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RESEARCH ARTICLE

Safety and Efficacy of Hydrus and I-Stent inject combined with Phacoemulsification in Primary Open Angle Glaucoma Patients: 2 year follow up study

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ABSTRACT

Aims: To compare the safety and efficacy of phacoemulsification combined with two individual kinds of trabecular bypass micro-stent device insertion. This study compares Phacoemulsification with Hydrus stent versus phacoemulsification combined with I-Stent inject W in patients with medically uncontrolled primary open-angle glaucoma (POAG).

Material and Methods: A retrospective comparative case series.

Results: Eighty eyes of 75 patients with 2 years completed follow-up after combined phacoemulsification with trabecular by-pass stent (s) were included. Forty eyes of 37 patients had Hydrus stent (Hydrus Group-PH) and the other 40 eyes of 38 patients had I-stent inject W (I-stent Group-Pi) insertion combined with phacoemulsification and intraocular lens implantation. Patient demographics and preoperative characteristics of the two groups studied are comparable. A post-operative decrease of 20 percentage or more in the IOP was achieved in 33 eyes (82.5%) in PH group and 30 eyes (75%) in Pi group (p=0.57). The Hydrus group (PH) had a post-operative reduction in the mean number of medications in 22 eyes (55%) in comparison to 18 eyes (45%) in the I-stent group (Pi). Second stage trabeculectomy was avoided in 31 eyes (77.5%) in the Hydrus group and 27 eyes (67.5%). There was no significant difference in rate of complications between two groups.

Conclusion: Both Hydrus stent and I-stent inject W combined with phacoemulsification and intra-ocular lens implantation, are efficacious and safe for treating patients with medically uncontrolled mild and moderate primary open-angle glaucoma (POAG). The reduction in the mean IOP and in the mean number of post-operative glaucoma medications was higher for the patients in Hydrus stent group than in I-stent inject W group.

Introduction:

Glaucoma affects an estimated 3% of the global population over 40 years of age[1]. The incidence of cataract & cataract surgery is also increasing with the increase in the aging population worldwide[2]. The strategy usually implemented in Glaucoma treatment is to slow the rate of disease progression by lowering the intraocular pressure (IOP). The reduction of IOP has been shown to reduce glaucoma progression and also the visual field loss[3]. In the last decade, it has increasingly become popular to combine cataract surgery with the relevant minimally (or micro) invasive glaucoma surgery (MIGS) procedures that shunt aqueous-humour into the Schlemm's canal (SC) with devices like I-stent inject W, Hydrus Stent or trabeculotomy ab-interno (e.g. with trabectome)[4,5,9,23]. MIGS devices are widely considered safer than the conventional filtering surgery and can reduce the need for adjunctive topical (Glaucoma medication) therapy without affecting the ocular surface for any subsequent filtration surgery[5]. The two most common schlemm's canal devices used in United Kingdom are the Hydrus Microstent (Ivantis, Inc, Irvine, CA) and the I-Stent Trabecular Micro-Bypass Stent System (Glaukos Corporation, San Clemente, CA). Both devices provide a bypass route for aqueous fluid into the Schlemm's canal through the trabecular meshwork (TM), which is the primary location of the outflow obstruction in open-angle glaucoma (OAG)[6-8]. There are several studies establishing their efficacy but there is a paucity of data directly comparing the two devices Hydrus stent and I-Stent inject W, with regards to their efficacy and safety[5, 9-15].

Our aim in this study is to compare the safety and efficacy profile of Hydrus stent with I-Stent inject W when combined with phacoemulsification in patients with primary open-angle glaucoma (POAG) in a single surgeon / single centre setting.

Material and Methods:

A comparative case-series of 75 consecutive patients undergoing Phacoemulsification combined with either Hydrus stent (Hydrus group-PH) or I-stent inject W (Pi) was undertaken retrospectively. We did not use any formal randomisation process but alternative cases were allocated to either PH or Pi. We got our study approved by the Worcestershire Acute Hospitals NHS Trust audit and research committee and it is also consistent with the Tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects. This single surgeon study only included POAG patients who underwent combined phacoemulsification and micro-invasive glaucoma surgery (MIGS) with Hydrus stent or I-Stent inject W devices in a single surgical centre. All patients who were unable to achieve the target IOP and showed worsening of visual fields, while on maximal-tolerated medical treatment but also with visually significant cataract were consented for combined phacoemulsification with MIGS as a first stage procedure. The target IOP was determined prior to surgery for every patient and set at a level expected to prevent further optic nerve damage and visual field loss.

