

BRIMONIDINA: NUOVE PROSPETTIVE OLTRE LA IOP

Renato De Natale

U.O.C. di Oculistica di Monselice
(Padova)

BRIMONIDINA:Alfa 2 agonista

1. Riduce la formazione dello U. A. nel corpo ciliare.
2. Accentua il deflusso uveo sclerale

Indicazioni:

- per il trattamento dell'ipertensione oculare e del glaucoma c.s.
- Quale farmaco di 1° scelta o in terapia associativa

Approvato dall' FDA 1997

Observations from the European Glaucoma Society (EGS) treatment guidelines³

IOP reduction

	β -blockers	Prostaglandins and Prostanoids	CAIs	α_2 Agonists
IOP reduction	20-25%	25-33%	15-20%	20-25%

Adapted from EGS Guidelines³

COMBIGAN (BrTFC)

combinazione fissa

Brimonidina 0,2% +

Timololo 0,50%

Approvato dall' FDA 2007

TOLLERABILITA'

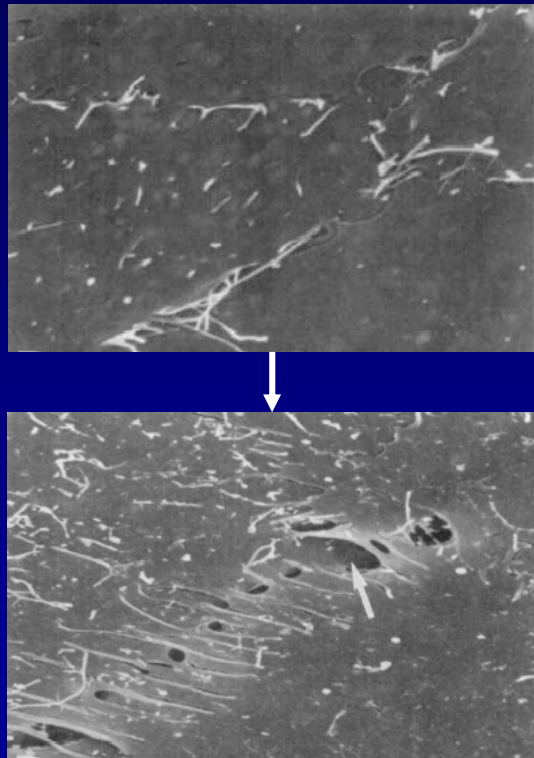
- In passato, problemi di tollerabilità, dovuti soprattutto ad allergia oculare, hanno limitato l'uso della brimonidina in monoterapia^{1,2}
- Il Combigan presenta una tollerabilità migliore rispetto alla brimonidina, quindi consente ad un maggior numero di pazienti di essere trattati con la brimonidina

1. Allergan Ltd. Combigan SmPC. November 2008

2. Motolko. Curr Med Res Opin 2008;24:2663-7

Un doppio meccanismo d'azione può migliorare la tollerabilità (1)

SEM of Schlemm's canal endothelial cells before and after treatment with beta-adrenergic agonist¹



