

Elevated intraocular pressure causes endothelial dysfunction in retinal arterioles of mice

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Background

Although high intraocular pressure is a risk factor for glaucoma, the role of ocular blood vessels in the pathophysiology of the disease is unknown at present. The purpose of this study was to test the hypothesis that elevated intraocular pressure causes vascular dysfunction in the retina.

Methods

High intraocular pressure was induced in one group of mice by cauterization of episcleral veins. The other group received sham surgery only (Fig. 1).

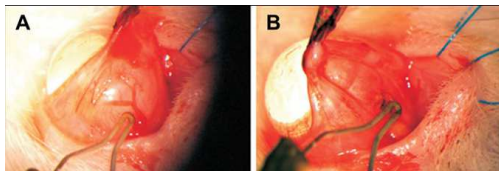
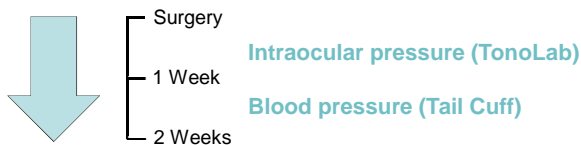


Fig. 1 Method of episcleral vein cauterization to reduce aqueous outflow. (A) Exposing the vein. (B) Cauterizing the vein.



Two weeks later, retinal vascular preparations were studied in vitro. Changes in luminal arteriole diameter in response to vasoactive substances and to different intraluminal pressures were measured by video microscopy (Fig. 2).

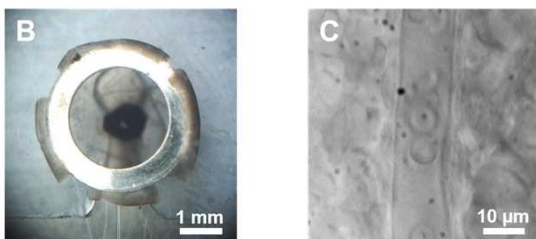
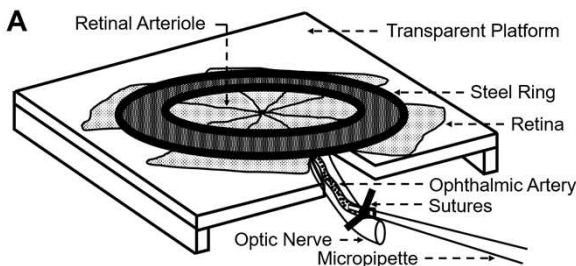


Fig. 2 (A) Sketch of the experimental setup. (B) Photograph showing the flat-mounted retina with the cannulated ophthalmic artery at the six o'clock position. (C) Retinal arteriole with red blood cells inside.

Results

Two weeks after surgery, intraocular pressure was markedly increased in cauterized compared to sham-treated mice. In contrast, mean arterial pressure and ocular perfusion pressure did not differ (Fig. 3).

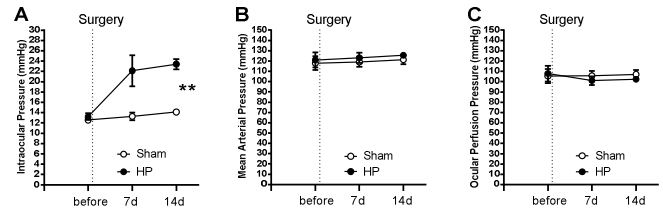


Fig. 3 Time course of intraocular pressure (A), mean arterial pressure (B) and ocular perfusion pressure (C) before, 7 days after and 14 days after surgery (** $P < 0.01$, $n = 5$ per group, RM ANOVA).

Retinal arteriole responses to the thromboxane mimetic, U-46619, and to the endothelium-independent nitric oxide donor, nitroprusside, were similar in both groups. In contrast, responses to the endothelium-dependent vasodilator, acetylcholine, were markedly reduced in mice with elevated intraocular pressure. Responses to stepwise intraluminal pressure elevation were also impaired in mice with high intraocular pressure (Fig. 4).

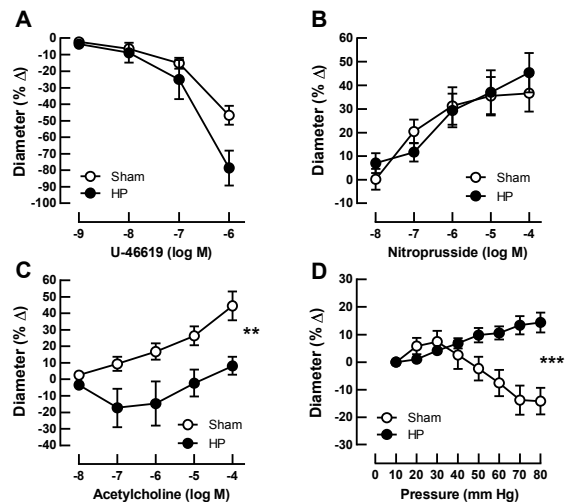


Fig. 4 (A) Responses to U-46619, nitroprusside (B), acetylcholine (C) and to intraluminal pressure elevation in mice with normal (sham) and high intraocular pressure (HP)(D); ** $P < 0.01$, *** $P < 0.001$, $n = 5$ per group, RM ANOVA.

Conclusion

Our data provide first-time evidence that intraocular pressure elevation induces vascular endothelial dysfunction and comprises autoregulation in mouse retinal arterioles even after a short time period of elevated intraocular pressure.