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GLAUCOMA

Prospective evaluation of CO_2 laser-assisted sclerectomy surgery (CLASS) with Mitomycin C

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Abstract

Purpose Our purpose was to evaluate the clinical safety and efficacy of CO_2 laser-assisted sclerectomy surgery (CLASS) with Mitomycin C (MMC) in open angle glaucoma (OAG).

Methods This was a prospective, uncontrolled, interventional case series. All subjects underwent CLASS procedure by a single surgeon. After the dissection of a partial thickness scleral flap, topical MMC 0.2 mg/ml was applied to the sclera and the conjunctiva for 3 min. The CO_2 laser with a beam-manipulating system was used to ablate the scleral tissue and expose the Schlemm's canal area. Primary outcomes: intraocular pressure (IOP) change, number of IOP-lowering medicaments change. Adverse events were evaluated as secondary outcomes.

Results Twenty-one eyes of 21 patients underwent the CLASS procedure. Thirteen were primary OAG (62%), two normal pressure glaucoma (10%), three exfoliative glaucoma (14%) and three others secondary OAG. With a mean (SD) follow-up of 15.3 (5.9) months, the IOP changed from 25.4 (6.7) mmHg at baseline to 10.9 (3.4) mmHg al the last visit. Mean reduction of IOP was −14.5 mmHg (95% CI, −17.7 to −11.2, $P < 0.001$). The median (IQR) number of IOP-lowering medication decreased from 3 (3–3) at baseline to 1 (0–1) at the last visit ($P < 0.001$). Visual acuity did not change significantly. Adverse events: five eyes (24%) developed iris adhesion to the filtration area that was successfully managed with office-based procedures. In one case (5%), CLASS was converted to trabeculectomy due to intraoperative perforation of the ablated area. There was one case of hypotony maculopathy successfully treated with placement of additional transconjunctival scleral flap sutures.

Conclusions The CLASS procedure with MMC is clinically safe and effective maintaining a large reduction in IOP and in the number of IOP-lowering medications with a mean follow-up of 15 months. Iris adhesion at the filtrating area warrants further evaluation and possibly reflects the surgeon's learning curve.

Keywords Glaucoma surgery · Deep sclerectomy · Laser · CO2 laser

Introduction

The goal of treatment for open angle glaucoma (OAG) is to achieve a target intraocular pressure (IOP) estimated to be compatible with a rate of progression of the damage sufficiently slow to maintain vision-related quality of life in the expected lifetime of the patient [1]. Thus, incisional surgery is considered when medicines fail to reach a target IOP or when medical therapy is not suitable due to poor adherence or side effects. Trabeculectomy is the most widely used surgical procedure in OAG with up to 90% of long-term success [2]. However, trabeculectomy may be associated with serious intraoperative and postoperative complications [3, 4]. It is widely accepted that intraoperative application of Mitomycin C (MMC) improves the success of trabeculectomy but its use has been associated with increased complication rates [5]. Even if the rate of complications of trabeculectomy has decreased with the improvement of the technique [6], deep sclerectomy (DS) has been developed with the aim to improve the safety of glaucoma surgery while maintaining high success guaranteed by subconjunctival filtration [7]. Contrary to trabeculectomy, DS does not require penetrating the anterior chamber, although, considerable technical skills are needed to

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preserve the integrity of the trabeculo-Descemet's membrane (TDM). Recently, a CO_2 laser with a beam-manipulating system has been developed to facilitate the surgeon exposing the Schlemm's canal reducing the risk of perforation of the TDM [8, 9]. Since the CO_2 laser energy is largely absorbed by water, the direct effect on the angle tissue reduced when aqueous starts to percolate [10]. Several groups have published reports on the success rates of DS [11–15]. Fewer studies investigated the CO_2 laser-assisted sclerectomy surgery (CLASS) procedure [9, 16–18]. In our prospective research, we evaluate the clinical efficacy and safety of the CLASS procedure with MMC in a cohort of patients with OAG.

