Abstract

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Glutamine supplementation, but not combined glutamine and arginine supplementation, improves gut barrier function during chemotherapy-induced intestinal mucositis in rats.


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BACKGROUND & AIMS: Increased intestinal permeability occurs during chemotherapy-induced intestinal mucositis. Previous data suggest that glutamine and arginine may have additive or synergic effects to limit intestinal damage. The present study aimed to evaluate the effects of glutamine and arginine, each alone or in combination, on gut barrier function during methotrexate (MTX)-induced mucositis in rats.

METHODS: Eighty Sprague Dawley rats received during 7 days (d) standard chow supplemented with protein powder (PP), glutamine (G, 2%), arginine (A, 1.2%) or glutamine plus arginine (GA). All diets were isonitrogenous. Rats received subcutaneous injections of MTX (2.5 mg/kg) from d0 to d2. The intestinal permeability and tight junction proteins were assessed at d4 and d9 in the jejunum by FITC-dextran and by western blot and immunohistochemistry, respectively.

RESULTS: At d4, intestinal permeability was increased in MTX-PP, MTX-A and MTX-GA rats compared with controls but not in MTX-G rats. The expression of claudin-1, occludin and ZO-1 was decreased in MTX-PP group compared with controls but was restored in MTX-G and MTX-A rats. In MTX-GA rats, occludin expression remained decreased. These effects could be explained by an increase of erk phosphorylation and a decrease of IκBα expression in MTX-PP and MTX-GA rats. At d9, Intestinal permeability remained higher only in MTX-GA rats. This was associated with a persistent decrease of occludin expression.

CONCLUSIONS: Glutamine prevents MTX-induced gut barrier disruption by regulating occludin and claudin-1 probably through erk and NF-κB pathways. In contrast, combined glutamine and arginine has no protective effect in this model.

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