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# Clinical Nutrition 2017: Effect of varying magnesium concentrations on NF-κB gene expression in human umbilical vein endothelial cells (HUVECs) – Lujain Almousa - The University of Nottingham

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Magnesium has anti-inflammatory and antioxidant effects, and it has a defensive role in triggering the body's immune cells. Moreover, magnesium enhances endothelial function and inhibits atherosclerosis. Inflammation is a risk factor for atherosclerosis progression and can be mediated by nuclear factor kappa light chain enhancer of activated B cells (NF-κB) activation, which plays a key role in the development of inflammation because when NF-κB transfers to the nucleus and binds to promoter regions, it initiates the transcription of many inflammatory mediators. In response to inflammation, NF-κB enhances the transcription of Intercellular Adhesion Molecule-1 (ICAM-1), Vascular Cell Adhesion Molecule-1 (VCAM1) and inflammatory cytokines, which aid in the transmigration of leukocytes from the blood vessel lumen through the barrier of the endothelial cells and into the sub endothelial space. In this study we determined the effect of different concentrations of magnesium on the expression of NF-κB. HUVECs were cultured in different MgSO4 concentrations: 0.1 mm, 5 mm and compared to the physiological circulating concentration. Expression of NF-κB was determined at the mRNA level by quantitative real-time PCR. Significantly elevated NF-κB expression was observed in magnesium-deficient (0.1 mm) cells that were stimulated with lipopolysaccharide 0.5 µg for 4 hours (34%, P=0.032), Moreover, a marked suppression of NF-κB expression in the magnesium-treated (5 mm), LPS stimulated HUVECs was observed (31%, P=0.048), relative to the 1 mm physiological concentration. These data shows that magnesium was inversely associated with the expression of NF-κB which induces an overexpression of the inflammatory phenotype in endothelial cells and has been connected to the pathogenesis of many cardiovascular diseases.

We investigated the effects of berberine on lipopolysaccharide induced apoptosis in human umbilical vein endothelial cells and the molecular mechanisms mediating the effect. The effects of berberine on LPS-induced cell apoptosis and viability were measured with 5-ethynyl-2-deoxyuridine staining, flow cytometry and Cell Counting Kit-8 assays. The expression and/or activation of proapoptotic and antiapoptotic proteins or signaling pathways, including caspase-3, polymerase, myeloid cell leukemia-1, p38 mitogen-activated protein kinase, C-Jun N-terminal kinase, and extracellular signal-regulated kinase, were determined with western blotting. The malondialdehyde levels, superoxide dismutase activity, and production of pro inflammatory cytokines were measured with enzyme-linked immunosorbent assays. The results demonstrated that berberine pretreatment protected HUVECs from LPS-induced apoptosis, attenuated LPS-induced injury, inhibited LPS-induced JNK phosphorylation, increased MCL-1 expression and SOD activity, and decreased pro inflammatory cytokine production. The effects of berberine on LPS-treated HUVECs were prevented by SP600125, a JNK-specific inhibitor. Thus, berberine might be a potential candidate in the treatment of endothelial cell injury-related vascular diseases. Endothelial cells, which act as a selective barrier between tissue and blood, play a potential role in the control of inflammatory responses, immunity, and homeostasis.In order to maintain normal organ function and vascular homeostasis, the integrity of the endothelial lining is critical. EC dysfunction and/or injury can disrupt the integrity of the endothelial lining and subsequently lead to vascular disease. EC dysfunction and/or injury, which are commonly mediated by lipopolysaccharide, are complications of sepsis, which is considered the major cause of several diseases, including diabetes mellitus, atherosclerosis and thrombosis. Therefore, agents that protect the vascular endothelium from injury and/or dysfunction are thought to reduce the incidence of cardiovascular disease. Because LPS is an integral part of the outer membrane of Gram-negative bacteria, it is considered a trigger of EC injury and its associated syndromes. In vitro, LPS stimulation alters multiple EC functions, including viability, apoptosis, malondialdehyde (MDA) release and tumor necrosis factor- (TNF-) and interleukin- (IL-) 6 synthesis. Increasing evidence suggests that oxidative stress that is induced by LPS stimulation can lead to apoptosis or death of ECs. In ECs, oxidative stress triggers various signal transduction pathways that are related to cell survival and apoptosis, induces damage to cell membranes and DNA structure and affects members of the mitogen-activated protein (MAP) kinase (MAPK) family and the cell biological processes that are regulated by MAP kinase, such as cell apoptosis, differentiation, and growth. Previous studies have shown that three MAPK subfamilies are activated in response to LPS stimulation, including c-Jun N-terminal kinase (JNK), p38 MAP kinase (p38) and extracellular signal-regulated kinase.

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