Outcomes of phacoemulsification combined with two iStent inject trabecular microbypass stents with or without endocyclophotocoagulation

Anca Delia Pantalon ,[1,2] Andre Diogo De Oliveira Barata,[1,3] Minas Georgopoulos,[1,4] Gokulan Ratnarajan [1]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bjophthalmol-2019-315434).

[1]Eye Unit and Eye Bank, Queen Victoria Hospital NHS Foundation Trust, East Grinstead, UK
[2]Ophthalmology, "St. Spiridon" University Hospital, Iasi, Romania
[3]Ophthalmology, Santa Maria Central Hospital, Lisbon, Portugal
[4]Ophthalmology, East Surrey Hospital, Redhill, UK

Correspondence to
Dr Gokulan Ratnarajan, Eye Unit and Eye Bank, Queen Victoria Hospital NHS Foundation Trust, East Grinstead RH19 3DZ, UK; g.ratnarajan@gmail.com

Received 23 October 2019
Revised 9 January 2020
Accepted 13 January 2020

To cite: Pantalon AD, Barata ADDO, Georgopoulos M, *et al*. *Br J Ophthalmol* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjophthalmol-2019-315434

ABSTRACT

Aim Comparing outcomes after combined phacoemulsification, two iStents insertion and endocyclophotocoagulation (ECP) versus phacoemulsification-iStents alone.

Methods This is a longitudinal retrospective 12 months study in eyes with ocular hypertension or early-to-moderate open angle glaucoma. Level of disease, intraocular pressure (IOP) and tolerance of glaucoma medication were considered before planning surgery. Best-corrected visual acuity (BCVA-logMAR), IOP (mm Hg), number of medications were assessed at baseline, week 1, week 5, month 3, 6, 12 postop. Main outcome: percentage (%) in IOP reduction at 12 months vs medicated baseline. Secondary outcomes: absolute values of IOP/medication reduction, BCVA and postop complications.

Results The ICE2 (two iStents-cataract extraction-ECP) group included 63 eyes and Phaco-iStent group included 46 eyes. Baseline IOP was higher in the ICE2 than phaco-iStent group (19.97±4.31 mm Hg vs 17.63±3.86 mm Hg, p=0.004) and mean deviation was lower (−7.20±2.58 dB vs −4.94±4.51 dB, p=0.037). Number of medications were comparable at baseline: 2.22±1.06 (ICE2) vs 2.07±1.02 (phaco-iStent), p=0.442. At month 12 postop, IOP in the ICE2 group decreased 35% from baseline vs 21% in the phaco-iStent group (p=0.03); absolute IOP reduction was significantly lower than baseline in each group (p<0.001), yet final IOP was lower in the ICE2 group than phaco-iStent group (13.05±2.18 mm Hg vs 14.09±1.86 mm Hg, p=0.01). Similar results were found for glaucoma medication (1.24±1.05 in ICE2 group vs 1.39±1.03 in phaco-iStent group, p=0.01). Final BCVA was 0.11±0.18 (phaco-iStent group) vs 0.08±0.08 (ICE2 group), p=0.309. Safety outcomes were comparable between groups.

Conclusion ICE2 procedure offers better results in IOP/medication reduction at 12 months than phacoemulsification-iStents alone.

INTRODUCTION

Glaucoma is the main cause of irreversible blindness worldwide[1] with intraocular pressure (IOP) remaining the only modifiable risk factor to prevent progression of the disease and further vision loss.[2] Traditionally, IOP lowering medications have been used as first-line treatment for ocular hypertension (OHT) or open angle glaucoma (OAG).[2] Topical glaucoma medications have the potential problems of ocular surface disease,[3] poor compliance, as well as difficulty administering the drops.[4]

Other treatments such as selective laser trabeculoplasty[5] (SLT) and minimally invasive glaucoma surgery (MIGS) have more recently been used to treat early glaucoma.[6] The cornerstone of MIGS remains a high safety profile while being able to prevent glaucoma progression, reduce medication burden, improve quality of life, as well as defer or negate the need for filtering surgery.[6–8]

The iStent (Glaukos, Laguna Hills, California, USA) is the first glaucoma device with ab interno delivery that has been approved for management of mild-to-moderate forms of OAG. Highly biocompatible (heparin-coated titanium), the iStent bypasses the trabecular meshwork (TM) to connect with the inner wall of the Schlemm's canal to enhance aqueous drainage by overcoming outflow resistance from the TM. Placed ab interno, through the TM directly into the Schlemm's canal under gonioscopic guidance,[9] both generations of iStents have proven safety and efficacy,[10] either when used as a standalone procedure[11] or when combined with cataract extraction for mid[12] or long-term follow-up intervals.[13]

In addition to the anterior chamber (AC) angle surgery, other MIGS procedures such as the laser endocyclophotocoagulation (ECP) have been found safe and effective,[14–16] decreasing the aqueous production by the thermal destructive effect on the ciliary processes. Satisfactory results in IOP reduction have been observed both when ECP was performed alone in pseudophakic glaucomatous eyes[17] and when combined with the cataract surgery.[18 19] Nevertheless, in selected cases, cataract removal is thought to have its own contribution in lowering the IOP in patients with glaucoma,[20] although the effect reduces in time.[20–23] Other studies mention a minor contribution after cataract extraction in terms of IOP reduction, estimated to be <2 mm Hg[23 24] and/or 16.5% reduced from baseline.[12 25] Yet, it has been acknowledged that eyes with higher IOP at baseline obtain a greater IOP reduction postoperatively.[12]

