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EFFECT OF QUERCITRIN ON STRUCTURAL CHANGES IN THE LARGE AND SMALL INTESTINE IN EXPERIMENTAL ENTEROCOLITIS

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Sensitization of rats with homologous antigen of large intestine together with Freund's adjuvant causes marked immunological changes in the large intestine of rats with manifestations of enteritis in the small intestine. Oral administration of the flavonoid quercitrin in a dose of 25 or 100 mg/kg daily for 10 days leads to a decrease of the focal lymphohistiomonocytic infiltration and eosinophilic exudation in the mucous membrane and of the sclerotic changes in the stroma of the large intestine. Meanwhile the structural disturbances in the small intestine are repaired. The effect of quercitrin on morphological changes in the epithelium of the mucosa of the large and small intestine was very slight. It is postulated that the therapeutic action of quercitrin may be due to restoration of the local circulation when disturbed by sensitization of the animals.

KEY WORDS: allergic enterocolitis; quercitrin.

Focal perivascular infiltration, edema, and disturbance of the local homeostasis and microcirculation arising in the intestinal mucosa during the antigen–antibody reaction [1, 7] lead to a disturbance of its specific function [4, 9]. For a long time now, to depress the autoallergic reaction in enterocolitis steroid hormones [5, 11, 14], immunodepressants [13], and antihistamine [3, 10] drugs have been given. However, these substances have side effects [6, 11, 15] and they are not always effective [6], especially in the late stages of sensitization [2]. During the development of a pathogenetic therapy of enterocolitis, especially in the period of allergic manifestations, substances regulating vascular permeability might prove effective.

The object of this investigation was to study the possibility of using the flavonoid quercitrin in order to depress immunomorphological changes arising in the intestinal mucosa during autosensitization of animals with homologous antigen of the large intestine.

EXPERIMENTAL METHOD

An allergic model of enterocolitis was produced by sensitizing animals with homologous antigen of the large intestine together with Freund's adjuvant. Experiments were carried out on 60 male albino rats weighing 170-190 g. Four injections of antigen were given at intervals of 7 days. The animals were divided into four groups: 1) intact rats, 2) sensitized but untreated animals (control), 3) sensitized animals receiving

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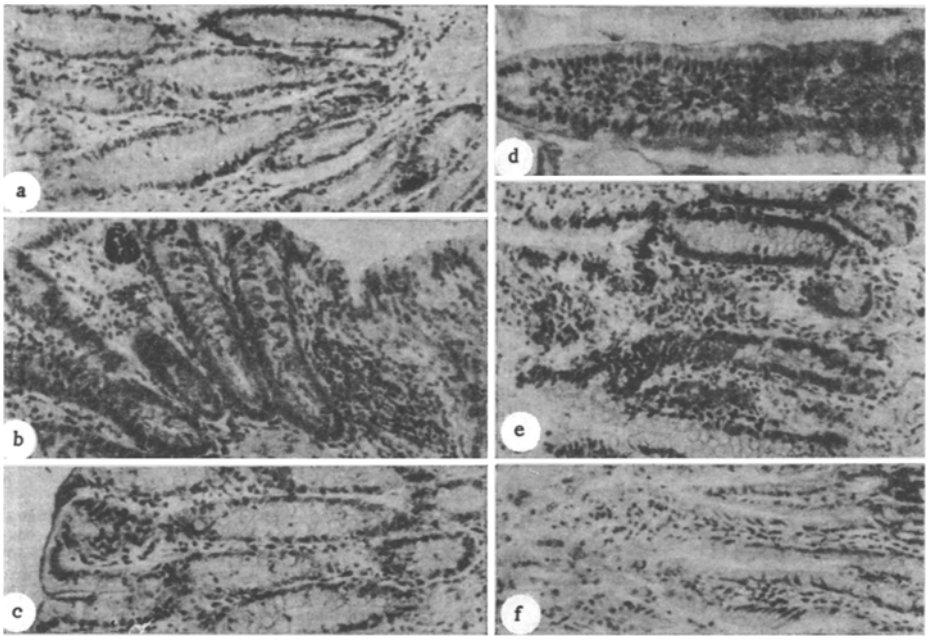

