Original article

Effect of posterior neodymium:YAG capsulotomy. Safety evaluation of macular foveal thickness, intraocular pressure and endothelial cell loss in pseudophakic patients with posterior capsule opacification

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ABSTRACT

Objective: To determine the effect of posterior capsulotomy on macular thickness, intraocular pressure and endothelial cell loss in pseudophakic patients with posterior capsule opacification using the other eye of every patient as a control.

Methods: An observational prospective study was conducted on 31 pseudophakic patients with posterior capsular opacification in one eye, using the other eye as a control. Patients did not suffer any other ocular pathology. All patients were treated by posterior capsular opacification with Nd:YAG capsulotomy, and followed up for a three-month period. The ocular examination included best corrected visual acuity (BCVA), intraocular pressure (IOP), macular optical coherence tomography (OCT), and endothelial cell assessment (including densitometry, cell size and coefficient of variation, hexagonal cell percentage and pachymetry), which were determined in both eyes before treatment, and one week, one month and 3 months after capsulotomy.

Results: Generalized estimating equations (GEE) were used to assess the capsulotomy effect adjusted by corresponding baseline measurements and time. No association was found between capsulotomy and IOP (p = 0.597), macular thickness (p = 0.085) or ECA densitometry (p = 0.422), average size of cells (p = 0.299), variation coefficient (p = 0.495), hexagonal cell percent (p = 0.093) and corneal pachymetry (p = 0.423). A significant increase of 0.15 Snellen units in BCVA was found during the 3-month follow-up period (p < 0.001).

Conclusion: This study shows that after Nd:YAG capsulotomy, BCVA improves significantly without any IOP, OCT or ECA changes during the three-month follow-up. Nd:YAG capsulotomy is a safe procedure in pseudophakic patients without any other ocular pathology.

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Efecto de la capsulotomía posterior con láser neodimio:YAG. Valoración de seguridad en el grosor foveal, la presión intraocular y el recuento de células endoteliales en pacientes pseudofáquicos con opacidad de cápsula posterior

PALABRAS CLAVE:
Opacidad de cápsula posterior
Capsulotomía
Presión intraocular
Edema macular
Recuento endotelial

RESUMEN
Objetivos: Determinar el efecto de la capsulotomía posterior en el grosor macular, presión intraocular (PIO) y pérdida de células endoteliales en pacientes pseudofáquicos que presentaban opacidad de la cápsula posterior, utilizando el eje adelfo de cada paciente como control.

Métodos: Se realizó un estudio prospectivo observacional en 31 pacientes pseudofáquicos con opacidad de la cápsula posterior en un ojo, utilizando el eje adelfo como control durante un período de 3 meses. Se excluyó a los pacientes que presentaban otras enfermedades oculares o cirugías intraoculares aparte de la facoexéresis. A todos los pacientes se les realizó una capsulotomía posterior con láser Nd:YAG. El examen ocular, que se realizó previamente a la capsulotomía y en revisiones a la semana, al mes y a los 3 meses, incluía: agudeza visual mejor corregida (AVMG), PIO, tomografía de coherencia óptica macular (OCT) y recuento endotelial.

Resultados: Se utilizaron ecuaciones de estimación generalizadas para valorar el efecto de la capsulotomía ajustado en función de situación basal y tiempo de seguimiento. No se encontró asociación significativa entre la capsulotomía y la PIO (p = 0,597), el grosor macular (p = 0,085) o el recuento endotelial densitometría (p = 0,422), tamaño celular medio (p = 0,299), coeficiente de variación (p = 0,495), porcentaje de células hexagonales (0,093) y paquimetria (p = 0,423). Un incremento significativo de la AVMG se observó en la revisión a los 3 meses (p < 0,001).

Conclusiones: Este estudio indica que, tras la capsulotomía posterior, la AVMG mejora significativamente, sin observarse cambios significativos en PIO, grosor macular o recuento endotelial. La capsulotomía con Nd:YAG es un procedimiento seguro en pacientes que no presenten enfermedades oculares asociadas.

