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Anatomical changes on the ciliary body after endocyclophotocoagulation

Cambios anatómicos en el cuerpo ciliar tras endociclofotocoagulación

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ABSTRACT

INTRODUCTION: Glaucoma is the first cause of irreversible blindness. Endocyclophotocoagulation is a cyclodestructive procedure that reduces the production of aqueous humour partially.To know the presence of ultramicroscopic changes on the ciliary body after endocyclophotocoagulation. **MATERIAL AND METHODS**: This is a prospective and longitudinal study about 10 eyes (9 patients). They were undergone to phacoemulsification and endocyclophotocoagulation doing an ultramicroscopic measurement before surgery, one week and three months after surgery. Measurements were compared with ANOVA and Friedman test. The statistical significance was $p < 0.05$. **RESULTS**: The values CBT0, CBTMAX, CBT 100 presented a reduction in all the measurements presenting statistical significance after 90 days. There were no changes in LV and ACD in the postoperative measurements. **CONCLUSION**: There are changes in the anatomical measurements of the ciliary body after endocyclophotocoagulation.

Keywords: eye; ciliary body; iris.

RESUMEN

INTRODUCCIÓN: El glaucoma es la primera causa de ceguera irreversible. La endociclofotocoagulación es un procedimiento ciclodestructivo que reduce parcialmente la producción de humor acuoso. El objetivo del estudio es conocer la presencia de cambios ultramicroscópicos en el cuerpo ciliar después de la endociclofotocoagulación. **MATERIALES Y MÉTODOS:** Se trata de un estudio prospectivo y longitudinal de 10 ojos (9 pacientes). Se les realizó facoemulsificación y endociclofotocoagulación realizándose una medición ultramicroscópica antes de la cirugía, una semana y tres meses después de la cirugía. Las mediciones se compararon con ANOVA y prueba de Friedman. La significación estadística fue $p < 0,05$. **RESULTADOS**: Los valores CBT0, CBTMAX, CBT 100 presentaron reducción en todas las mediciones presentando significancia estadística después de 90 días. No hubo cambios en LV y ACD en las mediciones postoperatorias. **CONCLUSIÓN**: Existen cambios en las medidas anatómicas del cuerpo ciliar después de la endociclofotocoagulación..

PALABRAS CLAVE: ojo; cuerpo ciliar; iris.

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INTRODUCTION

Glaucoma is defined as an optic neuropathy associated with characteristic structural damage to the optic nerve and visual field loss, glaucoma is the leading cause of blindness worldwide (1), genetic and genomic studies discovery of genes contributing to glaucoma (2), myocilin mutations are the most associated in glaucoma (3), other associated as OPTN and TBK1 mutations (4). In total sixteen genomic regions have been associated with glaucoma (5, 6). Glaucoma is more frequent with increasing age, increase after the age of 40 years (7). Various risk factors and systemic conditions can be associated with different types of glaucoma (8). Multiple mechanosensory mechanisms to be identified in the trabecular meshwork and optic nerve head (9). The level of intraocular pressure is related to retinal ganglion cell death, increased resistance to aqueous outflow through the trabecular meshwork, intraocular pressure can cause mechanical stress on the optic nerve, result in compression, deformation, remodeling of the lamina cribrosa, mechanical axonal damage and disruption of axonal transport (10). High levels of energy demand may be difficult to meet during periods of intraocular pressure-induced metabolic stress (11). This pathological process may cause secondary neurodegeneration of other retinal neurons and cells in the cervical visual pathway (12). Primary vascular dysfunction was also correlated; this syndrome was characterized by an insufficient or improper adaptation of blood flow, resulting in a transiently incorrect blood supply for the tissue needs (13,14). One-half of patients are undiagnosed because a diagnosed often requires monitoring over years to document changes in glaucoma (15), Diagnosis utilizes a comprehensive glaucoma evaluation. Several measures are employed to confirm an accurate diagnosis such as history, report of visual function, intraocular pressure, examination of anterior segments, optic nerve head, and retinal nerve fiber layers (16).