Proposal of effect of adrenergic agonists on corneal epithelium cells²

Adrenergic agonist binds to receptors in corneal epithelium cells¹

↓
Corneal epithelium cells shrink and open intercellular spaces in conjunctiva²

↓
↑ Permeability to airborne allergens, lipids, medications and preservatives²

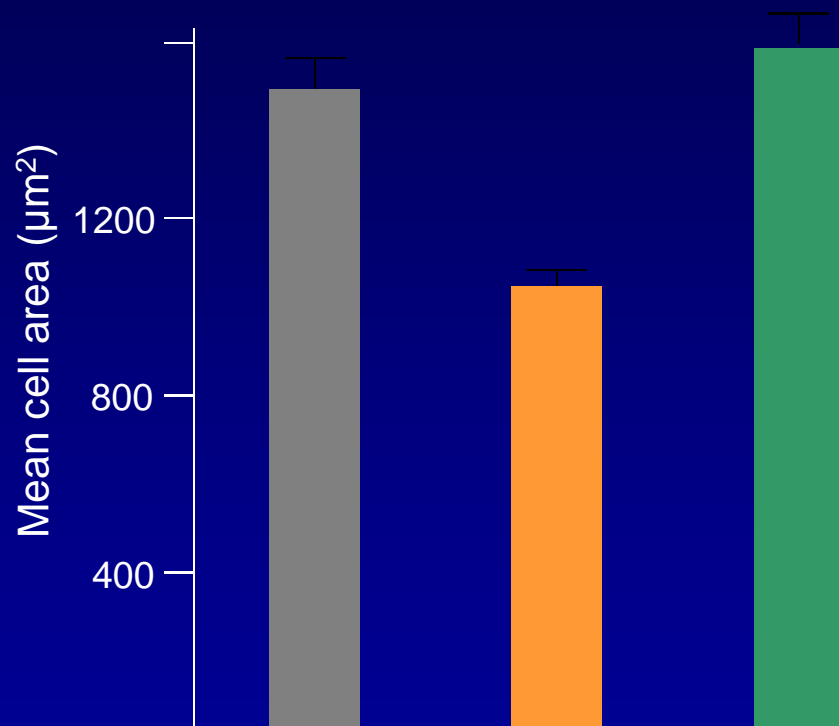
↓
↑ Cellular and vascular inflammatory response in subconjunctival space²

Gli agonisti adrenergici provocano una contrazione delle cellule epiteliali corneali, con allargamento degli spazi intercellulari e aumento della permeabilità ad allergeni e irritanti

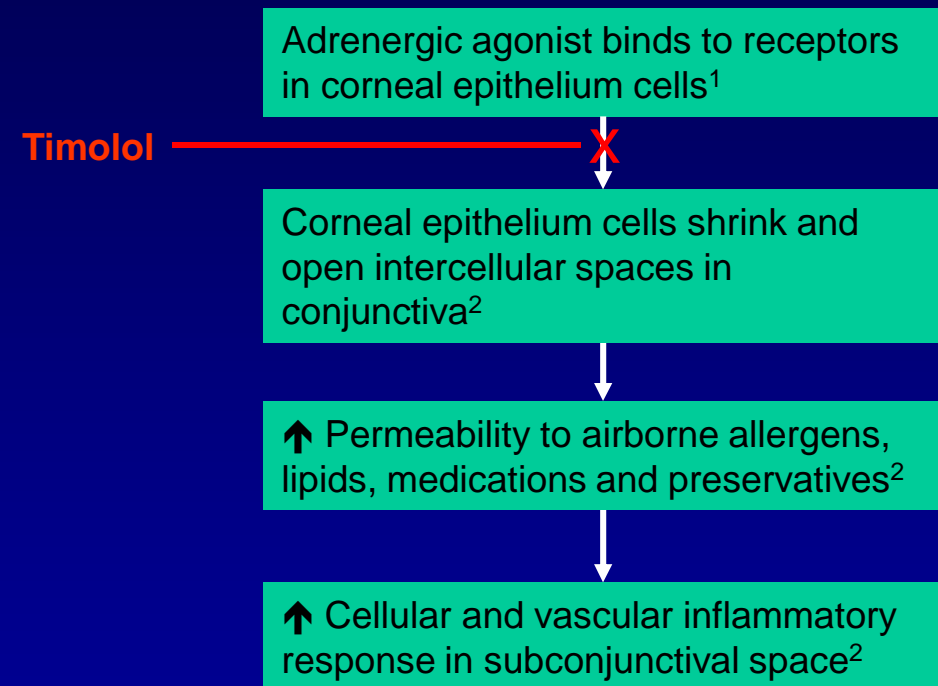
1. Alvarado et al. Invest Ophthalmol Vis Sci 1998;39:1813–22
2. Nixon, Turk. Medscape Ophthalmology 2008. Available at www.medscape.com. Accessed 18/02/09

Dual mechanism of action may improve tolerability (2)

Mean area of trabecular meshwork cells treated with adrenergic agonist +/- timolol¹



Proposal of effect of adrenergic agonists on corneal epithelium cells²



Il Timololo sembra inibire la contrazione delle cellule provocato dall'uso degli agonisti adrenergici. Ciò suggerisce che l'aggiunta del timololo al trattamento con gli agonisti adrenergici aiuti a mantenere la naturale barriera della congiuntiva.