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Introduction
Senile cataracts occur as a result of aging in 18% of the population between 65 and 74 years and in 46% between 75 and 85 years.\(^2\)\(^3\) Cataract surgery improves vision and quality of life.\(^2\)\(^3\) Posterior capsule opacity (PCO) is one of the most frequent complications of cataract surgery with intraocular lens (IOL) implant. It develops as a consequence of the proliferation of remaining epithelial cells and their migration to the space between the IOL and the posterior capsule.\(^5\)\(^6\) Epithelial cells contract and produce wrinkles and opacity in the posterior capsule. This opacity diminishes visual acuity, contrast sensitivity, stereoscopic and color vision. It also can produce glare and monocular diplopia.\(^7\)\(^8\)\(^9\) Opening the posterior capsule by means of capsulotomy with neodimium:YAG (Nd:YAG) laser restores the visual function when the PCO obstructs the visual axis. However, Nd:YAG capsulotomy can give rise to complications. Several studies have described damages in the IOL, increased intraocular pressure (IOP), glaucoma, retinal hemorrhage, iritis, vitreous prolapse, corneal injury, vitritis, pupil blockage, hyphema, cytokid macular edema, retina detachment, IOL dislocation or exacerbation of endophthalmitis.\(^13\)\(^14\)\(^15\)\(^16\)\(^17\) This study utilizes the technology provided by confocal mirror microscope and spectral domain optic coherence tomography (SD-OCT) for measuring the loss of endothelial cells and macular thickness changes after capsulotomy respectively.

Patients and methods
Overall, the study prospectively evaluated 31 consecutive pseudophakic patients scheduled for laser Nd:YAG capsulotomy. The patients were selected in the Ramón y Cajal Hospital of Madrid between February and October 2010. The patients had to fulfill the following inclusion criteria: operation for cataracts with phacoemulsification without events and exhibiting visual deficit symptoms (blurred vision or glare) and clinically observable PCO in the slit lamp examination in only one of the 2 eyes, they should be capable of being evaluated for at least 3 months after the capsulotomy intervention and exhibit a centered IOL with complete overlap between the anterior capsules and IOL. Patients who had previous laser treatments, ocular trauma or surgery during the follow-up period, ocular surface, corneal or retinal disease, uveitis or glaucoma were excluded. The study was approved by the Ethics Committee of the Ramón y Cajal Hospital. The patients signed an informed consent.

The information obtained from both eyes prior to the capsulotomy procedure comprised age, sex, PCO type (fibrous, in pearls or combined), eye subjected to the procedure (left or
right), date, best corrected visual acuity (BCVA), IOP, foveal thickness and endothelial count. The data obtained after the procedure comprised BCVA, IOP, foveal thickness at week one, month 1 and 3, endothelial count at month 1 and 3.

The main variables of the study were IOP, macular thickness and endothelial count. Secondary variables comprised a study of the energy applied on the basis of the surgical technique, complications on the basis of the applied energy and the applied energy for each PCO type.

Patient evaluation:

- BCVA measured by means of a Snellen projection plate at 6 m from the patient position. Visual acuity was always taken in the same room with similar lighting conditions.
- IOP measured by means of Goldmann applanation tonometry in slit lamp, registering the mean of 3 measurements.
- Foveal thickness, utilizing the Macular Cube acquisition protocol 512 × 128 of Cirrus SD-OCT (Carl Zeiss Meditec, Dublin, AC, USA), verifying that the foveal centering was precise. Otherwise, it was adjusted manually. The macular thickness and analysis protocol was applied to evaluate foveal thickness.
- Endothelial cell count, utilizing the EM 3000 Tomey specular microscope (Tomey Corporation, Nagoya, Japan) for measuring cell density, size (mean), variation coefficient, endothelial cell percentage and pachymetry.

Surgical technique

Prior to the procedure 0.5% tropicamide and 10% phenylephrine were instilled to achieve pupil dilatation. After applying topical anesthesia, a contact lens for capsulotomy was utilized. Capsulotomy was performed with Visulas YAG II Zeiss Nd:YAG laser (Carl Zeiss Meditec, Dublin, AC, USA) by 2 experienced surgeons (D.R.C. and C.B.J.). A circular or cross technique was carried out according to the surgeon preferences to obtain a capsulotomy of approximately 4 mm. Technique type, energy applied and complications were recorded. After the procedure, 0.1% praclonidine was administered, prescribing 5 mg/ml of trometamole ketorolac 4 times a day in the treated eye for one week.

