BETA-ADRENERGIC REGULATION OF THE BLOOD LYMPHOCYTE PHENOTYPE DISTRIBUTION IN NORMAL SUBJECTS AND SPLENECTOMIZED PATIENTS

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ABSTRACT

The beta-adrenergic effect on the release of immunoregulatory cells from the spleen was investigated by physical stress testing (bicycle ergometry up to submaximal work capacity) in 19 normal subjects (15 males, median 21 years) and in 10 male patients splenectomized for trauma (median 29 years). It was repeated in 6 subjects of each group during beta-blockade with 80mg oxprenolol. Blood samples for leucocyte analysis were taken before and at the end of the test. Leucocyte subpopulations were analyzed in a cytofluorograf after staining of buffy coat cells by direct (B cells) or indirect immunofluorescence with monoclonal antibodies directed against the phenotypes of T- (Leu-1), T helper- (Leu-3a), T suppressor/cytotoxic (Leu-2a) cells and natural killer (OKM1+ lymphocytes) cells.

In the controls all leucocyte subsets increased at ergometry, but B-, Leu-2a- and OKM1-cells increased more than Leu-3a cells. During beta-blockade the leucocyte changes reached only 50% of the value without treatment; the B- and Leu-2a cell mobilization was reduced more than the Leu-3a-, OKM1 cell- and monocyte changes. In splenectomized patients the proportional cellular changes were only half of those found in normal subjects, except for the Leu-3a cells which were not released. Beta-blockade during ergometry had no
effect on Leu-3a cells, a similar effect on B- and Leu-2a cells as in normal subjects and a stronger effect on granulocytes, monocytes and OKM1 cells than in controls. In conclusion, the B- and Leu-2a cell mobilization from the spleen (50%) was beta-adrenoceptor dependent, while the one from other lymphoid organs was beta-adrenoceptor independent. The strongly spleen dependent Leu-3a cell changes were not beta-adrenoceptor mediated. Granulocyte-, monocyte- and OKM1 cell changes were only partly spleen dependent. The spleen independent changes however were strongly beta-adrenoceptor dependent.

INTRODUCTION

In normal subjects adrenergic activation by injection of adrenergic agents or physical stress leads to granulocytosis and monocytosis; it produces a lymphocytosis, which is due to an increase of cells with surface immunoglobulin (sIg), with Leu-2a- or OKM1 phenotype. Beta-adrenergic stimulation by isoproterenol bolus injections in vivo mimics these changes to a lesser extent.

In the present study the beta-adrenergic specificity of the altered blood leucocyte distribution induced by adrenergic stimulation was further investigated by performing physical stress tests in normal subjects without and with beta-blockade. The qualitative and quantitative contribution of the spleen to the cell mobilization induced by sympathetic activation is not known. Therefore the effect of physical stress and beta-blockade upon lymphocyte phenotype distribution was also studied in splenectomized patients.

METHODS

Twenty normal subjects, fifteen males, aged 17 to 27 years (median 21 years) and ten male patients after splenectomy because of trauma were studied, their age ranged between 18 and 44 years (median 29 years). The time interval between splenectomy and the present investigation ranged from 1 to 18 years (median 7 years). At 8 am. an indwelling cannula was placed intravenously. After a rest of 30 minutes in the supine position, bicycle ergometry was carried out up to submaximal work capacity. Blood samples for the determination of the leucocyte distribution were taken before and at the end of ergometry. Heart rate was calculated from the electro-cardiogram which was recorded during ergometry. Six subjects of each group received 80mg of the beta-blocker oxprenolol orally, when their heart rate had reached basal values after the initial ergometry. They were then allowed a rest of 30 minutes in the supine position, after which they underwent a second ergometry with the same work load as before; Blood was again collected before and at