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Glucocorticoids and Acute Pancreatitis: Suggestions for Future Clinical Trials

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Corticosteroid administration for the treatment of acute pancreatitis is still being debated. In experimental acute pancreatitis, the results of this therapeutic option vary widely; some authors report an improvement of survival in different models of the disease in various animal species such as rats, rabbits, and dogs [1, 2, 3, 4] and others report an increase in the mortality rate after high-dose hydrocortisone treatment in rats with mild and severe disease, and a deteriorated outcome in hydrocortisone pre-treated rats with diet-induced acute pancreatitis [1, 2, 3, 4, 5]. Furthermore, a high-dose, long-term hydrocortisone treatment of 2 weeks was associated with an increased infection or sepsis rate, thereby worsening the outcome of experimental acute pancreatitis [5], and in high-dose, short term hydrocortisone therapy, no benefit regarding survival was shown [6, 7, 8]. However, recently published papers showed promising results with moderate and low dose hydrocortisone treatment over a period varying from 7 to 14 days and these positive effects regard the ameliorated hemodynamic status, the reduced number of organ failures, and the increased incidence of survival [9, 10, 11, 12, 13, 14].

At present, we are familiar with the role of various mediators in the development of systemic inflammatory response syndrome and multiple organ dysfunction syndrome in severe acute pancreatitis. This knowledge includes cytokines, tumor necrosis factor, platelet-activating factor and C-reactive protein, procalcitonin and granulocyte colony-stimulating factor, alfa-1-antitrypsin, elastase from polymorphonuclear granulocytes, phospholipase-A2, trypsin, and carboxy-peptidase B [15, 16, 17, 18, 19, 20, 21], capable of influencing glucocorticoids. The role of endogenous glucocorticoid metabolism itself and, respectively, its separate components, including total and free cortisol, corticosteroid-binding globulin, and adrenocorticotropic hormone, in the course of acute pancreatitis remains to be elucidated. For this reason, we welcome the paper of Muller *et al*. [22]; the authors measured how total cortisol, calculated free cortisol, corticosteroid-binding globulin and adrenocorticotropic hormone levels changed in the early course of human acute pancreatitis, and evaluated whether there was any relationship of those changes to the development of pancreatic necrosis. They found that, initially, highly elevated levels of calculated free cortisol and total cortisol, and depressed levels of adrenocorticotropic hormone and corticosteroid-binding globulin were observed. Moreover, daily measurements revealed increasing adreno-corticotropic hormone levels whereas cortisol levels decreased. Although an increase in adrenocorticotropic hormone levels is suggested to increase corresponding cortisol levels, cortisol levels decreased during the development of necrotizing acute pancreatitis. This phenomenon, along with the continuously decreasing corticosteroid-

binding globulin levels, brings up the hypothesis of a relative adrenal insufficiency which favors acinar cell apoptosis and may trigger the development of necrosis in the initial phase of acute pancreatitis.
According to the study by Muller *et al*. [22], early short-term therapy with hydrocortisone in low doses to prevent systemic inflammatory response syndrome and the development of necrosis in the early phases of acute pancreatitis may be hypothesized. Thus, studies evaluating dosage, application time, and a time period related to hydrocortisone therapy should be carried out.

Keywords Adrenal Cortex Hormones; Cytokines; Pancreatitis; Pancreatitis, Acute Necrotizing; Therapeutics

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