Statistical analysis

For the statistical analysis the STATA IC/11.0 4 for Windows application was used (Stata Statistical Software; Stata Corporation, College Station, TX, USA) and SPSS for Windows (version 15.0, SPSS, Inc., Chicago, IL, USA).

The descriptive analysis of the qualitative variables was performed calculating the absolute and relative frequencies. The numerical variations were described utilizing the mean and standard deviation (SD).

The main evaluated variables were BCVA, IOP, foveal thickness and endothelial count, comparing the treated eye with a non-treated eye in the same patient. Generalized estimation equations were applied to assess the effect of capsulotomy on BCVA, IOP, macular thickness and endothelial count (densitometry, size, CV, percentage of hexagonal cells and pachymetry) adjusted according to the baseline and follow-up time.

The secondary analyses were studied with the nonparametric tests of the SPSS software. The Mann–Whitney tests for 2 independent samples were utilized to assess the differences between the applied technique and the Kruskal–Wallis test for 3 independent samples in order to assess the differences between PCO types.

Results

Thirty-one patients were studied between February and October 2010. The follow-up period ranged between one week and 3 months due to the fact that 5 patients did not appear for the quarterly examination, 2 missed the monthly examination and one was lost immediately after the treatment. Overall, 23 patients completed the 3-month follow-up specified in the protocol. The mean follow-up was of 2.40 ± 1.05 months. All the patients underwent posterior capsulotomy, 17 with the circular technique and 14 with the cross technique, without intra- or post-surgery complications. Said loss of patients in the follow-up did not compromise the statistical analysis because the treated eyes were compared with the opposite eye in each patient at each step of the analysis.

Of the 31 patients, 20 were female (64.5%) and 11 were male (35.5%). The mean age was of 76.±7 years. Thirteen right eyes were treated (41.9%) and 18 left eyes (58.1%). The PCO type in 9 patients was the pearl type (29%), fibrous in 8 (25.8%) and combined in 14 (45.2%). The cross capsulotomy technique was applied in 14 patients (45.2%) and circular in 17 patients (54.8%); the mean applied energy was of 82.13 ± 51.38 mJ and the mean capsulotomy size was of 5.03 ± 0.45 mm (Table 1).

The mean BCVA, IOP, macular thickness and endothelial count parameters in the treated eye and the untreated eye prior to capsulotomy and at week one, month one and month 3 after the procedure are illustrated in Figs. 1–8.

The primary variables were analyzed applying the generalized estimation equations with the STATA software. Said
analysis compares the changes in BCVA, IOP, macular thickness and endothelial count in the treated eye as well as the untreated eye of each patient. This analysis was chosen to avoid confusion factors. A significant increase ($p<0.001$) of 0.15 Snellen mean BCVA in treated eyes at the three-month control. No association was found between the capsulotomy and IOP changes during the follow-up period ($p=0.597$). No significant differences were observed between treated and untreated eyes as regards foveal thickness ($p=0.085$), with a mean increase of $4.81 \mu m$. No association was found between the capsulotomy and the endothelial count parameters during the follow-up: cell density ($p=0.422$), mean cell size ($p=0.299$), variation coefficient ($p=0.495$), endothelial cell percentage ($p=0.093$) and corneal pachymetry ($p=0.423$).

The secondary analyses were carried out with nonparametric tests by means of the SPSS software. The mean energy applied in patients treated with the circular pattern was of $107.75 \pm 55.47 mJ$, while in patients treated with the cross pattern was of $52.86 \pm 24.64 mJ$, this difference being significant ($p=0.01$) calculated with the Mann–Whitney test for 2 independent samples. The mean size of capsulotomies was of $4.94 \pm 0.51 mm$ with the circular pattern and $5.14 \pm 0.36 mm$ with the cross pattern, without said differences reaching statistical significance ($p=0.262$). The mean energy utilized in patients with pearl PCO was $74 \pm 31.92 mJ$, in fibrous type $96.86 \pm 67.26 mJ$ and in combined type $80 \pm 54.82 mJ$. These differences were not statistically significant.

