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Research Article

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Retinal Pigment Epithelium After Application of the Cuban Treatment for Retinitis Pigmentosa.

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Summary

Purpose: To describe the possible effects on the retinal pigment epithelium generated by the application of the Cuban multitherapeutic treatment in patients with retinitis pigmentosa.

Methods: A retrospective longitudinal descriptive study was carried out, selecting 16 eyes with retinitis pigmentosa after the application of the Cuban treatment for this disease. Infrared laser scanning confocal ophthalmoscopy was performed to acquire and process images of the retinal pigment epithelium areas before treatment, at one year, 7 years and 15 years after treatment.

Results: Non-significant increases in central epithelial areas were observed in 6 right eyes and 5 left eyes at one year of the study, decreasing to their pre-treatment dimensions at 7 and 15 years. It is observed that in the same period 4 right and 4 left eyes that showed non-significant decreases at one year, maintained at 7 and 15 years similar dimensions to those obtained at the beginning of treatment.

Conclusion The application of Cuban multitherapeutic treatment to treat patients with Retinitis Pigmentosa is an alternative that attempts to preserve the retinal pigment epithelium.

Keywords: *Retinitis pigmentosa; Cuban treatment; Retinal pigment epithelium*

Introduction

The retinal pigment epithelium (RPE) is a monolayer of highly specialised pigmented cells located between the neural retina and the choroid, which degrades and digests approximately 3 billion photoreceptor outer segment discs over an average lifespan of 70 years. This important role is performed through a specific process of stepwise phagocytosis, where epithelial microvilli are in intimate contact with photoreceptor outer segments at a ratio of 30 to 50 photoreceptor outer segments per epithelial cell, allowing participation in many activities fundamental to visual function and photoreceptor viability such as retinol metabolism, blood-retinal barrier formation, light interaction through melanin granules, extracellular matrix synthesis and active transport of ions and metabolites [1,2].

Retinol metabolism is one of the highly specialised functions of the EPR, since as a result of photon absorption in photoreceptor outer segments the isomerisation of 11-cis-retinaldehyde to all-trans-retinol occurs, which is the initial reaction of the vision process. The re-isomerisation of all-trans-retinol to 11-cis-retinal in the EPR is

a crucial aspect of the visual cycle, with various transport mechanisms mediated by intracellular and extracellular retinol transport proteins and enzymes that convert retinol into various intermediates, to finally form the active 11-cis-retinaldehyde.

The RPE is the outermost portion of the blood-retinal barrier, which controls the exchange of fluids and molecules between the choriocapillaris and the outermost layers of the retina, such as the movement of water and catabolites from the retina to the choriocapillaris, helping to maintain intraocular pressure and also keeping the retina attached to the RPE by a very active suction mechanism, which removes fluids from the subretinal space. Control of sodium, potassium, ATP and taurine is also established through the RPE [3,4].

In retinal degenerative diseases, especially retinitis pigmentosa (RP), there is progressive atrophy of the RPE, generated by a programme of neuronal and vascular remodelling, which, together with other retinal alterations, leads to loss of visual function, with consequent clinical and social implications [5,6].

Professor Orfilio Peláez Molina, Doctor of Medical Sciences, began to apply a multi-therapeutic strategy in Cuban patients affected by RP, combining ophthalmological microsurgery using retro-orbital fatty tissue implanted in the suprachoroidal space, with ozone therapy, electro-stimulation and supplements used internationally [7,8]. The aim of this work is to learn more about the behaviour of RPE after applying the Cuban multitherapeutic strategy for RP, through a background infrared autofluorescence study. This technology will help to obtain more information and could lead to more objective prognoses [9-13].

Material and Method

A retrospective, longitudinal, descriptive study was carried out on 16 eyes of patients with RP who received treatment for the first time at the ¨Camilo Cienfuegos¨ International Clinic, Havana, Cuba.