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Trabecular meshwork is a sieve-like structure, which acts as a filter between the anterior chamber and Schlemm´s canal, a circular canal that collects the aqueous and evacuates it into the extraocular circulation. Which bridges the scleral sulcus, inserts anteriorly into the peripheral cornea at the level of Schlemm´s line, posteriorly; the trabecular lamellae are connected to the junction between the ciliary body, iris and scleral spur (17). The uveal meshwork is in indirect communication with the aqueous humor, pillars extending from the iris root and ciliary body to Schlemm´s line, the corneoscleral meshwork, represent most of the trabecular meshwork, lamellae transverse by orifices, which extend and grow from the anterior wall of the scleral sulcus to the scleral spur (18). The anterior situation of ciliary processes was extensively proved to be one of the predisposing factors of angle closure (19,20), ultrasound biomicroscopy is considered the conclusive method for acute diagnosis (21), the various ciliary body parameters that have been described are ciliary body thickness, ciliary body length and ciliary muscle thickness (22), provided ultrasound biomicroscopic descriptions of glaucoma, demonstrating rotation of the ciliary body and apposition of ciliary processes to the posterior iris (23), this technology uses ultrasound which allows noninvasive in vivo imaging of the anterior ocular segment (24), to evaluate the morphological changes of the ciliary body in treated glaucoma, furthermore the relation between the morphological changes is found (25),can be used to determine its dimensions and relationship with adjacent structures, therefore, the technique of choice for assessment of the posterior chamber and visualization of the zonula or ciliary processes (26). Ultrasound biomicroscopy can provide highdefinition images of the anterior segment, allowing reliable and repeatable quantitative measurements (27). Was performed to analized chamber structures imaged in primary angleclosure, that increase the likelihood of angle closure include basal iris insertion, mild iris angulation, and large ciliary body (28). Primary congenital glaucoma is a noninvasive technique that can visualize the anterior segment in infants, showed a large trabecular iris angle, decreased iris thickness, narrower or absent schlemm´s canal and increased zonular length (29).

Management of glaucoma on lowering intraocular pressure, which remains the principal proven method of treatment, it is recommended to reduce by 25% from baseline (30). A new glaucoma procedure, termed microinvasive glaucoma surgery, has emerged, which gap between conservative medical management and more invasive surgery (31). Cyclophotocoagulation was first introduced in 1970 as a last-line surgery to lower intraocular pressure (32), during the procedure, a semi-conductor diode laser is used to ablate the ciliary process (33), and two techniques are used to perform cyclophotocoagulation; transscleral diode cyclophotocoagulation (TCP) and endoscopic diode cyclophotocoagulation (ECP) (34). The surgeon is able to titrate the extent of ciliary body ablation to maximize intraocular pressure lowering, the goald of treatment is the reduction of aqueous humor formation through the destruction of ciliary body epithelium (35). Performed histologic analysis observed pigment clumping, coagulative necrosis, ciliary muscle destruction and vascular damage (36), endoscopic cyclophotocoagulation, a newer method that specifically targets the

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ciliary process under viewing, also used to treat refractory glaucoma (37), endoscopic cyclophotocoagulation containing a xenon light source, a helium-neon laser aiming beam, a video camara and a semiconductor diode laser probe, is inyected into the ciliary sulcus, across the anterior chamber, to visualized the ciliary process on the camera monitor, laser energy is titrated up until it just blanches and shrinks the ciliary process, can be amplied up to 270 degrees (38,39,40). Direct visualization of the ciliary body epithelium, with less unnecessary damage to other parts of the ciliary body, a significante adventage is the lowest laser energy, laser energy absorbed by melanin in the ciliary pigmented epithelium causes thermal demage, where aqueous humor production occurs (41). Direct visualization of the endoscope to be used for diagnosis, this therapy reduces intraocular pressure in patients with mild to moderate glaucoma (42), generates disrips ciliary body vasculature, causes coagulative necrotic demage to ciliary body epithelium to be sparing vasculature and ciliary muscle (43).

MATERIAL AND METHODS

This prospective and longitudinal study was realized in 10 eyes (9 patients) diagnosed with primary glaucoma (open or closure angle glaucoma). They underwent phacoemulsification and endocyclophotocoagulation in the Central Military Hospital in Mexico City. The Committee of Ethics approved this project based on the tenets of the Declaration of Helsinki.

Inclusion criteria were patients diagnosed with primary glaucoma in mild to moderate stages using at least one hypotensor eyedrop, no previous ocular surgeries, clinical cataracts, and who will undergo cataract surgery.

Before the surgical procedure, they recorded visual acuity (Log Mar), to measure intraocular pressure (IOP) Goldmann Applanation Tonometry was used, and glaucoma hypotensors eyedrops were used. IOL calculation was performed using IOL MASTER 700 (Carl Zeiss Meditec) for emmetropia.

Ultrabiomicroscopy was performed by only one expert operator using the platform AVISO with ClearScan ultrasonic probe, the meridians measured in triplicate were 4.5, 6, and 7.5 and the measurements previously described (9): Ciliary body Thickness (CBT max), Ciliary body thickness at scleral spur (CBT0), APCB (Anterior placement of ciliary body), Lens Vault (LV), Anterior chamber deep (ACD), Angle open distance at 500 µm of a scleral spur (AOD 500), Trabecular ciliary angle (TCA).

