EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Cryoglobulin Level in Patients with Ischemic Stroke and Effect of Selective Plasmapheresis on This Parameter

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Serum concentrations of cryoglobulins were measured in patients with ischemic stroke; inadequate changes in these concentrations over the course of the entire acute period of the disease were shown. Positive effect of selective plasmapheresis on the decrease in cryoglobulin concentration and recovery of patients was confirmed.

Key Words: *cryoglobulin; stroke; plasmapheresis*

Cryoglobulins (CG; proteins with abnormal thermal solubility) appear in the blood of patients with lymphoproliferative, autoimmune, malignant diseases, some hepatorenal diseases, *etc.* [3,7,8]. The levels of CG often correlate with the severity of patient's status, but the function of CG remains unknown. CG can be absent in normal subjects or their concentrations do not surpass 60-80 μg/ml [3]. Since stroke is an extremely severe and disabling condition, we hypothesized that CG are involved in its pathogenesis.

We measured serum CG concentrations at the debut of ischemic stroke and over the course of the acute period in patients receiving traditional treatment and selective plasmapheresis (SPP).

MATERIALS AND METHODS

Fifty patients aged 42-84 years were examined during the acute period of their first carotid ischemic stroke. The patients were divided into 2 groups by the pathogenetic variant of stroke: 1) 26 patients with atherothrombotic stroke (subgroup 1A: SPP (n=12) and 1B: no SPP (n=14) and 2) 24 patients with cardioembolic stroke (subgroup 2A: SPP (n=8) and 2B: no SPP (n=16).

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In addition to basic therapy, 20 patients received SPP aimed at elimination of CG on days 2, 4, and 6 of the disease. Control group consisted of 10 donors. Orgogozo International score was used for objective evaluation of patients' status.

Hemostasis was evaluated in all patients before, on day 7, and after treatment: coagulation hemostasis (activated partial thromboplastin time, prothrombin time, fibrinogen), fibrinolytic hemostasis (XIIa-euglobulin fibrinolysis), and cellular component (spontaneous and ADP-induced platelet aggregation) were studied by standard methods [2,4,5]. The level of CG in the peripheral blood was measured on days 1, 2, 3, 7, and 21 of stroke development as described previously [3].

RESULTS

The concentration of cryoproteins was elevated on day 1 of stroke development in all patients; it was 1.2 times higher in group 1 than in group 2 (Fig. 1). High level of CG directly correlated with the severity of clinical status on day 1 of stroke (r=0.6; p<0.01).

On day 2 the concentration of CG decreased irrespective of the stroke variant, while on day 3 it sharply increased: 1.2 times in subgroup 1B patients in comparison with day 2 (without surpassing the initial level) and 1.6 times in subgroup 2B (surpassing the

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initial concentration; Fig. 2, *a*). By day 7 of the disease CG concentration in subgroup 2B again decreased to the initial level, while in subgroup 1B it increased 1.03 times. By the end of the acute period (day 21) the concentration of CG slightly decreased irrespective of the pathogenetic variant of stroke. However the final concentrations of CG in the serum remained 1.4-1.6 times elevated in comparison with normal values. This inadequate relationship between CG concentration and period of observation can be due to different mechanisms of stroke development and course in patients with its different variants. The atherothrombotic variant of stroke is associated with prestroke progredient damage to the vascular wall caused by atherosclerosis, hypertensive crisis, leading to destructive injuries of the blood-brain barrier, release of neurospecific proteins persisting in the blood for a long time, development of autosensitization with neuroproteins [1]. By the stroke onset a basal level of CG is present in patient's blood and the phagocytic component of immunity is activated. Injury of the blood-brain barrier and release of neurospecific proteins into the blood lead to a potent immunological "burst" with repeated autosensitization. In cardioembolism the stroke develops suddenly, without appreciable pre-stroke antigenic stimulation, and therefore the initial serum level of CG is lower in these patients.

The relationship between CG level and time of development of acute cerebral ischemia is similar for patients receiving standard therapy and SPP (Fig. 2, *b*). By the end of the acute period (day 21) CG concentration in the blood of subgroup 1A patients approached the normal values and was about 90 μg/ml (normally 80 μg/ml). A significant reduction of CG concentration in comparison with the initial value correlated with the increment in the self-service score (r=-0.7; p<0.05). At the same time, the final concentration of CG in subgroup 2A was about 110 μg/ml, *i.e*. 1.4 times surpassed the normal, which does not differ from the values in patients receiving standard treatment.

