

MP-SS. Data from a general review of literature confirm that hypothesis (5).

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Meloxicam in hypersensitivity to NSAIDs

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Key words: angioedema; meloxicam; NSAID; tolerance; urticaria.

● CUTANEOUS adverse reactions to drugs are a common problem in clinical practice. Among them, the urticaria/angioedema syndrome is the most frequent. The drug categories responsible for the majority of cases are antimicrobials and nonsteroidal anti-inflammatory drugs (NSAIDs) (1). A patient with a history of allergic or pseudoallergic reaction to NSAIDs needs an alternative NSAID to take if necessary. The peroral challenge with an alternative NSAID is the most

common way to achieve this goal.

At the moment, there are no NSAIDs absolutely free of adverse reactions. The drugs that are the best tolerated are acetaminophen (paracetamol) and nimesulide. Meloxicam, floctafenine, and benzydamine seem to be tolerable as well (2–5).

Over a period of two and a half years (2 February 1998 to 25 June 2000), some of the patients referred to our outpatient department for unequivocal clinical history of urticaria with or without angioedema to NSAIDs were enrolled in the study. All subjects underwent single-blind, placebo-controlled peroral challenge with meloxicam after giving informed written consent. They presented a forced expiratory volume after 1 s (FEV₁) of >80% of predictive value. Antihistamines and other drugs had been discontinued 1 week (2 weeks for patients with chronic urticaria and 4 weeks for those treated with astemizole) before challenge.

Table 1. NSAIDs causing urticaria with or without angioedema in 148 patients

Drug	No. of patients	Percentage of patients
ASA	36	24.3
Pyrazolone derivatives	25	16.9
Propionic acid derivatives	25	16.9
Arylacetics	7	4.7
Others*	18	12.1
ASA + pyrazolone derivatives	13	8.8
ASA + propionic acid derivatives	6	4.0
ASA + arylacetics	1	0.7
ASA + others	3	2.0
Propionic acid derivatives + arylacetics	3	2.0
Propionic acid derivatives + others	1	0.7
Pyrazolone derivatives + propionic acid derivatives	1	0.7
Pyrazolone derivatives + arylacetics	1	0.7
Pyrazolone derivatives + others	3	2.0
Arylacetics + others	1	0.7
Arylacetics + propionic acid derivatives + others	1	0.7
Pyrazolone derivatives + ASA + others	1	0.7
ASA + propionic acid derivatives + others	1	0.7
ASA + propionic acid derivatives + arylacetics	1	
Total	148	100

*Others: nimesulide, paracetamol, morniflumate, niflumic acid, bromelein, and mefenamic acid.

On challenge day 1, three placebo capsules (talc) were administered, one per hour. After 1 week, increasing concentrations of meloxicam were used for the challenge until a total therapeutic dose was reached. There was a 1-h interval between each dose, and if no response appeared, the next dose was administered. The doses were 1, 2, and 4.5 mg, respectively, with a total therapeutic dosage of 7.5 mg.

All substances were given in identical opaque capsules. During its execution and at the end of the test, arterial pressure and FEV₁ were monitored. Each patient was kept under observation in hospital for at least 6 h after challenge and was then asked to return or telephone to the hospital after 24 and 48 h to exclude delayed reactions.

The test was considered positive if cutaneous and mucosal manifestations (erythema and/or wheals and/or angioedema) appeared, or when respiratory symptoms or a decrease of at least 20% in the FEV₁ or hypotension developed.

The study population comprised 148 NSAID-sensitive subjects (53 males and 95 females; mean age 33.9 years [16.22 SD]; range 14–79 years). Sixty-six had experienced urticaria alone (44.6%), 34 angioedema (23%), and 48 angioedema plus urticaria (32.4%) after the ingestion of different NSAIDs. The drugs causing symptoms in these patients are shown in Table 1.

Of the 148 patients who underwent the challenge test with meloxicam, only two showed a positive test (1.35%). The first subject presented generalized urticaria associated with abdominal pain after a total dose of 3 mg of meloxicam. The second patient developed diffuse wheals and labial edema about 45 min after the administration of a total dose of 7.5 mg of meloxicam. Both patients

suffered from chronic idiopathic urticaria. No delayed reaction was observed.

None of the patients suffered adverse reactions to the placebo challenge.

This study confirms that meloxicam is a tolerable NSAID. Similar findings have been published by Quarantino et al. (2) and Košnic et al. (3).

Meloxicam is an NSAID that exerts an inhibitory effect on PGHS enzymes with a high preference for the second isoform. The exiguity of the number of positive peroral challenges may be, at least in part, explained by the selectivity of action on the PGHS-2 isoform.

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Anaphylaxis to Japanese encephalitis vaccine

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Key words: adverse reaction; anaphylaxis; gelatin; IgE; Japanese encephalitis vaccine.

• We observed children who had systemic immediate-type reactions (cutaneous and respiratory symptoms) to Japanese encephalitis (JE) vaccine containing gelatin in amounts of 50–100 µg per dose (1). In addition, we found that vaccinees showed another pattern of cardiovascular symptoms without cutaneous symptoms after JE vaccination (2).

Physicians and vaccine manufacturers submitted 17 serum samples from vaccinees with systemic immediate-type reactions to JE vaccines, including anaphylaxis, to the National Institute of Infectious Diseases (Japan). Furthermore, some vaccine manufacturers provided us with clinical data from two vaccinees with systemic immediate-type reactions to JE vaccine. We used data from 19 vaccinees (3–14 years old; mean age ± SD, 5 years and 5 months ± 2 years and 9 months)

The incidence was 2.09 cases per million.