Abstract


Combined glutamine and arginine decrease proinflammatory cytokine production by biopsies from Crohn's patients in association with changes in nuclear factor-kappaB and p38 mitogen-activated protein kinase pathways.


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BACKGROUND: Glutamine (Gln) and arginine (Arg) are conditionally essential amino acids with immunomodulatory properties.

OBJECTIVE: The aim of the study was to assess the effects of Gln and Arg alone or in combination on cytokine release by cultured colonic biopsies from patients with active Crohn's disease (CD).

METHODS: Ten consecutive patients [mean (range) age 26 (18-39) y] with active colonic CD (mean CD activity index: 383.7 +/- 129.8) were prospectively included in the study. Eight colonic biopsies were obtained via a colonoscopy and incubated during 18 h with low (physiological) or high (pharmacological) doses of Arg (0.1 or 2 mmol/L designated as Arg(low) or Arg(high), respectively) and Gln (0.6 or 10 mmol/L designated as Gln(low) or Gln(high), respectively). The concentrations of cytokines [interleukin (IL)-4, IL-10, IL-8, IL-6, tumor necrosis factor-alpha (TNFalpha), IL-1beta, interferon-gamma] were assessed by ELISA, and nitric oxide (NO) production was evaluated by Griess assay. Nuclear factor (NF)-kappaB p65 subunit, inhibitor of NFkappaB-alpha, and p38 mitogen-activated protein kinase (MAPK) were assessed by immunoblotting.

RESULTS: Arg(high)/Gln(high) decreased the production of TNFalpha, IL-1beta, IL-8, and IL-6 (each P < 0.01). Arg(low)/Gln(high) decreased IL-6 and IL-8 production (both P < 0.01), whereas Arg(high)/Gln(low) did not affect cytokine and NO production. Arg(low)/Gln(high) and Arg(high)/Gln(high) decreased NF-kappaB p65 subunit expression, whereas p38 MAPK was decreased only by Arg(high)/Gln(high). Combined pharmacological doses of Arg and Gln decreased TNFalpha and the main proinflammatory cytokines release in active colonic CD biopsies via NF-kappaB and p38 MAPK pathways.

CONCLUSION: These results could be the basis of prospective studies evaluating the effects of enteral supply of combined Arg and Gln during active CD.

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