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Title page

Correspondence

Wheat allergy in a pediatric population from the Mediterranean area

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To the Editor,

The research performed by Nilsson *et al.*¹ highlighted the role of not routinely tested molecules (HMW and LMW glutenins) in addition to omega-5 gliadin in the diagnosis of wheat allergy (WA) in a population of children from the North of Europe (Sweden). Nevertheless omega-5 gliadin showed the best diagnostic performance in the outcome of the oral food challenge (OFC) with wheat, the additional analysis of further wheat components was helpful in predicting the positivity of OFC. In their conclusions, authors suggested the importance of these molecules in the diagnosis and follow-up of children with WA. Otherwise, in the population from the Mediterranean area, also the molecular components of plant-derived foods belonging to the family of the non-specific lipid transfer proteins (nsLTP) act as major allergens in patients with food allergy. As shown from previous studies, the nsLTPs of several seeds and fruits (e.g. Ara h 9 in peanuts or Pru p 3 in peaches), are relevant allergens in patients living in the Southern regions of Europe and are implicated in moderate to severe reactions, mainly due to their stability to high temperatures and to the gastric proteolysis². Nevertheless it has been ascertained the role of the nsLTP of wheat Tri a 14 as a professional allergen in baker's asthma, few data are available on its clinical relevance as a food allergen in patients with IgE-mediated reactions to ingested wheat^{3, 4}. To fill this gap, we sought at evaluating the relevance and the diagnostic accuracy of the wheat nsLTP Tri a 14, in addition to the omega-5 gliadin Tri a 19, in a population of children and adolescents from the Mediterranean area with sensitization to wheat grain [serum specific IgE (sIgE) to wheat ≥ 1 kU/L] Our cross-sectional study involved 19 patients (13 males, 6 females) with a mean age of 8 years old (range 0,6-17 years) referring to the Pediatric Allergy Outpatient Unit of S. Orsola-Malpighi Hospital of Bologna (Italy) from October 2013 to December 2014. All patients were assessed by skin prick test (SPT) with commercial extracts (Lofarma, Milan; Italy) for a standardized panel of inhalant and food allergens and sIgE against pollens, wheat, gluten and the two available molecular components of wheat rTri a 19 (omega-5

gliadin) and rTri a 14 (nsLTP) using the ImmunoCAP system (TFS, Uppsala, Sweden). The diagnosis of WA was confirmed with open OFC. Chi-square test and non-parametrical tests were applied when appropriate. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated for sIgE to rTri a 14 and rTri a 19. Receiver operating characteristics (ROC) curves were calculated for evaluating the diagnostic accuracy of sIgE to wheat, gluten and to the molecular components rTri a 14 and rTri a 19 in predicting the outcome of OFC to wheat. The study was approved by the Ethic Committee of S.Orsola-Malpighi Hospital (protocol name: Wheat Allergy; protocol number 194/2013/O/OssN)⁵. Within our study population, the diagnosis of WA was confirmed only in 6/19 patients (32%). The levels of sIgE (geometric mean) to wheat were almost 4 times higher in allergic patients compared to the tolerant ones (35.2 vs. 8.2 kU/L respectively, NS). Specific IgE to the nsLTP rTri a 14 were detected in most of our patients (11/19; 58%), while sIgE to rTri a 19 were found only in 5/19 (26%) children. Meanwhile, the comparison between the different patterns of sensitization showed, within the wheat-allergic group, a higher prevalence of sensitization to rTri a 19 (83% vs. 0%, $p < .05$), while the rates of sensitization against gluten (100% vs. 75%) and rTri a 14 (50% vs. 46%) were not statistically significant. Considering a cut off value of sIgE level ≥ 0.35 kU/L, the molecular component rTri a 19 showed the best sensitivity (83.3%) and specificity (100%) in diagnosing WA with high PPV and NPV (100% and 92.8% respectively), while the diagnostic performance of the wheat nsLTP was poor (sensitivity 50%, specificity 53.8%, PPV 33.8% and NPV 70%). The area under the ROC curve (AUC) for sIgE to omega-5 gliadin was 0.917 for a cut-off value of 0.34 kU/L, while the AUC for sIgE to wheat and to gluten were 0.763 and 0.798 for a cut-off value of 14.9 kU/L and 18.2 kU/L respectively (**Fig. 1**). The AUC for sIgE to the wheat nsLTP was not relevant (AUC=0.525).

In conclusion, our study showed comparable results to those presented by Nilsson *et al.*¹ concerning the relevant role of rTri a 19 as a diagnostic tool in WA, also in patients from a different geographical area (Italy). Interestingly, despite the high prevalence of the wheat nsLTP (rTri a 14) in our study population (58%), this allergen wasn't useful in predicting adverse reactions in wheat allergic patients, highlighting the controversial role of this molecule as a food allergen. To confirm the clinical relevance of our preliminary results, these data should be evaluated in a larger study population and compared to those from patients living in different geographical areas.

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Figures

Fig. 1 . Receiver operating characteristic (ROC) curves for specific IgE to wheat, gluten and omega-5 gliadin in predicting adverse reactions to the oral food challenge with wheat.