Yet there is little literature on IOP control and medication reduction in patients with glaucoma undergoing cataract surgery and two MIGS procedures, with different anatomical targets (aqueous production and aqueous outflow system).[26] In 2017, a single study reported that patients with OAG or OHT, who underwent insertion of a single,

first generation iStent, combined with cataract extraction and ECP (ICE1 procedure), obtained a better IOP reduction than those who did not have ECP included in the surgical protocol.[26] To the best of our knowledge, this is the first study to report the outcomes of combining two iStent devices (iStent inject) with ECP during cataract surgery (two iStents-cataract extraction-ECP (ICE2) procedure) in patients with early/moderate OAG or OHT.

MATERIAL AND METHOD

All procedures were approved by the Institutional Review Board of Queen Victoria Hospital, and respected the declaration of Helsinki. All patients signed an informed consent form. Clinical trial registration was not required, as the treatments being performed were standard of care at the hospital.

Study design

Our retrospective unmasked, longitudinal study included consecutive series of cases of eyes with early-to-moderate OAG, according to the Hodapp criteria[27] or patients with OHT, according to the EGS definition.[28] Eligible subjects were over 18 years old, requiring surgery for visually significant age related cataract, in addition to a better IOP control and/or a reduction in glaucoma topical treatment.

Level of disease (moderate versus early glaucoma), IOP (mm Hg) by Goldmann applanation tonometry (</=18 mm Hg vs >18 mm Hg) and local tolerance of glaucoma medication were all considered when the extent of surgery was planned (phaco-iStents versus ICE2).

Selection criteria

We included patients over 18 years of age with an established glaucoma diagnosis, based on criteria described earlier.[28 29] Gonioscopy was routinely performed in all cases, using Spaeth criteria.[30] Both primary and secondary OAG such as pseudoexfoliative and pigmentary glaucoma were included. Other inclusion criteria were best-corrected visual acuity (BCVA) better than 20/200 (ETDRS), and average mean deviation (MD) not below −12 dB in Humphrey Perimeter tests (central 24–2 test, SITA FAST strategy, II Humphrey Field Analyzer 750i, Carl Zeiss Meditech, Dublin, California, USA).

Exclusion criteria were closed angles, either appositional or synechial as found in gonioscopy, previous ocular trauma, uveitis, surgical interventions, including laser peripheral iridotomies or SLT within 90 days of surgery, MD equal to or worse than −12 dB, other ocular comorbidities that prevented full ocular examination or might have influenced the postop visual prognosis (eg, corneal scarring), unreliable visual fields (VF) at baseline or patients who failed to attend all follow-up visits.

Surgical technique

Topical anaesthesia was achieved using preservative free proxymetacaine hydrochloride 0.5% (Bausch&Lomb, UK) and tetracaine hydrochloride 0.5% (Bausch&Lomb, UK). A side port was created with a microvitreoretinal blade followed by intracameral introduction of 0.2 mL of preservative free lignocaine hydrochloride (1%) and AC fill with ophthalmic viscosurgical device (OVD) Healon GV (14 mg/mL sodium hyaluronate, Abbot Medical Optics, California, USA). A 2.2 mm temporal incision was made and the patient's head was tilted approximately 30° away from the surgeon, while the microscope was also tilted towards the patient to allow intraoperative gonioscopy with a Swan-Jacob gonio lens. Two preloaded iStents (iStent inject) were inserted into the nasal TM approximately 3 clock hours apart. Cataract surgery was then performed and the intraocular lens inserted. After OVD removal from the capsular bag, the sulcus space was inflated with Healon . Then, ECP was applied to the ciliary process using a standard power setting of 0.25 W, although this was titrated until a desired reaction was achieved. After viscoelastic removal, the wounds were hydrated; 0.2 mL intracameral dexamethasone (3.3 mg/mL solution, Hospira UK) and 0.1 mL cefuroxime (3 mg/0.3 mL, ITH Pharma, London, UK) were injected to complete the surgery.

Postoperative topical preservative free Chloramphenicol 0.5% (Bausch&Lomb, UK) was administered four times a day for 2 weeks in both study groups. Dexamethasone sodium phosphate 0.1%, preservative free (Bausch & Lomb, UK) was instilled each 2 hours (day time) for the first 2 weeks postop, then four times a day for the next 2 weeks in the ICE2 group; for the phaco-iStent group, Dexamethasone was used four times a day for 4 weeks postop. Non-steroidal anti-inflammatory drops were prescribed only if macular oedema was detected either by clinical or optical coherence tomograpghy (OCT) examination at any postop visit.

The patients continued their normal antiglaucoma medication immediately after the operation, regardless of class. Reduction in glaucoma drops was determined by the surgeon based on the IOP level at the postop visits in conjunction with the level of disease. Follow-up visits were at weeks 1 and 5, then at months 3, 6 and 12.

