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Decreasing the expression of LFA–1 and ICAM–1 as the major mechanism for the protective effect of glutamine on ischemiareperfusion injury

Letter to the Editor

Decreasing the expression of LFA-1 and ICAM-1 as the major mechanism for the protective effect of glutamine on ischemia-reperfusion injury

Sir—I read the article by Murphy and colleagues (1) with great interest. This work shows that glutamine markedly suppresses the functional activity of neutrophils, which is shown by reduced myeloperoxidase activity compared to placebo. I would like to complete the discussion from Murphy et al. by introducing a major route through which glutamine could suppress the activity of neutrophils.

Ischemia-reperfusion injury is complex, involving apoptosis, oxygen radicals, platelet aggregation, and leukocyte/endothelium interactions, and it results from acute interruption of blood flow within the microvasculature (2, 3). The recent focus on ischemia-reperfusion injury has mainly concerned the interaction between neutrophils and endothelial cells. The injury attributed to plugging of the microvasculature by neutrophils may initiate the cascade of injury by releasing free radicals, enzymes, and cytokines and by physically injuring the endothelium and obstructing the capillaries, thus impairing oxygen supply to the tissue. Also, transendothelial migration of neutrophils with release of reactive oxygen species and cytokines causes further damage to the injured tissue (4, 5). However, a key component in the pathogenesis of reperfusion syndrome is the upregulation of surface adhesion molecules on the vascular endothelium and their subsequent interaction with the activated neutrophils (6). The most important adhesion protein identified on neutrophils is the integrin lymphocyte function-associated antigen-1 (LFA-1; CD11a/CD18), which is the ligand for intercellular adhesion molecule-1 (ICAM-1) expressed on the endothelium. The LFA-1/ICAM-1 interaction is crucial for the ingress of neutrophils into the inflammatory sites (7, 8). Glutamine downregulates the expression of ICAM-1 and LFA-1, and through binding to LFA-1, it interferes with the interaction between ICAM-1 and LFA-1 (9, 10). This important mechanism should be borne in mind as possibly being the major mechanism of glutamine-induced inhibition of neutrophil activity.

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