Effects of latanoprost and pilocarpine combination on the intraocular pressure and pupil size of normal rabbits

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Summary

The aim of this study was to determine the combination effect of latanoprost and pilocarpine on the intraocular pressure and pupil size in normal rabbits. In this study, 18 rabbits were randomized to three groups of 6 animals each. The right eyes of rabbits in group 1 were treated topically with latanoprost, in group 2 with pilocarpine and in group 3 with latanoprost and pilocarpine. The left eyes received placebo. Drugs were instilled once a day at 8 am over 4 days. IOP and pupil diameter measurements were made at 8 am, 10 am, 12 noon, 2 pm and 4 pm during the 4 days of treatment, the 2 days that preceded treatment, and 3 days following treatment. The occurrence of blepharospasm and conjunctival hyperemia were also evaluated at the same times that the measurements were made. The mean IOPs were significantly lower than the contralateral eyes in 8 of the 20 time intervals (40%) in both latanoprost and pilocarpine-treated and in 18 of 20 time intervals (90%) in latanoprost plus pilocarpine-treated eyes in the treatment period. The mean daily hypotensive effects of latanoprost, pilocarpine and their combination were 4.5 (31%), 2 (14.4%) and 5 mmHg (34.7%), respectively. Although the mean IOPs in group 3 have decreased more than other groups, the differences between the three groups are not significant. Conjunctival hyperemia was observed in the treated eyes of the three groups. It is concluded that topical instillation of the combination of latanoprost and pilocarpine was not as effective in IOP reduction than by drugs alone and that hyperemia is the most frequent side effect observed during the treatment period.

Key words: Intraocular pressure, Latanoprost, Pilocarpine, Pupil diameter, Rabbit

Introduction

Glaucoma is the leading cause of irreversible blindness in the world (Weinreb and Khaw, 2004). Elevated intraocular pressure (IOP) is the major risk factor for the development of glaucoma and reducing IOP to a normal level is the primary goal of treatments for glaucoma and ocular hypertension (The AGIS Investigators, 2000). Latanoprost is a prostaglandin analog and a prostaglandin F (FP) receptor agonist that acts as an ocular hypotensive agent. Despite extensive research, controversies remain regarding the mechanism of action and relative clinical efficacy of the PGs (Eisenberg et al., 2002; Parrish et al., 2003; Orzalesi et al., 2006). Latanoprost increase aqueous humor outflow, either by enhancing the pressure-sensitive (presumed trabecular or conventional) outflow pathway or by increasing the pressure-insensitive (uveoscleral) outflow (Lim et al., 2008; Toris et al., 2008). Pilocarpine, a cholinergic agonist, in human eyes reduces intraocular pressure by stimulating postsynaptic muscarinic receptors in the ciliary muscle causing it to contract. This opens up the fluid channels in the trabecular meshwork, thus increasing trabecular outflow facility (Kaufman and Gabelt, 1997). Despite this, its effects in rabbit eyes is not decisively clear. In monkey eyes pilocarpine partially inhibited the reduction in intraocular pressure with topical prostaglandin F2a (Crawford and Kaufman, 1987; Millar and Kaufman, 1995), however, there are clinical reports that show the two drugs appeared to be additive (Fristrom and Nilsson, 1993; Toris et al., 2001). To the best of our knowledge there are no experimental reports regarding the combination effects of these