At each time point, identical parameters were collected: BCVA (ETDRS, then logMAR conversion), IOP (mm Hg) by Goldmann tonometry, number of glaucoma medications and presence of any postop complication. Gonioscopy was routinely performed at all visits to assess the stents placement and angle anatomy after surgery. All eyes underwent uncomplicated cataract surgery. The primary outcome was IOP (%) reduction at 12 months compared with medicated baseline IOP. Secondary outcomes quantified the absolute values in IOP and topical medication reduction, BCVA as well as postop complications. Safety outcomes included reporting the adverse reactions (IOP spikes, persistent inflammation or hyphaema, secondary surgical interventions).

Statistical analysis

IBM SPSS Statistics software (V.20.0) was used for all calculations. Data distribution was assessed by Shapiro Wilk's test. For variables with normal distribution, means±SD were calculated. For variables with non-Gaussian distribution, we used the median. A Wilcoxon signed rank sum test for non-Gaussian distribution was employed to compare the mean number of medications in each group from baseline to 12 months. A 2-independent sample t test was used to compare IOP changes, as well as for all parameters that needed comparisons between groups at week 1, week 5, months 3, 6 and 12 postop. Categorical variables, frequency distribution and percentages were evaluated and compared by χ^2 test. For correlations, we used the Pearson test; predictors in multivariate analysis were calculated based on a stepwise analysis of variance (ANOVA) model. Statistical significance was accepted at $p<0.05$.

RESULTS

A final number of 109 eyes were selected for the study, after meeting all the inclusion criteria: 63 eyes in the ICE2 group and 46 eyes in the phaco-iStent group. Table 1 shows comparative data between groups.

Glaucoma was more severe in the ICE2 eyes versus phaco-iStent eyes, as reflected by a higher IOP and a more decreased

Table 1 Demographics and baseline ocular characteristics in the study groups

Baseline parameter (mean±SD)	ICE 2 group	Phaco-iStent group	P value (t test)
Age (years)	77.49±6.45	76.24±8.37	0.380
Sex ratio M:F	1:1.62	1:1.7	0.789
BCVA (logMAR)	0.26±0.18	0.29±0.21	0.534
IOP (mm Hg)	19.97±4.31	17.63±3.86	**0.004**
No. of meds	2.22±1.06	2.07±1.02	0.442
MD baseline (dB)	−7.20±5.8	−4.94±4.51	**0.037**
RNFL thickness (µm)	78.37±11.82	81.91±12.67	0.146
ACD (mm)	2.86±0.48	3.00±0.40	**0.040**
AL (mm)	23.20±0.97	23.74±1.37	**0.018**
CCT (µm)	533±31.19	531±28.48	0.838

Bolded values point out the statistically significant differences between groups. ACD, anterior chamber depth; AL, axial lengths; BCVA, best-corrected visual acuity; CCT, central corneal thickness; ICE2, phacoemulsification+iStent inject+endocyclophotocoagulation procedure; IOP, intraocular pressure; logMAR, logarithm of minimum angle of resolution; MD, mean deviation; No. of meds, number of topical glaucoma medications; RNFL, retinal nerve fibre layer.

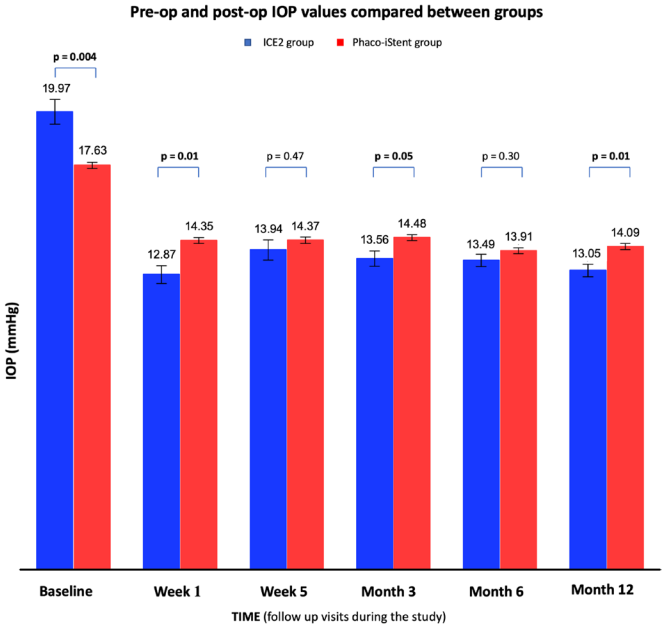

Figure 1 Mean intraocular pressure (mm Hg) in the two study groups (ICE2 versus phaco-iStent) before (baseline) and after the combined cataract and glaucoma procedure (week 1, week 5, month 3, month 6, month 12). Bolded values indicate the statistically significant difference (p<0.05) when t test was applied. Error bars represent SE of the mean. ICE2, two iStents-cataract extraction-endocyclophotocoagulation; IOP, intraocular pressure.

MD value at baseline. Statistically significant shorter axial lengths (AL) and anterior chamber depth (ACD) were also noted in the ICE2 group. Other parameters were comparable in terms of BCVA, intensity of treatment and so on.

