ECRONICON OPEN ACCESS

EC OPHTHALMOLOGY
Research Article

A Trabecular Micro-Bypass Stent Combined with Phacoemulsification Efficiently Reduces Intraocular Pressure in Primary Open Angle Glaucoma in Mexican Population

Sergio Ivan Escamilla Gallegos[1], Dora Aline Ochoa-Araujo[1]*, Elizabeth Dominguez[1], Daniel De La Torre-Tovar[1], Luis Ruben Martinez-Nava[1], Gabriela Valencia Rojas[1], Gabriela Esparza Rocha[1], Pablo Urzua de la Luz[1], Yuly Andrea Castellanos-Castellanos[1], Anani Vazquez Ramirez[1], Fernando Ruiz Magaña[1] and Oscar Medina-Contreras[2]

[1]*Glaucoma Department, Hospital Central Militar, Mexico City, Mexico*

[2]*Epidemiology, Endocrinology and Nutrition Department, Mexico Children's Hospital, Mexico City, Mexico*

***Corresponding Author:** Dora Aline Ochoa-Araujo, Glaucoma Department, Hospital Central Militar, Mexico City, Mexico.

Received: August 13, 2023; **Published:** September 07, 2023

Abstract

Purpose: The aim of this trial was to evaluate the safety and efficacy of a trabecular micro-bypass stent iStent combined with phacoemulsification in subjects with mild to moderate primary open angle glaucoma.

Methods: A prospective, randomized, open, controlled, clinical trial was performed an Mexico's Central Militar Hospital. The intervention was the implantation of a trabecular micro-bypass stent (iStent) combined with cataract surgery. 23 patients whom met the inclusion criteria were recruited into the trial. Intraocular pressure, best corrected visual acuity, visual field functional study, and the use of hypotensive drugs was documented and the patients were divided into two random groups, one underwent cataract surgery and the other underwent cataract surgery plus a trabecular microbypass stent (iStent) implantation.

Results: There was a reduction of up to 75% in the use of topical hypotensive drugs after one year iStent implantation.

Conclusion: The use of the iStent combined with phacoemulsification results in a sustained hypotensive effect in Mexican patients diagnosed with primary open angle glaucoma.

Keywords: *Glaucoma; Trabecular Stent; Microinvasive Glaucoma Surgery*

Introduction

Glaucoma is the second most common cause of blindness in the world after cataract, but this is the first one to be irreversibly. According to the World Health Organization, the prevalence of blindness in Latin America is 1 - 4% and 1.5% in Mexico L. IAPB [1,2], but there are no details about glaucoma-related blindness.

Primary open-angle glaucoma (POAG) is a chronic and progressive eye disease that causes loss of the optic nerve rim and the retinal nerve fiber layer with associated field defects [3]. POAG represents 80 - 85% of all glaucoma cases worldwide, and 53.7% of glaucoma cases in Mexico [4].

Risk factors include older age, Latino/Hispanic ethnicity, family history of glaucoma, and lower ocular perfusion pressure [3]. The main risk factor for its development and progression is ocular hypertension, and the major therapeutic option to prevent glaucomatous damage is to reduce the intraocular pressure (IOP) [5]. In Mexico POAG IOP has been reported as 17.1 in adults [4]. First line treatment for glaucoma is the use of topical hypotensives, often more than once a day, and usually in combination with double or triple therapy, and has been associated with poor compliance [6] and low tolerability [7-9] which can lead to treatment failure.

The ab externo surgery is still considered the gold standard, as it has good efficacy; however, it has a high complication rate [10-13].

However, surgery alone results in only a modest reduction in IOP [14-19]. However, there are several complications such as endophthalmitis, hypotonia, blister infections, blister leaks or fibrosis. Minimally invasive glaucoma surgeries (MIGS) require less surgical manipulation and are generally safer, with more benefits to IOP reduction and lower rates of serious complications [20].

First and second generation trabecular microbypass stent devices acts at the level of the trabecular meshwork, allowing to create a direct pathway from the anterior chamber to the drainage canal. This results in a decreased resistance to the aqueous humor outflow of up to 30% and a subsequent reduction in IOP of up to 6 mmHg [21,22].

Here we evaluated the effectiveness and safety of a trabecular micro-bypass stent implant combined with cataract surgery in Mexican population with POAG.

