Table 1. Drugs responsible for skin reactions in the patients' population

Drug	Number of patients (%)
Nimesulide alone	23 (32)
Nimesulide + ASA	3 (4.1)
Nimesulide + ASA + others*	18 (25)
Nimesulide + others*	28 (38.9)
Total	72 (100)

*Other nonsteroidal anti-inflammatory drugs (NSAIDs): Morniflumate, Diclofenac, Ketoralac, Arylpropionates, Acetaminophen, Oxicams and Benzydamine.
ASA, acetylsalicylic acid.

to the classic NSAIDs, with a very low rate of adverse events (3). Few studies have investigated the tolerability of CE in patients with severe NSAIDs hypersensitivity, therefore we attempted to address this aspect.

The main inclusion criterion for patients was a well-documented clinical history of erythema and/or urticaria/angioedema following the intake of N or other NSAIDs in addition to N. Pregnant/lactating women and patients with systemic diseases or chronic idiopathic urticaria were excluded. Respiratory symptoms, laryngeal oedema or anaphylaxis after NSAIDs were exclusion criteria as well. The diagnosis of N-induced skin reaction was confirmed by an oral challenge (4). Patients had to be asymptomatic since at least 1 month at the time of the challenge. At the first visit, patients underwent physical examination, spirometry and skin-prick tests with common allergens. The oral challenge was single-blind and placebo-controlled, under continuous medical supervision. The CE and placebo (lactose) were administered in identical capsules. Four doses of CE were used: 20, 60, 120 and 200 mg, being this latter the commercial therapeutic dose. On day 1, three placebo capsules were given at 1-h interval. After 3-4 days, the patients received 20, 60 and 120 mg CE hourly, and 3–4 days later a single 200 mg dose was given. In addition to clinical follow-up and vital signs recording, a spirometry was performed at baseline and after 6 and 24 h in each session. The challenge was positive if erythema and/or rush and/or urticaria-angioedema appeared.

Seventy-two patients (26 male, age 14–70, mean age 41) were included. Thirty (42%) had a clinical history of respiratory or food allergy, and 31 (42.6%) reported cutaneous symptoms also with other drugs (mainly antimicrobials). Twenty-three patients had a clinical history of adverse reaction to N alone (Table 1). Sixty-eight patients (93%) tolerated the therapeutic dose of CE (200 mg) without reactions. Two patients had moderate angioedema of the lips about 30–40 min after the administration of the 200 mg dose. Those events resolved in <2 h after oral cetirizine and intravenous methylprednisolone. One patient reported generalized itching, without objective signs 35 min after 120 mg (no treatment needed), and another subject reported mild stomachache 1 h after the higher dose.

An increasing number of publications is confirming that 'coxibs' are overall safe and well-tolerated, and severe reactions with them are only anecdotal (5). This is important, since the large use of N has increased the number of (or selected out) those patients intolerant to it. Those patients should be considered highly reactive, and CE is a reasonable alternative drug (3). In our study, only two of the four adverse events reported could be considered related to CE. In fact, generalized itching alone and stomachache are not considered typical of drug hypersensitivity. The finding of only two positive responses (2.77%) to challenge with CE in highly reactive patients confirms that the drug has a very good tolerability.

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No rHev b 12-specific IgE-response in children sensitized to natural rubber latex

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Latex allergy affects well-recognized risk groups. The highest prevalence appears in children requiring multiple surgeries, especially those with spina bifida (SB). Natural rubber latex (NRL) contains more than 200 proteins and peptides, some of which are capable of eliciting immunoglobulin E (IgE) responses. It is known that manu-

No specific IgE to rHev b12 was found in 31 latex sensitized children.

facturing processing of latex can alter the structure of proteins; thus, ammoniated latex contains less allergenic determinants and has been proved to offer inferior results to those of nonammoniated extracts for the study of sensitization to latex (1). Therefore, the isolation and synthesis of recombinant allergens is becoming an important tool both for clinical and research purposes. So far, 13 latex allergens have been registered by the IUIS (2). A lipid transfer protein, Hev b 12, is one of the latest registered allergens (3), and little information is currently available concerning its allergenic importance in sensitized patients.

We studied 20 Spanish children with SB with two to nine operations, eight non-SB children with two to eight operations, and three atopic nonoperated children. All displayed NRL-specific IgE antibodies in their serum (Pharmacia CAP class 7101), and 25 have had clinical symptoms in relation to latex. Serum IgE antibodies to recombinant Hev b 12 (rHev b 12) were analyzed by an ImmunoCAP method in leftover sera of all children. No rHev b 12-specific IgE antibodies were found (< 0.3 U/l). As positive controls, rHev b 12-specific IgE responses using the same technique were recently obtained in sera of fruit-allergic patients with and without NRL-sensitization (4).

The allergenic potential of NRL varies among risk groups. In health care workers, responses are found mainly to Hev b 5 and Hev b 6.01/6.02. In children with SB, Hev b 1 is the major allergen, with frequent responses also to Hev b 3 and Hev b 7. In nonoperated NRL-sensitized children, the pattern of sensitization resembles more that of health care workers (1, 5). This seems to depend on the physical properties of the allergens, and is important in order to develop suitable products for diagnosis and treatment of latex allergy. Extracts for diagnosis should contain a mixture of all allergens, to reach the highest sensitivity, and cover all cases of latex sensitization. Extracts for immunotherapy must contain sufficient amounts of the allergens relevant for the given patient. Until individualized extracts are commercially feasible and available, products for treatment must include those allergens known to sensitize most of the patients of each risk group. Regarding this, the importance of Hev b 12 had not been studied before. Our results revealed no rHev b 12-specific IgE antibodies in the sera of our 31 children. If these results are confirmed in more atopic children and in sensitized adults, the efforts to include rHev b 12 in diagnostic NRL-extracts should be limited. However, the relevance of this allergen in a recombinant form for cross-reactivity should be further studied.

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