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ORIGINAL RESEARCH

Protective Effects of Idebenone against Sepsis Induced Acute Lung Damage

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ABSTRACT

Background/Aims: Sepsis is an uncontrolled systemic infection, withcomplex pathophysiology that may result in acute lung organ damage and cause multiple organ failure. Although much research has been conducted to illuminate sepsis's complex pathophysiology, sepsis treatment protocols are limited, and sepsis remains an important cause of mortality andmorbidity in inten- sive care units.Various studies have shown that idebenone (IDE) possesses strong antioxidant properties, which inhibit lipid peroxidation and protect cells from oxidative damage. The present study aimed to evaluate the protective effects of IDE against lung injury in a cecal ligation and puncture (CLP)-induced sepsis rat model.

Methods: Male albino Wistar rats were used. The animals were divided into a healthy control (no treatment), CLP, IDE control (200 mg/kg), and CLP þ IDE subgroups (50 mg/kg, 100 200 mg/kg), with nine rats in each group.IDE was administered 1 h after CLP induction.To evaluate the protective effects of IDE, lung tissues were collected 16 h after sepsis for biochemical, immuno- histochemical staining, and histopathological examination.

Results: IDE significantly ameliorated sepsis-induced disturbances in oxidative stress-related fac- tors, with its effects increasing in accordance with the dose.IDE also abolished histopathological changes in lung tissues associated with CLP.Furthermore, interleukin 1 beta (IL-1*b*)and tumor necrosis factor-alpha (TNF-*a*) immunopositivity markedly decreased in the septic rats following IDE treatment.

Conclusions: IDE largely mitigated the inflammatory response in sepsis-induced lung injury by decreasing free radicals and preventing lipid peroxidation. The results suggest that IDE may repre- sent a potential novel therapeutic drug for sepsis treatment.

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Idebenone; sepsis; antioxidantlung injuryrat; oxidative stress

Introduction

Sepsis is a life-threatening syndrome that involves oxidative damage and multiple organ dysfunction, resulting from an imbalance in the inflammatory response to infections [1, 2].Sepsis can lead to high levels of morbidity and mortality [3], even death due to severe tissue damage, multiple organ failure, and hypotension [4]. Despite the availability of intensive treatment strategies for sepsis, sepsis-associated mortality rates have increased from 18% to 40% in recent years, with approximately 19 million cases of sepsis recorded worldwide annually [5, 6]. Given the high prevalence of sepsis, many studies have focused on its treatment and pathophysiology [7, 8]. A particular problem is the lack of an established treatment protocol for sepsis.The current high sepsis-related mortality rate indicates that the current treatment protocol for sepsis is limited and that a new therapeutic intervention for sepsis is necessary. In terms of the latter, there is a clear need to identify potential drug candidates.

A major cause of high mortality associated with sepsis is acute lung injury due to pulmonary sensitivity or acute respiratory distress syndrome, which plays a critical role in multiple vital organ failure [9]. Acute lung injury that develops early during the course of sepsis causes an excessive and uncontrolled inflammatory response by activating macrophages and neutrophils. Inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-*a*) and interleukins (ILs), which act as biomarkers of sepsis, directly contribute to the inflammatory response during sepsis [10, 11]. The secretion of inflammatory cytokines causes damage to lung epithelial and endothelial cells and sepsis-associated injuries, such as septic shock and multiple organ dysfunctions [12]. In addition, overexpression of proinflammatory cytokines leads to the secretion of secondary cytokines, lipid mediators, and reactive oxygen species [8]. The aforementioned factors lead

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