Exclusion criteria included patients with increased epi-scleral venous pressure, prior angle surgery or filtering procedure, any form of angle-closure glaucoma, presence of corneal oedema or opacity, a history of any refractive surgery, ocular trauma or presence of significant health conditions (bleeding and clotting disorders, uncontrolled diabetes,

serious cardiovascular problems, and chronic obstructive pulmonary disease). Patients with prior history of laser trabeculoplasty were considered acceptable. Patient demographics (age, sex); medical and ocular history including the stage and type of glaucoma and the number of ocular hypotensive medications were recorded. Pre-operative examinations included, best-corrected Snellen visual acuity, IOP measured by Goldman applanation tonometer, anterior chamber angle status, vertical cup-to disc ratio, and automated Humphrey visual field status. Glaucoma staging as per Hodapp classification (recorded as early, moderate, or advanced)[16] and the target IOP were established. Ocular hypotensive medications were not discontinued before surgery.

SURGICAL TECHNIQUE:

All patients were operated by a single surgeon using the same surgical protocol under local anaesthesia at a single centre. Both the Trabecular Bypass devices (Hydrus & I-stent inject W) insertions were performed after the standard phacoemulsification and intra-ocular lens implantation. Details of Hydrus & I-Stent inject surgical insertion techniques are well established and quite well published. Under gonioscopic view, two I-Stents inject W were implanted through the trabecular meshwork into the SC, approximately two clock hours apart. Hydrus stent insertion was also done under gonioscopic assistance via an incision perpendicular from insertion site of stent (usually in the quadrant involving the nasal to the superior angle). The Hydrus stent was then advanced to span approximately 90 degrees of SC, while the 1–2mm inlet segment was left to reside in the anterior chamber. After confirming the proper placement of the device, the implants injector was withdrawn and the viscoelastic was removed.

Postoperative treatment comprised a topical combination of steroids (dexamethasone 0.1% 4 × a day for 4 weeks) and antibiotics (chloramphenicol 0.5% 4 × a day for 2 weeks) following the intervention in each group. Post-operative, the glaucoma medications were continued at the pre-operative level initially. However, they were modified over the study period to achieve the target IOP in each case. There were no patients where glaucoma treatment was completely stopped in the postoperatively.

FOLLOW UP:

All Patients were seen post-operative on the day 1, day 7 and 1, 3, 6, 12, 18 and 24 months. Best corrected Snellen visual acuity (BCVA), IOP measurement with Goldman applanation tonometer, number of glaucoma medications, and number of post-operative complications were recorded. All patients completed the 2-year follow-up and hence, we had a data of all 100% of the eyes at each time point of the study.

SURGICAL SUCCESS:

The efficacy of the procedures performed was analysed based on all available data from the IOP measurements and the number of glaucoma medications. Surgical success was defined as either a post-operative reduction in IOP by 20% or more, or achieving the set target IOP post-operative, avoiding any second stage trabeculectomy surgery.

The primary parameters were the assessment of IOP reduction for each eye at the time of observation, and the reduction of the number

of glaucoma medications used in relation to pre-operative values.

We used the Student's t-test to compare the normally distributed variables. Mann–Whitney U test and the Wilcoxon-Rank-signed-test were applied for any numeric variables that were not normally distributed. Fisher exact test was used to compare the two groups for Sex, race and the incidence of postoperative adverse events. P-values lower than 0.05 were determined to be significant at all times.

