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Hydrogen and N-acetyl-L-cysteine rescue oxidative stress-induced angiogenesis in a mouse corneal alkali-burn model

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Abstract

Purpose: To investigate the role of reactive oxygen species (ROS) as the prime initiators of the angiogenic response after alkali injury of the cornea and observe the effects of antioxidants in preventing angiogenesis.

Methods: The corneal epithelia of SOD-1-deficient mice or wild-type (WT) mice were removed after application of 0.15 N NaOH to establish the animal model of alkali burn. ROS production was semiquantitatively measured by dihydroethidium (DHE) fluorescence. Angiogenesis was visualized by CD31 immunohistochemistry. The effects of the specific NF-κB inhibitor DHMEQ, the antioxidant N-acetyl-L-cysteine (NAC), and hydrogen (H2) solution were observed.

Results: ROS production in the cornea was enhanced immediately after alkali injury, as shown by increased DHE fluorescence (P<0.01). NF-κB activation and the upregulation of vascular endothelial growth factor (VEGF) and monocyte chemoattractant protein-1 (MCP-1) were significantly enhanced (P<0.01), leading to a significantly larger area of angiogenesis. Angiogenesis in SOD-1-/- mice corneas were significantly higher in WT mice (P<0.01), confirming the role of ROS. Pretreatment with the specific NF-κB inhibitor DHMEQ or the antioxidant NAC significantly reduced corneal angiogenesis by downregulating the NF-κB pathway (P<0.01) in both WT and SOD-1-/- mice. Furthermore, we showed that irrigation of the cornea with hydrogen (H2) solution significantly reduced angiogenesis after alkali-burn injury (P<0.01).

Conclusions: Immediate antioxidant therapy with H2-enriched irrigation solution is a new potent treatment of angiogenesis in cornea to prevent blindness caused by alkali burn.

Related information

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Gene
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Nucleotide (RefSeq)
Nucleotide (Weighted)
Protein (RefSeq)
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