Barrier Qualities of the Mouse Eye to Topically Applied Drugs


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Purpose: To learn if rapid intraocular pressure (IOP) responses to topical drugs measured by the invasive servo-null micropipette system (SNMS) reflect unusually rapid drug transfer across the thin mouse cornea and sclera.

Methods: IOP was measured by invasive SNMS and non-invasive pneumotonometry. Pupils were imaged with a digital camera, and diameters measured by IMAGE J.

Results: Topical application of 40 μM carbachol produced no miosis 10 min later unless the cornea was impaled with a micropipette as used in SNMS. Carbachol contracted impaled contralateral pupils by 0.76 ±0.09 mm (~38%, N=6, P<0.0005). We also compared mouse IOP responses to purinergic drugs, measured by SNMS and pneumotonometry. Responses to the previously-studied non-selective adenosine-receptor (AR) agonist adenosine, the A3-selective agonist CI-IB-MECA and the A3-selective antagonist MRS 1191 were all enhanced to varying degrees, in time and magnitude, by corneal impalement. Topical application of two novel A3 antagonists (LJ 979 and MRS 3771) lowered SNMS-measured IOP, but not IOP measured by pneumotonometry over similar times.

Conclusions: The thin ocular coats of the mouse eye actually present a substantial barrier to drug penetration. Corneal impalement with even fine-tipped micropipettes can significantly enhance entry of topicaly-applied drugs into the mouse aqueous humor, reflecting either direct diffusion around the tip or a more complex impalement-triggered change in ocular barrier properties. Comparison of invasive and non-invasive measurement methods can document drug efficacy at intraocular target sites even if topical drug penetration is too slow to manifest convincing physiologic effects in intact eyes. Using this strategy, we found that the novel cross-species A3 antagonists LJ 979 and MRS 3771 lowered mouse IOP, if their relatively poor baseline permeability is enhanced in intact eyes.

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