impair the safety of Hymenoptera venom immunotherapy build-up phase. *Clin Exp Allergy* 2014;44:747-55.
5. Sturm GJ, Varga EM, Roberts G, Mosbech H, Bilò MB, Akdis CA, et al. EAACI Guidelines on Allergen Immunotherapy: Hymenoptera venom allergy. *Allergy* 2018;73:744-64.
6. Golden DBK. Insect sting allergy: new guidelines from the European and USA consensus groups: algorithms and recommendations. *Curr Opin Allergy Clin Immunol* 2019;19:456-61.
7. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* 2018;39:3021-104.

<https://doi.org/10.1016/j.jaci.2020.09.029>