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Effect of α-Tocopherol on Vasoregulatory Gene Expression during Polymicrobial Sepsis

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Sepsis remains common surgical problems with high morbidity and mortality despite improvement in the management for septic patient. Although hepatocellular dysfunction occurs during sepsis, the mechanism responsible for this remains unclear. In sepsis, a state of severe oxidative stress is encountered, with host endogenous antioxidant defenses overcome. Therefore, the aim of this study was to determine the effect of α-tocopherol (AT) vasoregulatory gene expression during polymicrobial sepsis. Rats were subjected to polymicrobial sepsis by cecal ligation and puncture (CLP). AT (15 mg/kg) was intraperitonealy injected for 3 days prior to CLP. Blood samples were taken 24 h after CLP for measurement of the extent of hepatocellular damage. Liver samples were taken for RT-PCR analysis of mRNA for genes of interest: endothelin-1 (ET-1), its receptors ET_A and ET_B, nitric oxide synthases (iNOS and eNOS), cyclooxygenase-2 (COX-2), heme oxygenase-1 (HO-1), and tumor necrosis factor-α (TNF-α). The activities of serum alanine aminotransferase and lipid peroxidation level were significantly increased; an increase which was prevented by AT pretreatment. CLP significantly increased the mRNA levels of ET-1 and ET_B; an increase that was prevented by AT pretreatment. However, the level of ET_A mRNA significantly decreased after CLP; a decrease that was not prevented by AT pretreatment. There were significant increases in the mRNA expression of iNOS, HO-1 and COX-2 in CLP groups. This increase was prevented by AT pretreatment. The expression of eNOS and TNF-α mRNA significantly increased in CLP, which was not prevented by AT pretreatment. Our findings suggest that there was an imbalanced vasoregulatory gene expression in sepsis, and AT ameliorates this change through its free radical scavenging activity.