Results:

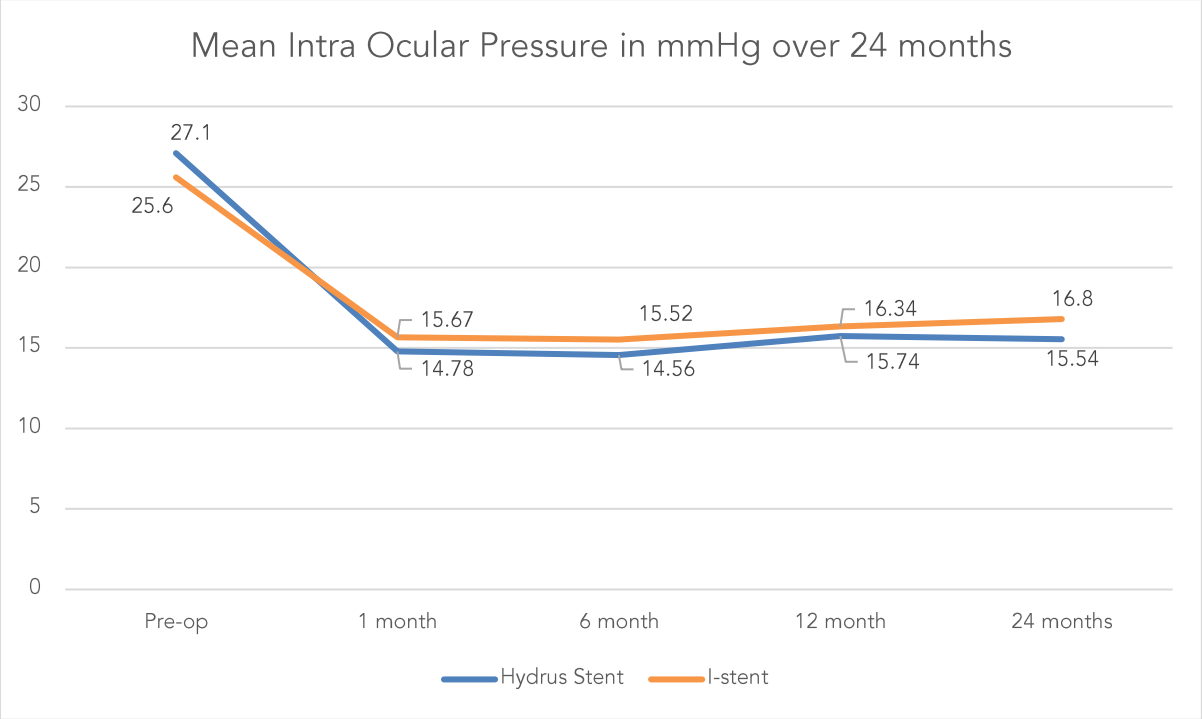
This study included 80 eyes of 75 consecutive patients. A total of 40 eyes underwent combined Phaco-Hydrus stent (PH); and 40 eyes underwent combined Phaco-I-Stent inject W (Pi). Those patients who required treatment in both eyes underwent the same procedure (MIGS device) in both eyes. There was no difference in the two groups with regards to the patient demographics and the pre-operative characteristics ($p > 0.05$) (Table 1).

Table 1. Demographic comparison between two groups: n=80 eyes

Pre-op variables		Phaco-Hydrus Stent (40 eyes/37 subjects)	Phaco-iStent (40 eyes/38 subjects)
Mean Age in Years		76.8±4.3	73.9±3.5
Gender	Male	17	18
	Female	20	20
Mean IOP mmHg		27.1±3.6	25.6±4.3
Mean Visual acuity		6/12	6/12
Mean number of drops		3.4±0.4	3.5±0.54
Stage of glaucoma	Mild	07	09
	Moderate	18	16
	Severe	12	13

The Mean IOP reduced by an average of 12.32 ± 2.4 mmHg in the Phaco-Hydrus (PH) group and 9.93 ± 2.6 mmHg in the Phaco-I-Stent inject W (Pi) group at the first post-operative visit ($p = >0.05$). This was maintained at 24 months as the Mean IOP was reduced by an average of 11.7± 2.2 in PH group and 8.8± 1.7 in the Pi group ($P=<0.05$). Mean IOP was at 15.4 ± 2.1 mmHg in PH group and 16.8 ± 2.9 mmHg in Pi group at 24 months postoperatively (Fig. 1). This shows that the effect of both the types of trabecular stents was satisfactorily maintained throughout the study period.