Methods

This study was a prospective, uncontrolled, consecutive case series involving 21 eyes with OAG that underwent the CLASS procedure at the Clinica Oculistica, DiNOGMI, Ospedale Policlinico San Martino, University of Genoa, Italy. In case of bilateral surgery, we have included in the series only the first operated eye. Exclusion criteria were history of any glaucoma incisional surgery, cyclodestructive procedure, clinically significant cataract and gonioscopically narrow or closed angle. History of cataract surgery, small-gauge vitreo-retinal surgery and laser treatments were not exclusion criteria. Preoperative data collected included demographics, systemic diseases, ophthalmic history, topical and systemic medications. Ocular examination performed at baseline and at each follow-up visit (1 week, 1 month, 3 months and, every 3 months) included best-corrected visual acuity (BCVA) with Snellen chart, careful slit-lamp examination, Goldmann applanation tonometry, gonioscopy, and fundus examination. Procedure related complications, the number of IOP-lowering medications administered postoperatively and additional surgical procedures were recorded. Variables conforming to normal distribution were summarized as means (SD) and otherwise as median (IQR). For preoperative and postoperative comparisons, the paired Student's t-test was used for parametric data (IOP), and the Wilcoxon paired signed rank test was used for nonparametric data (IOP-lowering medications, visual acuity). Statistical analysis was performed using MedCalc 16.8. Significance was determined as $P < 0.05$.

Intervention

Informed consent was obtained from all patients after a thorough explanation of the procedure and its risk. All procedures followed the tenets of the Declaration of Helsinki. A single surgeon (CET) performed all CLASS procedures using the IOPtiMate system (IOPtima Ltd., Tel Aviv, Israel) under peribulbar anesthesia. After dissecting a fornix-based conjunctival flap and performing a tenonectomy, a 6×4 mm partial thickness limbus-based scleral flap was fashioned. MMC 0.2 mg/mL was applied for 3 min using filter paper cut to cover an area of at least 10×12 mm. Then, the CO_2 laser with a beam-manipulating system was used to ablate the scleral tissue in favor of reservoir creation for the percolated aqueous absorption, and to expose the Schlemm's canal area until sufficient percolation was obtained. The scleral flap was repositioned with two 10/0 nylon sutures, one at each posterior corner. The conjunctival flap was then closed with two half purse-string 8/0 polyglactin sutures at each side and one mattress suture centrally. An inferotemporal anterior chamber clear-cornea peripheral paracentesis was always created before photoablation. Postoperative bleb manipulation and scarring modulation with needling or MMC injections were part of routine management.

Iris adhesion management with Nd:YAG laser

In case of iris adhesion at the filtrating area, a Nd:YAG laser was attempted first. Miosis was first obtained with pilocarpine 2% ophthalmic solution (Pilocarpina, Farmigea srl, Italy). The area of iris adhesion to the trabeculo-descemetic window was visualized using the gonioscopy contact glass CGAL (Haag-Streit AG, Switzerland). Then, two to 15 spots of Nd:YAG laser were applied with a power of 3–7 mJ on the area of the adhesion. When not effective, the management was as described below.

Iris adhesion management at the slit lamp

First, miosis was obtained. Under topical anesthesia and after the instillation of two drops of povidone iodine 5% ophthalmic solution (Oftasteril, Alfa Intes srl, Italy) a small amount of dispersive viscoelastic solution (Viscoat, Alcon, USA) was injected through the infero-temporal paracentesis. The 27-gauge cannula of the viscoelastic syringe was then carefully used to pull the iris centrally. The success of the procedure was always verified by gonioscopy.

Results

Patient demographics and baseline characteristics are summarized in Table 1. The mean follow-up was 15.3 (5.9) months with a minimum of 12 months. The IOP was 25.4 (6.7) mmHg at baseline and decreased to 10.9 (3.4) mmHg al the last visit. Mean reduction of IOP was −14.5 mmHg (95% CI, −17.7 to −11.2, $P < 0.001$). Figure 1 shows the IOP changes during the follow-up. As shown in Figs. 2, 3 and 4, the median number for