Efficacy of treatment

In both groups, there was a significant IOP reduction both at 6 and 12 months compared with baseline (p<0.001, for all paired groups). In the ICE2 group at 12 months postop, there was a 35% IOP reduction from the initial medicated IOP (19.97±4.31 mm Hg at baseline vs 13.05±2.28 mm Hg, p<0.001 mm Hg at 1 year follow-up), whereas in the phaco-iStent group, the per cent of IOP reduction from baseline was 21% at 1-year follow-up (17.63±3.86 mm Hg vs 14.09±1.86 mm Hg, p<0.001). Such IOP reduction in the ICE2 group was significantly more prominent than the phaco-iStent group, p=0.03. Figure 1 shows the comparison of IOP between groups throughout the study period. Absolute IOP values demonstrate that at month 12 in the ICE2 group, there is a more significant IOP reduction versus phaco-iStent group (p=0.01).

Approximately 2/3 of the ICE2 procedures were performed by the consultant (40 eyes, 63.5%), while the fellows performed the remaining 1/3 of cases (23 eyes, 36.5%). In the ICE2 group, there was a comparable (%) reduction in IOP at month 12 from the medicated baseline between consultant and fellow cases (34.3% vs 31.8%, p=0.08). In the phaco-iStent group, the consultant performed 27/46 (58.7%) of all cases and fellows operated on 19/46 eyes (41.3%), with a similar (%) IOP reduction at month 12 from medicated baseline, consultant versus fellow: 21.2% vs 19.1%, p=0.67.

There was a significant reduction in medication use in both groups at 6 months and 12 months compared with baseline. For the ICE2 group, we found a decrease from a mean number of 2.22±1.85 substances at baseline, to 1.35±1.03 substances at 6 months (p<0.001) and 1.24±0.98 at 12 months (p<0.001) with a final 45% reduction of medication use. In the phaco-iStent group, there was a final 33% reduction of medication from baseline, but significantly inferior to the ICE2 group (p=0.04). Reduction in eye drops usage in the phaco-iStent group was also significant at 6 months (1.46±0.97 substances vs 2.07±1.02 substances, p<0.001) and, respectively, at 12 months, compared with baseline (1.39±1.03 substances vs 2.07±1.02 substances, p<0.001). No differences in terms of medication reduction for fellow versus consultant cases were observed during the study at any time point (p>0.05).

At the last follow-up visit, 31.7% eyes in the ICE2 group did not require topical medication to control IOP, 27.1% required 1 class of IOP lowering medication and the rest (41.2%) required 2≥classes of antiglaucoma medications. In the phaco-iStent group, 19.6% eyes needed no treatment to control the IOP at month 12, 41.3% eyes needed 1 class of glaucoma medication with the remainder (39%) requiring ≥2 substances to lower the IOP. The proportion of medication-free eyes at 12 months was significantly higher in the ICE2 group versus phaco-iStent group (p=0.001).

A reduction in medication use at 12 months was noted individually in both groups. In the ICE2 group, a significant reduction was noted at week 5 (2.22±1.06 substances vs 1.63±1.17 substances, p<0.001) and month 12 postop (2.22±1.06 substances vs 1.24±0.98 substances, p<0.001). A similar trend was observed in the phaco-iStent group, decreasing significantly the medication at week 5 postop vs baseline (2.07±1.02 substances, p<0.001) or at month 12 postop vs baseline (1.39±1.03 substances vs 2.07±1.02 substances, p<0.001). At different time points, figure 2 compares the reduction of medication throughout the study between the study groups.

In the ICE2 group, a median area of 270° ECP treatment had been applied (range 180°–300°). ICE2 patients were grouped according to extent of ECP treatment: group A (ECP applied on less than/equal to 210°) and group B (ECP applied on more than 210°). Decision to treat a wider surface of ciliary processes was based on the baseline IOP, number of topical medications and the level of disease using the MD of VF test. The mean MD (dB) in group A was −4.33±3.94 vs −8.67±6.13 in group

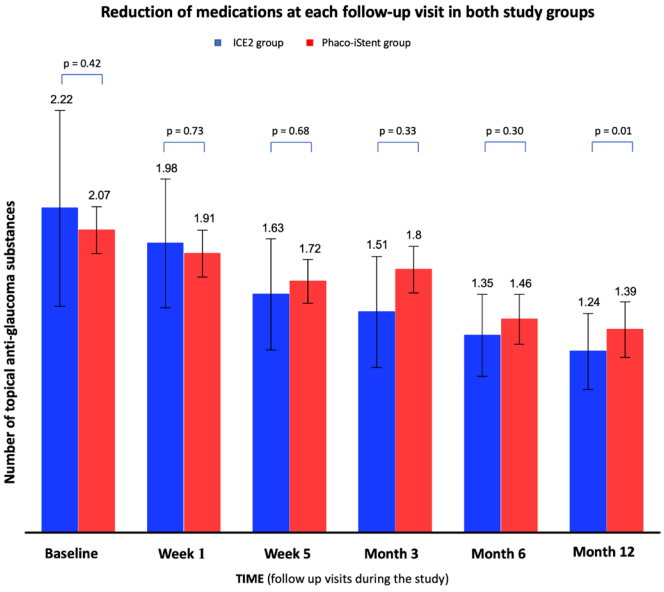

Figure 2 Mean number of glaucoma medications (absolute values) in the two study groups ICE2 versus phaco-iStent before (baseline) and after the combined cataract and glaucoma procedure (week 1, week 5, month 3, month 6, month 12 postop). A p<0.05 value was statistically significant (t test). Error bars represent SE of the mean. ICE2, two iStents-cataract extraction-endocyclophotocoagulation.

