Heparin Action in Pemphigus vulgaris: Clinical and Immunologic Studies

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Heparin administration to 34 patients with pemphigus vulgaris before the beginning of steroid treatment or in combination with it proved to be therapeutically useful. Its suppressive effect on T- and B-lymphocytes in vitro and in vivo was revealed in the examined patients by the test of rosette-formation. *Key words: T- and B-lymphocytes; Rosette-formation; Blood coagulation.* (Received January 15, 1985.)

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Five communications about clinical trials of heparin in pemphigus were published in the 1950s (1–5). Except in one case (3), good clinical results were registered. The reason for heparin administration in these cases was the disturbed balance between hyaluronidase and hyaluronic acid which, in the authors' opinion, took place in pemphigus. However, these reports have gone unnoticed.

We studied the action of heparin in vitro on the rosette-formation of T- and B-lymphocytes of the peripheral blood in patients with pemphigus vulgaris. On the basis of the data obtained, heparin was used as a treatment for 34 patients with active pemphigus. Heparin (10000 IU) was administered intramuscularly every 12 hours, 15 to 40 injections for the course of treatment under control of blood coagulation.

PATIENTS

The study material comprised 34 patients with a confirmed diagnosis of pemphigus vulgaris, 15 males and 19 females, 31–65 years of age, in the active stage of the disease. In 13 patients, steroid therapy had not yet been started. Twenty-one patients had a recurrence of the disease despite steroid administration. In 11 patients, pemphigus erosions were localized on the oral and laryngeal mucous membranes. A further 23 patients had widespread lesions on the skin, mucous membranes and genitalia. The general state of 18 patients was estimated as severe, and in all the other patients as moderately severe. The duration of pemphigus in 11 of 21 patients who were receiving steroids was 1.5–3 months. At the time of examination they were receiving 50–100 mg of prednisolone daily, giving a rather weak clinical effect. Two of these 11 patients also received methotrexate in 5-day courses. Other 10 patients had pemphigus for 1–7 years. In six of them the course of the disease was especially severe and they received 80–100 mg of prednisolone a day for 1–2.5 months.

METHODS

To evaluate possible hemostatic disorders in pemphigus and the possibility of heparin administration for the treatment of the disease, eight coagulation tests were screened before, during and after heparin administration (Lee-White clotting time, activated partial thromboplastin time, prothrombin time, prothrombin activity, thrombin clotting time, heparin cofactor assay, fibrinogen, euglobulin lysis time).

Lymphocytes were isolated from the samples of peripheral blood of patients by gradient centrifugation on Ficoll-Hypaque. T-lymphocytes were determined by E-rosette technique (6), and for the detection of B-lymphocytes we used a test of rosette-formation with mouse erythrocytes as described by Forbes & Zalewski (7). To evaluate the action of heparin in vitro on T- and B-lymphocytes, the same tests were performed in the presence of heparin (75 IU in 1 ml).

RESULTS

Coagulation tests showed that heparin in the used dosage did not significantly affect the state of blood coagulation. None of the registered deviations exceeded the normal level.

The mean quantity of T-lymphocytes after incubation with heparin decreased from 73±3% to 56±3%, and that of B-lymphocytes from 22±2% to 12±1%. At the same time there was no change in total lymphocyte quantity.

In the group of 13 patients to whom heparin was administered instead of steroid treatment the complete healing of erosions was obtained in three cases, and a considerable improvement with a partial healing of erosions in six cases. The epithelialization of erosions was not noted in three patients but no new lesions appeared during heparin therapy. In one patient with widespread pemphigus lesions on oral and laryngeal mucous membranes further exacerbation of the disease occurred and new lesions appeared. Therefore, heparin injection was discontinued after five days and steroid treatment started.

Clinical remission with a complete healing of all erosions was obtained in 12 of 21 patients who were treated with the combination of heparin and steroids, and the dose of steroid could be reduced. In 9 other patients of this group a gradual disappearance of pemphigus lesions occurred without an increase of steroid dose. No side effects or complications were registered during heparin administration.

The study of lymphocytes in the peripheral blood of 34 patients with pemphigus vulgaris

after clinical administration of heparin showed the decrease of T-lymphocyte mean quantity to be from 73±3% to 66±2% and that of B-lymphocytes from 22±2% to 14±1%.

DISCUSSION

Heparin is a drug with manifold biologic capabilities. It decreases cytotoxic action of antibodies on cells (8), influences the quantity of lymphocytes in the peripheral blood (9) and T- and B-lymphocyte cooperation (10), changes immunoproliferative capability of T- and B-cells (11). In the present study the suppressive effect of heparin on T- and B-lymphocytes in patiens with pemphigus vulgaris was revealed by the rosette-test. The results obtained in vitro, after lymphocyte incubation with heparin, and those obtained in vivo, after heparin administration for the treatment of pemphigus, were rather similar. However, the mechanism of heparin in pemphigus needs further investigations.

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