Table 1 Baseline characteristics

Demographics	
Women	11 (55%)
Age (years)	73.6 (8.8)
Ocular characteristics and previous treatments	
Study eye was right eye	11 (52%)
Diagnosis in the study eye	
POAG	13 (62%)
POAG/NPG	2 (10%)
XFG	3 (14%)
Other[a]	3 (14%)
Glaucoma topical medication	
One	1 (5%)
Two	4 (19%)
Three	12 (57%)
Four	4 (19%)
Glaucoma oral medication (acetazolamide)	12 (57%)
IOP (mm Hg)	25.4 (6.7)
Lens status	
No clinically significant cataract	10 (48%)
Pseudophakia, IOL in the bag	10 (48%)
Surgical aphakia	1 (5%)
Previous laser surgery	
ALT	4 (19%)
YLPI	1 (5%)
BCVA, (LogMAR)	0.10 (0.02, 0.22)

Data are number (%), mean (SD), or median (IQR)

POAG primary open angle glaucoma, *NPG* normal-pressure glaucoma, *XFG* exfoliative glaucoma, *IOP* intraocular pressure, *IOL* intraocular lens, *ALT* argon laser trabeculoplasty, *YLPI* Nd:YAG laser peripheral iridotomy, *BCVA* best-corrected visual acuity, *LogMAR* logarithmic minimum angle of resolution

[a] Uveitis (1), previous plana vitrectomy for Eales disease (1), aphakia for congenital cataract (1)

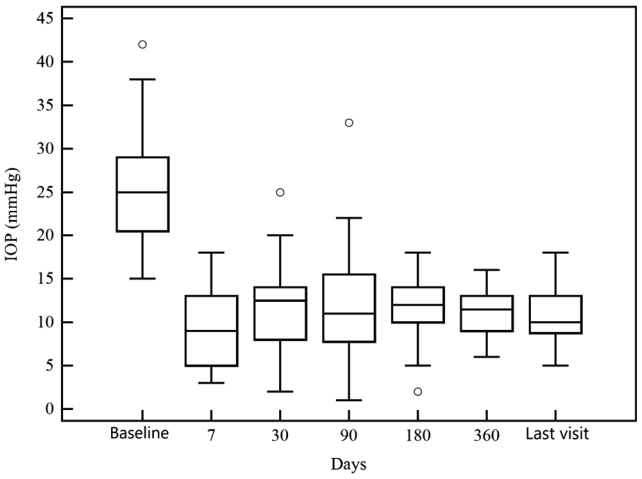

Fig. 1 Box plot for intraocular pressure at each study visit. Box-and-whiskers plot of the IOP measured during the follow-up visits. Values not included between the whiskers are plotted as outliers with a small circle

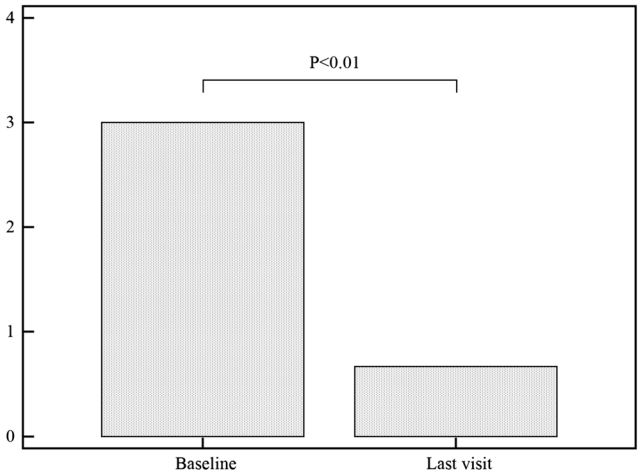

Fig. 2 IOP lowering medication. Median of preoperative and postoperative IOP lowering medication. The difference is statistically significant

the IOP-lowering medication was 3 (3–3) at baseline, and decreased to 1 (0–1) at the last visit ($P < 0.001$). During the follow-up, ten eyes (48%) did not require any IOP-lowering medication whereas eight (38%) received pilocarpine 1% ophthalmic solution q.d. to prevent iris adhesion. Postoperative bleb manipulation was performed in seven eyes (33%). Visual acuity was 0.10 (0.02–0.22) logarithmic minimum angle of resolution (logMAR) at baseline and 0.12 (0.04–0.40) logMAR at the last visit ($P = 0.06$). No patient required oral glaucoma medication at the last visit. Adverse events related to the procedure and their management are reported in Table 2. Of the five eyes (24%) that developed iris adhesion (Fig. 5), two were successfully managed only with Nd:YAG laser and three required iris repositioning at the slit lamp.