Methods

Study design: A prospective, longitudinal study was carried from January 2022 to February 2023 at the department of ophthalmology at the Central Military Hospital in Mexico City. The study protocol was approved by the local ethics committee and informed consent was obtained from all participants. Patients with mild to moderate glaucoma damage according to Hodapp criteria, and with a diagnosis of cataract at the were invited to participate in this study. Inclusion criteria: patients above 18 years old who had completed one year of follow-up after surgery. Exclusion criteria: follow-up of less than 12 months, neovascular, closed angle, or traumatic glaucoma, any previous glaucoma surgery (except laser trabeculoplasty), previous ocular trauma, patients with increased episcleral venous pressure (active thyroid orbitopathy, carotid-cavernous fistula, Sturge-Weber syndrome), corneal opacity that makes gonioscopy and cataract difficult, patients under 18 years of age.

Clinical evaluation: A clinical evaluation of the patients was carried out with a complete medical history and ophthalmological examination, including visual acuity, best corrected visual acuity, intraocular pressure measured with Goldmann tonometry, slit lamp examination, gonioscopy with a 4-mirror Sussman lens, and dilated fundus examination. Prior to the surgery, preoperative tests were taken, such as, axial length measurement, anterior chamber width, anterior chamber volume, specular microscopy, 24-2 visual fields, and optic nerve and ganglion cells optical coherence tomography.

Surgery: All subjects underwent phacoemulsification cataract extraction with IOL implant. Preoperative peribulbar anesthesia was used; after cataract extraction, acetylcholine was used in the anterior chamber to induce pupil contraction after implanting the IOL. A first generation heparin-coated, medical-grade titanium, 1 mm length, 0.3 mm diameter, 120 µm lumen trabecular micro-bypass stent (iStent; Glaukos Corporation, Laguna Hills, CA) was placed. The study subjects underwent the implantation of one iStent, so it was necessary to fill the anterior chamber with viscoelastic. This was pre-loaded in a single-use inserter that was advanced internally to the globe towards the inferior nasal sector of the iridiocorneal flexure, towards the pigmented portion of the trabecular meshwork, next to Schlemm's canal; guided by gonioscopy ab interno using a Swan-Jacobs gonioscope. After verifying the proper iStent implantation, the applicator was removed, the viscoelastic was washed and the cataract surgery ports were hydrated. At the end of the surgical procedure, simple

moxifloxacin topical antibiotic drops were placed. Postoperative care was performed with moxifloxacin 0.5% ophthalmic solution, which was continued for one week, in addition to prednisolone acetate 1% eye drops, with a reduced dose for 4 weeks.

Follow-up: Follow-up was carried out by the same doctor the following day, one week later, one, three, six and twelve months after surgery. At each visit visual acuity, best-corrected visual acuity and intraocular pressure by Goldmann tonometry were registered; the antihypertensive medication was continued (it was documented how many drugs the patient had and the need to withdraw or add another one). Also associated complications were documented, such as infection, eye pain, low vision, increased or low intraocular pressure. Visual fields, OCT and specular microscopy were performed at 6 and 12 months after surgery.

Ethical approval declarations: This protocol was approved by the Central Militar Hospital Ethics Committee and was carried out in accordance with the relevant guidelines and regulations. All participants received and signed an informed consent.

Data analysis: All records were collected in a database. Descriptive statistics, t-SNE dimensional analysis, and t-student were performed in R 4.4.0 and GraphPad Prism 10.0.0 (112) for all our analyses.

Results

A total of 23 patients with a diagnosis of glaucoma were studied. Females with primary open angle glaucoma were the predominant population (Table 1). The mean corneal endothelial cell count (RTO) pre-operatively was 2181.39 ± 362.14 cells/mm^2 while postoperatively at 1 month it was 1660.69 ± 341.84 cells/mm^2.

Variable	n = 23
Age, mean (SD)	71.2 (9.4)
Sex, n (%)	
Female	16 (69.6)
Male	7 (30.4)
Diagnosis, n (%)	
POAG	20 (87.0)
PXG	2 (8.7)
PG	1 (4.3)
Right eye	13 (56.5)
Left eye	10 (43.5)
RTO, mean (SD)	
Pre-surgery	2181.39 (362.14)
Post-surgery	1660.69 (341.84)

Table 1: *Descriptive statistics. POAG: Open Angle Glaucoma; PXG: Pseudoexfoliative Glaucoma; PG: Pigmentary Glaucoma; RTO: Corneal Endothelial Cell Count.*

A dimensional reduction analysis by tSNE was performed on all 26 variables from the 23 patients to identify the effect of the iStent implant. 3 distinct groups were identified and strongly associated with RTO and IOP (Figure 1).

