

Reply to the Letter ‘Multiple Nonsteroidal Anti-Inflammatory Drug-Induced Cutaneous Disease: Relevance, Natural Evolution and Relationship with Atopy’ by Blanca-López et al.

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Dear Editors,

I would like to thank Blanca-López et al. [1] for considering my recent paper [2] a relevant addition to the study of nonsteroidal anti-inflammatory drug (NSAID) hypersensitivity. In their comments, the Spanish authors raise three specific points.

The first one concerns the prevalence of hypersensitivity reactions induced by the different drug classes. In effect, several studies carried out by that group as well as by other authors seem to suggest that NSAIDs are the drugs most frequently involved in hypersensitivity reactions. However, looking at the clinical histories of patients seen in everyday practice, beta-lactam hypersensitivity is much more frequently reported than NSAID hypersensitivity. Obviously, it is not possible to check every single clinical history by oral challenges, particularly if the patient has been referred for other reasons (e.g., food or respiratory allergy). Thus, in the absence of specifically designed epidemiological studies, the question remains open. Anyway, since my paper did not deal with the prevalence of NSAID or antibiotic hypersensitivity in the general population, it seems to me that this point is not particularly relevant.

The second point concerns the natural history of NSAID-induced urticaria/angioedema patients. Although another study by the Spanish authors [3] does not seem to support this finding, the proneness of this subset of patients to develop chronic spontaneous urticaria confirms previous observations I made on a completely different population one decade ago [4]. Blanca-López et al. comment that there was no control population in my last study. They are right, but the control population was present in my former study [4], and the proportion of control subjects who developed chronic spontaneous urticaria was well below 20%. One further finding suggesting a similarity (I would be tempted to say a relationship) between patients with NSAID-induced urticaria/angioedema and NSAID-exacerbated cutaneous disease is the frequent detection of autoreactivity by autologous serum skin test in the former subset [5]. The discrepancies between Spanish and Italian studies might be due to differences in criteria adopted to diagnose chronic urticaria. In fact, along with classic cases of recurrent generalized wheals possibly associated with angioedema, sponta-

neous urticaria may sometimes be slight, appearing as dermatographism and/or recurrent pruritus in the absence of frank spontaneous wheal-and-flare skin lesions and/or angioedema, maybe induced by exercise, hot baths and showers, sun exposure, or appearing during menstrual periods.

The third point concerns the prevalence of atopic diseases in the different subsets of patients with NSAID hypersensitivity. I believe that the discrepancies between series of patients from different geographic areas may to a large extent reflect regional differences in the prevalence of sensitization to different airborne allergens. For instance, Sánchez-Borges et al. [6, 7] found an association between NSAID hypersensitivity and allergy to house dust mite (HDM) or *Blomia tropicalis* in Venezuela, and an extremely high prevalence of HDM hypersensitivity was also found by a Spanish team from Malaga [8]. Since in Milan and its surroundings HDM hypersensitivity is much less frequent than in those places, and *B. tropicalis* allergy is virtually absent, it is not very surprising that no such association was observed here. In

contrast, in keeping with the findings in Venezuela [9], in Milan atopy seems more frequent among single NSAID reactors than among multiple reactors either with or without chronic spontaneous urticaria (unpubl. data). A study by Quiralte et al. [10] which was quoted by Blanca-López et al. established an association between atopy and isolated periorbital angioedema, a

clinical pattern that was completely missing in the series I studied. In contrast, another study [11] found no difference in the prevalence of atopic diseases between patients with aspirin-exacerbated respiratory disease and subjects monosensitized to pyrazolones, although atopy was more frequent in either group than in the control group.

Altogether pharmacogenomic studies regularly show differences in the clinical responses to drugs as well as in features of drug hypersensitivity among patients from different parts of the world. In other words, it is not surprising that some findings from a certain geographic area may be slightly different from those in a homologous group studied elsewhere.

References

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