1. Alvarado et al. Invest Ophthalmol Vis Sci 1998;39:1813–22
2. Nixon, Turk. Medscape Ophthalmology 2008. Available at www.medscape.com. Accessed 18/02/09

OLTRE LA IOP.... ?

NEUROPROTEZIONE

INDIRETTA

Sui fattori di rischio:

- IOP
- Flusso oculare

DIRETTA

Previene e/o rallenta
l'apoptosi RGC agendo
direttamente su
meccanismi biochimici
parzialmente conosciuti

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Brimonidina e:

- a. Ocular blood flow
- b. Pressione di perfusione

Arch Ophthalmol 1998 Dec;116(12):1591-1594.

99020203

CLINICAL SCIENCES

Effect of Brimonidine Tartrate on Ocular Hemodynamic Measurements

Yves Lachkar, MD; Clive Migdal, MD; Surinda Dhanjil, MSc, RVT

Conclusion: The hemodynamics of the posterior segment of the eye as measured by color Doppler ultrasound do not appear to be altered by 2% brimonidine tartrate.

Accepted for publication August 14, 1998.

This study was supported by a research grant from Allergan Inc, Irvine, Calif.

Presented at the Association of Vision Research in Ophthalmology meeting, Fort Lauderdale, Fla, May 15, 1997.

Corresponding author: Clive Migdal, The Western Eye Hospital, Marylebone Road, London NW1 5YE, England.

Am J Ophthalmol
2000;129(3):297-301.
2000040382A

The Effect of Brimonidine Tartrate on Retinal Blood Flow in Patients With Ocular Hypertension

ANTHONY M. CARLSSON, BSc, BALWANTRAY C. CHAUHAN, PhD, A. ARLENE LEE, RN,
AND RAYMOND P. LeBLANC, MD

- **CONCLUSIONS:** Brimonidine reduces intraocular pressure without altering retinal capillary blood flow in patients with ocular hypertension. (Am J Ophthalmol 2000;129:297–301. © 2000 by Elsevier Science Inc. All rights reserved.)

This study was supported by the MacKeen Studentship from the Dalhousie Medical Research Foundation, Halifax, Nova Scotia, Canada (Mr Carlsson), and by a grant from Allergan Pharmaceuticals, Irvine, California (Dr Chauhan).

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AND THERAPEUTICS
Volume 17, Number 3, 2001
Mary Ann Liebert, Inc.

Effect of Brimonidine Tartrate on Ocular Hemodynamics in Healthy Volunteers

CHRISTIAN P. JONESCU-CUYPERS¹, ALON HARRIS^{1,2}, YOKO ISHII¹,
LARRY KAGEMANN¹, HANNA J. GAZOZI³, YGAL ROTENSTREICH¹,
HAK SUNG CHUNG¹, and BRUCE MARTIN²

Glaucoma Research and Diagnostic Center, Departments of ¹Ophthalmology and ²Physiology and Biophysics, Indiana University Medical Center, Indianapolis, Indiana

³Department of Ophthalmology, Central Emek Medical Center, Afula, Israel

It remains unknown if topical brimonidine can reach the posterior pole or, if having reached that site, it can constrict vessels within the retinal nerve fiber layer and optic nerve head. In this study, we evaluated the hemodynamic actions of topical brimonidine by studying its effects on retinal and retrobulbar vessels.

In conclusion, two-week treatment with brimonidine reduces IOP and does not reduce the bulk retinal or retrobulbar arterial perfusion in young healthy volunteers.

