

Correspondence and Replies

Drug-induced anaphylaxis in children: Nonsteroidal anti-inflammatory drugs and drug provocation test

TO THE EDITOR:

In a recent publication, Aun et al¹ demonstrated that 14.5% of drug hypersensitivity reactions (DHR) are anaphylactic in nature, and nonsteroidal anti-inflammatory drugs (NSAID) account for nearly half of these cases. In our practice, we observed a higher frequency of anaphylactic reactions in pediatric patients with DHR, which also highlights the importance of NSAIDs in this population. From June 2011 to May 2014, we evaluated 104 children (mean age, 10.4 years) with a history of DHR, from which 26 had anaphylaxis symptoms. Unlike adults, there was a predominance of male patients ($n = 16$). Most reactions were classified as moderate (85%), with dyspnea ($n = 18$), urticaria associated with angioedema ($n = 16$), and angioedema alone ($n = 8$) being the most frequent clinical manifestations.² All the patients were seen in the emergency department, except one, who had not received medical attention. However, only 5 received epinephrine, whereas most received antihistamines ($n = 12$) or corticosteroid injections ($n = 11$). Twenty patients presented fever and/or viral infection symptoms at the time of reaction.

NSAIDs were the main drug class involved in anaphylactic reactions (70.6%). Sixteen patients associated the reactions exclusively to NSAIDs, whereas 4 had used other drugs in combination (amoxicillin [2], azithromycin, and metoclopramide). Among those who presented reactions to NSAIDs alone, 12 reported 2 or more episodes with drugs of different chemical groups, with dipyrone being associated to all cases, followed by ibuprofen (75%) and paracetamol (acetaminophen) (50%). The other 4 patients reported only 1 episode of reaction (3 with dipyrone and 1 with paracetamol) (Table I). Eleven patients had atopy symptoms, and only 3 had a familial history of drug hypersensitivity.

In our department, we prescribe the drug provocation test (DPT) with paracetamol for all patients with a suspected reaction to this drug because paracetamol is a weak inhibitor of COX and rarely triggers symptoms in subjects with nonselective hypersensitivity reaction to NSAIDs. In 5 patients tested, only 1 had a reaction. During the study, this patient took ibuprofen and dipyrone on his own, without the occurrence of symptoms, which characterized a selective hypersensitivity reaction to paracetamol, with a positive skin test (by using paracetamol drops at 50 mg/mL concentration and negative in 10 controls), suggesting an IgE-mediated mechanism. The DPT also is indicated in cases in which the patient had a single episode in an attempt to characterize it as a selective or nonselective NSAID reactor. We also performed DPT with acetylsalicylic acid with 2 patients who presented a single episode of anaphylaxis associated with dipyrone, both with positive results. Finally, 1 patient was challenged with etoricoxib. The test result was negative, and the drug was offered as a safe therapeutic option. We concluded that NSAIDs are the most important cause of DHR-related anaphylaxis also in children, with most

TABLE I. NSAIDs and DPT in children with anaphylaxis

Patient no.	Sex	Age(y)	Drugs involved*	DPT
1	M	9	dip, pa, i	pa neg
2	M	9	dip, pa, i	pa neg
3	F	13	pa, dip	
4	M	12	dip, i	
5	M	2	dip	
6	M	11	dip, i	
7	M	11	pa	pa pos
8	F	11	dip, pa, i, dic	pa neg, e neg
9	F	18	dic	a pos
10	F	16	pa, dip, dic, n	
11	F	12	a, dip, dic	
12	M	8	dip, i	a pos
13	M	9	dip	
14	M	10	dip, i	pa neg
15	M	15	dip, i, pa, n	
16	M	14	dip, n	

e, etoricoxib; neg, negative; pos, positive.

*Drugs involved in the reaction that was evaluated and prior reactions: a, aspirin; dic, diclofenac; dip, dipyrone; i, ibuprofen; pa, paracetamol.

reactions being related to dipyrone. We also emphasize the importance of the DPT, mainly to exclude paracetamol as a cause of anaphylaxis because this is one of the few safe options for these patients.

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