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Micro-Invasive Glaucoma Surgery with the iStent inject: Impact on IOP and Medication Burden in a Real-World Setting

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Abstract

Background: The iStent inject is a Micro-Invasive Glaucoma Surgical (MIGS) device that has shown to reduce IOP and to be safe for glaucoma patients with fewer complications than regular surgery. **Objective:** To investigate, up to 15 - 20 months, the efficacy and safety of implantation of two second-generation trabecular microbypass stents in patients with or without prior glaucoma surgery. **Methods:** Fifty-seven eyes were implanted with the iStent inject. The population was comprised of eyes with primary open-angle glaucoma (n = 51), pseudoexfoliation glaucoma (n = 5) and ocular hypertension (n = 1). Major outcome parameters included IOP, medication needs and corrected distance visual acuity (CDVA). Follow-up time points were one day, 2 - 4 months, 9 - 14 months and 15 - 20 months. **Results:** The main reason to perform MIGS was IOP reduction in 68.4%, reduced number of medications due to drug intolerance in 24.6% and reduced medication due to compliance issues in 7.0% of the eyes. IOP decreased by 22.47%, from 19.40 ± 3.83 mmHg preoperatively (preop) to 15.04 ± 1.67 mmHg at 15-20 months postoperatively. IOP reduction was achieved at all follow-up time points ($p < 0.001$). A decrease in the number of medications was achieved in 32.1% of the patients after 15 - 20 months. **Conclusions:** Insertion of the iStent inject in patients with or without prior glaucoma surgery shows effective and sustained improvements in IOP with no safety concerns.

Keywords

iStent inject, MIGS, Glaucoma, Intraocular Pressure, Visual Acuity, Medication Need

1. Introduction

Glaucoma is the leading cause of blindness worldwide and the number of pa-

tients affected with this disease increased with life expectancy [1]. In 2020 it is estimated that the global prevalence of glaucoma will be 76 million people [2]. Glaucoma is characterized by progressive damage of the optic nerve associated with progressive visual field defect, that is often accompanied by elevated intraocular pressure (IOP) [1].

The main goal of treatment is to preserve vision loss and quality of life (QoL), which is clearly dependent on control of intraocular pressure [2].

Therefore, treatments aim to decrease IOP, given this is the primary, well established, modifiable risk factor for the progression of glaucoma [2] [3]. Topical medications are frequently used, although their effectiveness is limited by local and systemic side effects, ocular surface damage, and suboptimal patient adherence [1]. Traditional surgical treatment, trabeculectomy, involves the creation of a filtering bleb to reduce IOP. However, it carries the risk of failure and long-term complications [4] [5].

Micro-Invasive Glaucoma Surgery (MIGS) provides an alternative to more invasive or laser surgical methods, showing consistent reductions in IOP and medication burden, while also maintaining favorable long term safety [1] [3]. The iStent inject (Glaukos Corp., San Clemente, CA, USA) is an ab interno glaucoma implant in the MIGS treatment field, [5] which includes two trabecular stents, designed to be implanted into the Schlemm canal that augments the physiologic outflow through the conventional outflow pathway [1] [5]. This device can be implanted in a standalone procedure or in combination with cataract surgery [2]. In both investigational and real-world settings, the iStent inject revealed a significant decrease in IOP and medication burden in the long term (reduction or elimination of the need for IOP-lowering medications), accompanied by a favorable safety profile [1] [2] [3].

After iStent inject treatment, costs are higher in year zero compared with pharmacological therapies. However, annual costs thereafter are lower. Therefore, treatment with MIGS surgery may reduce health costs directly or indirectly [6].

The aim of this study is to present the results of iStent inject implantation up to 15 - 20 months after surgery in glaucoma patients, with or without prior glaucoma surgery.