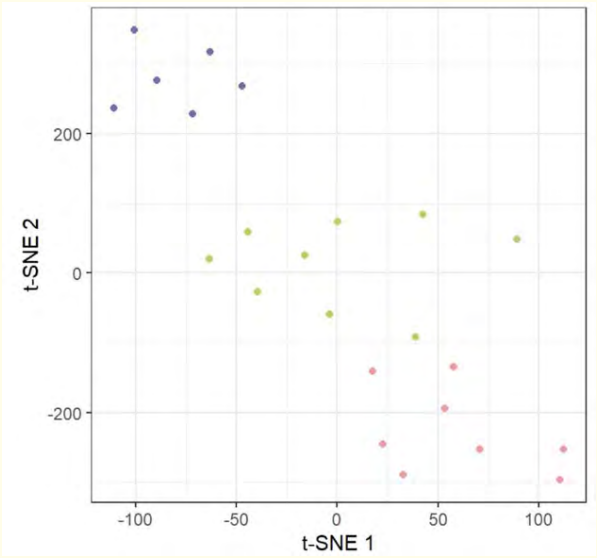

Figure 1: *Multidimensional analysis. A t-sne analysis indicates RTO and IOP are the main variables that can predict an improvement after the iStent procedure.*

Consistent with this observation, the iStent implant produced a strong and sustained hypotensive effect. The intraocular pressure showed a rapid and constant decrease (Figure 2). A 12% reduction was achieved just 1 day after surgery, and reached a 19% reduction at 1 week. It kept stabled at an average of 14.5% reduction, from 1 month up to 1 year. Importantly, the corneal endothelial cell count showed only a 23.8% decrease 1 month after surgery compared with the mean pre-surgery count (Figure 3).

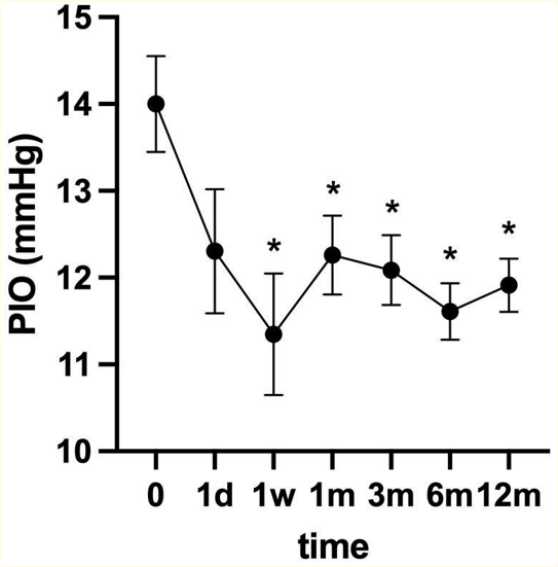

Figure 2: *Intraocular pressure. iStent implants reduce intraocular pressure. p = 0.05.*

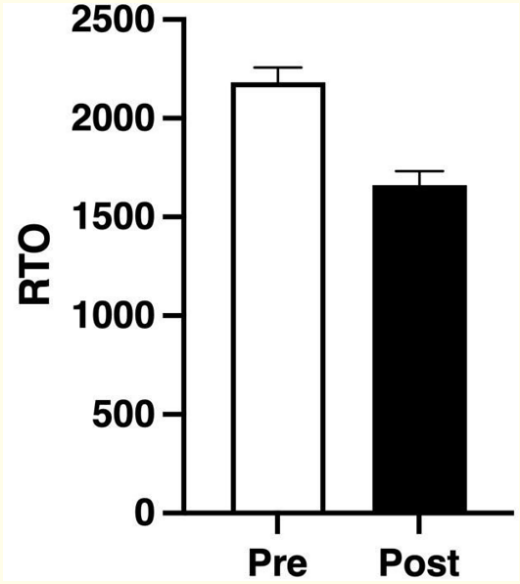

Figure 3: *Endothelial cells. iStent implant reduces corneal endothelial cell count. p = 0.00005.*

These clinical improvements resulted in a dramatic decrease in the number of conventional treatments received after surgery (Figure 4). On average, all subject required no treatment in the first month following the iStent implantation, and then required an average of 0.5 treatments for the following 11 months.