**Table 1 – Pretreatment demographic and clinical characteristics.**

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<td>0.45</td>
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<td>5.50</td>
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**Fig. 2 – Evolution of IOP during the follow-up in treated and untreated eyes. CAP, eyes treated with capsulotomy; Control, untreated eyes; IOP, intraocular pressure (mmHg).**

**Fig. 3 – Evolution of foveal thickness measured with OCT during follow-up in treated and untreated eyes (µm). CAP, eyes treated with capsulotomy; Control, untreated eyes; OCT, optic coherence tomography.**
Fig. 4 – Evolution of cell density during follow-up in treated and untreated eyes. AC, eyes treated with capsulotomy; CO, untreated eyes; D, endothelial cell density (cells/mm²).

Fig. 5 – Evolution of meanness and size and during follow-up in treated and untreated eyes. AC, eyes treated with capsulotomy; CO, untreated eyes; T, endothelial cell size (μm).

Fig. 6 – Evolution of said size variation coefficient during follow-up in treated and untreated eyes. AC, eyes treated with capsulotomy; CO, untreated eyes; CV, variation coefficients.

Fig. 7 – Evolution of hexagonal cell percentage during follow-up in treated and untreated eyes. AC, eyes treated with capsulotomy; CO, untreated eyes; HEX, percentage of hexagonal cells.
significant with the Kruskal–Wallis test for 3 independent samples \( (p = 0.892) \). The mean size of the pearl capsulotomy was \( 5.06 \pm 0.68 \text{ mm} \), for the fibrous type \( 4.86 \pm 0.38 \text{ mm} \) and the combined type \( 5.11 \pm 0.29 \text{ mm} \), without reaching statistical significance \( (p = 0.252) \). No post-surgery complications were observed and for this reason the complications variable based on the applied energy was not analyzed.

### Discussion

Several studies have assessed IOP changes after Nd:YAG capsulotomy. The IOP peak has been described previously\(^{18-21}\) although the existence of IOP changes in the mid or long term is not clear. One study suggests that IOP does increase in the long term in glaucomatous patients but this could be due to the course of the glaucoma and not the capsulotomies.\(^{22}\) A further study has observed that IOP increases in glaucomatous patients and found a correlation of this increase with the post-surgery peak.\(^{23}\) In addition, long-term IOP increases have also been described in patients without ocular hypertension.\(^{24}\) On the other hand, IOP increase has been related with the position of the IOL or the overlap of the anterior capsule over the IOL, finding little or no increases in patients with sac lenses.\(^{25,26}\)

This study did not assess the IOP peak after capsulotomy and all the patients were prophylactically treated with apraclonidine. None of these patients had glaucoma and all had been intervened with phacoemulsification without events, with sac lens and adequate anterior capsules overlapping. No differences were observed in the IOP between treated and untreated eyes. Even though the follow-up period was of 3 months, posterior IOP increases seem unlikely because the IOL was covered over the edges of the anterior capsule in all cases and this seems to prevent the capsulotomy detritus from reaching the anterior chamber and blocking the trabeculum.

Cystoid macular edema is a frequent complication in intraocular surgery, arising generally about 2 months after surgery.\(^{27-29}\) Even though the “gold standard” for diagnosing cystoid macular edema is fluorescein angiography, several studies have demonstrated a good correlation with OCT, particularly the new generation spectral domain systems.\(^{30}\) Therefore, cystoid macular edema is routinely evaluated by means of OCT.\(^{31}\) The appearance of late retinal complications has been described after posterior capsulotomies, including macular edema.\(^{32}\) However, said macular changes could also be due to other concurring diseases. The presentation of macular edema after capsulotomy has already been studied with temporal domain OCT\(^{33}\) without observing objective differences in macular thickness. This study has not found differences in the foveal thickness or presentation of macular edema in any of the patients during the three-month follow-up as examined with spectral domain OCT. Accordingly, capsulotomy seems to be a safe procedure in what concerns macular edema presentation in pseudophakic patients with ocular comorbidity.