Inclusion criteria were people aged between 18 and 45 years, Snellen visual acuity between 1.0 and 0.4, and Goldmann visual field greater than 10 degrees in central areas, who maintained disease control and treatment every 6 months for 15 years after surgery.

Exclusion criteria were patients with any other local or systemic pathology that may affect the blood vessels and RPE, as well as absence from any of the annual check-ups.

A Heidelberg type 2 videoangiograph (HRA-2) programme was used to acquire, store and process images of the retinal pigment epithelium, in the central epithelial areas, performing confocal infrared laser scanning ophthalmoscopy (between 810-830 nanometres) in areas of 15, 20 and 30 degrees, to obtain the necessary images at the five moments of the study.

The images were acquired and processed over a 30-degree area, 768 by 768 pixel speed, 1536 by 1536 pixel resolution, which allows defining details with 5 millimicron resolution, 8 kHz line scan frequency, 100% intensity, low sharpness, low noise reduction, adjustable brightness and contrast, with sensitivity adjustment to obtain the best quality. The processing and analysis of the information on the central EPR areas was performed and checked seven times, which is facilitated by the database integrated in the HRA-2 software, which allows real-time imaging and subsequent processing of the information as many times as necessary. Peripheral areas of retinal pigment epithelium were excluded.

Procedures specific to the technique used

Microsurgery performed as revitalising surgery is an autologous, pedicled transposition of retro-orbital fatty tissue into the retro-orbital space.

Suprachoroid. A conjunctival incision was made in the inferior temporal quadrant to identify and fix the inferior and lateral rectus muscles, exposing the surgical area and performing a non-perforating sclerotomy, 3 millimetres from the scleral insertion of the muscles, approximately 2 millimetres away from the path of the muscles. The incision was deepened using a scalpel at an oblique angle until the dark colouring of the choroid was visible through the deepest scleral fibres. Lateral, parallel incisions were made, which allowed advancing in a posterior direction, lifting a scleral lamina of approximately 3 millimetres in the inferior temporal quadrant, behind the insertion of the lateral and inferior rectus. The orbital fatty tissue was identified by pedicle dissection and extended over the entire exposed area and attached to the most posterior edge of the anterior lip of the sclerotomy. The fatty tissue autoimplant was covered over with the scleral lamina, fixed with loose stitches or surget, closing with 6/0 polyglycolic acid, replacing muscles and finishing with conjunctival surget, 7/0 silk, which was removed 7 days after surgery.

The following day, treatment was continued with ozone therapy by rectal insufflation (100 cc), one application per day for 14 days.

This therapy was carried out using a 50cc syringe, which allows the extraction of a mixture with an ozone concentration between 20 - 40 mcg/ml, from a device fitted on the ozone therapy equipment. At the end, sinusoidal electro-stimulation was applied to the reflexology points on the eyelids and back of the hand, once a day for 14 days. This was carried out with Scyfix 600 equipment, approved by the Food and Drug Administration (FDA).

In order to meet the objectives, statistical measures were used by calculating and estimating parameters depending on the type of variable being evaluated.

To evaluate the existence of changes in the retinal pigment epithelium, it was necessary to estimate the mean value of this variable and to evaluate its behaviour at different points in time (before treatment, 15 days, one year, 7 years and 15 years after treatment).

For the analysis, the one-factor repeated measures Anova test was used, and the result obtained from each hypothesis test that was contrasted was verified. In all statistical tests, a reliability level of 95% with a statistical significance level of 0.05% was considered.

Results

When studying the retinal pigment epithelium 15 days after the start of treatment, only one right and one left eye of different patients showed non-significant increases of more than one millimicron compared to pre-treatment measurements. One right eye showed a decrease of one millimicron in a similar comparison, corresponding to a third patient.

One year later it was observed that 6 right eyes and 5 left eyes in monocular form showed non-significant differences with an increase of one millimicron when comparing the results with those obtained at 15 days. At the same time, 4 right and 4 left eyes showed non-significant differences of one millimicron less, corresponding to two patients with binocular response and two patients with monocular response.