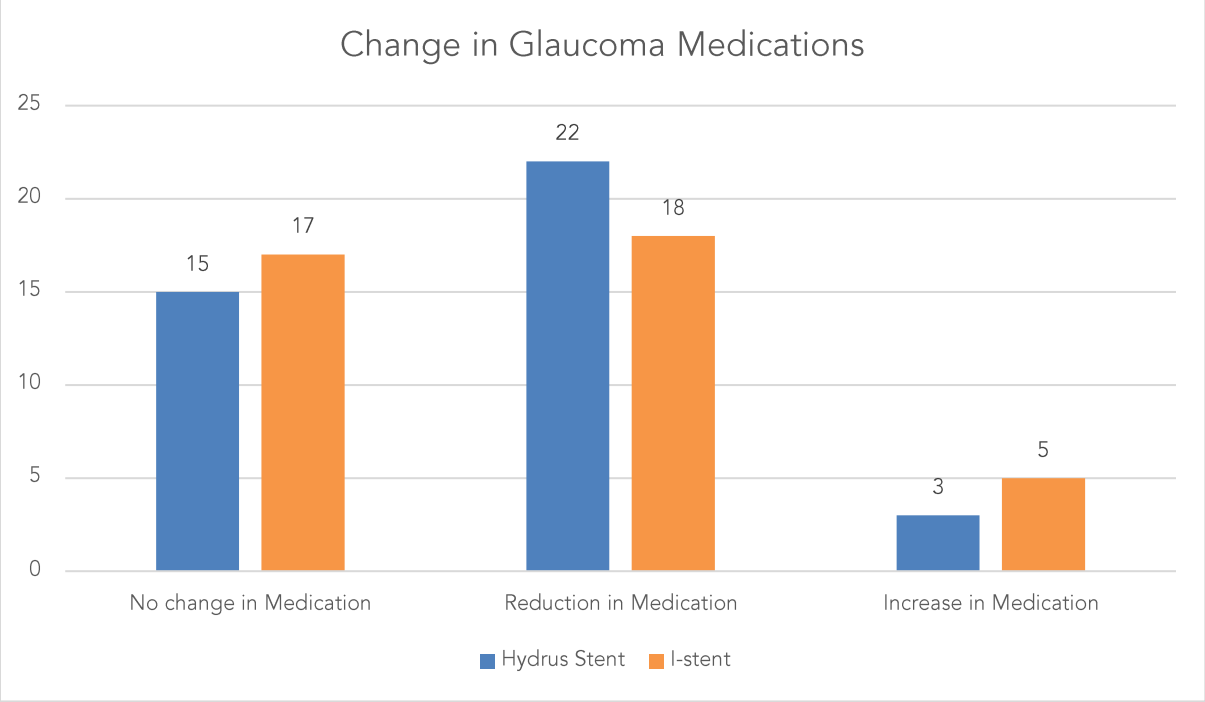
Figure 1. Mean Intra Ocular Pressure in mmHg over 24 months



GLAUCOMA MEDICATIONS:

In this study, 45% of the Pi group had a decrease in post-operative drop use at 24 months compared to the 55% in the PH group (p = >0.05). Following surgery 7.5% in the PH group needed additional glaucoma drops to achieve target IOP compared to 12.5% of the Pi group (p = >0.05) (Fig. 2).

