PLASMA LEUKOTRIENE B_4 and C_4 LEVELS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Familial Mediterranean fever (FMF), or periodic fever, is a hereditary disease characterized by pain and febrile syndromes and associated with inflammation of the serous membranes [2]. The pathogenesis of this disease is still unknown and it may perhaps be connected with leukocyte function or, in particular, degranulation of neutrophils and secretion of lysosomal enzymes and pyrogens [2, 3]. An important role in inflammatory reactions in the body is played by the eicosanoids, a large group of highly active bioregulators which are arachidonic acid metabolites [7]. The writers showed previously that platelets from patients with FMF produce thromboxane A_2 (TxA_2) and 12-hydroxyeicosatetraenic acid (12-HETE) much less actively during incubation with arachidonic acid than healthy human platelets [4]. TxA_2 and 12-HETE formation show little change during an episode, or after sessions of hyperbaric oxygenation (HBO), which cuts short attacks [4]. Since 12-HETE inhibits leukocyte 5-lipoxygenase [5], we suggested that exacerbation of FMS may be linked with increased formation of leukotrienes and other oxidation products of arachidonic acid via the C-5 pathway [4]. Leukotriene B_4 is a stimulator of chemotaxis and chemokinesis of leukocytes, and induces degranulation of polymorphs and secretion of lysosomal enzymes, as well as aggregation of polymorphs and their adhesion to vascular endothelial cells [6]. Leukotriene C_4 increases capillary permeability and secretion of mucous, it is a mediator of inflammation and allergy, and it plays an important role in several pathological states [9].

The aim of this investigation was to study leukotriene B_4 and C_4 levels in peripheral blood plasma from patients with FMF.

EXPERIMENTAL METHOD

Leukotrienes B_4 and C_4 were determined in peripheral blood plasma by radioimmunoassay using kits from Amersham International (system for analysis of [^{3}H]-leukotriene B_4 and specific system for analysis of [^{3}H]-leukotriene C_4 – monoclonal antibody) and a Mark III (Tracor) β-scintillation counter, using the recommended methods.

Preliminary purification of the blood plasma samples was carried out by solid-phase extraction of the leukotrienes by means of a Sep-Pak C_{18} attachment (Waters) with alkylated silica-gel by Powell's method [10].

Blood from 10 patients with FMF and eight healthy blood donors was used.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that the levels of leukotrienes B_4 and C_4 in the plasma of patients with FMF was twice and 3 times higher than the normal level, respectively. During an episode it rose by a further 54 and 74 mg/ml, respectively, for leukotrienes B_4 and C_4. After a session of HBO, their levels in the patients' plasma returned close to the basal values.

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TABLE 1. Blood Plasma Leukotriene B_4 and C_4 Levels (in pg/ml) in Healthy Individuals and Patients with FMS during an Episode and after a Session of HBO ($M \pm m$)

Group of subjects	Leukotriene B_4	Leukotriene C_4
Healthy blood donors	25±4	67±19
Patients with FMF:		
receiving colchicine	48±10*	116±6*
not receiving colchicine	58±20*	196±39*
mixed group	53±10*	175±22*
during episode	107±21*	249±34*
after HBO, without colchicine	33±6	58±20

Legend. *$p < 0.05$.

Some workers pay particular attention to the constant (irrespective of the phase of the disease) and considerable increase in the blood histamine concentration of patients with FMF [2]. A similar picture in relation to leukotrienes also was observed in the present case. In this connection it should be recalled that histamine secretion is directly dependent on leukotriene biosynthesis [8].

Colchicine, which is used to prevent episodes of FMF [1], selectively inhibits biosynthesis of leukotriene B_4 in human polymorphs [11]. As Table 1 shows, the blood levels of leukotrienes B_4 and C_4 in patients receiving colchicine was somewhat lower than in patients not so treated. Probably the fall of the leukotriene B_4 level is linked to the action of colchicine, administration of which, however, as our observations show, is coupled with undesirable after-effects.

Thus leukotrienes B_4 and C_4 are involved in the mechanism of the febrile and pain syndrome in patients with FMF.

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