Gastric Ulcers Induced by Systemic Hypoxia

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ABSTRACT

Aim: *to assess the effect of systemic hypoxia on gastric mucosa and the activation of stress-responsive transcription factors induced by hypoxia.*

Methods: *in this experimental study, rats were allocated to control and experimental groups. The experimental group was divided into subgroups and subjected to hypoxia conditions for 1, 7, 14 or 21 days. Afterwards, histopathological evaluation and study of the protein expression of the gastric mucosa were performed.*

Results: *the results showed that longer exposure to hypoxic conditions leads to more severe gastric ulceration. Twenty-four hours after induction, 60% of rats had developed gastric ulcers. Seven days after induction, 80% of rats developed gastric ulcers. In the 14-day and 21-day hypoxia conditions, epithelialization (a sign of gastric ulcer healing) was observed. Evaluation of the average ulcer depth on the day of treatment showed that the greatest depth was on day 7, and the shallowest was on day 21 of treatment. Western blot analyses demonstrated that systemic hypoxia resulted in the expression of heat shock factor (HSF) and heat shock protein 70 (HSP-70), which were highest on day 7 and then regressed gradually. In control, HSF-1 and HSP-70 were not detected by Western blot analysis in the control group (normoxia).*

Conclusion: *in this study, systemic hypoxia caused gastric ulcers, and during the time of exposure to hypoxia, an adaptation process in the form of gastric epithelialization occurred in the rats. This development of gastric lesions was in line with the expression pattern of HSF-1 HIF-1α and HSP-70.*

Key words: *gastric ulcer, systemic hypoxia, heat shock factor expression.*

INTRODUCTION

Gastric mucosal lesions are defects in the gastric system that extend through the muscularis mucosae. Helicobacter pylori infection, Non-steroidal anti Inflammatory drug (NSAID) use, stress ulcers and acute mucosa-damaging lesions are the most common aetiologic factors. Under normal conditions, a physiological balance exists between peptic acid secretion and gastroduodenal mucosal defence.[1,2] Mucosal injury and subsequent peptic ulcers occur when the balance between the aggressive factors and the defensive mechanisms is disrupted. The imbalance between aggressive and defensive factors determines the outcomes of the gastric lesions that result from these common causes. The imbalance depends on whether there is an increase in aggressive factors or a decrease in defensive factors. The defensive mechanisms include tight intercellular junctions, mucus and bicarbonate, gastric mucosal blood flow, cellular restitution and epithelial renewal. The decrease in these mechanisms can be induced by many factors, including hypoxia.[3,4] Prostaglandin enhances these protective mechanisms, and it is believed to be a major gastric mucosal defensive factor. Heat shock proteins (HSPs) have proved to be an equally effective key protective mechanism.[5]

Cells respond to stressful conditions by activating genetic programmes whose evolutionarily conserved mechanisms have common ancestral origins, from the simplest bacteria to complex organisms, including humans. In recent years, one such genetic programme that has gained increased attention involves the families of HSPs.[6,7] HSPs, also called stress proteins, are a group of proteins that are present in all cells in all life forms. They are induced when a cell undergoes various types