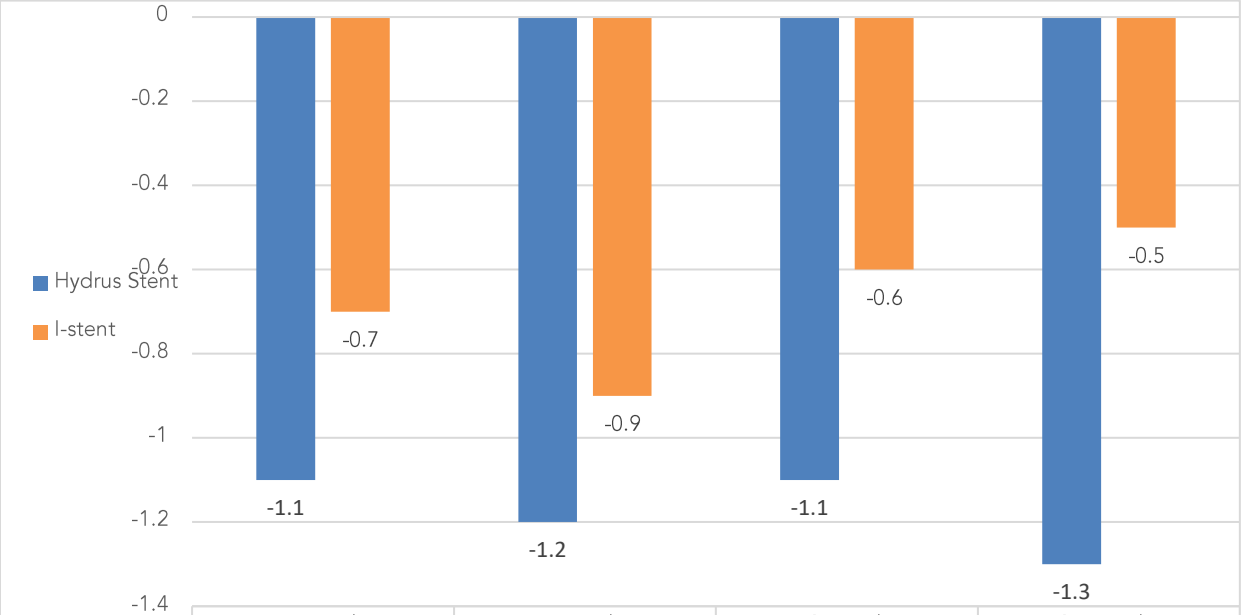
Figure 2. Number of Eyes & change in glaucoma medications



The PH group went from an average of 3.4±0.4 drops to 2.10 ± 0.28 drops post-operative at 24 months. The Pi group averaged 3.52 ± 0.32 drops pre-operative, reducing to needing an average of 3.02 ± 0.38 drops at the 24 months follow up (Fig. 3).

The reduction in the mean number of medication was 1.3 in PH group vs 0.5 in Pi group at 24 months (P=<0.01). The PH group consistently showed more reduction in the medications than Pi group throughout the study period.

