

LETTER TO THE EDITOR

Comment on “Caution against injudicious vaccine allergy skin test and adverse reactions after intradermal COVID-19 vaccine testing”

To the Editor,

We read with great interest the article “Caution against injudicious vaccine allergy skin tests: adverse reactions after intradermal COVID-19 vaccine testing” by Chiang et al,¹ who reported the case of a woman with generalized urticaria ~1 hour after Sinovac CoronaVac SARS-CoV2 vaccination. The patient underwent skin prick test and intradermal test (IDT) with fresh and undiluted Sinovac CoronaVac SARS-CoV2 and Pfizer-BioNTech vaccines. Skin tests were negative at immediate readings but in the following few days the patient developed erythema and swelling evolved into blistering lesions at both IDT sites. Two weeks later the patient tolerated the second dose of Sinovac CoronaVac vaccine uneventfully.

We agree with the authors who warn against the injudicious use of vaccine skin testing in the assessment of suspected adverse drug reaction (ADR) to coronavirus disease 2019 (COVID-19) vaccines. In our study cited by the authors we hypothesized that the reactions to COVID-19 vaccine at IDT sites in six patients with referred ADR to Pfizer-BioNTech vaccine were false positive reactions due to a cellular type IVa immune protection rather than an allergy to SARS-CoV-2 viral S protein or to vaccine components.² To confirm the “not allergic” cellular immune protection against SARS-CoV-2 viral S protein, we performed the same IDT in healthy volunteers who had received one or two doses of Pfizer-BioNTech vaccine, observing the same delayed reactions in all controls. Consequently, all of our patients and vaccinated controls tolerated the second vaccine dose, as well as the patient reported by Chiang et al.

Contrary to what the authors reported, in our article we did not judge the IDT reactions in subjects who received at least the first COVID-19 vaccine dose as “mixed results” and we advised against the vaccine IDT to investigate suspected ADR to COVID-19 vaccines. Moreover, we noticed that the modality to perform IDT with undiluted vaccines was not in accordance with what was suggested by the European network of drug allergy/European Academy of Allergy and Clinical Immunology Drug Allergy Interest Group.³ This position paper recommends that IDT is performed with a 1:100 vaccine dilution to avoid strong bullous reactions and subsequent permanent scars. According to this position paper and to a recent review on skin tests in the ADR diagnosis,⁴ we used 1:1000 and 1:100 diluted Pfizer-BioNTech vaccine to perform IDT,³ documenting in all six patients and vaccinated volunteers a delayed (12 hours after) erythematous, edematous, and infiltrated asymptomatic reaction without blistering at IDT sites.

In conclusion, in the light of our findings, IDT with anti-SARS-CoV-2 vaccines in subjects who received at least one dose is not advisable as they cause false-positive reactions, and in case of immediate-type

reactions, skin prick testing should be performed. Moreover, we believe that the blistering IDT reactions observed by Chiang et al. could have been prevented by using appropriate dilution without modifying the meaning of the assumed pathomechanism underlying them.

CONFLICT OF INTEREST

All authors have no interests to report.

AUTHOR CONTRIBUTIONS

Leonardo Bianchi: Conceptualization (equal). **Katharina Hansel:** Conceptualization (lead). **Filippo Biondi:** Conceptualization (equal). **Nicola Murgia:** Conceptualization (equal). **Marta Tramontana:** Conceptualization (equal). **Luca Stingeni:** Conceptualization (lead).

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