B (p=0.005). There was an IOP reduction from baseline of 33.34% in the group A vs 35.4% in group B, p=0.315. Table 2 shows the differences between the subgroups in terms of IOP control, medication and BCVA outcome throughout the study.

Application of previous SLT treatment (single session, range between 3 and 24 months before surgery) in OAG or OHT eyes did not influence the final postop IOP result at 12 months. Subgroup analysis (no previous SLT versus previous SLT) showed similar age (77±7.5 vs 76±8.49 years, p=0.910), comparable IOP (18.42±4.23 mm Hg vs 18.57±3.43 mm Hg, p=0.902) and intensity of treatment (2.1±1.01 substances vs 2.5±0.76 substances, p=0.165) at baseline. At 12 months, we found a similar number of topical medications used to control the IOP ('no previous SLT' group versus previous SLT' group=1.15±1.0 vs 1.69±0.75 substances, p=0.09), regardless of previous SLT application. Table 3 summarises the IOP levels for both groups at each time point in the study.

In the ICE2 group, we found significant correlations between elevated IOP at baseline and IOP at week 1 (r^2=0.302, p=0.009), week 5 (r^2=0.220, p=0.043) and 12 months postop (r^2=0.552, p=0.000). Wider area of ECP treatment was correlated with lower IOP at week 5 postop (r^2=−0.256, p=0.022). Based on this correlation, a stepwise ANOVA analysis was used to create prediction models. As such, we found that for the final IOP level, there was a significant effect of the initial IOP [F(1,61)=27.66, p<0.001], explaining alone 31.2% (R Square) of the final IOP result. Baseline IOP and IOP at week 5 postop explained together 36.6% (R Square) of final IOP level, [F(2,60)=17.29, p<0.001], as shown in online supplementary table 1.

In the phaco-iStent group, the IOP at 12 months was weakly correlated with two parameters: elevated IOP at baseline (r^2=0.288, p=0.026) and IOP at week 5 postop (r^2=0.436, p=0.001). Based on the correlation analysis, a significant effect was detected for a single parameter (IOP at week 5 postop), which predicted 19.0% of the final IOP (F(1,44)=10.33, p=0.002), as shown in online supplementary table 2.

Table 2 ICE2 group—parameters comparison at all time points of the study according to the ECP extent of treatment

Parameter (mean±SD)	Group A—ECP≤210° (n=20 eyes)	Group B—ECP>210° (n=43 eyes)	P value (t test)
Baseline			
BCVA (log MAR)	0.20±0.13	0.29±0.19	0.06
IOP (mm Hg)	20.85±5.0	19.56±3.95	0.318
No. of meds	2.40±0.99	2.14±1.1	0.372
Week 1			
BCVA (log MAR)	0.12±0.08	0.12±0.09	0.845
IOP (mm Hg)	12.30±3.06	13.14±3.11	0.328
No. of meds	2.25±1.11	1.86±1.08	0.193
Week 5			
BCVA (log MAR)	0.11±0.07	0.13±0.11	0.542
IOP (mm Hg)	15.60±4.29	13.16±2.82	**0.009**
No. of meds	1.85±0.98	1.53±1.16	0.299
Month 3			
BCVA (log MAR)	0.1±0.1	0.11±0.08	0.579
IOP (mm Hg)	14.15±3.03	13.28±2.45	0.284
No. of meds	1.70±0.99	1.42±1.07	0.338
Month 6			
BCVA (log MAR)	0.06±0.06	0.06±0.01	0.713
IOP (mm Hg)	14.05±2.19	13.00±1.96	0.161
No. of meds	1.25±0.96	1.28±1.09	0.793
Month 12			
BCVA (log MAR)	0.07±0.09	0.09±0.08	0.305
IOP (mm Hg)	13.90±2.29	12.65±2.03	**0.03**
No. of meds	1.15±1.04	1.29±1.06	0.636

'n' represents the total number of eyes in each subgroup; bolded values point out the statistically significant differences between groups when t test was applied. BCVA, best-corrected visual acuity; ECP, endocyclophotocoagulation; IOP, intraocular pressure; logMAR, logarithm of minimum angle of resolution; No. of meds, number of topical glaucoma medications.

