

The Effect of β -Blocker Eye Drops on Pulse Rate, Ocular Blood Flow, and Glaucoma Progression: A Retrospective Longitudinal Study

Authors: Naoki Kiyota¹, Yukihiro Shiga¹, Takahiro Ninomiya¹, Satoru Tsuda¹, Kazuko Omodaka¹, Noriko Himori^{1,5}, Yu Yokoyama¹, Kyongsun Pak⁶, and Toru Nakazawa¹⁻⁴

Affiliations:

¹ Department of Ophthalmology, Tohoku University Graduate School of Medicine, Miyagi, Japan

² Department of Ophthalmic Imaging and Information Analytics, Tohoku University Graduate School of Medicine, Miyagi, Japan

³ Department of Retinal Disease Control, Tohoku University Graduate School of Medicine, Miyagi, Japan

⁴ Department of Advanced Ophthalmic Medicine, Tohoku University Graduate School of Medicine, Miyagi, Japan

⁵ Department of Aging Vision Healthcare, Tohoku University Graduate School of Biomedical Engineering, Sendai, Japan.

⁶ Division of Biostatistics, Department of Data Management, Center for Clinical Research, National Center for Child Health and Development, Tokyo, Japan

Correspondence: Toru Nakazawa, MD, PhD

Department of Ophthalmology, Tohoku University Graduate School of Medicine, 1-1 Seiryō-machi, Aoba-ku, Sendai, Miyagi, 980-8574, Japan. Tel: +81 22 717 7294, Fax: +81 22 717 7298
e-mail: ntoru@oph.med.tohoku.ac.jp

Supplementary Table S1. The effects of anti-glaucoma eye drop add-ons on BP, PR, and IOP

Add-on eye drops	Number of eyes and subjects	PR (β , P)	IOP (β , P)	SBP (β , P)	DBP (β , P)
PGs	251 eyes of 158 subjects	+1.74, 0.018*	-0.39, < 0.001*	-5.24, < 0.001*	-0.58, 0.411
CAIs	387 eyes of 236 subjects	+0.73, 0.162	-0.25, 0.021*	-0.22, 0.781	-0.42, 0.456
α_2 stimulators	1276 eyes of 774 subjects	-0.05, 0.878	-0.24, < 0.001*	-3.25, < 0.001*	-0.70, 0.027*
α_1 blockers	57 eyes of 35 subjects	+1.33, 0.245	-0.97, < 0.001*	-3.82, 0.082	-0.16, 0.899
Rho kinase inhibitors	679 eyes of 414 subjects	+0.40, 0.320	-0.49, < 0.001*	-0.65, 0.350	-0.13, 0.760

CAI = carbonic anhydrase inhibitor; DBP = diastolic blood pressure; IOP = intraocular pressure; PG = prostaglandin analogue;

PR = pulse rate; SBP = systolic blood pressure.

Age at add-on start date, gender, year from add-on start date (-: before, +: after), and being after cataract surgery or glaucoma surgery (reference, before) were adjusted. β indicates the partial regression coefficient; * indicates statistical significance.

Supplementary Table S2. Linear mixed-effects model assessing the effect of clinical factors on PR at add-on start date and PR change after the β blocker add-on

	Effect on PR at add-on start date		Effect on PR change after add-on	
	β	<i>P</i> value	β	<i>P</i> value
Pulse rate at add-on start date (1 bpm higher)	0.88	< 0.001*	-0.42	< 0.001*
Age at add-on start date (1 year older)	-0.11	0.218	-0.02	0.689
Female (reference, male)	6.37	0.005*	-2.36	0.059
MD (1 dB higher)	-0.06	0.377	0.12	0.101
Overall cpRNFLT (10 μ m higher)	0.00	0.995	0.10	0.766
BMI (1 kg/m ² higher)	-0.15	0.686	0.11	0.572
Axial length (1 mm longer)	-0.04	0.944	-0.04	0.917
CCT (10 μ m longer)	-0.20	0.329	0.45	0.006*
d-ROM level (10 U. Carr higher)	0.53	0.005*	-0.40	< 0.001*
BAP (100 mmol/L higher)	0.46	0.322	-0.08	0.763
Smoking habit (yes:1, no: 0)	-3.66	0.126	-0.54	0.688
Hypertension (yes:1, no: 0)	-4.54	0.081	0.79	0.576
DM (yes:1, no: 0)	-8.06	0.137	7.24	0.027*
Dyslipidemia (yes:1, no: 0)	-2.38	0.385	-0.83	0.589
Heart disease (yes:1, no: 0)	-9.62	0.004*	2.01	0.285
Sleep apnea syndrome (yes:1, no: 0)	-2.82	0.523	3.27	0.171
Dosage of eye drop: 2 times a day (reference, once a day)	4.14	0.132	-0.74	0.630
Added-on eye drop: carteolol (reference, timolol)	0.70	0.827	1.99	0.262
Diagnosis of “POAG” (reference, “NTG”)	-1.11	0.693	3.03	0.106
Diagnosis of “other” (reference, “NTG”)	-2.25	0.216	3.55	0.052

Year from add-on start date (-: before, +: after) was adjusted.

BAP = biological antioxidant potential; BMI = body mass index; CCT = central corneal thickness;

cpRNFLT = circumpapillary retinal nerve fiber layer thickness; DM = diabetes mellitus; d-ROM = diacron reactive oxygen metabolite;

MD = mean deviation; NTG = normal-tension glaucoma; POAG = primary open-angle glaucoma; PR = pulse rate.

β indicates the partial regression coefficient; * indicates statistical significance.