Glutamine Antioxidant Properties and its Role in VEGF-Akt Pathways in Portal Hypertension Gastropathy

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This study aims to investigate glutamine effects on oxidative/nitrosative stress and, VEGF-AKT-eNOS signaling pathway in a portal hypertension (PH) experimental model induced by partial portal vein ligation (PPVL). We evaluated the expression and the immunoreactivity of proteins involved in VEGF-AKT-eNOS pathway. Oxidative stress was measured by quantification of the TBARS, GSH levels, SOD activity, NO production and nitrotyrosine immunoreactivity. TBARS and NO production were significantly increased in PPVL animals. SOD activity reduction was detected in PPVL+G group. In the nitrotyrosine, Akt and eNOS immunohistochemical analyses the PPVL group exhibited significant increases, whereas decreases were observed in PPVL+G group, but no difference in VEGF was detected. Western blot analysis detected increased expression of IP3K, p-Akt and eNOS in PPVL group compared with the PPVL+G group, which was not observed for the VEGF expression when comparing these groups. Glutamine administration alleviated oxidative/nitrosative stress, normalized SOD activity, increased total GSH level, blocked NO overproduction and, peroxynitrite formation. In conclusion, results suggested the use of molecules with an antioxidant capacity could provide a new therapeutic modality for protection of gastric tissue in portal hypertension. Glutamine treatment can be useful to reduce oxidative/nitrosative damage but does not reduce angiogenesis by stimulating the overproduction of VEGF induced by PH in gastric tissue, demonstrating a beneficial role for the IPK3-Akt-eNOS pathway.

Key words: Partial portal vein ligation, Oxidative stress, Glutamine, Portal hypertension

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