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Letter to the Editor

Treating through in drug allergy: The considerations of allergists^{*}

Traiter l'allergie aux médicaments de bout en bout : les considérations des allergologues

To the Editor

Drug hypersensitivity reactions (DHR) constitute a major health problem affecting one tenth of the world's population. On the one hand, patients can suffer from early or delayed reactions, which may even have life-threatening consequences, while on the other, as a precaution, they may be labelled as having multiple drug 'allergies', resulting in restrictions in prescription and limitations in treatment strategies [1]. Investigations to check the possibility of a real drug allergy or to identify the drug responsible for the reaction are not straightforward and can be only performed in specialized centres after risk-benefit analysis.

The primary principle of DHR management is prompt withdrawal of the culprit drug and switching to an alternative treatment [2]. Drug desensitization may be considered where the offending drug is crucial and either no alternatives exist or they are less effective. However, with some 'benign' reactions, the benefits and risks of continuing the drug may be considered in the absence of danger signs [2]. In such cases, once the symptoms of the current hypersensitivity reaction are under control, the medication(s) may continue to be taken under close clinical and laboratory monitoring. This approach, termed "treating through" (TT), appears to afford a practical option in the management of certain mild forms of DHR [3,4].

Although this method has been proposed as a therapeutic option in consensus reports, it is rarely discussed among allergists, and thus data reflecting physicians' opinions about TT is scarce and is mostly shared through case reports by physicians from outside the field of allergy [3,5].

The aim of this study was to determine the attitudes and experiences of adult/paediatric allergists regarding the TT approach in DHR. To this end, following approval by a local ethics committee (2019.022.IRB2.011), a 20-item questionnaire in open-label and multiple choice formats was created and sent to 312 members of the Turkish National Society of Allergy and Clinical Immunology (TNSACI) using the Society's e-mail network in February 2019. One hundred and fifty specialists and registrars practicing in adult ($n=81$) or paediatric ($n=69$) allergy responded to the e-mail by answering questions.

The majority (57%) reported seeing at least one patient per day with suspected drug allergy. According to the results, paediatric

allergists were less familiar with TT, with 22% of adult allergists not having heard of this concept versus 39% of paediatric allergists ($P=0.031$). A total of 56 physicians (37%) reported having no experience in TT, with 83% describing it as a risky procedure and 11% as highly risky.

Respondents with experience of this method were asked about the evidence they reviewed before opting for their position, such as the possible culprit drug, the nature of the reaction presented by the patient, the reason why the particular medication was given, and details about the patients in question.

The majority of adult allergists reported that they would not try TT with allopurinol (61%) or with bleomycin (54%). Paediatric allergists indicated that in addition, they would not try TT where the suspected drugs were allopurinol (61%) or bleomycin (54%); in addition, they would not attempt this option with other medications such as taxanes (70%), platins (68%), monoclonal agents (65%), aspirin (64%) or NSAIDs (53%). Systemic steroids in adults and amoxicillin in children were the most encouraging drugs for TT in our survey according to the adult and paediatric allergist respondents, with 78% and 77% respectively indicating that they would try TT with these agents. Reluctance to use these supplementary agents was the main difference between the approaches of paediatric and adult allergists.

Regarding the nature of the reaction, urticaria, flushing and maculopapular exanthema appeared to be the only three presentations for which respondents would be prepared to try TT. The other possible clinical or laboratory findings where TT would not be considered by the majority of our respondents were: angioedema, anaphylaxis, acute generalized exanthematous pustulosis, fixed drug eruption, intense facial involvement, atypical target or bullous lesions, widespread dark-red erythema, extensive pustulosis, painful skin, mucosal involvement, generalized lymphadenopathy, hepatopathy and nephropathy. As well as medication and clinical presentation or laboratory findings, responders were also asked about patient-related factors that would make them reluctant to adopt this approach, and they indicated psychological issues, presence of anxiety or anxious parents, presence of other drug allergies in both adults and children, and presence of asthma in adults only.

Our responders reported previous experience of this method mainly in patients having chronic spontaneous urticaria (CSU), or flare-up after NSAIDs or antibiotics, or in patients having maculopapular exanthema (MPE) after chemotherapeutic agents or antibiotics. According to their past experience, the general outcome was successful for 30% of participants, successful with mild adverse effects for 21%, and successful with moderate side effects for 9% (Fig. 1). Only one paediatric allergist had to withdraw the medication due to severe side effects, and no other unsuccessful cases or serious side effects were reported.