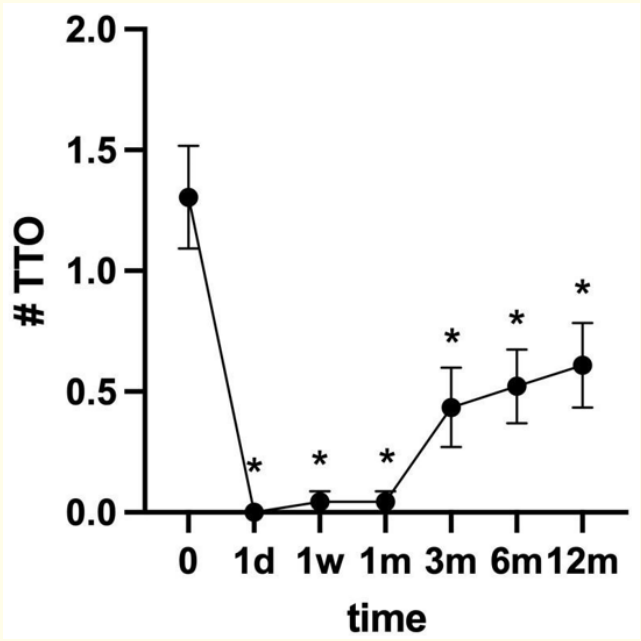

Figure 4: *Treatment. Number of conventional treatments after iStent implant. p = 0.05.*

Discussion

From all the variables that were studied, our analysis indicated IOP and RTO, both pre- and post-surgery, are crucial for an effective glaucoma surgery using a trabecular micro-bypass stent. These highlights the importance of a good procedure to minimize the loss of corneal endothelial cells, and the intraocular pressure as the main benefit from these kind on implants.

Typical glaucoma hypotensive treatment includes a combined therapy of at least 2 drugs. Here we show that iStent implantation achieves an average reduction of 78% in the use of topical hypotensive drugs during the first year after surgery. This results in less adverse effects on the ocular surface caused by the constant use of the hypotensive eye drops, and promote better adherence to treatment. Thus, this represents a significant decrease in expenses for both the institution and the patient. Further, it has been reported that the annual cost of hypotensive eye drops in Mexico was $360 in 2013 [23]. The current annual cost adjusted by inflation is approximately $696 dollars, this is comparable to the $864 cost of the iStent implant in Mexico. Together, the benefits of the iStent become economically more evident after the first year.

Corneal endothelial cells are crucial in maintaining clarity of vision [24]. Normal adults have between 2000 - 3000 cells/mm^2, in line with our patients average of 2181 cells/mm^2 despite being 71 years old. Interestingly, we observed only a modest 23% decrease in these cells after surgery, suggesting the iStent has not a great impact, and might be one of the reasons the IOP decrease was sustained for the whole year follow-up. Our results in endothelial cells decrease after surgery are slightly above of what has been reported before for a similar microbypass, they also concluded there were no significant differences in the percentage of eyes with central endothelial cell density > 30% between the iStent inject and control groups at any timepoint within the 60-month follow-up period. None of the eyes in this study developed corneal edema and/or required keratoplasty, none had central endothelial cell density < 750 cells/ mm^2 at the 60- month [25]. This may be related to the surgery performed by glaucoma-training ophthalmologist, rather than fully-trained glaucoma ophthalmologists, and shows a potential improvement. However, this also highlights the safety and reproducibility of the iStent implantation.

Finally, the strong hypotensive effect induced by the iStent implant, together with the small corneal endothelial cell loss, was constant and showed little variability during the follow-up period. These observations suggest the iStent implant has long-term positive effects, with great efficacy, safety, and benefits for the eye after surgery, but also promotes greater adherence to treatment in the long term [26,27].

Conclusion

iStent implant represents a cost effective alternative to traditional open angle glaucoma surgery plus conventional hypotensive drugs. The use of the iStent implant has long-term safety, and promotes greater adherence to treatment in the long term.

Bibliography

1. IAPB, Latin America. "Estimates of Blindness in Latin America". *Vision* (2020).
2. IAPB. "Estimates of Vision Loss in Central Latin America". (2020).
3. Gedde Steven J., *et al*. "Primary Open-Angle Glaucoma Preferred Practice Pattern". *Ophthalmology* 128.1 (2021): 71-150.
4. Galvez-Rosas Arturo., *et al*. "Association of risk factors with primary open angle glaucoma in adults over the age of 40". *Gaceta Médica de México* 154.1 (2018).
5. EGSTGG. "European Glaucoma Society Terminology and Guidelines for Glaucoma". *British Journal of Ophthalmology* 105.1 (2021): 1-169.

6. Newman-Casey., *et al*. "The Most Common Barriers to Glaucoma Medication Adherence". *Ophthalmology* 122.7 (2015): 1308-1316.

7. Schuman Joel S. "Antiglaucoma Medications: A Review of Safety and Tolerability Issues Related to Their Use". *Clinical Therapeutics* 22.2 (2000): 167-208.

