Poster T017

Two simple animal models of intraocular pressure elevation for testing therapeutic drugs in glaucoma

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Introduction

Glaucoma is a progressive optic neuropathy and elevated intraocular pressure (IOP) is one of the most important risk factors. There are many experimental models to test the effect of new drugs but they are often expensive or require invasive techniques. The purpose of this poster is to present two simple animal models of intraocular pressure elevation for testing therapeutic drugs in glaucoma.
One is related to the side effects of corticosteroids in rats[1,2] and the other one is related to the hypersaline stress in rabbits eye[3].

Materials and methods

The rat model:

Elevation of IOP
Young female Sprague-Dawley rats received bilateral topical application of dexamethasone 0.1% twice daily over 42 days[1]. The animals of naive group were instilled by 0.9% NaCl only (n=10 per group).

Hypotensive drug assay
On day 28, the IOP lowering effect of bilateral single drop application of latanoprost (0.002%)[4] or brimonidine/timolol (0.2%/0.25%) was evaluated in high IOP rats. The naive group and an induced group treated with bilateral single drop application of 0.9% NaCl served as controls (n=10 per group).

IOP measurement
The IOP was measured using an Icare® TonoLab tonometer at different time-points.

The rabbit model:

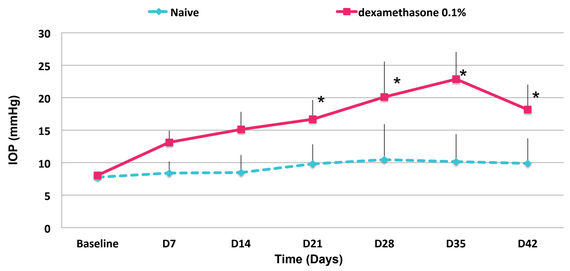
Elevation of IOP
Elevation of IOP in male New Zealand rabbits was induced by intravitreal (IVT) injection of a hypertonic saline solution (2.5% NaCl). The animals of the control group received an IVT injection of isotonic saline solution (0.9% NaCl) (n=10 per group).

Hypotensive drug assay
In order to test efficacy of hypotensive drug in the model, brimonidine (0.2%) or 0.9% NaCl were applied five time during the two hours preceeding the IVT injection of hypertonic saline solution (n=10 per group).

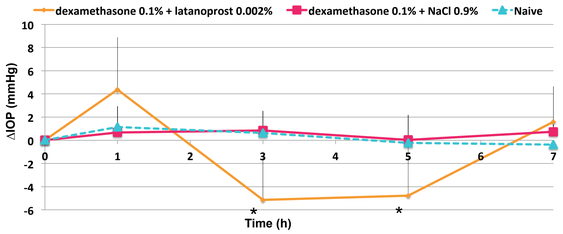
IOP measurement
The IOP was recorded with a Reichert MODEL 30 CLASSIC™ pneumatonometer at different time-points.

Results

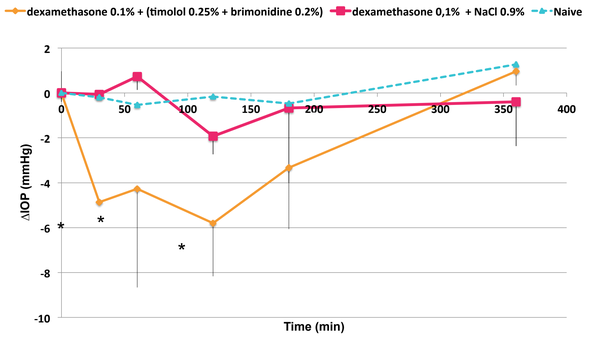
The rat model



0.1% dexamethasone instillations induced a significant and chronic increase of the IOP over 35 days.

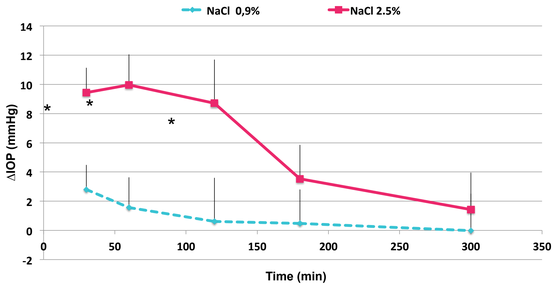


The high IOP was significantly decreased after treatment with single drop application of latanoprost (0.002%).



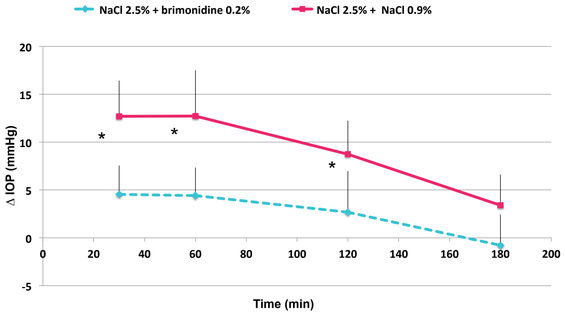
The high IOP was significantly decreased after treatment with single drop application of brimonidine/timolol (0.2%/0.25%).

The rabbit model



2.5% NaCl intravitreal injection induced a significant increase of IOP during 2 hours.

Statistical analysis
Data were compared using two-way ANOVA p<0,05



The pretreatment with brimonidine 0.2% prevented the raise of IOP induced by the 2.5% NaCl intravitreal injection.

Conclusion

Here we described two models of high intraocular pressure, a chronic in rat and an acute in rabbit. Two different classes of drug, a prostanglandin analogue and a combinaison of beta blocker and alpha agonist eye drops, have been efficient to lower IOP in the rat model and the alpha agonist eye drops, in the rabbit model. These two models with simple experimental handling and low cost, can be used as a tool for discovering therapeutic drugs in glaucoma targeting the outflow.

References

1. Argawal et al. ISOPT (Paris 2013).
2. Jain D et al. Journal of Current Glaucoma Practice. 4(3):109-113 (2010).
3. Orihashi M et al. Biol. Pharm. Bull. 28 (1) 65-68 (2005).
4. S. Husain et al. Exp. Eye Res. 48, 707-716 (2006).

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