The cataract surgery was performed in a standard way using the phaco-chop technique. There were recorded complications. The endocyclophotocoagulation was performed by E2 Beaver Visitec equipment (Endo Optiks Inc, Little Silver, Nj) before the placement of the intraocular lens by a straight probe, power applied was 200 mW, the meridians treated were from m2 to m8 (180 grades). The exposition time was until the ciliary body presented whitening and shrinkage.

Posterior of the surgery, recorded visual acuity (Log Mar), intraocular pressure, number of glaucoma eyedrops used and Ultrabiomicroscopy which was performed by the same expert operator using the platform AVISO with ClearScan ultrasonic probe, making the same measurements done in the preoperative examination: CBT,

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CBT0, APCB, LV, ACD, AOD 500 and TCA all the measurements were done at a week and 90 days after surgery.

The values measured on the ciliary body by UBM were compared using the SPSS v25.00 software ((SPSS, Inc., Chicago, IL, USA) and Excel Microsoft Office 2013. For analysis, we divided into 3 groups (presurgical, 1 week, and 90 postoperative (PO)). The data were analyzed using ANOVA or Friedman test depending on the data distribution. Post-hoc tests were done (Tukey Test and Bonferroni-Dunn Test). Statistical significance was set at $p < 0.05$.

RESULTS

The study included 10 eyes (9 patients) all were included in the analysis. The average age was 71.5 years old (± 5.3). The diagnosis was separated into two groups primary angle-closure glaucoma 60 % (6 patients) and primary open-angle glaucoma 40% (4 patients) (Table 1).

Table 1. Demographic and clinical characteristics

	Group (*n* = 10)
Mean age ± SD (range)	71.5 ± 5.29 (59–78)
Male/female	4/6
Eyes affected, *n* (right/left)	6/4
IOP (preoperative) mmHg, mean ± SD (range)	14.5 ± 2.06 (11–17)
IOP (postoperative 90 days) mmHg, mean ± SD (range)	10.8 ± 1.35 (9–12)

The glaucoma stage in the study was 30% moderate and 70% mild based on Hodapp Parrish Andersen criteria (44) (Table 1). The visual acuity has a meaning of 0.63 Log Mar (± 0.35), 1 one week after surgery was reported 0.29 (± 0.19) and 90 days after 0.26 (±0.19) with no statistical significance between one with and 3 months after. The hypotensive eyedrops used had a mean of 1.3 (± 0.48) preoperative and 0.6 (± 0.69) 90 days after surgical, presenting a reduction with statistical significance on 1 week (p 0.01) and 90 days postoperative (p 0.01). (Figure 1).

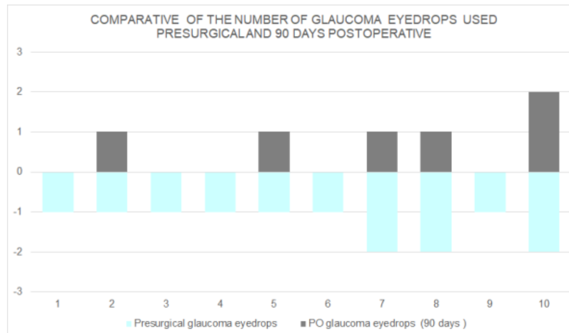

Figure 1. Comparative of the number of glaucoma eyedrops used presugical and 90 day postoperative

The IOP has a mean of 14.5 mm Hg (± 2.06) showing a 24.23% reduction (10.8 mm de Hg (± 1.13) at 90 days after surgery compared with the presurgical values. As shown in Figure 2.

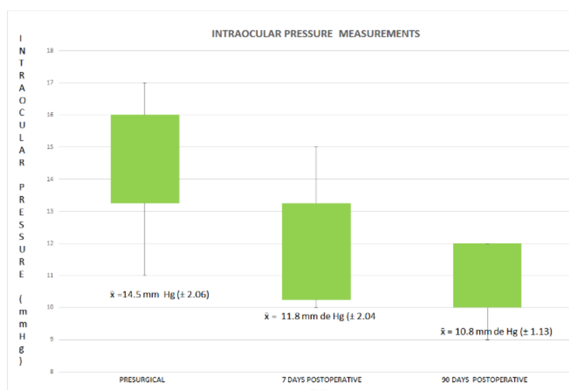

Figure 2. Intraocular pressure measurements

CBT0 Showed a mean of 1.14 mm ((±0.08) presurgical, 1.05 (±0.18), and 0.80 (±0.20)

