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Paracetamol sensitivity without aspirin intolerance

INTOLEANCE reactions to acetylsalicylic acid (ASA) manifested as rhinitis, asthma, or urticaria-angioedema are well known. However, allergy-like reactions to paracetamol (1) have been rarely reported in spite of widespread consumption of this analgesic. Selective sensitivity to paracetamol without ASA or nonsteroidal anti-inflammatory drug (NSAID) intolerance is even more uncommon (2-5).

In this paper, we report five cases, studied at our department, with paracetamol sensitivity confirmed in four of them by oral challenge. In all cases, we confirmed ASA tolerance by oral challenge.

Case 1: A 27-year-old woman experienced several episodes of facial angioedema or tongue edema and dyspnea 15 min after ingesting drugs containing paracetamol.

Case 2: A 48-year-old woman developed an itching erythematous plaque on her right mammary areola 60 min after ingestion of one tablet of Gelocatil® (paracetamol 650 mg).

Case 3: A 48-year-old woman developed generalized urticaria 60 min after ingestion of one tablet of Gelocatil (paracetamol 650 mg).

Case 4: A 27-year-old woman experienced two

episodes of generalized urticaria 10 min after ingestion of one tablet of Gelocatil (paracetamol 650 mg).

Case 5: A 24-year-old woman presented two episodes of generalized urticaria 30 min after ingestion of different medicaments containing paracetamol.

In Table 1, we report the results of skin prick test, leukocyte histamine release test with paracetamol, and oral challenges with paracetamol and ASA carried out in our patients. All of them gave written, informed consent to participation in the study.

In cases 1 and 5, we also performed oral challenge with indomethacin 50 mg (Inacid®) and codeine 30 mg (Codeisan®), respectively, with tolerance. In case 1, we did not perform oral challenge with paracetamol because of the severity of the symptoms.

Four patients with positive oral challenges with paracetamol tolerated ASA orally.

Paracetamol is a commonly used analgesic-antipyretic drug with weak anti-inflammatory action. Its underlying mechanism seems to be a weak inhibition of cyclooxygenase, thus

blocking prostaglandin synthesis. Should inhibition of cyclooxygenase be the underlying mechanism of our patients' symptoms, adverse reactions to ASA would be expected in all of them.

Although we suspected an immunologic basis of the paracetamol sensitivity, the skin prick test performed in two patients and the histamine release test in three patients were negative. In another case studied in our department a few years before, the skin prick test and specific IgE determination by RAST to paracetamol (2) were positive.

Reports of paracetamol sensitivity with ASA tolerance are uncommon (3-4), and the underlying mechanism is not known. Recently, three cases of children with paracetamol hypersensitivity were reported, and one of them was confirmed by patch

Table 1. Results of tests in patient group

	Case 1	Case 2	Case 3	Case 4	Case 5
Paracetamol skin prick test 100 mg/ml	Neg	ND	ND	ND	Neg
Paracetamol histamine release	ND	Neg	ND	Neg	Neg
Paracetamol oral challenge	ND	160 mg FE	60 mg Urticaria	650 mg Urticaria	80 mg Urticaria
ASA oral challenge 500 mg	Neg	Neg	Neg	Neg	Neg

ND: not done; Neg: negative; FE: fixed eruption.

test with paracetamol and later biopsy, showing that delayed hypersensitivity was responsible for the reaction (5).

In one case of urticaria caused by paracetamol, as confirmed by oral challenge, the relationship between paracetamol and another NSAID was studied, and tolerance of ibuprofen was also confirmed by oral challenge (6). In case 1, we performed oral challenge with indomethacin with good tolerance.

On the other hand, asthmatic and nonasthmatic patients with ASA intolerance have been extensively studied (7). In those studies, the prevalence of cross-sensitivity between paracetamol and NSAID seemed to be dose-dependent, demanding high doses of paracetamol to reproduce the symptoms. They have also demonstrated that the higher the intolerance of aspirin, the lower the paracetamol dose that induced symptoms.

Fixed eruption is one common adverse reaction caused by different drugs, but paracetamol is not a usual cause (8). In one of our patients, we reproduced the fixed eruption in the same place by oral challenge with only 160 mg paracetamol, with further ASA tolerance.

When we deal with a reaction to paracetamol, it is difficult to choose another analgesic as an alternative because the underlying mechanism of intolerance reactions to this drug appears to be similar to that for ASA. We demonstrated by oral challenge that there was good tolerance of ASA in our patients, so other mechanisms may be implicated. Further studies are

needed to clarify the mechanism of paracetamol sensitivity in patients who tolerate ASA.

Key words: acetylsalicylic acid; oral challenge; paracetamol.

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