Effect of Disodium Cromoglycate (Intal®) on Antigen-Induced Histamine Release from Passively Sensitized Human Lung in vitro

H. Morr

1. Medizinische Universitätsklinik Hamburg-Eppendorf und Abteilung für klinische Immunologie und Allergologie

Abstract. Human lung passively sensitized with anti-grass pollen IgE antibodies releases histamine upon exposure to a specific antigen. In the present experiments disodium cromoglycate is shown to be a potent inhibitor of histamine release. When it was added in concentrations of $10^{-3}$ and $10^{-5}$ mol prior to the antigen, histamine release was reduced to 56% and 29%, respectively. The results clearly demonstrate the protective effect of disodium cromoglycate in IgE-mediated allergic reactions and underline its value in the treatment of extrinsic allergic asthma.

Key words: Histamine release - DSCG - Human lung tissue - Bronchial asthma - Passive sensitization

The initial event in the pathogenesis of allergic bronchial asthma is an immediate hypersensitivity reaction when the precipitating allergen becomes bound to specific tissue mast cells which are passively sensitized with IgE antibodies, thus inducing the release of pharmacologically active mediators (histamine, slow reacting substance of anaphylaxis (SRS-A), eosinophil chemotactic factor of anaphylaxis (ECF-A), bradykinin, kallikrein and prostaglandins). In spite of our advances in understanding the immune mechanisms in allergic bronchial asthma, therapy is not yet satisfactory. Improved control of immune responses and mediator release will require better understanding of the pathogenesis of the disease.

Experiments in vivo with drugs in patients with allergic bronchial asthma present considerable disadvantages. Such studies on the protective effect on antigen-induced bronchial obstruction may cause considerable risk for the patient because the allergic reactions brought on by bronchial provocation tests cannot be satisfactorily controlled. In addition, since these trials only provide information on airway caliber, they do not offer conclusive evidence about whether the tested substance (1) merely acts on the bronchial smooth muscle, (2) interferes with the intracellular events accounting for the histamine release, or (3) has influence on both mechanisms.
Appropriate tests with isolated cells or cell cultures therefore provide a remarkable advantage. The procedure whereby antigen-induced histamine is released from passively sensitized human lung ensures the differentiated assessment of the efficacy and mode of action of those drugs which are being used in the treatment of bronchial asthma [10, 12, 16, 18]. This is supported by the results of the following experiments using disodium cromoglycate (DSCG).

Methods

The procedure is itemized in Figure 1. Human lung tissue was obtained from thoracic surgeons who were operating on patients mainly affected with pulmonary and bronchial carcinomata. After removal of the pleural parts, visible bronchioles and vessels, the lung tissue was chopped and washed several times with Tyrode’s solution to reduce the remaining blood constituents. Passive sensitization with IgE antibodies was carried out for 3 h with the serum of patient E. F., who was suffering from allergic asthma. The tissue was washed again several times with Tyrode’s solution to remove the non-cell attached IgE antibodies and then exposed for 5 min in concentrations of $10^{-3}$, $10^{-7}$ and $10^{-9}$ mol to disodium cromoglycate (Fisons, Loughborough, England) and finally incubated for 15

---

1 We are grateful to Prof. Dr. V. Bay (1. Chirurgische Abteilung des Allgemeinen Krankenhauses Harburg) and Prof. Dr. K. von Windheim (Krankenhaus Grosshansdorf) for providing the lung tissue specimens.