

ZINC PROTECTS HUMAN ENDOTHELIAL VASCULAR CELLS AGAINST THE GLUCOSE INDUCED CYTOTOXICITY

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Morphological and functional abnormalities of vascular endothelium may represent a pathway to the accelerated atherosclerotic complications of diabetic patients.

The mechanism underlying the effects of high glucose on endothelium are not clear even if it is almost certain that oxidative stress may play a significant role in these pathological events. It known that glucose may induce apoptosis of these cells and that antioxidant may protect them against the deleterious effect of glucose.

To investigate the cell damage induced by glucose-dependent oxidative stress, we have employed an *in vitro* system of human endothelial veins cultured in elevated glucose concentrations. The effects of an essential micronutrient, zinc, was experimented in this model.

Cytotoxicity of glucose was determined by the blue trypan technique, 7 or 14 days after glucose incubation (25 and 50mM) or Zinc (5, 25 and 50 μ M).

We found indeed that, the number of survival endothelial cells, incubated with glucose significantly decreased at J7 as well as J14 in a dose dependent manner.

Moreover, endothelial cells preincubated with Zinc 25 and 50 μ M, were protected from glucose induced cytotoxicity. Complementary studies will be performed in order to measure the effect of zinc on endothelial cell redox state including reduced glutathione and antioxidant enzymes. Moreover the effect of metformin alone or associated with zinc will be experimented in this system as we recently demonstrated that this antidiabetic agent leads to an antioxidant effects (1) *in vivo*. Coculture technique will be used associating endothelial and vascular smooth cell in order to evaluate the effect of zinc on vascular smooth cells as their proliferation is linked to the endothelial cell functions.

REFERENCE

P. Faure, E. Rossini, N. Wiernsperger, M.J. Richard, A. Favier, and S. Halimi. Diabetes, In press, 1998.