It was observed that the 6 right eyes and 5 left eyes, which showed non-significant increases at one year, decreased to the dimensions they had before treatment. In the same period, 4 right eyes and 4 left eyes, which showed non-significant decreases at one year, maintained similar dimensions as before starting treatment.

Pigmentary Epithelium		Half millimicrons (SD)	95% CI
Right Eye (n = 8)	formerly	2,19 (0,80)	1,89 - 2,48
	15 days	2,19 (0,80)	1,89 - 2,48
	1 year	2,19 (0,81)	1,89 - 2,48
		P=0,992	
Left Eye (n= 8)	formerly	2,18 (0,84)	1,88 - 2,48
	15 days	2,18 (0,84)	1,88 - 2,49
	1 year	2,19 (0,84)	1,88 - 2,49
		P=0,239	

Table 1: *Behaviour of the pigment epithelium.*

Pigmentary Epithelium		Half millimicrons (SD)	95% CI
Right Eye (n = 8)	7 years	2,19 (0,80)	1,89 - 2,48
	15 years	2,19 (0,81)	1,89 - 2,48
		P = 0,992	
Left Eye (n= 8)	7 years	2,18 (0,84)	1,88 - 2,49
	15 years	2,19 (0,84)	1,88 - 2,49
		P = 0,239	

Table 2: *Behaviour of the pigment epithelium.*

It was observed in the statistical results that in the right eyes studied before the Cuban multitherapeutic treatment, the mean of the central epithelial areas was 2.19 millimicrons with a standard deviation of 0.80. When comparing the results obtained before treatment with those observed at 15 days and at one year, the mean of the epithelial areas studied remained the same, with the same standard deviation of 0.80, as shown in table 1. In the evaluation carried out 7 and 15 years after the start of treatment, no significant changes were observed in relation to those obtained at previous times, with a p=0.992, as shown in table 2.

In the left eyes studied, the mean of the epithelial areas studied before treatment was 2.18 millimicrons, with a standard deviation of 0.84. At 15 days and one year after the start of treatment, the epithelial areas remained within the same parameters as those obtained before treatment, with a p=0.239 as shown in table 1.

In the evaluation carried out 7 and 15 years after the start of treatment, no significant changes were observed in relation to those obtained at previous times, p=0.239 as shown in table 2.

Discussion

When assessing the behaviour of the retinal pigment epithelium during the period studied, no new areas of epithelial atrophy were detected in the central areas, which may suggest a delay of the degenerative process in this structure, with great clinical implication in trying to favour the survival of the cones, which is in accordance with the desire to develop strategies for the rescue of these important cells [14].

The dimensions of the central circular areas studied by means of the programme incorporated in the Heidelberg type 2 video angiograph show that when comparing the results before treatment, 15 days after treatment, one year later, at 7 and 15 years, no reduction in these areas was detected.

The limitation of not being able to study the peripheral areas where there were still remnants of retinal pigment epithelium is important, as the programme prevents them from being adequately quantified and they must be excluded.

The criterion of this author in relation to the behaviour of the retinal pigment epithelium is that no increase was detected in the central areas of epithelial atrophy, perhaps due to the possible improvement in metabolic support generated by the treatment applied to the cells that survived the remodelling process, which could prolong cell survival and the possible preservation of cones, from our point of view valued as a positive result.

In models studied, cone survival appears to delay the onset of advanced stages of the disease, keeping the retina at an early or intermediate stage indefinitely. The effect is local and small areas of cones that preserve their structure connected to bipolar cell dendrites survive even when cones are severely affected [15]. It is therefore of interest to continue to evaluate the responses obtained after the application of this multitherapeutic alternative on the retinal pigment epithelium.

Conclusions

The application of the Cuban multitherapeutic treatment to treat patients with Retinitis Pigmentosa is an alternative that preserves the retinal pigment epithelium.

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