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The effects of prostaglandin $F_{2\alpha}$ in the human eye

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Abstract. The ocular effects of 200 μg of topically applied prostaglandin $F_{2\alpha}$ were studied in 18 nonglaucomatous volunteers. A fall in intraocular pressure was seen in the prostaglandin-treated eyes when compared with the placebo-treated control eyes. The maximum intraocular pressure reduction was observed at the 7th h and hypotensive ocular effect persisted for 24 h. Prostaglandins did not produce any change in pupillary diameter or signs of intraocular inflammation visible by anterior segment biomicroscopy or iris fluorescein angiography. The drug caused side effects: conjunctival hyperemia was constant and many patients complained of ocular smarting and headache. It could be useful in the treatment of ocular hypertension, although its usefulness would be limited by the side effects.

Introduction

Prostaglandins (PGs) are know to be important mediators of ocular inflammatory responses (Eakins 1977). Early reports indicated that PGs can induce an acute rise in intraocular pressure (IOP), miosis (Waitzman and King 1967), as well as an increase in the protein content of aqueous humor, particularly in rabbits (Beitch and Eakins 1969). In addition, PGE_2 and $PGF_{2\alpha}$ have been shown to cause a prolonged reduction in IOP when administrated intravenously, intracamerally (Starr 1971), or topically (Camras et al. 1977). Relatively small doses of PGs instilled in the conjunctival sac of primates also lowered the IOP without causing any apparent inflammatory reaction (Camras and Bito 1981; Stern and Bito 1982).

The purpose of this study was to evaluate the effects of topically administrated $PGF_{2\alpha}$ (200 μg) on the intraocular pressure and pupillary diameter of the human eye. Changes in anterior chamber trasparency were recorded, as well as iris reactions and ocular side effects.

Subjects and methods

Eighteen patients referred to our clinic for nonglaucomatous ocular diseases were investigated. Individuals with anterior segment diseases, uveitis, aphakia, and those under topical drug treatment were excluded. The volunteers comprised 12 females and 6 males with an average age of 64.11 (range 25–78) and an IOP between 9 and 23 mm Hg.

At 8 and 9 a.m. bilateral measurements of the IOP (Goldmann tonometer) and the pupillary diameter (Goldmann perimeter with standard background luminance) were performed, along with a biomicroscopic examination of the anterior segment. A 200-μg aliquot of the tromethamine salt of $PGF_{2\alpha}$ dissolved in 40 μl of sterile water was randomly applied on one eye of the volunteers. An equal volume (40 μl) of sterile water was instilled into the control eye of the same subject. The above-mentioned examinations were again performed 1, 2, 4, 7, 10, and 24 h after treatment. The patient's subjective tolerance to the drug was recorded throughout the study. Each patient underwent fluorescein iridography between 10 min and 5 h after instillation of the PG. The significance of the results were valued by Student's paired t-test.

Results

Application of $PGF_{2\alpha}$ to the eye produced a drop in the IOP about the 4th h and a further drop between the 7th and the 10th h. The placebo-treated eyes showed little fluctuation in the IOP (see Fig. 1).

The difference in IOP between the PG-treated and the control placebo-treated eye in each of the 18 patients is shown in Fig. 2. The IOP differences are statistically significant in the 4th and 24th h ($P<0.01$) and in the 7th and 10th h ($P<0.001$). The pupillary diameter measured in the two series of eyes showed no difference (see Fig. 3).

Immediately after topical instillation of the $PGF_{2\alpha}$, a marked conjunctival hyperemia developed in the treated eye in all patients. The effect was reduced after 2 h, but in some cases a noticeable hyperemia persisted for the entire 24-h period of observation. Anterior chamber biomicroscopy did not reveal any aqueous flare or cells in any subject at any stage of the 24-h period.

Fluorescein iridography was employed to detect possible signs of PG-induced iritis (vascular dilation and leakage). Ten pateints exhibited normal angiographic pattern, but eight subjects showed some bilateral leakage of fluorescein from the pupillary border vessels. Since these latter patients were elderly, the leakage from the pupillary plexus was not considered abnormal.

The subjective symptoms reported by the patients included smarting (11 subjects) and foreign body sensation (2 subjects) in the treated eye following PG instillation. Moreover, in one-third of all our volunteers headache of variable intensity was reported. All the symptoms generally disappeared after 2–3 h.

