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THE EFFECT OF ... ANOPROST (PHXA41) ON THE INTRAOCULAR PRESSURE AND AQUEOUS HUMOR PROTEIN CONCENTRATION
A RANDOMIZED, DOUBLE MASKED COMPARISON WITH TIMOLOL AS CONTROL

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Purpose To study the dose response-relationship between PhXA41 15 µg/ml bid and PhXA41 50 µg/ml once daily concerning the IOP lowering effect and ocular side effects.
Methods A randomized, double-masked study with 2 cross-over and one parallel group and 3 treatment periods of 3 weeks each. 30 patients with bilateral POAG were enrolled after written informed consent and IOP > 22 mm Hg after washout. Eyes were treated with 15 µg/ml bid and 50 µg/ml once daily compared to a third group with timolol 0.5% bid. Flare was studied using the KOWA flare meter 500 at day 1, 21 and 42. Conjunctival hyperaemia was graded using visual analogue scales and standard photographs.
Results PhXA41 50 µg/ml once daily reduced IOP (-9.8 mm Hg) significantly compared to both timolol 0.5% (p = 0.001, students t-test) and PhXA41 15 µg/ml bid. Timolol 0.5% bid showed a significant (p = 0.001) increase of aqueous humor flare. There was no significant difference in change from baseline in aqueous humor protein concentrations between patients treated with PhXA41 and timolol (p = 0.08). No significant difference in hyperaemia was found between the 2 PhXA41 concentrations (p = 0.37, ANOVA).
Conclusions Our results suggest that PhXA41 50 µg/ml once daily is a clinically useful ocular hypotensive agent which is superior to PhXA41 15 µg/ml and timolol 0.5% twice daily when compared for reduction of IOP. The relative lack of ocular side effects in this study suggest that this agent has promise for the treatment of chronic glaucoma.

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TITLE: OCULAR HYPOTENSIVE EFFECTS OF PhXA41 IN GLAUCOMA PATIENTS AND IOP CHANGE DURING DAY AND NIGHT IN NORMAL VOLUNTEERS

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Purpose We evaluated the clinical efficacy of 0.005% PhXA41, a new phenyl-substituted prostaglandin $F_{2\alpha}$-isopropyl ester analogue, in primary open angle glaucoma (POAG) and ocular hypertension (OH) patients. We also investigated the effect of PhXA41 on diurnal and nocturnal IOP changes in normal volunteers.

Methods 1) A multicentral randomized, double-masked study in which the efficacy on IOP and safety was evaluated for 12 weeks with daily once administration of 0.005% PhXA41 or with daily twice administration of 0.5% Timolol Maleate as a control drug in thirty five patients with POAG or OH.
2) Sixteen normal volunteers were recruited for the study to evaluate the diurnal and nocturnal change of IOP with daily once administration of 0.005% PhXA41.

Results The mean IOP reduction from baseline after 12 weeks treatments 6.2±2.7 mmHg for PhXA41 and 4.4±2.3 mmHg for Timolol Maleate, respectively. The mean IOP reduction of PhXA41 group was greater than the other one. Major symptoms were only conjunctival hyperemia and smarting in both groups. PhXA41 kept reducing IOP with daily once administration either in day and night.

Conclusions 1) PhXA41 showed significantly better IOP reduction than Timolol Maleate. 2) PhXA41 reduces the IOP in normal volunteers with daily once administration either in day and night.

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COMPARISON OF MITOMYCIN C AND 5 FLUOROURACIL IN 100 CASES OF HIGH RISK TRABECULECTOMIES.

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Purpose: A comparison of long term effect on IOP and complications of trabeculectomies performed with the adjunct of either postoperative 5 fluorouracil(5FU) or peroperative mitomycin C(MMC) in 100 cases of high risk glaucoma.
Method:We prospectivly studied 52 eyes of 46 patients treated with MMC (Follow up 15±8,7m) and compared it with a retrospective serie of 48 eyes of 35 patients treated with 5FU (Follow up 14,31± 11,25m).
Results:84% of MMC patients but 46% of 5FU group had a normalized IOP without treatment, and 23% of 5FU vs 5,7 % of MMC patients required systemic glaucoma therapy. Early adverse effects were more frequently observed with 5FU (cornea 39%, conjonctiva 17% or hypotony 29%) than with MMC (13,46%, 3,85%,13,46% respectivly). At last examination, bleb failure requiring additional surgery was more frequent in 5FU group (10%) than MMC (3%), and was mostly associated to anterior chamber factors (i.e. vitreous or lens related obstruction), rather than episcleral cellular factors.Long term hypotony was observed in in 17,3 % of the MMC eyes, in this later group 5 of 9 patients had more than 2 lines of best corrected visual acuity reduction.
Conclusion: These results suggest that MMC is at least as efficient to reduce IOP.The use of MMC may be associated with a higher rate of long term hypotony.

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INTRAOPERATIVE TREATMENT WITH MITOMYCIN C IN EXPERIMENTAL GLAUCOMA FILTERING SURGERY: DOSE EFFECT ON CONJUNCTIVAL AND SCLERAL FIBROBLASTS.

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PURPOSE: To evaluate the effect of mitomycin C on fibroblasts outgrowth in a model of glaucoma filtering surgery.
METHODS: Pigment rabbits undergoing filtering surgery were exposed to several intraoperative treatments: Group 1 (n=5): balanced saline solution; Group 2 (n=5): mitomycin C 0.2 mg/ml; Group 3 (n=5): mitomycin C 0.4 mg/ml. Tissue samples were taken one hour after surgery and included conjunctival and scleral tissue at 0° and 90° area and the adjacent cornea 2 mm from the limbus. The biopsies were placed in tissue culture media (trimix media with 20% fetal calf serum) and incubated at 37° and PCO_2 5%, in a humified atmosphere. Fibroblast outgrowths were measured every 3 days for 12 days; cell morphology was evaluated as well. Repeated-measures analysis of variance was performed each time. Significance was defined as $p<0.05$.
RESULTS: The average scleral and conjunctival outgrowth from the mitomycin-C treated tissues were significantly less than the outgrowth of the eyes treated with BSS, throughout all the experiment to day 12. The outgrowths from the 90° tissues of mitomycin treated eyes, were significantly higher than 0° tissues and similar to BSS group. There were no differences between eyes treated with mitomycin 0.2 mg/ml and eyes treated with mitomycin 0.4 mg/ml at any time point. The cells growing out from the mitomycin C treated areas were abnormal in appearance.
The outgrowths corneal samples were similar in all groups.
CONCLUSIONS: Intraoperative exposure to mitomycin C has an inhibitory effect on the local conjunctival and scleral fibroblasts population. In our serie, this effect is similar with mitomycin 0.2 and 0.4 mg/ml. Mitomycin C treatment induces abnormal fibroblasts morphology.