

that 'One of the many weaknesses of the authors' informed consent process is that they did not mention disclosure to the patient of the risks associated with LP, nor was there any mention of the presence or absence of complications related to the LP in the Results Section'. We agree with Dr Grzybowski that the article (Ren et al. 2011b) does not contain information whether the patients were informed about the risks associated with a lumbar puncture, nor were potential complications owing to the lumbar puncture mentioned in the article. Thanking Dr Grzybowski for this advice, we hereby state that all patients were informed about the risks related to a lumbar puncture, and it is hereby also stated that none of the patients has been experiencing any complications owing to the lumbar puncture.

Thirdly, Dr Grzybowski mentions that 'While the authors mention an ethical review process, their description lacks sufficient detail to satisfy concerns that adequate attention was paid to protecting patients during their recruitment as research subjects. ...' The authors would like to turn Dr Grzybowski's attention to that they did not consider the study participants as 'research subjects' but as patients in need of diagnosis and treatment. In addition, the study had a therapeutic consequence. The results of the study showed that the study participants with a low CSF-P may not receive systemic carbonic anhydrase inhibitors to avoid a further lowering of the CSF-P.

Fourthly, Dr Grzybowski finally remarks that 'There is much concern about ethical issues in the design and conduct of clinical trials in developing countries It was shown in many studies that patients in developing countries can easily be exploited. It was also pointed out that studies in developing countries are more easily carried out because of less stringent controls and restrictions. This should not be a justification for conducting studies in developing countries' Although the statements given by Dr Grzybowski may potentially hold true for some countries, they are not valid for China, where patients have usually been better protected against malpractice by physicians than in other, even higher developed, countries. Perhaps, Dr Grzybowski may never have come to China nor may have had contact with many physicians from China. Dr

Grzybowski should understand that in China, after the reform and opening up policy more than 30 years ago, many clinical scientists have become fellows from leading institutions in Europe and the US, and that we have been conducting our research in accordance with international standards [e.g., as shown in the Handan Eye Study (Yang et al. 2011)]. For our study on the potential role of a low CSF-P in the pathogenesis of glaucoma, our work and the study protocol were approved and supervised by The Medical Ethics Committee of Beijing Tongren Hospital, which as a third party was independent of our research team. In addition, the CSF-P in patients with glaucoma has also been examined in other investigations made in Western Europe (Jaggi et al. 2011). In those studies, not only lumbar puncture but also CSF sampling and computer tomographic cisternography including an intrathecal injection of iopamidol were performed (Jaggi et al. 2011). Does Dr Grzybowski measure by different yard sticks?

In conclusion, we thank Dr Grzybowski for his letter, and we were very cognizant of his concern. We completely agree with him in his general concerns about the welfare and protection of patients. With respect to the specific points he listed in his letter, we refer to the remarks given above.

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Correspondence:

Ningli Wang
Beijing Tongren Eye Center
Beijing Tongren Hospital Affiliated to
Capital Medical University
1 Dongjiaominxiang Street
Dongcheng District
Beijing 100730
China
Tel: + 8610 58269920
Fax: + 8610 58269920
Email: wningli@trhos.com.

No retinal morphology changes after use of riboflavin and long-wavelength ultraviolet light for treatment of keratoconus

Mario R. Romano, Grazia Quaranta, Marsel Bregu, Elena Albe and Paolo Vinciguerra

Department of Ophthalmology, Istituto Clinico Humanitas, Rozzano, Milan, Italy

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Editor,

Retinal phototoxicity is a very well-known phenomenon and best defined as the noxious effect of

light on retinal tissue (Roberts 2001). During corneal cross-linking (CXL) treatment, the eye is exposed to a selected UVA light with a wavelength of 370 nm (Vinciguerra et al. 2009).

The photomechanical effect on the retina occurs when incident light interacts with an endogenous chromophore in the ocular tissue, causing chemical changes related to the formation of free radicals. UVA radiation should not pass through the crystalline lens, so it cannot theoretically reach retinal tissue (Glickman 2002).

UVA light used in cross-linking has an irradiance of 3 mW/cm² for a total time of 30 min. This exposes the cornea to a total dose of 3.4 J on a total radiant exposure of 5.4 J/cm². This is far superior to the maximum dose recommended by the 'Guidelines on limits of exposure to ultraviolet radiation of wavelengths between 180 and 400 nm of 1 J/cm²' (2004). However, the shielding effect of riboflavin-saturated cornea should lower such a dose to 0.22 J/cm² at the posterior lens surface (Spoerl et al. 2007). Using a slit lamp with the blue filter, the surgeon confirmed the presence of riboflavin in the anterior chamber before UV irradiation. Moreover, pilocarpine drops 2% were also administered to minimize the retinal and lens exposure. A prospective, nonrandomized comparative single-centre clinical study on 42 eyes has been performed. Twenty-one eyes (10 right, 11 left) of 17 consecutive patients (36 ± 7 years) affected by progressive keratoconus were assigned to group A and treated with CXL treatment. The control group (Group B) was composed of 21 (9 right, 12 left) eyes of 21 healthy patient of the same age (34 ± 4 years). The aim of this study was to detect any morphological change in the retina of cross-linked eyes using retinal tomography comparing scans at baseline, 1, 3 and 6 months after CXL with those of the control group.