Complications

Final BCVA (logMAR) was 0.11±0.18 (phaco-iStent group) vs 0.08±0.08 (ICE2 group), p=0.309, both significantly improved in both groups when compared with baseline (p<0.001). In the ICE2 group, we found that incidence of cystoid macular oedema (CMO) detected either by OCT or clinical examination was 1.8% (2 eyes). In 5.5% cases (six eyes) at week 5 postop, the IOP was slightly higher than baseline (2–5 mm Hg); this was attributed to the transitory corticosteroid (CS) response; therefore, no change in their glaucoma medication was done at this visit; at the month 3 visit, when the CS had been completely washed out, the IOP was lower than baseline in all eyes and no additional medication was needed. An IOP spike was defined as an increase in IOP more than 10 mm Hg compared with baseline. Two eyes in the ICE2 group developed IOP spikes at week 1 postop due to the patients mistakenly stopping all glaucoma medication. Reinitiation of glaucoma medication decreased the IOP to satisfactory levels. Otherwise, in respect to baseline, no increase in medication was needed throughout the study in the ICE2 group. Anterior segment inflammation did not persist after week 5 in either groups and also no patients required additional surgical intervention in the first year postop. In the phaco-iStent group, 2 eyes (4.3%) developed CMO. All cases of CMO resolved with topical steroids and non-steroidal anti-inflammatories in both groups. By month 3, additional glaucoma medication was required in 10.9% (5 eyes) in phaco-iStent group and this could not be linked to CS response, persistent AC inflammation or

Table 3 Influence of previous SLT treatment on IOP levels during the study

IOP (mm Hg)—mean±SD	No previous SLT (n=71 eyes)	Previous SLT (n=14 eyes)	P value (t test)
Baseline	18.42±4.23	18.57±3.43	0.902
Week 1	13.82±2.94	13.57±3.48	0.783
Week 5	13.85±2.73	14.86±2.71	0.219
Month 3	13.61±2.59	14.07±2.97	0.550
Month 6	13.37±1.8	13.57±2.1	0.596
Month 12	13.15±1.94	12.77±2.08	0.526

'n' represents the total number of eyes in each subgroup; bolded values point out the statistically significant differences between groups when t test was applied.
IOP, intraocular pressure; SLT, selective laser trabeculoplasty.

patients incompliance. In either group, there were no cases of stent obstruction, malposition or hyphaema.

DISCUSSION

The global burden to health systems of diagnosing and treating glaucoma is increasing.[31 32] Much attention and research has gone into developing new therapeutic strategies which aim to increase both the quality of life and efficacy of glaucoma treatment, for which MIGS is one key area.[33] Prior to MIGS, patients would have been offered filtering surgery, if topical medication or laser could not control their glaucoma. Good results with iStent devices have been reported either as stand-alone procedures[11 34] or combined with phacoemulsification[12 35] with various rates of IOP reduction.[10] Second generation of stents (iStent inject) has been proven superior to first generation of iStent in terms of IOP and medication reduction.[4] Similarly, phacoemulsification combined with ECP[17–19] has been shown to lower IOP, although there are scarce prospective data.[14–16 36]

Our results demonstrate that the ICE2 procedure leads to a more significant reduction in IOP at 12 months compared with the phaco-iStent group (35% vs 21%, p=0.03). These findings support previously published data regarding treated patients with primary open angle glaucoma (POAG), where the higher the baseline IOP, the larger the IOP reduction was with therapeutic intervention.[34] Yet we adapted the intensity of treatment (ICE2 versus phaco-iStent procedure) based on more variables (eg, glaucoma severity, intensity of treatment, local tolerance and medicated baseline IOP), so we could achieve a 'individualised IOP' level at 12 months for each patient. The ICE2 procedure also results in a more significant reduction in glaucoma medication use at 1-year postop compared with the phaco-iStent group, with 31.7% of patients on no glaucoma medication, and a further 27% only on one class. In the phaco-iStent group, fewer eyes could be taken completely off medication (19.6%), and 41.3% were on one class of medication. Although no formal quality of life assessment was carried out in this study, many patients reported high level of satisfaction and improvement in their quality of life now that they were medication free or used less eye drops. An economic evaluation of the two treatment groups was outside of the scope of the current study, but will be evaluated in future planned studies.

Longitudinal analysis of the ICE2 group showed a small increase in IOP at week 5 compared with week 1 (13.94mm Hg vs 12.87mm Hg), as this was the period when medication use was often reduced or stopped; also, the CS response should be taken into account for some cases (six eyes). The IOP at subsequent time points were gradually declining, with no evidence that the efficacy of the treatment was tailing off. In fact, the IOP level achieved at month 12 (13.05 mm Hg) was the lowest recorded, except immediate postop results at week 1.

A curved ECP probe was used in all cases to allow a greater treatment area, with 210°−240° easily treated using the 2.2mm main phacoemulsification incision alone. For more than 240°, the side port was also used to treat the subincisional ciliary processes. As noted by Kahook *et al*,[16] patients who underwent combined ECP and phacoemulsification, a greater reduction in IOP has been found if a larger area of ECP has been applied (360° vs 300°). Similarly, we noted a significantly lower IOP achieved at 12 months if more than 210° ECP has been delivered in comparison with the eyes that have been treated with less than 210° ECP.

Cataract surgery alone is known to lower IOP,[37] with the effect more pronounced in smaller eyes.[37 38] The difference in AL and ACD between the two groups was statistically significant; however, such small differences are unlikely to be clinically significant and certainly does not translate to the ICE2 group having a greater phacomorphic component compared with the phaco-iStent group.

