

Correspondence and Replies

Predictive models in drug allergy: An appropriate patient selection is needed



To the Editor:

We read with great interest the article by Hierro Santurino et al,¹ who proposed a mathematical model to predict the risk of allergic drug reactions using the data collected in the medical history. As they state, this work was performed at the Allergy Service of the University Hospital of Salamanca (Spain). Indeed, it was the dissertation work of the first author² and it was originally designed to describe the adverse reactions evaluated throughout 2010, characterizing patients, reactions, tests, results of the allergy evaluation, and number of visits needed for reaching a diagnosis. Because authors have later used these data for elaborating a predictive model, we are concerned about several possible biases.

From a methodological point of view, we are wondering how the authors obtained the a priori probability formula of a patient having an allergic drug reaction or not. It is remarkable that the variable “sex” has a -0.226 coefficient, independently whether it is a male or a female, whereas other categorical variables receive different values for each category. Another concern resides in the selection of the “simple and most useful model.”¹ The authors discarded variables such as 60 IgE median, emergency department visits, and duration of the episodes for being nonsignificant. But in the final model they include nonsignificant variables such as sex ($P = .49$), number of drugs involved ($P = .385$), and number of doses. In this last variable, the categories “first dose” ($P = .919$) and “several doses” ($P = .103$) were nonsignificant, whereas the only significant category was “unknown number of doses” ($P = .034$), which seems inconsistent with a predictive model. Furthermore, immediate and nonimmediate reactions are considered together, whereas clinical manifestations, mechanisms, and diagnostics methods are very different. In the case of betalactams, different protocols are recommended for immediate and nonimmediate reactions.^{3–5} Authors state that there were 626 active principles but indeed they were 132 because several of them were repeated (most principles were represented 1–3 times).² In addition, in a quarter of cases the diagnosis was presumptive, considerably reducing the sample. However, in the global sample, betalactams accounted for one-third of patients with a positive or a negative diagnosis (although there were only 46 confirmed and 113 ruled-out cases). Thus, the β coefficient for betalactams is very high. To build up a predictive model, an allergic diagnosis or a discarded diagnosis should have been obtained in 100% of the patients and much more cases should have been included. In this sense, we studied the performance of an artificial neuronal network in the classification of patients only with suspected immediate reactions to betalactam allergy.⁶ We evaluated 656 patients (169 with a final diagnosis of allergy), achieving a receiver operating characteristic curve area of 0.939. Finally, the a priori possibility of having an allergic reaction is different for different drugs and it seems that the authors have not considered it. We do believe that predictive mathematical models can be useful, but our opinion is that they should be based

on prospective protocols specifically designed, with accurate diagnosis following practice guidelines.

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Mathematical models are not sufficient for the diagnosis of drug allergy



To the Editor:

In the article published by Hierro et al¹ in the April 2016 issue of the *Journal of Allergy and Clinical Immunology: In Practice*, the authors described a mathematical model that could improve the discriminatory capacity of the medical history in drug hypersensitivity reactions (DHRs). The DHRs are an important health problem affecting many subjects of all ages and are related to a higher use of health care services, particularly in adults in whom the diagnosis is complex.²

Although the quantification of the risk of an allergic drug reaction through the medical history is essential in the clinical decision making, the use of models alone will never be sufficient for confirming the diagnosis of patients with suspicion of DHR. A clinical history recording the temporal association, the identification of the drug/drugs involved, the biological

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