Since case reports of successful outcomes with TT do not reflect the reality, more evidence concerning this approach is needed to

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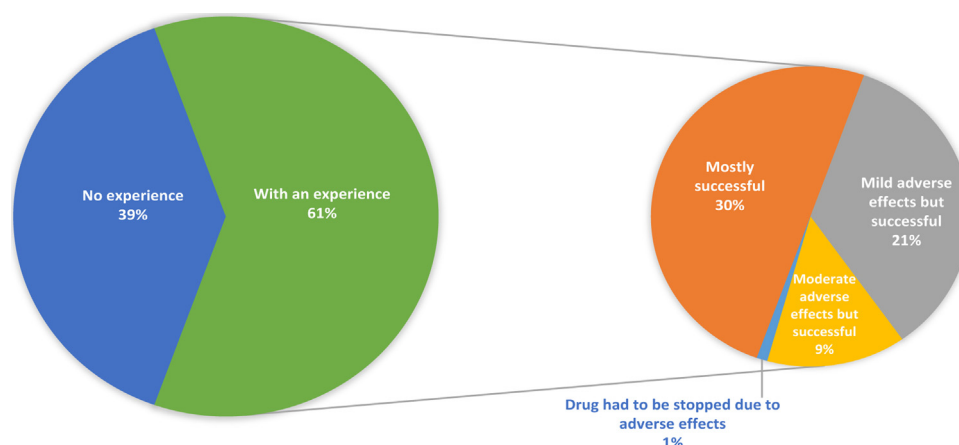


Fig. 1. The percentage of experience of 'threatening through' among allergist, together with the outcome of this previous experience.

enable safe use of this approach. In a recent study, Trautmann et al. retrospectively reviewed a homogenous group of 18 patients developing delayed MPE after initiation of intravenous antibiotic treatment for severe cellulitis [4]. TT was reported to work well under close monitoring in 12 patients, but was unsuccessful in three patients due to elevated liver enzymes or clinical progression of MPE.

In conclusion, the responses we collated in our study suggest that flushing, urticaria and maculopapular exanthema with absence of danger signs may be defined as benign reactions enabling TT to be considered in selected cases with certain medications under close medical observation, following joint decision-taking with the patient and/or the patient's family members. However, a standardized recommendation for a general approach is needed for consideration of TT, and which takes into account inadequate knowledge and reticence.

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S.B., O.S. and L.P.O. developed the original idea. L.P.O. and A.B.O. obtained ethics committee approval. L.P.O. constructed the survey. A.B.O., O.S. and S.B. distributed the survey to the participants. L.P.O. analysed the results and S.B. supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Torres MJ, Romano A, Celik G, Demoly P, Khan DA, Macy E, et al. Approach to the diagnosis of drug hypersensitivity reactions: similarities and differences between Europe and North America. *Clin Transl Allergy* 2017;7:7, <http://dx.doi.org/10.1186/s13601-017-0144-0>.
- [2] Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, et al. International Consensus on drug allergy. *Allergy* 2014;69(4):420–37, <http://dx.doi.org/10.1111/all.12350>.
- [3] Putterman C, Rahav G, Shalit M, Rubinow A. "Treating through" hypersensitivity to co-trimoxazole in AIDS patients. *Lancet* 1990;336(8706):52, [http://dx.doi.org/10.1016/0140-6736\(90\)91563-p](http://dx.doi.org/10.1016/0140-6736(90)91563-p).
- [4] Trautmann A, Benoit S, Goebeler M, Stoevesandt J. "Treating Through" decision and follow-up in antibiotic therapy-associated exanthemas. *J Allergy Clin Immunol Pract* 2017;5(6):1650–6, <http://dx.doi.org/10.1016/j.jaip.2017.03.032>.
- [5] Vishnevsky A, Savage MP, Fischman DL. Treatment of clopidogrel hypersensitivity: the Jefferson approach. *Curr Vasc Pharmacol* 2019;17(2):123–6, <http://dx.doi.org/10.2174/1570161116666180730100346>.

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