The presentation of vitreous synesesis, posterior vitreous detachment and retinal tears or detachments have been described after the execution of posterior capsulotomy.\(^{34}\) The 3-month follow-up period of this study does not allow an assessment of said presentations, which were not the objective of the study. Prospective studies assessing the effect of posterior capsulotomy on vitreous degeneration are necessary to understand the role played by this procedure in vitreoretinal complications.

Studies on rabbits have described diminished endothelial counts 6 h after posterior capsulotomy.\(^{35}\) However, the authors have not found studies in humans which directly evaluate endothelial count reductions after said procedure. One study has assessed corneal endothelium and 3 months after cataract surgery assisted with erbium:YAG\(^{36}\) and several papers have studied the loss of endothelial cells after various surgical procedures.\(^{37-39}\) Endothelial cell loss is observed at an early stage after anterior segment surgery and maintain significant differences at 3 months after the intervention. This study evaluates various endothelial characteristics such as cell density, mean cell size and variation coefficient, hexagonal cell percentage and pachymetry, without finding differences in the corneal endothelium between treated and untreated eyes. Probably, the fact that posterior capsulotomy with Nd:YAG is a procedure that occurs behind the IOL could mean that the lens itself protects the endothelium. In accordance with our results, Nd:YAG posterior capsulotomy appears to be a safe procedure in pseudophakic patients without corneal endothelial disease.

By comparing the most frequent laser application patterns the authors found that less energy is applied in the cross than in the circular pattern, without observing differences in capsulotomy to justify said differences. In this study, the authors had no post-surgery complications and for this reason the presentation of complications based on the applied technique was not evaluated. The cross-shaped technique involves
greater risk of central damage for the lens, secondary to unintended central impacts which, in the circular pattern, have less repercussion due to being peripheral. However, we consider that for experienced surgeons this risk is low and does not justify the application of a circular pattern that would offset the potential benefits of lower energy. Accordingly, for experienced surgeons the cross is recommended in order to diminish the amount of applied energy and its possible associated complications. On the other hand, no differences were observed in the energy required for the capsulotomy on the basis of the PCO type.

The results of this study must be regarded taking into account its limitations. The sample comprises a limited number of patients without ocular diseases apart from cataracts and PCO. Accordingly, said results might not be applicable in patients with ocular disease. Patients affected by endothelial dystrophy could suffer endothelial cell loss while glaucomatous patients could suffer IOP decompensation, and patients with retinal disease could present macular edema. Prospective studies are necessary to assess the safety of posterior capsulotomy with Nd:YAG laser in patients with ocular disease. The effects of vitreous syneresis, posterior vitreous detachment, retinal tears, retina detachment or other late complications secondary to Nd:YAG laser capsulotomy were not the objective of this study. The follow-up period of 3 months did not enable the assessment of long-term changes after the procedure. However, significant changes in IOP, endothelial count or foveal thickness beyond 3 months seem unlikely. Despite said limitations, the results of this study suggest that posterior capsulotomy with Nd:YAG laser is a safe procedure in pseudophakic patients without other ocular diseases, without inducing IOP increases, loss of endothelial cells or macular edema.

The strength of the study lies in its prospective design, utilizing the opposite eye as control for the studied variables, thus reducing the presence of confusion factors. On the other hand, technology for assessing endothelial count on macular thickness has improved in recent years which increases the precision of measurements.

This study was designed to assess safety of posterior capsulotomy with Nd:YAG laser in pseudophakic patients without corneal or macular disease or glaucoma. Expected BCVA improvement was found without observing objective effects in IOP, macular thickness or endothelial count in the post-surgery period. This study maintains that capsulotomy with Nd:YAG laser does not seem damaging for IOP, macular thickness or endothelial count in patients without ocular comorbidity. It is necessary to carry out studies assessing said parameters in patients with ocular disease in order to determine the overall safety of this procedure. It has been demonstrated that the cross-shaped pattern is associated to a reduction in the amount of energy applied for the procedure whereas the PCO type does not modify the amount of energy. Accordingly, the authors recommend the cross pattern as method of choice.

**Conflict of interests**

No conflict of interests has been declared by the authors.

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