

Urticaria induced by meperidine allergy

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Key words: allergy; meperidine; narcotic analgesics; urticaria.

● ALLERGIC reactions to narcotic analgesics are extremely rare (1–6). We report a case of generalized urticaria and angioedema after administration of meperidine.

A 42-year-old woman was admitted to the emergency department with renal colic. The patient was treated intramuscularly with metamizole 2 g. One hour later, due to the persistence of pain, Dolantina® (100 mg meperidine) was

given intramuscularly. Within 15 min of the injection, she developed generalized pruritus, erythema, urticaria, facial angioedema, dysphagia, dysphonia, and dizziness. Physical examination showed laryngeal edema and generalized urticaria. Blood pressure was 110/70 mmHg. Immediate treatment with subcutaneous epinephrine and intravenous dextchlorpheniramine and methylprednisolone resulted in a noticeable

improvement after 2 h, enabling the patient to be discharged several hours later.

Three months after the events described, and after the patient gave written consent, an allergy study was carried out.

Skin tests were performed by prick tests and intradermal tests with metamizole, meperidine, and other narcotic analgesics, as described in Table 1. The skin tests were all negative except for the prick test with meperidine and morphine (Table 1). All concentrations employed were also skin-tested in a group of 10 controls subjects (two patients had allergic rhinitis, two chronic urticaria, and six urticaria during general anesthesia). All tests but the skin test with morphine proved to be nonirritant in this group. The skin prick test with morphine was also positive in seven controls. Commercial RAST for meperidine was not available.

A single-blind, placebo-controlled oral challenge test with metamizole at a 2-g dose was negative. The patient did not consent to the meperidine challenge.

The narcotic analgesics are among the most commonly administered drugs in hospitals. The most serious immediate adverse effect, respiratory depression, is a predictable effect related closely to analgesia. Although these drugs are potent histamine releasers, anaphylactoid reactions

have rarely been described, and the antigenic safety of the drugs is impressive (1, 2).

Levi & Rockoff (5) reported the first case of true anaphylaxis developing after meperidine treatment in a child. They demonstrated the presence of specific IgE antibodies to meperidine by RAST. No controls were tested for this method, and skin tests with meperidine were not performed.

We report a patient with immediate urticaria and angioedema induced by meperidine. The meperidine allergy was confirmed by skin prick test. The negative result of this test in controls excluded the direct pharmacologic release of histamine at the tested concentration (50 mg/ml). There was no documentation of our patient having received meperidine previously, but its previous administration could have been unrecorded.

Anaphylactic reactions to other narcotic analgesics (fentanyl and papaveretum) also have been reported (3, 4). Some authors have demonstrated the presence of an IgE-mediated mechanism by positive skin tests or RAST to narcotic analgesics (3–6). Too few patients have been studied to determine accurately the likelihood of clinical cross-sensitivity among narcotics. Possible cross-reactivity among fentanyl, alfentanil, sufentanil, and meperidine has been suggested (6). Furthermore, after hapten-inhibition studies with morphine, clear cross-reactivity was demonstrated with codeine, partial cross-reactivity was reported with meperidine and methadone, and no cross-reactivity was demonstrated with fentanyl, naltrexona, and bupremorphine (4). We could not demonstrate any cross-sensitivity to the other narcotics skin-tested in our patient. All skin tests with these agents were negative.

The positive result of the prick test with morphine was considered to be nonspecific,

A case documented by positive SPT to meperidine and morphine.

Table 1. Skin-test response to narcotic analgesics

Drug	Prick-test (concentration)	Wheal* (mm)	Intradermal (concentration)	Wheal* (mm)
Meperidine	50 mg/ml	8	ND	ND
Morphine	10 mg/ml	5	ND	ND
Fentanyl	50 µg/ml	–	0.5 µg/ml	–
Alfentanil	0.5 mg/ml	–	5 µg/ml	–
Methadone	10 mg/ml	–	0.1 mg/ml	–
Metamizole	400 mg/ml	–	40 mg/ml	–
Saline solution	0.9%	–	0.9%	–
Histamine	10 mg/ml	8	ND	ND

*Wheal diameter greater than 3 mm, compared with negative control, was considered positive response. ND: not done.

due to the positive result of this test in most controls, probably because of the potent cutaneous histamine-releasing effect.

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Chronic urticaria: a mystery

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Key words: chronic urticaria; causes; diagnosis.

● CHRONIC urticaria (CU) has various causes such as intolerance to certain food additives and nonsteroidal anti-inflammatory drugs, and presence of

various internal and infective diseases (1, 2). Despite careful research, the pathogenesis of CU has not yet been identified. We present the results of a study performed at the departments of dermatology of Milan and Bergamo, Italy, on patients with chronic urticaria.

A total of 348 (208 women and 140 men aged 24–59 years) consecutive patients, excluding those with obvious physically induced urticaria (3), underwent a complete investigation consisting of their medical history and objective signs of the episode, and their personal and family history of allergies. Laboratory and instrumental investigations were carried out on all patients at their first visit, including routine blood tests and specific tests: CAP PRIST, CAP Phadiatop test (4), ELISA for specific IgG antibodies to *Helicobacter pylori* (HP), free T3, free T4, TSH, urine and stools tests for blood, parasites, and yeast, and chest radiograph. A psychosomatic examination of the last 66 patients and an autologous intradermal test in 113 were performed. The results are shown in Table 1.

There were more female than male patients (208 vs 140), and we found a high total eosinophil count in 129 patients, a high level of total IgE in 102 patients, and positive Phadiatop tests in 96 patients. The specific allergens included at least one of the allergens in the pollen/inhalant series and/or foods. A total of 202 patients whose history led to suspicion of a dietary causative factor were also prescribed a standardized diet, as described by Zuberbier et al. (5). Forty-one patients discontinued the diet because of low compliance, and 35 declared that they followed regularly without real improvement. A total of 126 patients who were fully compliant for the prescribed period reported an improvement in

subjective symptoms lasting for at least 3 months; 47 out of 126 were positive to placebo-controlled tests of food additives.

The other 75 patients underwent commercially available food prick tests and the CAP-RAST test. When positive, a double-blind, placebo-controlled oral challenge (DBPCOC) was used: 15 patients were positive, the majority to peas and peanuts, as confirmed by DBPCOC with the suspected foods. ESR was high in 48 patients, but only 20 patients had also markedly increased inflammation indexes. Further specific diagnostic tests revealed that 20 of these patients presented a clear focus of infection in dental arcades, paranasal sinuses, urogenital tracts, and gallbladder. Only five were relevant, showing remission on appropriate therapy. Intestinal parasitic infections caused by *Giardia* or other organisms (eight cases of *Ascaris lumbricoides*, one case of *Tenia solium*) were detectable by means of parasitologic stool examinations.

Four patients suffering from urticaria showed a reduced value of complement-altered inflammation indexes and joint pains, and biopsy showed a classical picture of cutaneous vasculitis that could be considered definitely relevant. An association between CU and neoplastic diseases was observed in only two cases. Only 10 patients of the 113 patients who underwent an intradermal autologous serum test were positive. The relevance was difficult to assess because the response to treatment did not correlate with the test. In terms of thyroid alterations, four patients had a hypothyroid state with positive antimicrosomal and antiperoxidase antibodies, whereas six had a hyperthyroid state. Of the 125 patients studied, 78 had circulating antibodies to HP (62%) (6). Eradication of the bacterium led to the subsidence of urticaria in only 4 of 31 patients who received eradication therapy.

In only 100 of 348 consecutive cases was a pathogenic mechanism found.