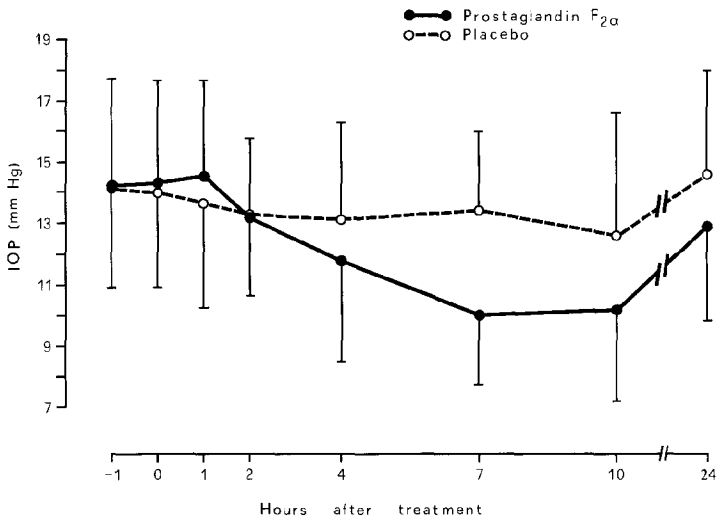

Fig. 1. Mean change in IOP of 18 patients versus time. $PGF_{2\alpha}$ (200 µg) – treated eyes: *points*; placebo-treated eyes: *circles*; ±1 SD: *bars*

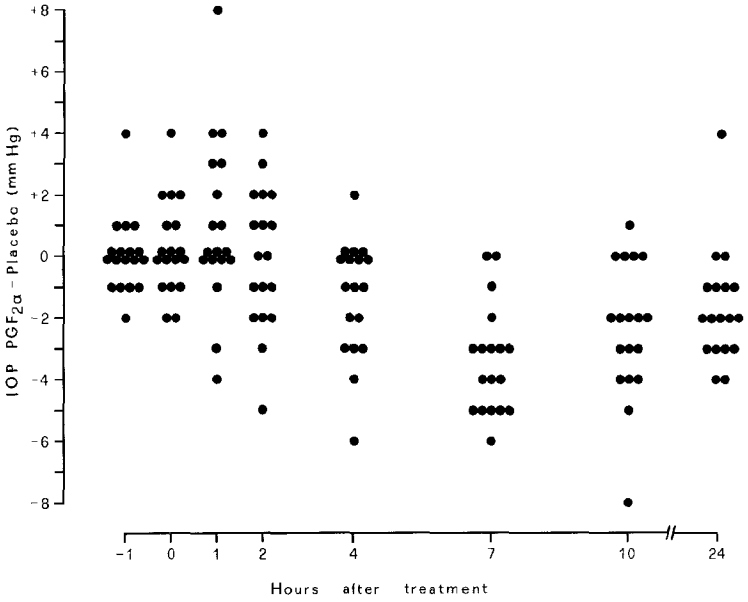

Fig. 2. IOP difference between the PG-treated and the placebo-treated eye in each of 18 patients versus time. *Points* represent the IOP differences in each patient

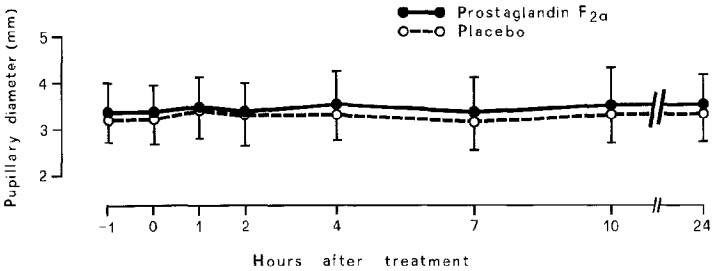

Fig. 3. Mean change in pupillary diameter of 18 patients versus time. $PGF_{2\alpha}$ (200 µg) – treated eyes: *points*; placebo-treated eyes: *circles*; ±1 SD: *bars*

Discussion

This study indicates that topical PGs can reduce IOP in humans. In nonglaucomatous subjects 200 µg of $PGF_{2\alpha}$ reduces IOP up to about 30% of pretreatment values and produces some hypotension for 24 h at least.

Zajacs et al. (1976) has found an IOP reduction in pregnant women after intravenous or intrauterine administration of PGs to induce abortions. Although ocular hypertension induced by exogenous PG in humans has not been reported before now a similar effect has been shown in experimental animals. In the rabbit, Camras et al. (1977) have observed that topical $PGF_{2\alpha}$ and PGE_2 produce an immediate rise in the IOP, followed by a reduction that

lasts many hours. The initial hypertensive response did not occur with the use of 5 µg or less of $PGF_{2\alpha}$. A similar biphasic response has been shown by Stern and Bito (1982) in the cat and in the rhesus monkey. The higher doses of $PGF_{2\alpha}$ produced an initial rise in IOP before the hypotony, without aqueous flare. Miosis occurred in the cat eye but not in the monkey eye. In our patients no change in the pupillary diameter or the blood-aqueous barrier permeability was evoked by $PGF_{2\alpha}$, which is similar to the results obtained by Stern and Bito (1982) in the rhesus monkey. The ocular hypotensive effect of the PGs may be due to an increase in the aqueous-humor outflow facility, which Green and Kim (1975) and Moses et al. (1981) have demonstrated in the rabbit eye.

Since PGs reduce IOP and do not change the pupillary diameter and blood-aqueous barrier, they could represent a new pharmacological approach to the therapy of ocular hypertensions. However, a serious handicap in their use is the unfavorable side effects of ocular pain, conjunctival hyperemia and headache, which could discourage their use in chronic therapy.

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