The presence or absence of previous SLT treatment did not seem to influence the final IOP, but medication usage at 12 months was lower in patients who did not have previous SLT. The small sample size (14 patients) of this subanalysis means little clinical significance can be drawn from this. Complication rates were low and comparable in both groups with all CMO and IOP increases managed conservatively and resolved completely. Of note, all patients with CMO were using prostaglandin analogue both preoperatively and postoperatively, and this was stopped after CMO detection in all eyes.

In the ICE2 group, significant predictors for month 12 IOP were IOP at baseline and at week 5, whereas in the phaco-iStent group, only the IOP at week 5 had a significant predictive value. This suggests that if target IOP is achieved at the week 5 visit, this serves as a good predictor for continued control of IOP over a 12-month period. Such a finding might have a positive impact on reducing postop outpatient visits as well as improving the patient postop experience, yet caution should be taken before generalising the need for a less frequent follow-up as more variables outside IOP determine the frequency of follow-up. Further studies should be employed in this direction with larger samples and longer follow-up intervals to validate our predictors.

Study limitations

Several factors can be considered as limitations in this study: sample size with unequal distribution among study groups, lack of randomisation, study design (retrospective) and single-centre data which could be subject to selection bias. Inadequate power calculation for assessing the secondary outcomes (eg, prior SLT treatment) could not be improved due to the retrospective nature of the study. Our results demonstrate that ICE2 procedure is both efficacious and safe. Despite lacking a statistical significance, the slightly greater IOP reduction (%) achieved by the consultant may suggest a learning curve present in fellows. Further prospective, randomised multicentre studies with longer follow-up need to be undertaken for assessment of long-term efficacy and safety of the ICE2 procedure in patients with early-to-moderate OAG and OHT.

CONCLUSION

In patients with OHT and early-to-moderate OAG, iStent inject combined with cataract extraction and ECP offers a greater reduction in IOP and glaucoma medication at 12 months compared with phacoemulsification and iStent inject alone. Our study is the first to report postop results after the ICE2

procedure at 12 months, including predictive factors for 1-year IOP outcome. Longer-term outcomes, patient quality of life assessment as well as economic evaluation need to be considered in future work that is planned.

Contributors ADP, ADDOB, MG and GR contributed to the design of the study, data collection, analysis and interpretation. ADP and GR drafted the manuscript and ADP, ADDOB, MG and GR critically revised it. All authors approved the final version published.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests GR is a consultant for Glaukos Inc.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to this study are included in the article or uploaded as supplementary information. Databases containing the deidentified participant data and clinical parameters are available on request from the corresponding author. Reuse is prohibited under all circumstances.

ORCID iDs
Anca Delia Pantalon http://orcid.org/0000-0002-4095-0751
Gokulan Ratnarajan http://orcid.org/0000-0001-7990-5053

