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Chemopreventive effects of resveratrol in a rat model of cerulein-induced acute pancreatitis

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Abstract In the past decades, a greater understanding of acute pancreatitis has led to improvement in mortality rates. Nevertheless, this disease continues to be a health care system problem due to its economical costs. Future strategies such as antioxidant supplementation could be very promising, regarding to beginning and progression of the disease. For this reason, this study was aimed at assessing the effect of exogenous administration of resveratrol during the induction process of acute pancreatitis caused by the cholecystokinin analog cerulein in rats. Resveratrol pretreatment reduced histological damage induced by cerulein treatment, as well as hyperamylasemia and hyperlipidemia. Altered levels of corticosterone, total antioxidant status, and glutathione peroxidase were significantly reverted to control levels by the administration of resveratrol. Lipid peroxidation was also counteracted; nevertheless, superoxide dismutase enzyme was overexpressed due to resveratrol pretreatment. Related to immune response, resveratrol pretreatment reduced pro-inflammatory cytokine IL-1β levels and increased anti-inflammatory cytokine IL-10 levels. In addition, pretreatment with resveratrol in cerulein-induced pancreatitis rats was able to reverse, at least partially, the abnormal calcium signal induced by treatment with cerulein. In conclusion, this study confirms antioxidant and immunomodulatory properties of resveratrol as chemopreventive in cerulein-induced acute pancreatitis.

Keywords Resveratrol · Acute pancreatitis · Cerulein · Interleukins · Antioxidants

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Introduction

Acute pancreatitis is an inflammatory disease with a wide clinical variation, ranging from self-limiting mild form (75–80 % of the cases) to serious form, which may present multisystem organ failure, sepsis, and even death [1]. Nowadays, the treatment of this illness is limited to palliative cares such as monitoring of vital signs, arterial oxygen saturation, and hydration status of the patient, as well as analgesic therapy [2]. In patients with poor prognosis, antibiotics and/or surgery are also recommended to avoid necrosis [3]. In addition, the treatment of human severe acute pancreatitis with some promising molecules such as lexipafant [4], a powerful platelet activating factor (PAF) antagonist, had not shown to be effective against systemic inflammatory response syndrome (SIRS) and organ failure, responsible for the high mortality and morbidity rates of this illness [5].

Previous studies have confirmed the participation of reactive oxygen species (ROS) at early stages of acute pancreatitis, independently of the underlying etiology [6, 7]. It is supposed that an imbalance between the production of free radicals and the antioxidant system of an organism would predispose to acute pancreatitis. Afterward, premature activation of pancreatic enzymes, leukocyte infiltration, and cytokine production could aggravate local injury and produce the spread of the inflammation to the rest of the organism [8–11].

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