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CORRESPONDENCE

Paediatric perioperative hypersensitivity: the performance of the current consensus formula and the effect of uneventful anaesthesia on serum tryptase. Reply to *BJA Open* 2024; 9: 100254

Nils Vlaeminck[1], Marie-Line van der Poorten[2], Vera Saldien[1], Vito Sabato[3] and Didier G. Ebo[3,*]

[1]Department of Anaesthesiology, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp University Hospital, Antwerp, Belgium, [2]Department of Paediatrics, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp University Hospital, Antwerp, Belgium and [3]Department of Immunology, Allergology, Rheumatology and the Infla-Med Centre of Excellence, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp University Hospital, Antwerp, Belgium

*Corresponding author. E-mail: immuno@uantwerpen.be

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Editor—It was with great interest that we read the response by Green and colleagues[1] to our publication on tryptase in paediatric hypersensitivity.[2] We would like to thank the authors for their prompt response to our request for external validation of the new paediatric consensus formula for mast cell activation. Some aspects of their validation study and our original study warrant further discussion. Although the Australian cohort is smaller than the cohort in our previous study (38 *vs* 190 patients with paired acute and baseline tryptase sampling), it significantly strengthens the validity of our conclusion, both in terms of numerical representation and geographical distribution. The perioperative hypersensitivity (POH) cohort appears to be comparable between studies, with a similar distribution of severity (~55% grade 1–2 and 45% grade 3–4) and age of POH patients (median age 13 and 14 yr). The reported culprits, predominantly cefazolin and neuromuscular blocking agents, are also consistent with those reported in our region.[3] However, it is important to note that the control cohort was defined differently. We used healthy controls who were uneventfully exposed to general anaesthesia, whereas Green and colleagues used patients who had been referred for investigation of POH and who were considered to have not exhibited an immunological reaction. The authors do not report the criteria for confirmation of an immunological reaction. As they report a causative agent for each POH patient, they may have required a positive skin or *in vitro* test to confirm an immunological reaction. However, the diagnosis of POH is clinical and diagnostic investigations are not always conclusive in identifying the culprit agent. The Immediate Hypersensitivity Consensus Clinical Score (IHCCS) is a novel tool to standardise the clinical diagnosis of POH. Although it is often difficult to gather all the required information in retrospective studies, as was the case in our own study, we recommend that future prospective studies use the IHCCS to standardise cohorts.[4] However, it should be noted that the IHCCS is not specifically designed for or validated in children. The application of (overly) strict criteria for the confirmation of POH reaction by Green and colleagues could possibly explain the increased sensitivity of both the new paediatric consensus formula and the adult consensus formula, when compared with our study (72.7% *vs* 53.3% and 50.0% *vs* 31.9%, respectively). It is noteworthy that of the five additional cases identified by the new paediatric consensus formula, three were grade 3. This highlights the lack of sensitivity of the adult formula in children. Conversely, the specificity of both the new paediatric and the adult consensus formulae is lower than that observed in our study (70.0% *vs* 93.3% and 59.3% *vs* 99%, respectively). This may be as a result of the aforementioned differences in the definition of the control cohort. The overall performance of tryptase in paediatric POH remains lower than that reported in adults,[5] which may be owing to increased haemodilution in paediatric POH compared with adults. It would, therefore, be interesting

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to analyse the volume of fluid administered in both cohorts. In addition, in a research setting we could advocate that a surrogate for haemodilution such as haematocrit be measured simultaneously with both acute and baseline tryptase sampling. Alternatively, the lower incidence of transient tryptase elevations may also imply mechanistic differences in POH and this should be further investigated in future studies.[6]

In conclusion, Green and colleagues have made a valuable addition to the diagnosis of POH in children and are the first to confirm our previous findings on tryptase in children. Because of the smaller number of patients in the paediatric population, international collaborations are necessary to further validate the new paediatric consensus formula for mast cell activation. To standardise and facilitate this collaboration, we suggest the use of the IHCCS to standardise cohorts across studies and facilitate comparisons. Finally, we note that the International Suspected Perioperative Allergic Reaction group (ISPAR) is currently working on a common database to further enhance international collaboration, which we hope will be disseminated in the near future.

Declarations of interest

The authors declare that they have no conflicts of interest.

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