Independent Study, No Grant for this paper

Effects of Topical Hypotensive Drugs on Circadian IOP, Blood Pressure, and Calculated Diastolic Ocular Perfusion Pressure in Patients with Glaucoma

Luclano Quaranta, Federtco Gandolfo, Raffaele Turano, Federtco Rovlida, Teodoro Ptzzolante, Andrea Mustg, and Enrtco Gandolfo

CONCLUSIONS. Latanoprost seemed to induce a uniform reduction in IOP during the 24-hour period, although timolol was as effective as latanoprost during the daytime, and dorzolamide are as effective as latanoprost at night. SBP and DBP were significantly decreased by either timolol or brimonidine. In this study of patients with newly diagnosed POAG, only dorzolamide and latanoprost significantly increased mean 24-hour DOPP. (*Invest Ophthalmol Vis Sci.* 2006;47:2917-2923) DOI: 10.1167/iovs.05-1253

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be marked "advertisement" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Comparative Analysis of the Effects of Brimonidine and Dorzolamide on Ocular Blood Flow Velocity in Patients with Newly Diagnosed Primary Open-Angle Glaucoma

TULAY SIMSEK,¹ BAHAR YANIK,² ISIK CONKBAYIR,² and ORHAN ZILELIOGLU¹

There was little difference, in terms of ocular blood flow velocity, between newly diagnosed glaucoma patients and control subjects. Both topical brimonidine and dorzolamide significantly reduced the intraocular pressure without altering ocular blood flow velocity in patients with newly diagnosed POAG.

Independent Study, No Grant for this paper

$$\text{Pressione di perfusione oculare} = \text{Pressione diastolica} - \text{P.I.O.}$$

La pressione di perfusione è il risultato di un “**gradiente**” di due parametri

A Randomized Trial of Brimonidine Versus Timolol in Preserving Visual Function: Results From the Low-pressure Glaucoma Treatment Study

THEODORE KRUPIN, JEFFREY M. LIEBMANN, DAVID S. GREENFIELD, ROBERT RITCH, AND STUART GARDINER, ON BEHALF OF THE LOW-PRESSURE GLAUCOMA STUDY GROUP

- **PURPOSE:** To compare the alpha₂-adrenergic agonist brimonidine tartrate 0.2% to the beta-adrenergic antagonist timolol maleate 0.5% in preserving visual function in low-pressure glaucoma.

Am. J. Ophthalmol. 2011; 151:671-681

In summary, in this randomized clinical trial, twice-daily treatment with topical brimonidine tartrate 0.2% preserves visual field better than treatment with topical timolol maleate 0.5% in a subset of open-angle glaucoma patients with statistically normal IOP. Given the similar IOP-lowering efficacy of the 2 compounds, this finding is consistent with a non-IOP-related mechanism of action favoring brimonidine-treated patients. The effectiveness of brimonidine in delaying or preventing visual field progression has to be judged in context of brimonidine's adverse event profile, primarily localized external ocular allergy. Validation of a neuroprotective mechanism of action requires additional basic science and clinical research to confirm the present results prior to altering current clinical patient care paradigms.

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La Brimonidina in studi su animali da lab.

Brimonidine rescues RGCs from ischemia-induced cell death, preserves retrograde axonal transport in surviving RGCs and protects against ischemia-induced degeneration of the retinotectal projection.

- a) Lafuente MP, et Al. Transient ischemia of the retina results in altered retrograde axoplasmic transport: Neuroprotection with brimonidine. *Exp Neurol.* 2002;178:243-258.
- b) Vidal-Sanz M, et Al. Retinal ganglion cell death induced by retinal ischemia: Neuroprotective effects of two alpha-2 agonists. *Surv Ophthalmol.* 2001;45(Suppl 3):S261-S267.

Take Home Message:

1. La brimonidina abbassa la IOP > CAI
2. Il Combigan presenta < eff. coll. dell'Alphagan per la presenza del timololo
3. Non vi sono evidenze per sostenere che la Brimonidina riduca la pressione di perfusione oculare, anzi preserva il c.v. nel LTG e potrebbe pertanto svolgere un ruolo neuroprotettore clinicamente apprezzabile nel LTG.

GRAZIE

Disponendo di una molecola a forte azione ipotonizzante oculare, con proprietà neuroprotettive accertate in lab. e empiricamente dimostrate in clinica.

La usereste quando.....?

Come ultima spiaggia o..... ?