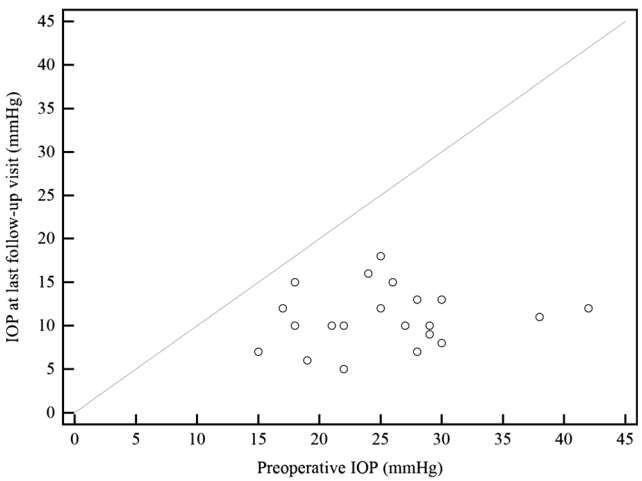

Fig. 3 Pre-Post intraocular pressure graph. A favorable IOP-lowering effect of the procedure is evident at the last follow-up visit for all the cases

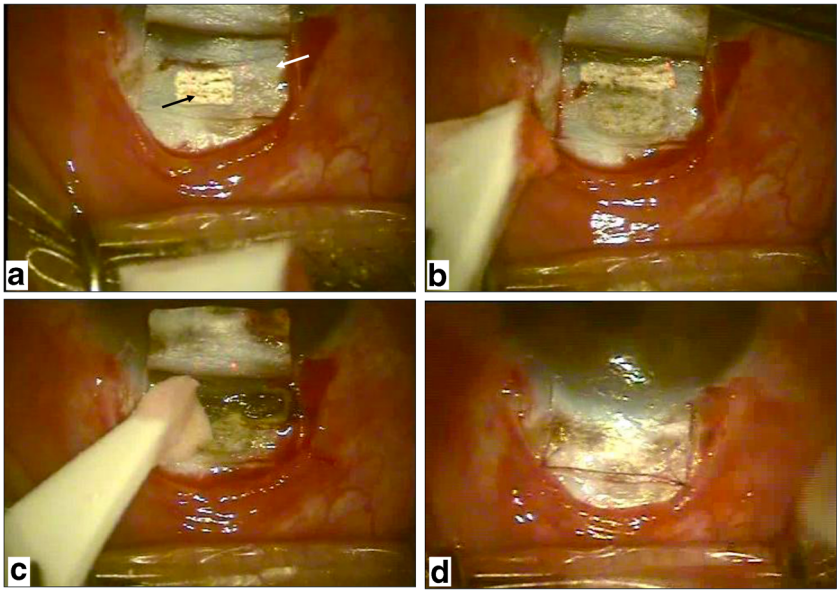

Fig. 4 The CLASS procedure. **a** After the creation of a scleral flap with a blade, initial CO_2 laser dissection is performed. The squared red laser aiming beam with four dots at the corners (white arrow) is visible near a treated area within the deep sclera (black arrow). Tissue ablation begins posteriorly and then the laser beam is repeatedly applied over an area including the Schlemm's canal (**b**) until sufficient percolation is clearly evident (**c**). The scleral flap is then repositioned with single 10–0 nylon sutures (**d**)

Table 2 Adverse events and management

Iris adhesion	5 (24%)	managed as described in the methods section
Cataract progression	2 (10%)	phacoemusification and IOL implantation
Intraoperative perforation	1 (5%)	converted to trabeculectomy
Hypotony maculopaty	1 (5%)	successfully treated with placement of additional transconjunctival scleral flap sutures

Data are number (%)