Optical coherence tomography (Stratus OCT 3000; Carl Zeiss Meditec Inc., Dublin, CA, USA) was used to image the macular area and nerve fibre layer at each time-point.

A p value of ≤0.05 was considered significant, and the statistical power of the study was 0.8 and beta error 0.2.

In the group A, the central macular thickness (CMT) was 189 (SD 30), 187 (SD 24), 195 (SD 22) and 184

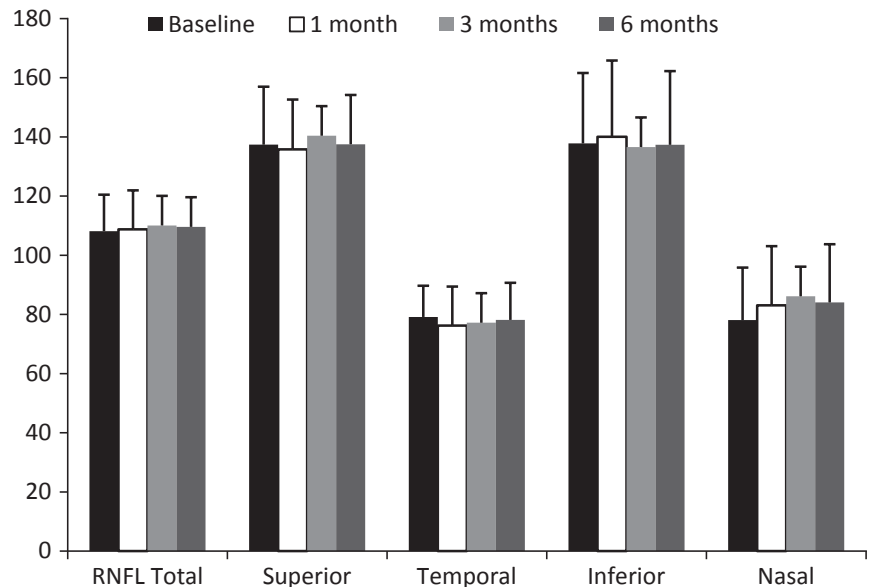


Fig. 1. Retinal nervous fibre layer thickness changes after cross-linking treatment trough 6-month follow-up.

(SD 27) microns, respectively, at baseline and at 1-,3-,6-month follow-up. No changes of outer retinal layers such as interruption of ELM or IS/OS were recorded at any time of the follow-up. The average retinal nervous fibre layer (RNFL) thickness on OCT was 108 (SD 7.2) microns at baseline and 109 (SD 7.2), 110 (SD 7.3), 110 (SD 7.4), respectively, at each follow-up visit (Fig. 1).

Group B (control group) had only one assessment time-point: CMT was 180 (SD 28) and the average RNFL thickness was 112 (SD 6.9).

The differences between the group A and control group were not statistically different at any time of the follow-up. (p = 0.8; p = 0.8; p = 0.7; p = 0.8 for CMT and p = 0.8; p = 0.9; p = 0.8; p = 0.8 for RNFL, respectively, at baseline and at 1-,3-,6-month follow-up.)

In group A, an improvement in uncorrected and best spectacle-corrected VA (0.6 ± 0.20 at baseline versus 0.7 ± 0.17 at 6 months) was recorded, but was not statistically significant (p = 0.12). The mean spherical equivalent recorded was -4.0 (SD 4.9), -6.2 (SD 5.1), -5.1(SD 5), -4.8 (SD 4.9), respectively, at each follow-up visit.

Having the patient stare at the UVA light source for 30 min during the CXL procedure has raised concerns regarding the risk for retinal damage, despite the fact that UVA should not pass through the crystalline lens (Spoerl et al. 2007).

Our results showed no statistically significant changes in retinal morphology with a concomitant improvement of visual function after CXL treatment. It is therefore correct to assume that no immediate toxic effect can be found on the retinal structures on the treated eyes.

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Correspondence:

Dr Mario Romano
 Department of Ophthalmology
 Istituto Clinico Humanitas
 Rozzano
 Milan
 Italy
 Tel: + 390282244647
 Fax: + 390282244640
 Email: romanomario@email.it