ARVO

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The **Abstract Program Book** is mailed to all ARVO members and pre-registered non-member participants in March. **Everyone is expected to bring this book with them to the Meeting as additional copies are limited and can only be given out after the third day of the Meeting.** Remember that abstracts are referred to by Program Number, as opposed to Page Number, in the Author and Permuted Keyword indices.

Hernando Desoto Hall North & South
Wednesday 8:30 — 12:00 noon

Glaucoma
Clinical Pharmacology

MODERATORS: David K. Dueker
Donald S. Minckler

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1574	9:30	Van Best, Kuppens, Stolwijk, de Keizer
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WEDNESDAY

1570 — 8:30

EFFECT OF TOPICAL INDOMETHACIN AND APRACLONIDINE HYDROCHLORIDE ON INTRAOCULAR PRESSURE IN NORMAL SUBJECTS

Fi —Jung Lin, Por-Tying Hung, Tsing-Hong Wang and Tzyy-Chang Ho
Department of Ophthalmology, National Taiwan University, Taipei, Taiwan, ROC

Indomethacin inhibits the ocular hypotensive action of topical epinephrine in glaucoma patients. This study is to assess whether the intraocular hypotensive effect of apraclonidine can also be altered by the application of topical indomethacin. We performed a randomized double-masked crossover study in ten normal volunteers.

The subjects were randomly divided into two groups of five. They underwent two successive study days in two periods seperated by one-week washout time. Each subject received 0.1% topical indomethacin four times daily in one eye and placebo in the other eye for the two study days in both periods. For group I subjects, one drop of 1% apraclonidine was placed in the eye receiving indomethacin concurrently and placebo in the fellow eye at 8 A.M. on the second day of the first period. In the second period, apraclonidine and placebo were exchanged for comparison. Group II subjects received the same eyedrops but in reverse sequence. Each subject thus served as his own control.

We examined intraocular pressure (I.O.P.) of each subject immediately before the first dose at 8 A.M. , then 2, 5 and 8 hours later for every study day.

We found the intrsocular hypotensive effect of apraclonidine was not significantly ($p>0.1$) changed by the administration of topical prostaglandins-inhibitor, indomethacin.

	Percent IOP Change from Baseline 2 hr	5 hr	8 hr
Apraclonidine + Placebo:	27.1±9.4%	37.1±11.0%	28.9±11.1%
Apraclonidine + Indomethacin:	29.3±8.5%	36.4±9.4%	30.1±10.4%

These results [illegible] in the mechanisms by which apraclonidine decreases ocular pressure in normal subjects.

1571 — 8:45

APRACLONIDINE: REFORMULATION AND DROP SIZE ALTERATION

Mark J. Vocci†, Alan L. Robin†*, John C. Wahl† and James Sutton†
†Sinai Hospital of Baltimore and *The Johns Hopkins University, Baltimore, Maryland

Chronic administration of apraclonidine ([A]) may be somewhat limited by symptoms of dry mouth and eyes. These may be dose dependent. Reformulation could enhance [A]'s corneal adherance and/or alter penetration, reducing the need for higher concentrations of [A] while maintaining the same magnitude and duration of intraocular pressure (IOP) lowering as the conventional 1% solution. This could decrease side effects while maintaining efficacy. Similarly, a reduction in drop size from 30 µl to 16 µl might also increase ocular bioavailability. We compared three different formulations of [A] (a 0.5% viscous solution, a 0.5% viscous solution with lysolecithin and 0.5% conventional ophthalmic solution) and the vehicle of the conventional formulation all delivered with a standard 30 µl drop size. We also compared the conventional 1% solution to the 0.5% solution in an 16 µl drop. The effect of these formulations on IOP lowering and on local and systemic side effects were monitored in 29 healthy adult volunteers in a prospective double-masked, placebo-controlled, randomized six period cross-over study. Each received all six medications in a random order with a one week washout between periods. Diurnal data was collected on day one and day seven of each period. Maximum IOP lowering effect at three hours ranged from 21.9% ± 16.6% to 26.1% ± 12.0% for all formulations. All formulations were significantly different from placebo ($p<.05$) but none were statistically significantly different from each other. The 0.5% formulation produced less dry mouth, fatigue, and drowsiness than the 1% apraclonidine solution, but the differences were not statistically significant. Hydroxypropyl methylcellulose produced transient blurred vision. There was no statistical difference in either symptoms or IOP lowering; however, the smaller drop size did show a trend toward fewer side effects.

1572 — 9:00

A PILOT STUDY OF THE EFFICACY AND SAFETY OF AGN 190342-LF 0.02% AND 0.08% IN PATIENTS WITH ELEVATED INTRAOCULAR PRESSURE.

Thomas R. Walters,[1] Rex L. Repass,[1] Julia P. Sargent,[1] Elaine P. Kelley,[2] Jack F. Stoecker,[2] Kuankuan S. Chen[2], David G. Harper[2], Biomedical Research Group,[1] Austin, TX., Allergan, Inc.,[2] Irvine, CA.

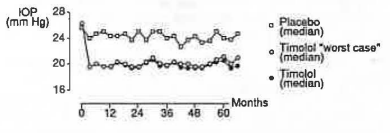
AGN 190342-LF is a relatively selective alpha$_2$-adrenoceptor agonist under investigation as an ocular hypotensive agent. Structurally similar to clonidine, both compounds possess a 2-amino-imidazoline group. Topically administered, AGN 190342-LF lowers intraocular pressure (IOP) in normotensive and ocular hypertensive monkeys, rabbits, and cats over a dose range of 0.001% to 1%. IOP reduction appears to be produced by a decrease in aqueous humor flow, caused by stimulation of alpha$_2$-adrenoceptors located, in part, on ocular sympathetic nerve endings. In this randomized, double-masked, pilot study, we evaluated the efficacy and safety of bilateral, twice-daily administration of AGN 190342-LF 0.08%, 0.02% or vehicle in 13 patients with open-angle glaucoma or ocular hypertension. Overall mean reductions in IOP were 6.0 mm Hg (23.9%), 3.4 mm Hg (13.8%), and 2.0 mm Hg (7.2%) for the 0.08%, 0.02%, and vehicle groups, respectively, following three days of treatment. Mean decreases in heart rate and blood pressure were not clinically significant. The results of this pilot study indicate that AGN 190342-LF has potential in the treatment of elevated intraocular pressure.

1573 — 9:15

LACK OF SUBSENSITIVITY TO TOPICAL TIMOLOL IN OCULAR HYPERTENSION,

Boel Bengtsson, Anders Heijl, and Jan Lanke. Dept of Ophthalmolgy in Malmö and Dept of Statistics, University of Lund, Sweden

132 eyes of 82 patients were followed up to 66 months in a masked, prospective, randomized study of patients with high risk ocular hypertension. Patients were randomly assigned to treatment with topical timolol or placebo. IOP was monitored as office hour tension curves every third month. Patients who developed glaucoma or in whom mean IOP rose to ≥ 35 mmHg left the study. Mean baseline IOP was 0.6 mm Hg higher in the timolol-treated eyes than in the placebo eyes. At three months IOP was 4.3 mm Hg lower in the timolol than in the placebo group. This treatment-induced difference between groups showed no signs of diminishing over time in the eyes remaining in the study.



Those eyes which had to leave the study complicate the picture. However, the conclusion is not substantially altered even when we assume a worst-case scenario, viz. that all excluded timolol would have had higher IOP than all remaining timolol eyes, while placebo eyes were a random sample of all excluded placebo eyes (cf. the middle curve in the figure). Thus, in the present material there was no evidence of any decrease over time in the pressure-reducing effect of timolol.