2. Materials and Methods

2.1. Patients and Procedures

This was a retrospective study including patients with iStent inject implantation with or without prior glaucoma surgical interventions from May 2016 until June 2019 at the Department of Ophthalmology at the Klinikum Region Hannover Nordstadt, Hannover, Germany. The procedures were performed by a single surgeon at one center. All patients who underwent iStent inject implantation at the clinic were followed over a period of two years. Data were obtained preoperatively and at 1 day, 2 - 4 months, 9 - 14 months and 15 - 20 months after sur-

gery. Inclusion criteria were eyes with primary open angle glaucoma (POAG), pseudoexfoliation glaucoma (PEX) and ocular hypertension. This study was conducted in accordance with the Declaration of Helsinki in its latest amendment (Brazil, 2013). Due to the type of study and since it was a retrospective analysis of anonymous data, submission to ethical approval was not necessary. International data protection guidelines were followed for all data processing.

2.2. Device Description

The second-generation trabecular microbypass stent, or iStent inject, encompasses two trabecular microbypass stents that are pre-loaded on a single device to permit insertion of both in the same procedure. In comparison to the first-generation device, the iStent, the two stents included on the iStent inject are smaller in size (0.36 mm × 0.23 mm) and each includes 4 lateral outlet lumina that aim to produce multidirectional outflow.

2.3. Main Outcome Measures

Primary outcome measures included mean postoperative IOP via Goldmann applanation tonometry and ocular hypotensive medication burden. The proportion of patients with a decrease of IOP and mediation needs from preoperatively compared to follow-up visits was considered as a surgical success. All patients included in this evaluation were scheduled for IOP profile measurement and the IOP was measured with the Goldmann tomometer. A visual field measurement was performed and target IOP was defined prior to the iStent inject surgery and the postoperative medication was adjusted accordingly. Visual acuity outcomes were also evaluated using standard charts.

2.4. Statistical Analysis

Descriptive statistics were used to summarize pre- and postoperative data. Statistical inference of preoperative IOP vs postoperative IOP at all follow-up time points was performed using a paired samples t-test. The McNemar test was used to compare pre- and postoperative proportions. An $p < 0.05$ (two-sided) was considered statistically significant.

3. Results

Forty-five patients with a total of 57 eyes with POAG (51 eyes), PEX (5 eyes) and ocular hypertension (1 eye) were included. Prior glaucoma surgical interventions were performed in 15.8% (9 eyes). A total of 63.2% (36 eyes) were from female patients and 36.8% from males (21 eyes), with a mean age and standard deviation of 73.32 ± 8.17 years and a range of 55-89 years. The main reason to perform MIGS was IOP reduction in 68.4%, reduced number of medications due to drug intolerance in 24.6% and reduced number of medication due to compliance issues in 7.0% of the eyes. A stand-alone MIGS procedure was performed in 49.1% (28 eyes) of the patients, the other 29 eyes underwent iStent inject im-

plantation combined with cataract surgery.

The preoperative corrected distance visual acuity (CDVA) was 0.29 ± 0.25 LogMar. Besides not reaching the target IOP in all patients, no complications occurred. Table 1 shows the demographic and preoperative data for the cohort.

3.1. Intraocular Pressure Reduction

Mean IOP reduction was achieved for the entire cohort and the standalone as well as the combined surgery group at all time points of follow-up compared to preoperative IOP ($p < 0.001$). A mean IOP decrease of 22.47%, from baseline 19.40 ± 3.83 mmHg to 15.04 ± 1.67 mmHg at 15 - 20 months post-operatively, was observed in Table 2.

All eyes achieved an IOP ≤ 18 mmHg after 15 - 20 months of surgery. Almost half of the eyes (49.12%) attained an IOP ≤ 15 mmHg after 15 - 20 months of follow-up and 59.65% of the eyes had an IOP decrease of ≥20% vs preoperative, at 15 - 20 months of follow-up. However, these differences were not statistically significant in Table 3.

3.2. Medication Burden

More than 32% of the eyes achieved a reduction in glaucoma medication at 15 - 20 months of follow-up compared to preop, although it did not reach statistical significance at any time point. None of the eyes at 15 - 20 months of follow-up were completely medication-free. The number of medications was reduced from preoperative 2.94 ± 1.01 to 2.75 ± 1.04 after 15 - 20 months, but this difference was not statistically significant. There was a slight non-significant decrease of eyes on ≥3 medications (62.26%) compared with preop (66.04%) and during follow-up 83.02% of the eyes maintained or decreased their medication needs in Table 4.

Table 1. Demographic and preoperative characteristics.

