Effect of the ophthalmic preservative thimerosal on rabbit and human corneal endothelium

Diane L. Van Horn, Henry F. Edelhauser, Gary Prodanovich, Richard Eiferman, and Harlan J. Pederson

Widespread use of the mercurial-containing preservative thimerosal as an antibacterial agent in ophthalmic drugs and solutions warranted an investigation into its possible cytotoxic effects on the functional and ultrastructural integrity of the corneal endothelium. No changes in corneal thickness were observed during 5 hours' perfusion of the endothelium of rabbit and human corneas with 0.0001 and 0.0005 percent thimerosal in glutathione bicarbonate Ringer's solution (GBR). Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) of the endothelium of the 0.0001 percent group revealed normal ultrastructure. SEM and TEM of the endothelium of corneas perfused with 0.0005 percent thimerosal for 5 hours revealed condensed mitochondria, cytoplasmic vacuoles, and cytoplasmic flaps at the apical end of the cellular junctions. Perfusion of higher concentrations (0.001 and 0.005 percent) of thimerosal in GBR resulted in increases in corneal thickness after 2 hours and irreversible ultrastructural damage to the endothelial cells by 5 hours. Corneas perfused with 0.01 and 0.1 percent thimerosal in GBR showed a rapid and immediate increase in corneal thickness and endothelial cell death and necrosis within 1 hour. It is postulated that the mercury in thimerosal becomes bound to the cell membrane protein sulfhydryl groups, causing an increase in cellular permeability. These results suggest that the prolonged exposure of the corneal endothelium to thimerosal in the accepted antimicrobial dosage of 0.005 to 0.001 percent may result in functional and structural damage to the endothelium.

Key words: cornea, corneal endothelium, preservatives, scanning and transmission electron microscopy, thimerosal, toxicity.

From the Departments of Ophthalmology and Physiology, The Medical College of Wisconsin, Milwaukee, and Research Service, Veterans Administration Center, Wood (Milwaukee), Wisc.

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Reprint requests: Diane L. Van Horn, Ph.D., Department of Physiology, The Medical College of Wisconsin, 561 North 15 St., Milwaukee, Wisc. 53233.