

Cytoprotective effect of hyaluronic acid and hydroxypropyl methylcellulose against DNA damage induced by thimerosal in Chang conjunctival cells

Juan Ye · Huina Zhang · Han Wu · Changjun Wang ·
Xin Shi · Jiajun Xie · Jinjing He · Jun Yang

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Abstract

Background To investigate genotoxicity of the preservative thimerosal (Thi), and the cytoprotective and antioxidant effects of hyaluronic Acid (HA) and hydroxypropyl methylcellulose (HPMC) on Chang conjunctival cells.

Method Cells were divided into three groups. One group was exposed to Thi at various concentrations (0.00001 %–0.001 %) for 30 min; the other two groups were pretreated with 0.3 % HA or 0.3 % HPMC for 30 min before the Thi exposure. After cell viability was evaluated, alkaline comet assay and detection of the phosphorylated form of the histone variant H2AX (γ H2AX) foci were used to determine DNA damage. Reactive oxygen species (ROS) production was assessed by the fluorescent probe, 2', 7'-dichlorodihydrofluorescein diacetate (DCFH-DA).

Results A significant change of cell viability was observed after exposure to 0.001 % Thi for 30 min. DNA single- and double-strand breaks were significantly increased in a dose-

dependent manner with Thi exposure. In addition, intracellular ROS induced by Thi was dose-dependent, except at 0.001 % less ROS was induced than at 0.0005 %. However, cells pretreated with 0.3 % HA or 0.3 % HPMC showed significantly increased cell survival, decreased DNA damage, and decreased ROS production compared to cells exposed to Thi alone. Pretreatment with 0.3 % HA was found to be even more protective than 0.3 % HPMC.

Conclusion Thi can induce DNA damage in human conjunctival epithelial cells, probably due to oxidative stress. HA and HPMC are protective agents that have antioxidant properties and can decrease DNA damage induced by Thi. Pretreatment of 0.3 % HA may be more protective of the ocular surface than 0.3 % HPMC.

Keywords Thimerosal · Hyaluronic acid · Hydroxypropyl methylcellulose · DNA damage · Cytoprotective · Chang conjunctival cells · ROS · γ H2AX foci

J. Ye (✉) · H. Zhang · H. Wu · C. Wang · X. Shi · J. Xie · J. He
Department of Ophthalmology, The 2nd Affiliated Hospital
of Zhejiang University, College of Medicine,
Hangzhou, Zhejiang, China
e-mail: yejuan@zju.edu.cn

J. Ye
e-mail: Yejuan_99@yahoo.com.cn

J. Yang
Department of Toxicology,
Zhejiang University School of Public Health,
Hangzhou, Zhejiang 310058, China

J. Yang
Department of Toxicology, Hangzhou Normal University School
of Public Health,
Hangzhou, Zhejiang 310036, China

Introduction

Thimerosal (Thi) is an organomercurial compound that is widely used as an antiseptic/antifungal agent in cosmetics, pharmaceutical products, and vaccines. It is also widely used in ophthalmic preparations, mainly drugs and contact lens solutions. Its usual concentration in ocular drugs ranges from 0.001 % to 0.004 %. Recently, deleterious effects on the ocular surface and corneal endothelium have been observed with long-term use of topical drugs containing Thi. Thi might cause structural and functional damage to the endothelium with prolonged, direct exposure [1]. In addition, evidence suggests that Thi might be responsible for delayed hypersensitivity, which can cause conjunctival hyperemia and corneal infiltrates [2].