		N = 57 eyes (45 patients)
Age (years)	Mean ± SD	73.32 ± 8.17
	Range	55 - 89
Gender	Male/Female	21/36
Eye	OD/OS	25/32
Prior Glaucoma Surgical Interventions	N (%)	9 (15.79)
CDVA (LogMar)	Mean ± SD	0.29 ± 0.25
Type of Glaucoma	N (%)	
	POAG	51 (89.47)
	PEX	5 (8.77)
	Ocular hypertension	1 (1.75)

POAG, primary open angle glaucoma; PEX, pseudoexfoliation glaucoma; CDVA, Corrected Distance Visual Acuity; SD, Standard deviation; OD, oculus dextrus; OS, oculus sinistro.

Table 2. Intraocular pressure by visit (available eyes at each visit).

	Preop	1D	2 - 4 M	9 - 14 M	15 - 20 M
Total cohort					
N	57	57	54	57	57
Mean (mmHg)	19.40	13.18	15.26	14.89	15.04
SD	3.83	3.19	2.47	1.86	1.67
p-value compared to preop	--	<0.001	<0.001	<0.001	<0.001
Stand-alone surgery group					
N	28	28	28	28	28
Mean (mmHg)	19.21	12.43	14.89	14.89	14.93
SD	4.42	3.38	2.77	2.28	1.98
p-value compared to preop	--	<0.001	<0.001	<0.001	<0.001
Combined surgery group					
N	29	29	26	29	29
Mean (mmHg)	19.59	13.90	15.65	14.90	15.14
SD	3.22	2.86	2.08	1.37	1.33
p-value compared to preop	--	<0.001	<0.001	<0.001	<0.001

D, Day; M, month; Preop, preoperative; SD, Standard deviation. *p-values from paired samples t-test.

Table 3. Proportional analysis of postoperative IOP (Available eyes at each visit).

	Preop n (%)	1D n (%)	2 - 4 M n (%)	9 - 14 M n (%)	15 - 20 M n (%)
Available at Visit	57	57	54	57	57
IOP ≤ 15 mmHg	6 (10.53%)	44 (77.19%)	26 (48.15%)	30 (52.63%)	28 (49.12%)
IOP ≤ 18 mmHg	22 (38.60%)	56 (98.25%)	50 (92.59%)	56 (98.25%)	57 (100.00%)
IOP decreased ≥ 20% vs preop IOP		46 (80.70%)	29 (53.70%)	36 (63.16%)	34 (59.65%)

D, Day; IOP, Intraocular Pressure; M, month; Preop, preoperative; SD, Standard deviation.

3.3. Visual Acuity

Table 5 shows the changes in visual acuity (VA) from baseline. At all follow-up time points except for one day ($p = 0.104$), all patients had an improved VA compared to preoperatively ($p < 0.001$) and 83.63% of the eyes had a similar or improved VA at 15 - 20 months postoperatively. VA was significantly improved at all follow-up visits in the combined surgery group. No significant VA differences to the preoperative value were found in the stand-alone group.

Overall, at the end of the follow-up period, 66.67% (26 of 39 eyes) achieved an IOP reduction, and 38.89% (7 of 18 eyes) reached the goal of reducing the medication burden in Table 6.

Table 4. Medication analysis (available eyes at each visit).

	Preop n (%)	2 - 4 M n (%)	9 - 14 M n (%)	15 - 20 M n (%)
Available at Visit	53	51	53	53
Eyes on 0 med	0 (0.00%)	2 (3.92%)	0 (0.00%)	0 (0.00%)
Eyes on 1 med	5 (9.43%)	6 (11.76%)	8 (15.09%)	8 (15.09%)
Eyes on 2 meds	13 (24.53%)	13 (25.49%)	13 (24.53%)	12 (22.64%)
Eyes on 3 meds	15 (28.30%)	12 (23.53%)	14 (26.42%)	18 (33.96%)
Eyes on 4 meds	20 (37.74%)	18 (35.29%)	18 (33.96%)	15 (28.30%)
Mean no. of meds	2.94	2.75	2.79	2.75
SD	1.01	1.18	1.08	1.04
No change in meds from preop		32 (62.75%)	29 (54.72%)	27 (50.94%)
Increase in meds from preop		7 (13.73%)	9 (16.98%)	9 (16.98%)
Decrease in meds from preop		12 (23.53%)	15 (28.30%)	17 (32.08%)

med, medication; M, month; Preop, preoperative; SD, Standard deviation.

