able improvement was noted on the 5th day, and the patient became symptom-free on the 10th day. In the summer she was able to sunbathe, yet remained and has been symptom-free up to now.

Discussion

The deposition of acid mucopolysaccharides in the dermis in cutaneous mucinoses and in REM syndrome is most probably a secondary phenomenon due to a hitherto unknown cause. In the first group of diseases it is accompanied by an increased number of fibroblasts; in the second condition by a perivascular or/and perifollicular infiltrate of patchy character. The infiltrate is composed mainly of lymphocytes, but lymphoblasts or stimulated lymphocytes also occur in them (6, 11). These cellular elements may play a part in the deposition of acid mucopolysaccharides in which connection no immunoglobulin deposition was found (1, 2, 4).

The eruptions appear mostly after sun exposure (10, 11) although the MED values are usually normal (1, 2, 11), as in our case. Another interesting point is the good therapeutic response to chloroquine derivates (1, 4, 6, 10, 11, 12). The action mechanism of these preparations in photosensitive eruptions is thought to be the drug's binding to the DNA (9). In REM syndrome the infiltrations contain stimulated lymphocytes (6, 11), and the chloroquine derivates might have something to do with their DNA-rich nuclei. Their action in other forms of mucinoses (5, 7) might be connected with the fibroblasts which normalize their activity.

Investigations into the action mechanism of chloroquine might throw some light on the pathogenesis of mucinoses and REM syndrome.

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Topical Application of Zinc-Solutions: A New Treatment for Herpes Simplex Infections of the Skin?

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Abstract. Eighteen patients experiencing 22 episodes of recurrent herpes simplex skin infections were treated with topical applications of a solution containing 4% zinc sulphate in water. In all patients, pain, tingling and burning stopped completely within the first 24 hours of zinc therapy. Crusting occurred within 1–3 days and no adverse effects were observed.

Recurrent herpes simplex infections, although usually self-limited, are an annoying source of discomfort and embarrassment. Topical therapy with iododeoxyuridine (6), adenine arabinoside (2), cytosine arabinoside (8) and ether (2) have been shown to be without effect on the clinical course of this condition. Photodynamic inactivation has been reported to be effective in the treatment of orolabial and genital herpes Simplex (4); however, the safety of this form of therapy has been questioned, since photodynamically inactivated herpes simplex virus can induce neoplastic transformation in vitro (10) and in vivo (7).

Solutions of zinc salts have been reported to be effective in the treatment of herpetic keratitis in man (3). More recently, zinc ions have been shown to cause irreversible inhibition of herpes simplex

virus replication in vitro (5). On a molecular basis, zinc ions were found to inhibit the activity of herpes simplex virus specified DNA polymerase (11). It was therefore decided to try to treat patients suffering from recurrent herpes simplex infections of the skin with topical applications of zinc. The results of this preliminary trial are reported in this paper.

PATIENTS AND METHODS

Eighteen patients experiencing 22 episodes of recurrent herpes simplex skin infections were treated with topical applications of a solution containing 4% zinc sulphate in water. Only patients who had visible evidence of recurrent herpes simplex virus infection for less than 48 hours were included. All patients were otherwise healthy young adults and none of them was receiving any systemic medication; 12 of them were female and 6 were males. In 16 of the patients, the diagnosis was confirmed by virological culture. Fourteen of the patients had orolabial lesions, while the remaining 4 had genital infections.

At their first visit, a detailed history was obtained from each of the patients and the following information was recorded: duration of the disease, causes of recurrence, frequency of recurrences, previous treatments, and the average time required for crusting and for complete healing. The vesicles were ruptured and unroofed with a sterile 23-gauge needle and a 4% aqueous solution of zinc sulphate was applied in the form of a wet dressing for a period of one hour at least. In cases of labial lesions, patients were cautioned to take care not to ingest the solution. Instructions were given to repeat the treatment at home four times daily for a total of 4 days. The patients were re-examined every 1 to 3 days in order to evaluate symptomatic improvement and the time required for crusting and for complete healing.

RESULTS

Previous treatments had included iododeoxyuridine ointment, 70% ethanol, tincture of iodine and solutions of silver nitrate. According to the patients' accounts, in previous attacks, the time needed for crusting had ranged between 4 and 10 days (mean: 7 days) whereas the time needed for complete healing had ranged between 10 and 21 days (mean: 16 days).

Sixteen of the patients noted symptomatic relief superior to that experienced with other therapeutic modalities previously used. In all patients, pain, tingling and burning abated and stopped completely within the first 24 hours of zinc therapy. In 2 of the zinc-treated episodes, crusting occurred within 24 hours; in 14 episodes, within 48 hours, and in 3 episodes, within 72 hours after zinc therapy was instituted. In 2 patients new vesicles appeared in adjacent areas 48 and 72 hours after therapy was started. The time needed for complete healing in the 22 zinc-treated episodes ranged between 6 and 12 days (mean: 9.5 days). No adverse reactions of therapy were reported.