Figure 3. Mean drop in number of medications at each follow up

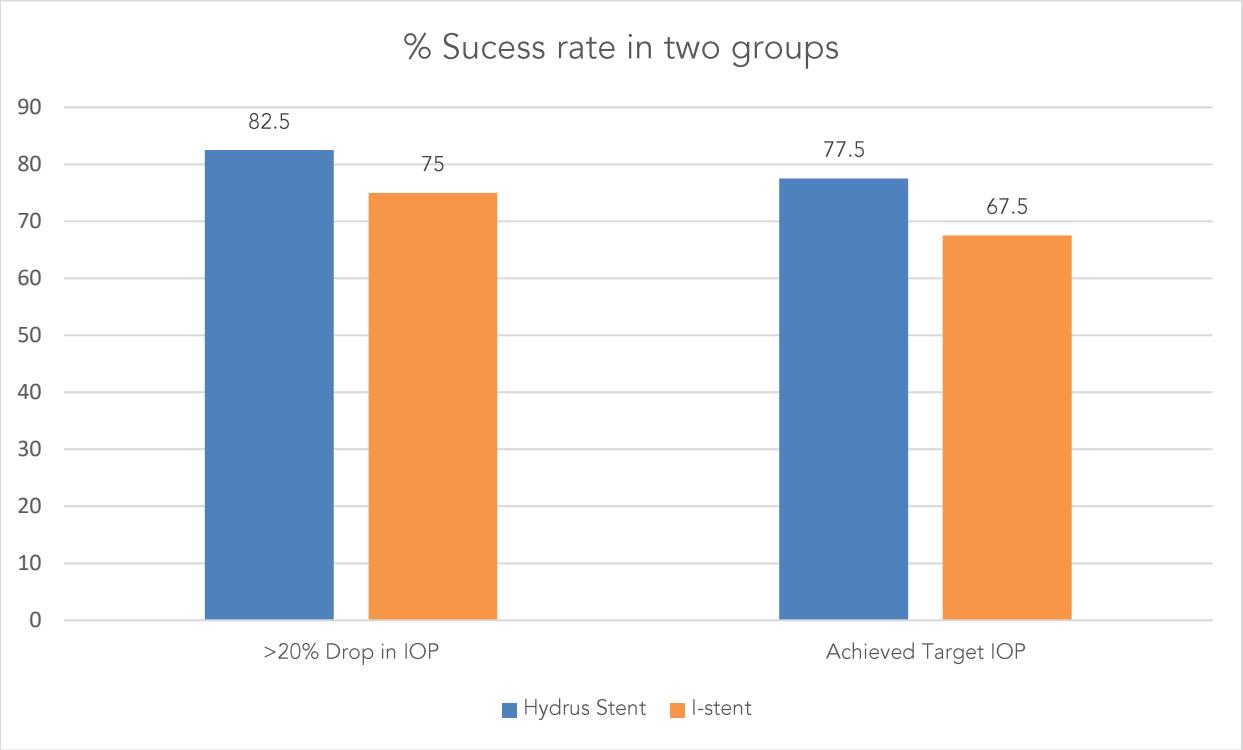


	1 month	6 months	12 months	24 months
Hydrus Stent	-1.1	-1.2	-1.1	-1.3
I-stent	-0.7	-0.9	-0.6	-0.5

SURGICAL SUCCESS:

Figure 4 shows that Hydrus stent group achieved higher success rate for both the primary success outcome criteria, but this was not statistically significant due to small patient population in this study. A 20% drop in post-operative IOP was observed in 33 eyes (82.5%) in PH group and in 30 eyes (75%) in Pi group (p = 0.89). Thirty-one eyes (77.5%) in the PH group and 27 eyes (67.5%) in Pi group achieved and maintained the target IOP and avoided a second stage trabeculectomy over the 2-year period (p = 0.72). Nine eyes (22.5%) in PH group and thirteen eyes (32.5%) in Pi group failed to achieve their set individualised target IOP and, therefore required a subsequent trabeculectomy

Figure 4. Percentage of eyes achieving success rate as per agreed definition



VISUAL ACUITY:

Visual acuity improved or remained at the pre-operative level in 37 eye (92.5%) in both PH & Pi group. Both groups had 3 eyes (7.5%) with poorer post-operative BCVA (at least 1 or more-line drop in Snellen visual acuity) at the 24-month period. The cause for poor visual outcome was cystoid macular oedema related changes in one study-eye in each of the groups. Two eyes in the PH group showed worsening of vision related to age related macular degeneration and ischaemic optic neuropathy while the Pi group had 2 eyes with wet Age related Macular Degeneration related visual deterioration.

COMPLICATIONS:

Complication rates in both the groups were low. Cystoid macular oedema was seen in one study-eye in each group. OCT of macula was done if the post-operative BCVA was less than 6/6. Both cases of CMO resolved but did leave residual epi-retinal membrane. We did not see any cases of ocular hypotony where the IOP drop below 8 mmHg at any stage, in either of the groups. Other comorbidities seen were wet Age related macular degeneration and ischaemic optic neuropathy.

Discussion:

Primary open-angle glaucoma (POAG) is a significant cause of ocular morbidity Worldwide. It leads to blindness in a significant number of individuals, even while the patients remained under glaucoma treatment[17,18,19, 20, 21]. Glaucoma progression and visual field loss can be reduced by a sustained reduction in intraocular pressure[3]. The advent of trabecular bypass stent insertion at the time of cataract surgery has allowed improvement in the conventional aqueous outflow with a good safety profile.

There are several studies showing that the MIGS devices may be safer than conventional Glaucoma filtering surgery, can eliminate or reduce adjunctive topical medication therapy, and do not impede or preclude subsequent filtration surgery[22]. I-stent inject & Hydrus stent are the most common trabecular bypass stents used currently and have been shown to be effective in lowering the IOP with minimal side effects.[4,11,14,15,23,24]. There is paucity of data on direct comparison of I-stent inject & Hydrus stent[5,10].

