

deflazacort generally follows the same metabolic route of all the corticoids.

The patient has shown a positive reaction to betamethasone in three ways of presentation (betamethasone sodium phosphate, belonging to group C, and betamethasone dipropionate and valerate, both included in group D (4). Momethasone also belongs to group D, and is a substance tolerated as well by the patient, confirming in this case that this corticoid does not usually cross-react with others (7).

The final diagnosis was hypersensitivity type IV to betamethasone, dexamethasone, budesonide, hydrocortisone, and deflazacort, but we could not find any bibliographic reference on the last drug. We have indicated for the patient treatment with topical momethasone or 6-methylprednisolone by oral or parenteral administration if needed.

Key words: contact dermatitis; corticosteroid cross-reactivity; deflazacort.

DRA. ANA M^a NAVARRO PULIDO*, J. C. ORTA, G. BUZO

*c/ Argantonio 4, 7° C

41008 Seville

Spain

Accepted for publication 23 April 1996

REFERENCES

1. Doms-Gossens A, Meinardi M, Degreef H. Contact allergy to corticosteroids: the results of a two-centre study. *Br J Dermatol* 1994;130:42-7.
2. Doms-Gossens A, Morren M. Results of routine patch testing with corticosteroid series in 2073 patients. *Contact Dermatitis* 1992;26:182-91.
3. Lepoittevin JP, Drieghe J, Doms-Gossens A. Studies in patients with corticosteroids contact allergy. *Arch Dermatol* 1995;131:31-7.
4. Coopman S, Degreef H, Doms-Gossens A. Identification of cross-reaction patterns in allergic contact dermatitis from topical corticosteroids. *Br J Dermatol* 1989;121:27-34.
5. Doms-Gossens A. Contact dermatitis by corticosteroids. In: *Proceedings (I) of XVI European Congress of Allergology and Clinical Immunology*. Bologna: Monduzzi, 1995:841-5.
6. Gonzalo MA, Bobadilla P. Cutaneous-mucosal allergic contact reaction due to topical corticosteroids. *Allergy* 1995;50:833-6.
7. Rasanen I, Tuomi ML. Cross-sensitization to momethasone furoate in patients with corticosteroids contact allergy. *Contact Dermatitis* 1992;27:323-5.

Anaphylactic-type reaction to hymecromone

HYMECROMONE (H) (7-hydroxy-4-methylumbelliferone, 7-hydroxy-4-2H-1-benzopyran-2-one), a coumarin derivative without anticoagulant effect, has both true choleretic and antispasmodic effect (1-3) when administered orally or intravenously (1, 2). Furthermore, it is used as a reagent in the determination of nitric acid (3). H has a low molecular mass (176.16 Da). It is soluble in meth-

anol and glacial acetic acid, slightly soluble in ether and chloroform, and practically insoluble in cold water (3). This drug rarely produces adverse effects in therapeutic doses. Diarrhea may occasionally occur (2). Accordingly, we reviewed the literature (Medline database from 1966 to January 1996, inclusive) with emphasis on adverse reactions to H, but no associated reactions have been reported; hence, the interest of our case.

A 63-year-old woman, without previous history of allergy, presented cutaneous pruritus, systemic urticaria, and angioedema of the face and hands 20-30 min after eating codfish, eggs, potatoes, lettuce, tomatoes, and cake, and taking one tablet (400 mg) of Bilicanta[®] (hymecromone). The patient had tolerated these foods previously and after the reaction, but she did not remember taking Bilicanta before. Six months after this episode, she was referred to the Allergology Department to determine the cause of the reaction. She had not taken Bilicanta again. The patient gave her written informed consent before the study.

Total serum IgE was 25 UI/ml. Skin prick tests with a standard allergen panel (pollens, mites, molds, animal dander, and food allergens) were negative (ALK Abelló SA, Madrid, Spain).

In addition to H, other drugs with a similar chemical structure were selected for *in vivo* and *in vitro* tests: warfarin and acenocoumarol (coumarin derivatives) and cromoglycate (chromone derivative) (Fig. 1). They were obtained as pure products from the trade-name dealers in Spain. Lymphocyte-transformation tests, human basophil-degranula-

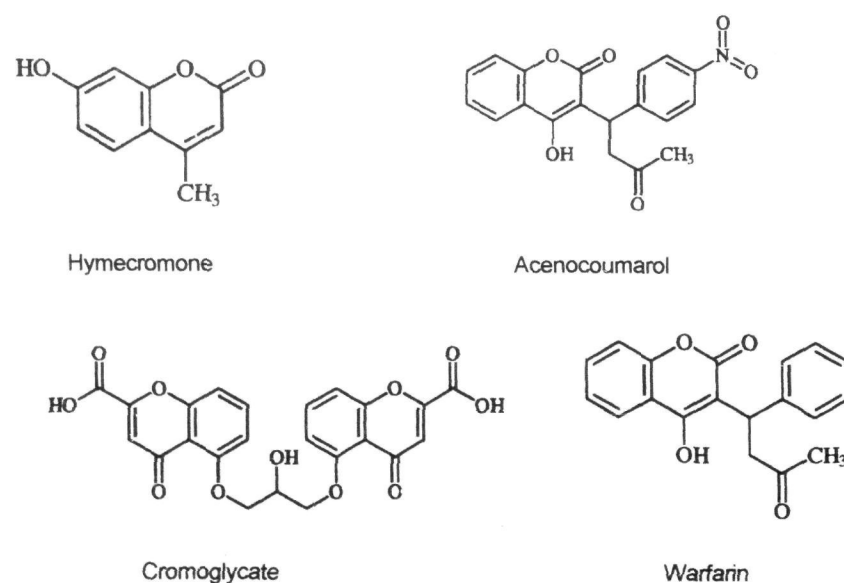


FIGURE 1 Chemical formulas of hymecromone, two other coumarins (warfarin and acenocoumarol), and cromoglycate (chromone derivative).

