Occupational contact dermatitis due to pyritinol

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Key words: allergic contact dermatitis; occupational; laboratory assistant; pharmaceutical industry; pyridoxine; pyritinol; pyrithioxine; airborne contact dermatitis; cross-sensitivity.

Pyritinol, originally developed as a cerebroactivating agent, is a compound of 2 molecules of pyridoxine (vitamin, B_6) (1). The structural analogy of its metabolite, 5-mercapto-pyridoxine, with d-penicillamine led to its use in rheumatoid arthritis (2, 3).

Case Report

A 17-year-old laboratory assistant, 4 months after starting to work on quality control in a pharmaceutical company, developed eczema on the face and hands. She had previously had seasonal rhinoconjunctivitis, with positive prick tests to pollens. Her symptoms coincided with working on pyritinol and other derivatives of pyridoxine used in the synthesis of Encephabol® (pyritinol hydrochloride). Patch tests with the European standard, medicaments and preservatives series (Hermal) were negative. Patch tests with pyridoxine derivatives (2% aq.) used in the laboratory resulted in +++ reactions to pyritinol, pyritinol hydrochloride and 2 bases used in the synthesis of Encephabol® after 2 and 3 days. The bases contained pyritinol, pyritinol hydrochloride and precursor molecules, the exact nature of which was unknown. 10 unexposed persons tested as controls were negative.

Discussion

Pharmaceutical workers feature among high-risk occupations for allergic contact dermatitis (4–6). The risk to chemists and laboratory workers is higher than from well-contained synthetic processes (7, 8). Compared to other branches of the chemical industry, morbidity is 3× higher and dermatoses show a shorter induction time (9). Many groups of therapeutic agents cross-react (4, 10), which is true of pyridine derivatives (11, 12). Pyridoxine is 1 of the 3 interchangeable compounds referred to as vitamin B_6, the other 2 being pyridoxal and pyridoxamine (13). Contact sensitization to pyridoxine and its derivatives (13–16) is well-known and often occurs in the production of vitamin B_6 (11), the derivative 2-methyl - 3 - nitro - 4 - methoxymethyl - 5 - cyano - 6 - chlorpyridine being the sensitizer. A similar derivative, ricinine (1-methyl-3-cyano-4-methoxy-2-pyridon), has caused occupational contact allergy in the production of castor oil (11). Tanaka et al. (17) reported a photoallergic drug eruption due to pyridoxine hydrochloride and Morimoto et al. (18) a patient with photosensitivity due to pyridoxine hydrochloride in a multivitamin preparation (18).

Pyritinol hydrochloride (pyrithioxine), the active ingredient in Encephabol®, is the dihydrochloride monohydrate of pyritinol, which has the formula bis(4-hydroxymethyl-5-hydroxy-6-methyl-3-pyridylmethyl) disulfide (Fig. 1). Pyritinol has previously been described as causing cutaneous side-effects such as pemphigus and pemphigus-like-reactions (19–22), lichenoid reactions (23, 24), lichen-planus-like eruptions from photosensitive dermatitis due to oral pyritinol (1), and erythema-multiforme-like eruptions (25). The free sulfhydryl (SH-) group in thiol drugs may contribute to the induction of the skin lesions (25, 26). However, to our knowledge, this is only the 2nd reported case of allergic contact dermatitis from pyritinol. Dooms-Gossens et al. (27) reported a nurse who developed airborne contact dermatitis due to Encephabol® tablets, which she had to crush between 2 spoons prior to administration.Because of the powder form of many products in the pharmaceutical industry, airborne contact dermatitis, as in our case, is not uncommon (27, 28).

It is not clear whether our patient was sensitized to pure pyritinol and pyritinol hydrochloride only, or to precursor molecules in the bases. Pyridine, the base structure of pyridoxine, is widely used in laboratories as a solvent (10). Our patient changed her job, terminating exposure to all pyridine derivatives, though she was not tested to pyridine itself, and the dermatitis healed quickly.

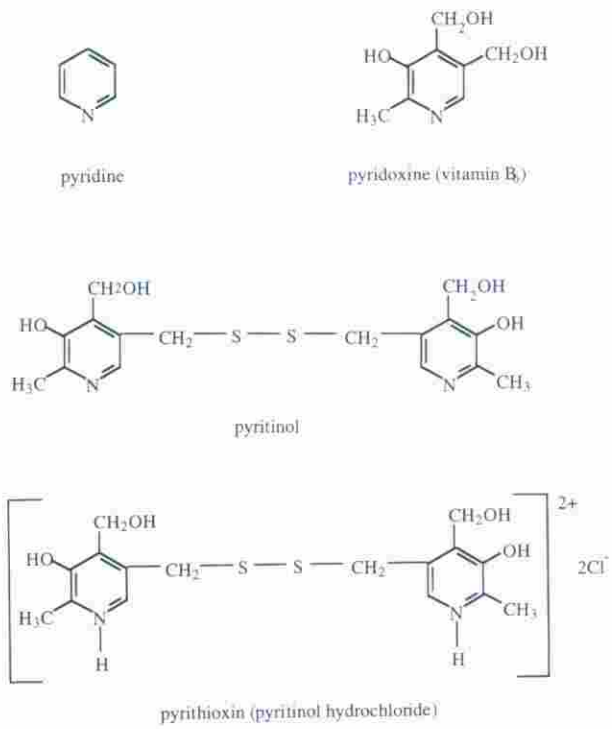

Fig. 1. Chemical structures of pyridine and pyridoxine derivates.

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Induction of contact sensitization to monotertiary butyl hydroquinone

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Key words: monotertiary butyl hydroquinone; TBHQ; contact sensitization; photosensitization; repeat insult patch test; antioxidant; CAS 1948-33-0; antioxidants; foods; cosmetics.

Monotertiary butyl hydroquinone (TBHQ) is an antioxidant. It has FDA clearance for use in foods at levels not to exceed 0.02% of oil or fat content (1). In addition, the Cosmetics Ingredients Review (CIR) Expert Panel has approved its use in cosmetics at concentrations not to exceed 0.1% (2, 3). Included in their review were 4 human repeat insult patch test (RIPT) studies in a total of 271 participants. No sensitization reactions were induced using concentrations ranging from 0.054–0.15%.

Methods and Results

There were 114 participants in an RIPT and 25 in a photosensitization study. Both studies used 0.20% TBHQ in pet., 0.2 ml of which was applied under an occluded Webril® patch (Kendall Health Care Products, Greenwood, SC, USA).

In the RIPT, induction patches were applied 3×/week for 3 weeks (4). After a 2-week rest period, a challenge