

Nitric Oxide and Tumor Necrosis Factor- α Production of Kupffer Cells In Rats with Obstructive Jaundice and Its Relief by External Biliary Drainage

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Abstract

Background: Preoperative biliary drainage in obstructive jaundice has been the subject of controversy and the role of Kupffer cells in obstructive jaundice is still unclear. The aim of this study was to investigate the production and time course of nitric oxide (NO) and tumor necrosis factor- α (TNF α) released from Kupffer cells in obstructive jaundice.

Methods: Nitrite (NO₂⁻) as the stable end product of NO production of Kupffer cells in response to lipopolysaccharide (LPS) was measured together with TNF α production in bile duct ligated (BDL) rats and in its relieved rats by external biliary drainage.

Results: In systemic endotoxemia of BDL rats, plasma levels of nitrite/nitrate and TNF α were significantly elevated, and returned to the levels of sham-operated control rats in 7 to 14 days after external biliary drainage. The time course of TNF α production showed its peak level 3 hours after incubation of isolated Kupffer cells with 1 μ g/ml LPS. Kupffer cells isolated from BDL rats produced 2-fold greater amounts of nitrite and TNF α than those from sham-operated control rats in response to LPS stimulation, and its nitrite accumulation increased in a time dependent manner. After external biliary drainage, nitrite production by Kupffer cells isolated from BDL rats and its dependence on LPS decreased as well as TNF α production.

Conclusions: These results indicate that Kupffer cells play a key role through the production of NO and TNF α in the development of pathogenesis of obstructive jaundice, and preoperative biliary drainage in obstructive jaundice might be significant due to decrease of detrimental amount of NO and TNF α .

Key words: Rat, bile duct ligation, obstructive jaundice, Kupffer cell, lipopolysaccharide, nitric oxide, tumor necrosis factor- α external biliary drainage

Listing of Abbreviations

NO - nitric oxide, NOS - nitric oxide synthase, iNOS - inducible NOS, TNF α - tumor necrosis factor- α , LPS - lipopolysaccharide, BDL - bile duct ligated, ED - external biliary drainage, Sham - sham-operated control, PBD - preoperative biliary drainage

Introduction

Obstructive jaundice in patients who undergo surgery leads to a high rate of postoperative morbidity and mortality¹⁾ due to renal failure²⁾, gastrointestinal bleeding, coagulopathy³⁾, cardiovascular instability

manifested as systemic hypotension⁴⁾, and immune suppression. These complications are closely related to gram-negative sepsis and systemic endotoxemia is integral to the pathophysiology of obstructive jaundice⁵⁾. In fact, endotoxins were positive in 11 of 13 jaundiced patients before, during, and after surgery⁶⁾.

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