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at 90 days after surgery respectively. Showing statistical significance comparing presurgical among the 90 days postoperative values. CBT max analysis shows the Tukey honestly significant difference (HSD) >0.20 ($p < 0.05$) between presurgical- 90 days PO (0.35) and 7-week PO-90 days PO (0.21) (45). No statistical significance between presurgical-1-week PO. CBT1000 showed a reduction in the mean size of 2% compared to presurgical 1-week PO and 22% at 90 days PO. The Tukey honestly significant difference (HSD) > 0.15 presented no statistical significance between presurgical – 1-week PO (0.5), presurgical- 90 days PO, and 1 week PO – 90 days PO presented a HSD 0.21 and 0.16. Comparisons between APCB showed a statistical significance compared to the presurgical with the 90-day PO values (p 0.0002), with no differences presented on the first week. TCA values presented a significant difference between the presurgical values with the postoperative values ($P< 0.05$). No differences were shown between 1 week and 90 days PO. AOD500 presented an important difference between the measurements ($p< 0.05$) at 7 days 75%, and 90 days 78%.

LV. The mean preoperative values were 0.66 mm (± 0.16), 1 week PO was -0.73 mm (± 0.42) and -0.69 (± 0.40) at 90 days PO, showing a statistical difference between the preoperative and PO values (p 0.016 1 week, p0.030 at 90 days PO) no difference among the PO values (p 1.0). ACD presented a mean of 2.5 mm (±) 0.09 presurgical and postsurgical of 4.33 mm (±0.12) 7- and 90-day PO. Statistical significance of p 0.02 and p 0.04 respectively, attributable to the cataract surgery.

DISCUSSION

Based on the results, we documented a decrease in the size of the ciliary body after endocyclophotocoagulation (Figure 3). The results obtained are related to Rathi (46), Noecker (47), Lima (48), and Francis (49). The effectiveness of ECP, achieving an average reduction of one ocular glaucoma Eyedrop (± 0.35).) in most patients with mild to moderate glaucoma is enough for treatment, as well as reducing the costs generated on the glaucoma hypotensive eyedrop. All patients in the study showed lower intraocular pressure concerning preoperative IOP, independently of the reduction or not of topical medication. The decrease in intraocular pressure showed a decrease of 24.2% (± 0.12) in the last measurement of the study, which is similar to what has been described in the literature (50).

Figure 3.A

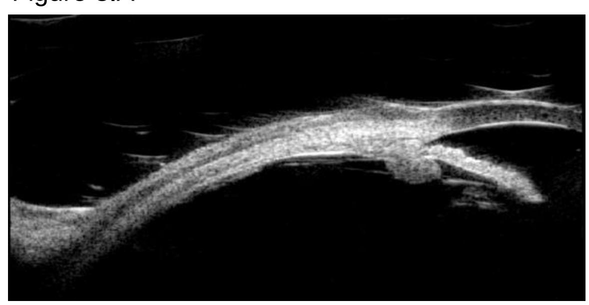

Figure 3.B

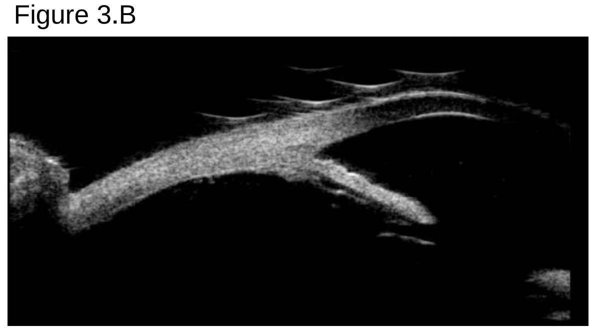

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Figure 3.C

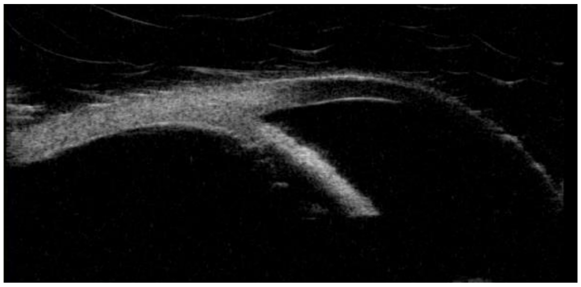

Figure 3. **A**. Presurgical UBM image of the ciliary body. **B**. UBM at 7 days after ECP. **C**. Atrophy of ciliary body compared with the presurgical image.

