Study Synopsis

Study title	A randomized, placebo-controlled study investigating the effects of moxaverine on ocular blood flow after oral administration in healthy subjects
Development phase	Phase II a
Principal Investigator	Department of Clinical Pharmacology, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Wien, Austria
Study coordinator	Department of Clinical Pharmacology, Medical University of Vienna Währinger Gürtel 18-20, 1090 Wien, Austria
Co-investigators	Department of Clinical Pharmacology, Medical University of Vienna Währinger Gürtel 18-20, 1090 Wien, Austria
Statistics	Department of Clinical Pharmacology, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna Währinger Gürtel 18-20, 1090 Wien, Austria
Studied period	Date of first enrolment: 25-11-2010 Date of last completed: 29-03-2011
Background	A number of common eye diseases such as age-related macular degeneration and glaucoma are associated with ocular perfusion abnormalities. Although this is well recognized there is not much possibility to improve blood flow to the posterior pole of the eye in these diseases. For many years, moxaverine has been used in the therapy of perfusion abnormalities in the brain, the heart and the extremities. This is based on a direct vasodilatatory effect of the drug, but also on the rheological properties of red blood cells. In two recent studies we have shown that intravenous moxaverine increases choroidal and retrobulbar blood flow in healthy young subjects, in elderly people with healthy eyes and in patients with eye diseases associated with hypoperfusion. The present study aimed to investigate, whether ocular blood flow is also improved after oral administration of moxaverine.
Study objectives	To investigate the effect of orally administrated moxaverine on ocular blood flow in young healthy subjects
Study design	randomized, double-masked, placebo-controlled, two-way crossover study with moxaverine or placebo
Study population	16 healthy volunteers, age 18-35 years, non-smokers
Study medication	Moxaverine-hydrochloride, coated tablets containing 150 mg moxaverine (Kollateral forte, Ursapharm, Saarbrücken, Germany), dosage: 900 mg, administrated per os in three equal doses of 300 mg at two hour intervals or matching placebo. Placebo: coated tablets identical in number and appearance
Methods of evaluation	Laser Doppler flowmetry (choroidal and optic nerve head blood flow) Color Doppler imaging (retrobulbar vessels) Non-invasive measurement of systemic blood pressure

	Applanation tonometry (intraocular pressure)
Study endpoints	Primary endpoint: Choroidal and optic nerve head blood flow (Laser Doppler Flowmetry) Secondary endpoint: Retrobulbar flow velocities (Color Doppler imaging) Intraocular pressure (Applanation tonometry) Systolic and diastolic blood pressure (non-invasive)
Statistical methods	Statistical significance was assessed by an ANOVA model for repeated measurements. Post hoc comparisons were done using planned comparisons. A $p < 0.05$ was considered the level of significance.
Results	None of the measured parameters showed any difference between moxaverine and placebo. The p-values of ANOVA testing between moxaverine and placebo were as follows: Choroidal blood flow ($p = 0.52$), optic nerve head blood flow ($p = 0.54$), peak systolic velocity in the ophthalmic artery ($p = 0.33$), end diastolic velocity in the ophthalmic artery ($p = 0.58$), resistance index in the ophthalmic artery ($p = 0.59$), peak systolic velocity in the posterior ciliary arteries ($p = 0.38$), end diastolic velocity in the posterior ciliary arteries ($p = 0.26$), resistance index in the posterior ciliary arteries ($p = 0.86$), peak systolic velocity in the central retinal artery ($p = 0.35$), end diastolic velocity in the central retinal artery ($p = 0.51$), resistance index in the central retinal artery ($p = 0.91$).
Summary/Conclusion	The present results indicate that oral moxaverine, in contrast to parenteral moxaverine, does not increase ocular blood flow. This may be related to the relatively low bioavailability of moxaverine after oral administration.