REFERENCES

1 Tham Y-C, Li X, Wong TY, *et al*. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology* 2014;121:2081–90.
2 Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA* 2014;311:1901–11.
3 Baudouin C, Liang H, Hamard P, *et al*. The ocular surface of glaucoma patients treated over the long term expresses inflammatory markers related to both T-helper 1 and T-helper 2 pathways. *Ophthalmology* 2008;115:109–15.
4 Popovic M, Campos-Moller X, Saheb H, *et al*. Efficacy and adverse event profile of the iStent and iStent inject trabecular Micro-bypass for open-angle glaucoma: a meta-analysis. *J Curr Glaucoma Pract* 2018;12:67–84.
5 Gazzard G, Konstantakopoulou E, Garway-Heath D, *et al*. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet* 2019;393:1505–16.
6 Ahmed IIK. MIGS and the FDA: what's in a name? *Ophthalmology* 2015;122:1737–9.
7 Fingeret M, Dickerson JE. The role of minimally invasive glaucoma surgery devices in the management of glaucoma. *Optom Vis Sci* 2018;95:155–62.
8 Richter GM, Coleman AL. Minimally invasive glaucoma surgery: current status and future prospects. *Clin Ophthalmol* 2016;10:189–206.
9 Manasses DT, Au L. The new era of glaucoma Micro-stent surgery. *Ophthalmol Ther* 2016;5:135–46.
10 Wellik SR, Dale EA. A review of the iStent(®) trabecular micro-bypass stent: safety and efficacy. *Clin Ophthalmol* 2015;9:677–84.
11 Ahmed IIK, Fea A, Au L, *et al*. A prospective randomized trial comparing Hydrus and iStent microinvasive glaucoma surgery implants for Standalone treatment of open-angle glaucoma: the compare study. *Ophthalmology* 2020;127:52–61.
12 Guedes RAP, Gravina DM, Lake JC, *et al*. Intermediate results of iStent or iStent inject implantation combined with cataract surgery in a real-world setting: a longitudinal retrospective study. *Ophthalmol Ther* 2019;8:87–100.
13 Craven ER, Katz LJ, Wells JM, *et al*. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: two-year follow-up. *J Cataract Refract Surg* 2012;38:1339–45.
14 Yip LW, Yong SO, Earnest A, *et al*. Endoscopic cyclophotocoagulation for the treatment of glaucoma: an Asian experience. *Clin Exp Ophthalmol* 2009;37:692–7.
15 Lima FEL, Carvalho DMde, Avila MPde. [Phacoemulsification and endoscopic cyclophotocoagulation as primary surgical procedure in coexisting cataract and glaucoma]. *Arq Bras Oftalmol* 2010;73:419–22.
16 Kahook MY, Lathrop KL, Noecker RJ. One-site versus two-site endoscopic cyclophotocoagulation. *J Glaucoma* 2007;16:527–30.
17 Cantor AJ, Wang J, Li S, *et al*. Long-Term efficacy of endoscopic cyclophotocoagulation in the management of glaucoma following cataract surgery in children. *J Aapos* 2018;22:188–91.
18 Francis BA, Berke SJ, Dustin L, *et al*. Endoscopic cyclophotocoagulation combined with phacoemulsification versus phacoemulsification alone in medically controlled glaucoma. *J Cataract Refract Surg* 2014;40:1313–21.
19 Lindfield D, Ritchie RW, Griffiths MF. 'Phaco-ECP': combined endoscopic cyclophotocoagulation and cataract surgery to augment medical control of glaucoma. *BMJ Open* 2012;2. doi:10.1136/bmjopen-2011-000578. [Epub ahead of print: 30 May 2012].
20 Armstrong JJ, Wasiuta T, Kiatos E, *et al*. The effects of phacoemulsification on intraocular pressure and topical medication use in patients with glaucoma: a systematic review and meta-analysis of 3-year data. *J Glaucoma* 2017;26:511–22.
21 Poley BJ, Lindstrom RL, Samuelson TW, *et al*. Intraocular pressure reduction after phacoemulsification with intraocular lens implantation in glaucomatous and nonglaucomatous eyes: evaluation of a causal relationship between the natural lens and open-angle glaucoma. *J Cataract Refract Surg* 2009;35:1946–55.
22 Shingleton BJ, Laul A, Nagao K, *et al*. Effect of phacoemulsification on intraocular pressure in eyes with pseudoexfoliation: single-surgeon series. *J Cataract Refract Surg* 2008;34:1834–41.
23 Friedman DS, Jampel HD, Lubomski LH, *et al*. Surgical strategies for coexisting glaucoma and cataract: an evidence-based update. *Ophthalmology* 2002;109:1902–13.
24 Vizzeri G, Weinreb RN. Cataract surgery and glaucoma. *Curr Opin Ophthalmol* 2010;21:20–4.
25 Mansberger SL, Gordon MO, Jampel H, *et al*. Reduction in intraocular pressure after cataract extraction: the ocular hypertension treatment study. *Ophthalmology* 2012;119:1826–31.
26 Ferguson TJ, Swan R, Sudhagoni R, *et al*. Microbypass stent implantation with cataract extraction and endocyclophotocoagulation versus microbypass stent with cataract extraction for glaucoma. *J Cataract Refract Surg* 2017;43:377–82.
27 Chakravarti T. Assessing precision of Hodapp-Parrish-Anderson criteria for staging early glaucomatous damage in an ocular hypertension cohort: a retrospective study. *Asia Pac J Ophthalmol* 2017;6:21–7.
28 European Glaucoma Society Terminology and Guidelines for Glaucoma. European Glaucoma Society Terminology and Guidelines for Glaucoma, 4th Edition - Chapter 2: Classification and terminologySupported by the EGS Foundation: Part 1: Foreword; Introduction; Glossary; Chapter 2 Classification and Terminology. *Br J Ophthalmol* 2017;101:73–127.
29 National Institute for Health and Care Excellence. *NICE guideline - Glaucoma: diagnosis and management*, 2017.
30 Spaeth GL. The normal development of the human anterior chamber angle: a new system of descriptive grading. *Trans Ophthalmol Soc U K* 1971;91:709–39.
31 Flaxman SR, Bourne RRA, Resnikoff S, *et al*. Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. *Lancet Glob Health* 2017;5:e1221–34.
32 Bourne RRA, Stevens GA, White RA, *et al*. Causes of vision loss worldwide, 1990-2010: a systematic analysis. *Lancet Glob Health* 2013;1:e339–49.
33 Saheb H, Ahmed IIK. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol* 2012;23:96–104.
34 Katz LJ, Erb C, Carceller Guillamet A, *et al*. Long-term titrated IOP control with one, two, or three trabecular micro-bypass stents in open-angle glaucoma subjects on topical hypotensive medication: 42-month outcomes. *Clin Ophthalmol* 2018;12:255–62.
35 Gallardo MJ, Supnet RA. Three-year outcomes of combined trabecular micro-bypass and phacoemulsification in a predominantly Hispanic population with primary open-angle glaucoma. *Clin Ophthalmol* 2019;13:869–79.
36 Clement CI, Kampougeris G, Ahmed F, *et al*. Combining phacoemulsification with endoscopic cyclophotocoagulation to manage cataract and glaucoma. *Clin Exp Ophthalmol* 2013;41:546–51.
37 Ling JD, Bell NP. Role of cataract surgery in the management of glaucoma. *Int Ophthalmol Clin* 2018;58:87–100.
38 Day AC, Donachie PHJ, Sparrow JM, *et al*. The Royal College of ophthalmologists' national ophthalmology database study of cataract surgery: report 2, relationships of axial length with ocular copathology, preoperative visual acuity, and posterior capsule rupture. *Eye* 2015;29:1528–37.