tion tests, and histamine-release tests were negative for all of these drugs. Specific IgE antibodies against H could not be determined for technical reasons. Prick tests with the same drugs in different vehicles (ether and methanol) and in different concentrations (0.1, 1, and 10 mg/ml) were negative. We did not perform intradermal tests because both ether and methanol were irritants. The oral provocation tests began with a dose of 40 mg of pure H (provided by Boehringer Mannheim SA, Barcelona, Spain). Within 30 min, the patient developed a severe reaction with hypotension (60/30 mmHg); heart rate of 140 beats/min; edema of the face, hands, and uvula; dyspnea; dysphagia; and dysphonia. She required admission to an intensive care unit and administration of subcutaneous epinephrine, as well as intravenous fluids, dexchlorpheniramine, and methylprednisolone. Recovery from this reaction was obtained over the next 2 h. Intravenous dexchlorpheniramine and methylprednisolone were continued for 48 h, enabling the patient to be discharged. Laboratory investigation, including urinalysis; tests for blood cell and differential counts, electrolyte levels, coagulation, arterial blood gases, creatine phosphokinase, lactic dehydrogenase, immunoglobulins, C3 and C4 components of complement, total hemolytic complement (CH50), and circulating immune complexes; and biochemistry profile gave normal results. We did not perform oral provocation tests with other coumarins or cromoglycate because of the serious reaction to H.

H was introduced for human use over 20 years ago. However, we have not found any references in the literature about adverse reactions with this drug, excepting diarrhea (2). We describe an anaphylactic-type reaction by H, a previously unreported complication of this drug. Clinically, it is clear that H caused the syndrome suffered by our patient. A definitive diagnosis can be established from the algorithm of Karch & Lassagna (4) and the "imputability concept" (5). However, it is more difficult to establish the mechanisms implicated in the reaction. In our case, the clinical history made it possible to exclude drug overdose, drug side-effect, and drug interaction. But other conditions, such as drug intolerance, drug idiosyncrasy, drug allergy, or pseudoallergic reaction, which can occur in certain susceptible patients, should be taken into account (6). To confirm drug allergy, one must demonstrate a relevant immunologic reaction to the drug or its metabolites. H has a low molecular mass (176.16 Da) so it is not immunogenic and requires complexing with a carrier protein to elicit an immunologic response. Often, the organic radicals formed by these complexes do not cross-react antigenically with the parent compound, and testing with the drug itself does not utilize the antigen responsible

for the symptoms (7, 8). For those reasons, we cannot come to definitive conclusions regarding our *in vivo* and *in vitro* negative results with H. It is clear that our patient suffered a severe immediate reaction to this drug, but we cannot establish the exact mechanism. Neither an IgE-mediated reaction nor other possible mechanisms of an immediate reaction (such as direct mediator release, anaphylotoxins of the complement cascade, immunocomplex aggregation, etc.) could be demonstrated.

We advised the patient to avoid drugs with similar chemical structure, such as other coumarins and chromones, because of the severity of the reaction.

Key words: anaphylaxis; drug allergy; hymecromone; hypersensitivity; umbelliferones.

DRA. M. A. GONZALO-GARIJO*, F. REVENGA-ARRANZ,
I. MONEO-GOIRI

*Hospital Infanta Cristina
Sección de Alergología
Carretera de Portugal s/n
06080 Badajoz
Spain
Tel. +34 24 21 81 00
Fax: +34 24 21 81 10

Accepted for publication 26 April 1996

REFERENCES

1. Garret ER, Venitz J, Eberst K, Cerda JJ. Pharmacokinetics and bioavailabilities of hymecromone in human volunteers. *Biopharm Drug Dispos* 1993;14:13-39.
2. Reynolds JEF. Martindale: The extra pharmacopoeia. 30th ed. London: Pharmaceutical Press, 1993:1378.
3. Merck index. Windholz M, editor. 10th ed. Rahway: Merck, Inc., 1983:709.
4. Karch FE, Lassagna L. Toward the operational identification of adverse drug reactions. *Clin Pharmacol Ther* 1977;21:247-54.
5. Bégaud B, Evreux JC, Jouglard J. Imputabilité des effets inattendus ou toxiques des médicaments. *Thérapie* 1985;40:111-18.
6. Vervloet D, Pradal M, Charpin D, Porri F. Diagnosis of drug allergy reactions. *Clin Rev Allergy* 1995;13:265-80.
7. Gruchalla RS, Sullivan TJ. *In vivo* and *in vitro* diagnosis of drug allergy. *Immunol Allergy Clin North Am* 1991;11:595-610.
8. Sullivan TJ. Drug allergy. In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, editors. *Allergy: principles and practice*. 4th ed. St Louis, Mo: Mosby, 1993:1726-46.

Tryptase – at last a useful diagnostic marker for anaphylactic death

THE postmortem diagnosis of anaphylactic shock has previously been based on the circumstances of death and absence at autopsy of specific pathologic and toxicologic findings which could explain death. Analysis of histamine and degradation products in blood is not feasible after death (1). Measurement of total IgE and IgE antibody with

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.