The COMPARE study compared the efficacy of Hydrus microstent or 2 I-Stent Trabecular Micro Bypass devices for reducing intraocular pressure (IOP) and medications in open-angle glaucoma (OAG) in a prospective, multicentre, randomized, single-masked clinical trial. This trial found that at 12months, the Hydrus had a greater rate of complete surgical success ($P < 0.001$) and reduced medication use ($P=0.004$). There were more patient's medication-free at 12 months in Hydrus stent group ($P =0.0057$). Holmes compared the Hydrus implant with the I-Stent inject implant. He showed a sustained IOP reduction with a good safety profile for both groups at 24 months. There was no significant difference in the IOP outcomes between the groups[9].

Hu et al[10] carried out a systematic review and a network meta-analysis comparing the efficacy and safety of two Schlemm's canal-based micro invasive glaucoma surgery (MIGS) devices, the Hydrus Micros tent and the I-Stent Trabecular Bypass combined with phacoemulsification and intra-ocular lens implantation for the treatment of open-angle glaucoma. This systemic review included six prospective RCTs comprising a total of 1397 patients. This study found that regarding the absolute value and the percentage of IOPR (IOP reduction), the Hydrus and 2-iStent implantation combined with phacoemulsification were significantly more effective than phacoemulsification alone. It also concluded that the Hydrus implantation may have a slight advantage over the 1-iStent or 2-iStent implantation in combination with phacoemulsification to treat open-angle glaucoma.

In our study, there was no statistically significant difference between the two groups in regard to demographic characteristics. The drop in mean IOP post-operative was consistently more in the Hydrus group at all stages of the study. The drop in mean IOP was maintained at 24 months as the Mean IOP was reduced by an average of 11.7 ± 2.2 in PH group and by 8.8 ± 1.7 in the Pi group ($P<0.05$). Our results suggest that though both the devices and procedures are reasonably effective in reducing IOP post-operative, Hydrus stent achieved significantly lower IOP than I-stent inject W. In our study, the PH group achieved higher success rate (82.5% in PH group vs 75% in Pi group). We also compared the groups to find if they achieved the target IOP and prevented subsequent 2nd stage trabeculectomy surgery. The PH group achieved higher success of 77.5% in comparison to 67.5% in Pi group in achieving the target IOP and avoiding the second stage trabeculectomy over a 2-year period ($p = 0.79$). There was no statistically significant difference between the two groups with either of the success outcome criteria. Medication use was reduced by a greater margin in PH group. The statistically significant difference in the reduction in mean number of glaucoma medications post-operative was -0.8 in favour of PH group at 24

months (P<0.01). The PH group consistently showed more reduction in the number of glaucoma medications than the Pi group throughout the study period. Our results are consistent with the COMPARE study as well as with the findings of Hu et al.

We found that both groups were similar with regards to the safety observations, even with the generally moderate disease severity in our study population. The Visual acuity score was comparable between the 2 study groups throughout the 24-month postoperative follow-up period. The rate of cystoid macular oedema was also similar. The predominant cause for poor visual outcome was wet type of age-related macular degeneration.

The most serious risks of conventional glaucoma surgery such as Ocular hypotony, significant vision loss, infections, and bleb-related complications, were not noted in both the treatment groups, as expected for a Minimally Invasive Glaucoma procedure. There has been some concern with regards to corneal endothelial cell loss in glaucoma surgery[18]. Horizon trial proved that there was sustained loss of endothelial cell after 3 months of the surgical insult[23]. We did not find any corneal oedema, decompensation or failure in any of our cases in either of the groups throughout the study period.

Conclusion:

Our study supports that trabecular bypass stent surgery combined with phacoemulsification may help a significant number of primary open angle glaucoma patients to achieve and maintain a lower IOP with reduced medication burden, thus improving their quality of life by slowing / stabilising the disease progression with significantly less risks taken.

The limitations of this study include the retrospective data collection, lack of true randomisation and the potential bias in choosing one technique over the other. The study did not have attrition and has a relatively long follow-up period of 2 years.

Conflicts of Interest:

All authors report no financial relationships (including employment, grants, patent ownership, and other interests) with any commercial entities that have an interest in the subject matter or materials discussed in the manuscript. The authors have no conflicts of interest to declare.

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