Discussion

In our study of a cohort of patients who underwent the CLASS procedure, we found a significant reduction in IOP and IOP-lowering drug during the follow-up. At the last visit, the mean IOP was reduced by 57% compared with baseline, and this was achieved with a marked reduction of IOP-lowering drugs. These results were comparable with other studies that showed a reduction of IOP between 42% and 49% after the CLASS procedure [9, 16, 17]. We mainly treated POAG patients. However, the procedure been successfully performed also in one eye with history of pars plana vitrectomy, in Fuchs heterochromic uveitis and in surgical aphakia. In our case series, iris adhesion to the filtrating area was the main adverse event related to the procedure (24%). This event happened spontaneously in three cases whereas in one case it was noted after needling and in one case after an ocular blunt trauma occurred one month after the surgery. We have not identified any ocular characteristics, such as lens status or anterior chamber depth, that were associated with the iris adhesion; in a patient who underwent CLASS procedure in both eyes, iris adhesion occurred only in one eye. All patients had wide and open angles at the baseline visit. Two other independent studies reported the occurrence of iris adhesion in 7% and 48% of cases [16, 17]. Thus, the risk of iris adhesion could be related to intraoperative factors such as the dimensions and the location of the ablated area; this hypothesis needs further evaluations. As suggested by other authors, in case of suspected

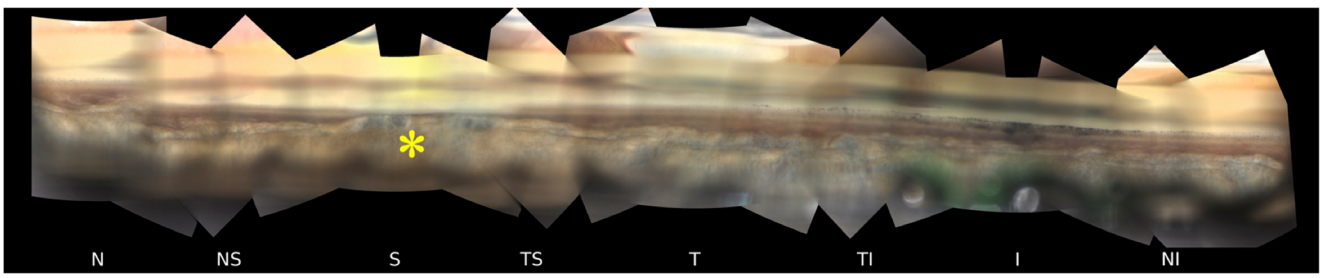

Fig. 5 360° Goniophotography. Automatic 360° goniophotography obtained with NGS-1 (Nidek srl, Italy). The image shows some iris adhesion at the filtration area (yellow asterisk)

overfitration, pilocarpine should be administered [17]. We also suggest long-term treatment with pilocarpine for patients who manifested iris adhesion. In our study, all cases of iris adhesion were managed by disengagement at the slit-lamp or with Nd:YAG laser. Of the treated eyes, only one underwent intraoperative perforation of the ablated area that required the conversion to trabeculectomy. In manual DS, perforation of the TDM is the most frequent intraoperative adverse event during the early learning curve [19]. The CLASS procedure seems to compare favorably with manually performed DS with IOP in the range of that reported with DS [12, 20]. CO2 is not the only type of laser to have been proposed to improve DS. In the past, also the excimer laser has been successfully used to ablate the sclera over the Schlemm's canal and obtain percolation [21, 22]. Although the authors reported good preliminary results, more extensive studies are missing. Early in vitro studies have also tested Erbium:YAG and femtolaser lasers for the dissection of the deep lamella but no clinical studies have been yet conducted [23, 24]. Hence, the CLASS system is the only laser commercially available for deep sclerectomy. Intraoperative application of MMC has been demonstrated to reduce the risk of failure of trabeculectomy and DS and, hence, is commonly used [5]. In the author's view, MMC should always be applied during the CLASS procedure because the thermal injury to the tissues adjacent to the ablated area may represent a stimulus for fibroblasts to proliferate. Our results indicate that this procedure can be considered as an alternative to traditional deep sclerectomy for the control of IOP in patients with OAG. Our study is limited by the small sample size. Further larger prospective studies with longer follow-up periods are required to establish the long-term effectiveness and safety of CLASS procedure in the management of glaucoma.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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