DISCUSSION

The results of the present study suggest that topical applications of zinc salts might be helpful in alleviating the symptoms and in enhancing the healing of recurrent herpes simplex virus infections. However, since it is known that in every therapeutic study of herpes simplex infections there is an important placebo effect and a great amount of subjectivity on the part of both patient and physician, one should be very careful in evaluating the results of such uncontrolled studies as the present one. On the other hand, these results seem to be sufficiently encouraging to warrant well-controlled, double-blind and long-term studies conducted on a large number of patients. Such studies are essential in order to confirm the therapeutic efficacy of topical zinc solutions in herpetic skin infections. In such cases, topical zinc may prove to be a safe, easily available and inexpensive form of treatment for this condition. Moreover, topical applications of zinc solutions may prove to be especially helpful in the treatment of the more rare and more severe herpes simplex infections of the skin such as primary genital infections or those occurring in patients with hematological malignancies (9, 12).

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Plasma Concentrations after Bath Treatment and Oral Administration of Trioxsalen

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Abstract. An analytical method comprising homogenous extraction and determination by gas chromatography mass spectrometry has been developed for the quantitation of trioxsalen in plasma. The limit of sensitivity of the method has been 2 ng/ml of trioxsalen. The method was used to monitor concentrations of trioxsalen in plasma after a 40 mg oral dose or after trioxsalen bath treatment. The concentrations in plasma after oral administration did not exceed 3 ng/ml, while in 2 patients after bath treatment trioxsalen could be determined (2–3 ng/ml). The low plasma concentrations found throw light on the poor UV-sensitizing properties found after oral trioxsalen therapy.

Key words: Trioxsalen; Photochemotherapy; Plasmaconcentrations; Skin absorption

Photochemotherapy implies sensitization of the skin, usually with psoralens, followed by UV-irradiation. This method (PUVA) is increasingly used in the treatment of psoriasis and other dermatoses (3, 4, 6, 12).

The most commonly used sensitizing agent is 8-methoxy-psoralen (8-MOP) given orally (12). Oral trioxsalen is less commonly used but the sensitizing properties of this therapy are not well documented. Local administration with 8-MOP in an ointment or in a bath also gives the skin high UV-sensitivity, but the highest sensitization is achieved with trioxsalen bath treatment (3, 4, 6).

Several studies have been performed on the pharmacokinetics of 8-MOP in human, after both oral and local treatment (7, 11). Studies on the disposition of trioxsalen have only been reported in rats (10).

SUBJECTS AND METHODS

Patients

Blood samples were drawn from 4 patients with psoriasis at different time intervals after taking a trioxsalen bath. The bath was prepared by adding 50 mg trioxsalen (Paul B. Elder Co., Bryan, Ohio) in 0.1 litre of alcohol to 150 litres of 37°C water. After the 15 min bath and drying, the patient was exposed to unfiltered light of the dysprosium solarium (3). Blood samples were drawn before, immediately after and at 30 min after the bath. In another 2 patients, samples were also drawn at 1, 2, 4, 6 and 8 hours after the bath. Two patients were given 40 mg of trioxsalen (Trisoralen; Elder Co, Bryan, Ohio) orally after a breakfast consisting of milk, two slices of bread and butter with marmalade or cheese, and coffee (2). Blood samples were drawn at 0, 1, 2, 3, 4, 6 and 8 hours after the administration. After sampling, the plasma was immediately separated and stored at −18°C until analysis not more than 3 days later.

Analytical procedure

Extraction. Four different extraction procedures were tested.

1. One ml of plasma was, after addition of an internal standard (8-methoxypsoralen 50 ng in 0.1 ml of alcohol) and 1 ml of phosphate buffer 0.1 M, pH 7.4 and water to 5 ml, shaken with 5 ml of distilled toluene for 60 min. After removal of the aqueous phase, the toluene layer was washed for 15 min in order with 2 ml of 0.05 M phosphoric acid and then with 2 ml of 0.1 M phosphate buffer, pH 10. The organic layer was evaporated to dryness and reconstituted in 30 μl of heptane.

2. The composition of the extraction mixture was the same as in 1. The mixture was shaken at 50°C for 20 min and, after centrifugation, the toluene layer was evaporated to dryness and redissolved in heptane.

3. One ml of plasma was, after addition of an internal standard (8-methoxypsoralen 50 ng in 0.1 ml of alcohol) shaken with 5 ml of acetone for 15 min. Four ml of toluene and 5 ml of water were added and the mixture was shaken