8. Dreer Laura E., *et al*. "Determinants of Medication Adherence to Topical Glaucoma Therapy". *Journal of Glaucoma* 21.4 (2012): 234-240.

9. Gatwood Justin., *et al*. "Facilitators and Barriers to Glaucoma Medication Adherence". *Journal of Glaucoma* 31.1 (2021): 31-36.

10. Shah Manjool. "Micro-Invasive Glaucoma Surgery - an Interventional Glaucoma Revolution". *Eye and Vision* 6.1 (2019).

11. Birnbaum Faith A., *et al*. "Microinvasive Glaucoma Surgery: An Evidence-Based Review". *Seminars in Ophthalmology* 36.8 (2021): 772-786.

12. Garudadri Chandra Sekhar., *et al*. "Three-Year Follow-up of the Tube Versus Trabeculectomy Study". *American Journal of Ophthalmology* 149.4 (2010): 685-686.

13. Nassiri Nariman., *et al*. "Three-Year Outcomes of Trabeculectomy and Ahmed Valve Implant in Patients with Prior Failed Filtering Surgeries". *International Ophthalmology* 40.12 (2020): 3377-3391.

14. Tennen Debra G and Samuel Masket. "Short- and Long-Term Effect of Clear Corneal Incisions on Intraocular Pressure". *Journal of Cataract and Refractive Surgery* 22.5 (1996): 568-570.

15. Shingleton Bradford J., *et al*. "Long-Term Changes in Intraocular Pressure After Clear Corneal Phacoemulsification: Normal Patients Versus Glaucoma Suspect and Glaucoma Patients". *Journal of Cataract and Refractive Surgery* 25.7 (1999): 885-890.

16. Shingleton Bradford J., *et al*. "Three and Five Year Changes in Intraocular Pressures After Clear Corneal Phacoemulsification in Open Angle Glaucoma Patients, Glaucoma Suspects, and Normal Patients". *Journal of Glaucoma* 15.6 (2006): 494-498.

17. Qassim Ayub., *et al*. "Effect of Phacoemulsification Cataract Surgery on Intraocular Pressure in Early Glaucoma: A Prospective Multi-Site Study". *Clinical and Experimental Ophthalmology* 48.4 (2020): 442-449.

18. Hayashi Ken., *et al*. "Effect of Cataract Surgery on Intraocular Pressure Control in Glaucoma Patients". *Journal of Cataract and Refractive Surgery* 27.11 (2001): 1779-1786.

19. Poley Brooks J., *et al*. "Long-Term Effects of Phacoemulsification with Intraocular Lens Implantation in Normotensive and Ocular Hypertensive Eyes". *Journal of Cataract and Refractive Surgery* 34.5 (2008): 735-742.

20. Ferguson Tanner J., *et al*. "Trabecular Microbypass Stent Implantation with Cataract Extraction in Pseudoexfoliation Glaucoma". *Journal of Cataract and Refractive Surgery* 43.5 (2017): 622-626.

21. Zhou Jianbo and Gregory T Smedley. "A Trabecular Bypass Flow Hypothesis". *Journal of Glaucoma* 14.1 (2005): 74-83.

22. Samuelson Thomas W., *et al*. "Randomized Evaluation of the Trabecular Micro-Bypass Stent with Phacoemulsification in Patients with Glaucoma and Cataract". *Ophthalmology* 118.3 (2011): 459-467.

23. Lazcano-Gomez., *et al*. "Topical Glaucoma Therapy Cost in Mexico". *International Ophthalmology* 34.2 (2013): 241-249.

24. Islam Qamar Ul., *et al*. "Age Related Changes in Corneal Morphological Characteristics of Healthy Pakistani Eyes". *Saudi Journal of Ophthalmology* 31.2 (2017): 86-90.

25. Ahmed Iqbal Ike K., *et al*. "Long-Term Endothelial Safety Profile With iStent Inject in Patients with Open-Angle Glaucoma". *American Journal of Ophthalmology* 252 (2023): 17-25.

26. Mojca Hudovernik and Dusica Pahor. "Intraocular Pressure after Phacoemulsification with Posterior Chamber Lens Implantation in Open-Angle Glaucoma". *Klinische Monatsblätter für Augenheilkunde* 220.12 (2003): 835-839.

27. Quigley HA. "The Number of People with Glaucoma Worldwide in 2010 and 2020". *British Journal of Ophthalmology* 90.3 (2006): 262-267.

Volume 14 Issue 10 October 2023