

Author(s) Douglas H. Johnson, M.D.

Principal: Douglas H. Johnson

Presenting: Douglas H. Johnson

Contributing: Cindy K. Bahler, Kyle G. Howell, Cheryl R. Hann, Michael P. Fautsch, PhD

Abstract Title: Prostaglandins increase outflow facility in cultured human anterior segments

Purpose: To determine the affect of latanoprost and PGE1 on outflow facility in cultured human anterior segments. Although all clinical studies find an increase in pressure insensitive outflow (uveoscleral flow) after prostaglandin treatment, some clinical studies also find an increase in pressure sensitive outflow (“trabecular outflow”).

Design: Open label lab study

Participants: Lab study; donor eyes

Main Outcome Measures: Pressure effect

Methods: Anterior segments from human eyes were placed in perfusion organ culture within 20 hours of death. One eye received either latanoprost or PGE1 (free acid) by anterior chamber exchange followed by constant perfusion of the drug for 72 hours while the fellow eye received vehicle control (10^{-7} M final concentration of each

drug). Zymography was performed on effluents to measure MMP 2, 3, and 9 activity. Western blots were used to assess MMP 3 levels. Scleral permeability was measured to fluorescein.

Results: Latanoprost increased facility $81\% \pm 7\%$ compared with the fellow control eye increase of $6\% \pm 9\%$ ($n=9$ eyes, $p=0.001$). PGE1 was less effective, increasing facility $13\% \pm 17\%$ vs fellow eye increase of $1\% \pm 11\%$ ($n=9$, $p=0.02$). MMP activity in effluent media was increased in only 1 latanoprost eye (MMP 3, 9) and none of the 3 PGE1 eyes tested. Scleral permeability was unchanged.

Conclusion: Prostaglandins increased outflow facility in perfusion organ culture, with latanoprost more effective than PGE1. The conventional pathway (trabecular meshwork) is most likely the site of outflow increase. Scleral permeability did not change.