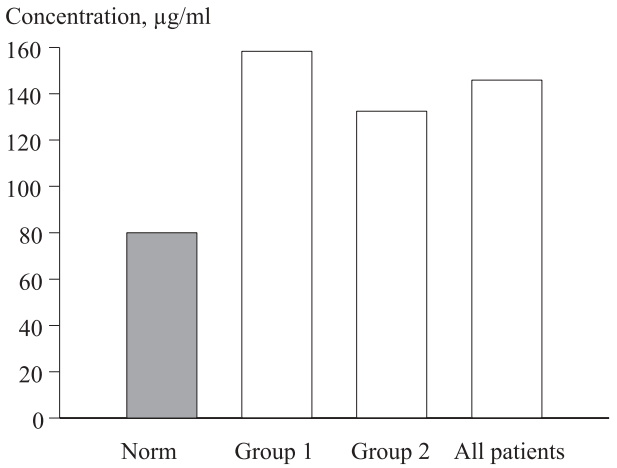

Fig. 1. Cryoglobulin concentration on day 1 of stroke.

Hence, CG were detected in all patients; their concentrations 1.5-2 times surpassed the normal values and correlated with disease severity. The use of SPP decreased CG concentrations significantly and improved the patients' condition. Traditional protocol of SPP was effective in patients with the atherothrombotic variant of ischemic stroke. Now it is interesting to clear out the prognostic significance of CG concentrations for each of the pathogenetic variants of stroke.

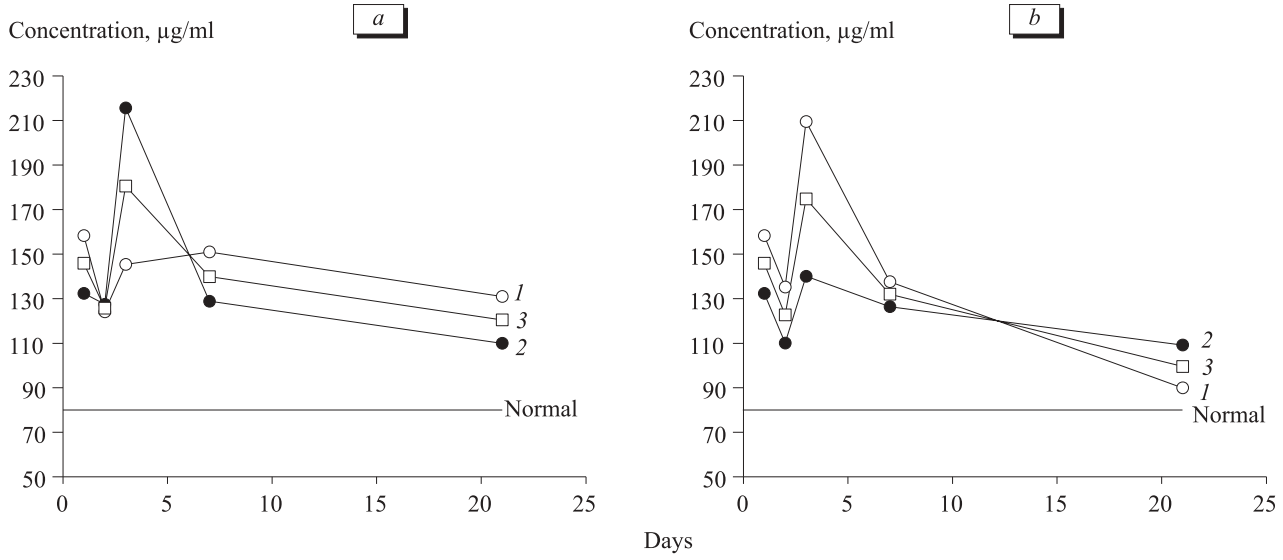

Fig. 2. Time course of cryoglobulin concentrations in patients receiving therapy (*a*) and selective plasmapheresis (*b*). *1*) group 1; *2*) group 2; *3*) all patients.

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