The anatomical changes attributable to cataract surgery are the ACD, LV, and AOD (Table 2). These values did not change postoperatively, comparing the values obtained at one week and third months postoperatively, studies are showing an increase in LV and ACD in patients with zonular weakness (51), in our study we can infer that there were no changes in the effective position of the intraocular lens; considering this as an important factor because of the zonule is inserted into the ciliary body as an anchor; an article has been published about the induction of changes in the effective position of the lens after endocyclophotocoagulation being attributed to an anteriorization of the complex ciliary-zonule body originating postoperative myopic refraction (-0.50) (52), these results had not been corroborated by imaging studies. This is the first report documenting the anatomical changes of the ciliary body presented after endocyclophotocoagulation. The values of CBT_o, CBT MAX, CBT 1000 showed a decrease in all their measurements but at one week after surgery did not present statistical significance (Table 2), which is striking because the trans-surgical marker for laser placement is the evident reduction of the size and change to a grayish-white color of the ciliary process treated, so we inferred that the most marked change would be at a week, which was not the expected result in the statistical analysis; It can be attributed to an inflammatory reaction with consequent edema of the ciliary body similar to that reported in patients with uveitis (53).

Table 2. Comparison of the preoperative and postoperative parameters of the anterior segment UBM

MEASUREMENTS (n=10)	**Presurgical**	**Post 1 week**	***Post 90 days***	**Statistical analysis**	**Pre vs 1 week . p**	***1 week – 90 days***	**Pre – 90 days PO**
CBT0, mean ± SD (mm)	1.13 ± 0.11	1.03± 0.23	0.84± 0.21	Tukey HSD >018 (p<0.05)	0.10 (p>0.05)	**0.25** (p<0.05)	**0.34** (p<0.05)
CBT Max, mean ± SD (mm)	1.30 ± 0.13	1.16 ± 0.25	0.97 ± 0.15	Tukey HSD > 0.20 (p<0.05)	0.15 (p>0.05)	**0.21** (p<0.05)	**0.35** (p<0.05)
CBT 1000, mean ± SD (mm)	0.85 ± 0.19	0.79± 0.09	0.63± 0.11	Tukey HSD >0.15 (p<0.05)	0.05 (p>0.05)	**0.16** (p<0.05)	**0.21** (p<0.05)

APCB, mean ± SD (mm)	0.54 ± 0.15	**0.29 ± 0.18**	**0.22 ± 0.14**	Bonferroni-Dunn ($p<0.05$)	**0.76**	**0.00**	**0.076**
LV, mean ± SD (mm)	0.58 ± 0.13	-0.66 ± 0.47	-0.54± 0.72	Bonferroni-Dunn ($p<0.05$)	**.003**	1.00	**.001**
ACD , mean ± SD (mm)	2.56 ± 0.09	4.33 ± 0.10	4.34 ± 0.11	Bonferroni-Dunn ($p<0.05$)	**0.002**	1.00	**.004**
TCA, mean ± SD (mm)	70.58 ± 12.12	89.94 ± 10.26	92.00 ± 12.65	>12.0 ($p<0.05$)	**21.50** ($p<0.05$)	2.97 ($p<0.05$)	**24.47** ($p<0.05$)
AOD, mean ± SD (°)	0.26 ± 0.88	0.42 ± 0.11	0.43 ± 0.09	>0.11 ($p<0.05$)	**0.18** ($p<0.05$)	0 ($p<0.05$)	**0.18** ($p<0.05$)

Changes in measurements of the ciliary body CBT_o, CBT MAX, CBT 1000, and APCB can be directly attributed to the ECP since there is a study in patients who underwent to cataract surgery where changes are not reported at the level of ciliary body measurements (54).

One limitation of this study lies in the size of the sample; enlarging it would give us a greater statistical weight. A limitation is the inference we gave from the measurement of UBM to the same ciliary body at the level of a given meridian, not being able to ensure that the data is from the same ciliary body in all measurements for reducing this limitation were taken 3 meridians for each measurement. In the absence of a study reported in the literature regarding the anatomical changes of the ciliary body, it is not possible to compare the results obtained by opening a panorama to carry out further research on this same line. The results in this study about the decrease in intraocular pressure (> 20%) and the reduction of one glaucoma eye drop are similar results that have been described in the literature.

CONCLUSION

This investigation concludes the existence of anatomical changes in the measurements of the ciliary body (APCB, CBT_o, CBT1000, CBTMAX) after endocyclophotocoagulation which are statistically significant presenting the reduction values at 90 post-surgical days.

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