Fig. 1. Structural changes in mucosa of large and small intestine of rats with experimental enterocolitis: a) mucous membrane of large intestine of intact animals; b) intestinal mucosa of rat with enterocolitis; foci of lymphohistiomonocytic infiltration in its stroma; c) mucosa of large intestine of rat receiving quercitrin in dose of 100 mg/kg; diminution of infiltration and eosinophilic exudation; d) small intestine in intact animals; e) mucous membrane of small intestine of rat with enterocolitis; marked inflammatory changes with disturbance of architectonics of villi; f) mucosa of small intestine of rat receiving quercitrin in a dose of 100 mg/kg; repair of structural changes in small intestine. Hematoxylin–eosin, 150 ×.

quercitrin in a dose of 25 mg/kg; 4) sensitized rats receiving quercitrin in a dose of 100 mg/kg. The flavonoid was given by mouth from the 28th day after the beginning of sensitization for a period of 10 days.

Pieces of small and large intestine were taken from the experimental animals for histological study, fixed in 10% neutral formalin, and embedded in paraffin wax. Sections were stained with hematoxylin–eosin.

The degree of allergic inflammation was judged from the extent of the perivascular lymphohistiomonocytic infiltration of the mucosa and of eosinophilic exudation. The severity of the nonspecific inflammation was assessed relative to the intensity of polymorphonuclear infiltration.

EXPERIMENTAL RESULTS

On histological examination of the mucosa of the large intestine of the sensitized control animals (group 2) signs of allergic inflammation were found. They consisted mainly of focal perivascular lymphohistiomonocytic infiltration of the stroma (Fig. 1b), plasmorrhagia of the vessel walls, and infiltration with plasma cells. Other characteristic features were accumulation of eosiniophils in the stroma of the mucosa and swelling, edema, and focal sclerotic changes in the submucous layer. Taken together, the morphological changes found in the mucosa of the large intestine pointed to the immunological nature of the pathological process.

Marked polymorphonuclear infiltration of the stroma, congestion, and hemorrhagic foci were found in the mucosa of the small intestine of the animals of group 2. By contrast with the changes in the large intestine, no perivascular foci of lymphohistiomonocytic infiltration were observed in the stroma of the small intestine. Otherwise the morphological picture found in the small intestine of the experimental animals was similar to the changes in enterocolitis of infectious etiology (Fig. 1e) [8].

Changes in the epithelium of the large and small intestine were similar in character: The cells became flatter, their nuclei were displaced toward the apical end, their regular orientation was altered, and their outlines became indistinct. The number of goblet cells in the epithelium of the small and large intestine was appreciably reduced.

Administration of quercitrin accelerated restoration of the normal structure of the mucosa of the large intestine (Fig. 1c). The perivascular foci of lymphohistiomonocytic infiltration were reduced in size, the edema of the mucosa diminished, and no sclerotic changes were seen in the stroma of the submucosa. Infiltration of the mucous membrane with eosinophils was much less marked than in the sensitized, untreated animals. Meanwhile structural changes in the epithelial cells persisted for a longer time. The increase in the number of goblet cells under these experimental conditions should be noted.

The morphological changes in the mucosa of the small intestine of the animals receiving quercitrin also were appreciably less severe and the mucous membrane acquired its normal structure (Fig. 1f).

From the combination of morphological changes observed in the epithelium and stroma of the mucosa of the large intestine in the sensitized animals it can be deduced that the structural changes were due to the action of substances liberated during the antigen–antibody reaction [1, 6].

The beneficial effect of quercitrin on the immunomorphological changes in the intestinal mucosa of the sensitized animals was evidently due to the action of several factors.

1. Quercitrin, it can be assumed, depresses the antigen-binding capacity of the mucosa of the large intestine. This is shown indirectly by the decrease in size of the foci of lymphohistiomonocytic infiltration in the mucosa of the large intestine of the animals receiving quercitrin.

2. Second, quercitrin reduces the manifestations of the inflammation in the small intestine of the sensitized rats ordinarily accompanying immunomorphological changes in the large intestine.

3. Quercitrin can evidently restore normal vascular permeability in the allergic reaction of delayed type [12]. At the same time, it must be emphasized that the effect of quercitrin on the structural changes in the intestinal epithelium was less marked.

Analysis of the results of these experiments and of data in the literature thus indicates a positive action of quercitrin on the structural changes in the intestinal mucosa of animals with experimental enterocolitis. The action of quercitrin can be considered to be aimed mainly at improving the local circulation when disturbed by organ-specific sensitization.

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