Table 5. Visual acuity (LogMar) and changes from baseline by visit (available eyes at each visit).

	Preop	1D	2 - 4 M	9 - 14 M	15 - 20 M
Total Cohort					
N		55	52	55	55
Decrease vs. preop. n (%)		20 (36.36%)	23 (44.23%)	25 (45.45%)	25 (45.45%)
Increase vs. preop. n (%)		9 (16.36%)	10 (19.23%)	10 (18.18%)	9 (16.36%)
No change vs. preop. n (%)		26 (47.27%)	19 (36.54%)	20 (36.36%)	21 (38.18%)
Stand-alone surgery group					
N	28	28	28	28	28
Mean (LogMar)	0.28	0.32	0.27	0.29	0.28
SD	0.25	0.25	0.24	0.24	0.24
p-value compared to preop	--	0.115	0.676	0.865	0.764
Combined surgery group					
N	29	29	26	29	27
Mean (LogMar)	0.30	0.21	0.19	0.18	0.18
SD	0.26	0.29	0.27	0.27	0.27
p-value compared to preop	--	<0.001	<0.001	<0.001	<0.001

D, DAY; M, month; Preop, preoperative; SD, Standard deviation.

Table 6. Goal achieved (IOP reduction or reduction of medication needs).

	IOP reduction (N = 39)			Reduction of medication needs (N = 18)		
	2 - 4 M	9 - 14 M	15 - 20 M	2 - 4 M	9 - 14 M	15 - 20 M
achieved N (%)	24 (61.54%)	29 (74.36%)	26 (66.67%)	4 (22.22%)	6 (33.33%)	7 (38.89%)
not achieved N (%)	15 (38.46%)	10 (25.64%)	13 (33.33%)	14 (77.78%)	12 (66.67%)	11 (61.11%)

M, month; IOP, Intraocular Pressure.

Table 7. IOP development in group with primary goal "IOP reduction".

Better IOP reduction group	Preop	2 - 4 M	9 - 14 M	15 - 20 M
IOP				
N	39	38	39	39
Mean (mmHg)	19.90	15.13	14.72	15.03
SD	3.64	2.61	1.85	1.65
p-value compared to preop	--	<0.001	<0.001	<0.001
Reduce medication group (compliance and tolerance issues)	**Preop**	**2 - 4 M**	**9 - 14 M**	**15 - 20 M**
Reducing Medication				
N	17	15	17	17
Mean (mmHg)	2.73	2.73	2.65	2.59
SD	1.03	1.10	1.12	1.00
p-value compared to preop	--	1.000	0.651	0.508

M, month; IOP, Intraocular Pressure; Preop, preoperative; SD, Standard deviation.

Table 7 shows the IOP development for the group with the major intention of IOP reduction and the number of medications at each visit. Significantly lower IOP than baseline was achieved at all visits in the group for which a better IOP reduction was intended. The mean number of medications was reduced after 9 - 14 and 15 - 20 months, but the difference was not statistically significant.

4. Discussion

This is a real-world study of MIGS in patients with different types of glaucoma. The data presented aimed at evaluating the effects of the iStent inject implantation in patients with glaucoma, after one day, 2 - 4 months, 9 - 14 months, and 15 - 20 months post-op. Surgeries were performed by a single surgeon in a real-world clinical setting, therefore these data can be relevant to ophthalmologists with patients with different types of glaucoma [5] [7].

At 15 - 20 months post-operatively, the iStent inject implantation achieved an IOP reduction of 22.47%. This statistically significant reduction was observed at all follow-up time points ($p < 0.001$). Moreover, more than half of the eyes

(59.55%) had an IOP decrease ≥ 20% compared to preop. The effect of iStent inject on lowering IOP may be related to the characteristics of the device that uses an ab interno microincisional approach, which minimizes trauma, [1] enhances aqueous outflow using the physiological pathway via Schlemm's canal, and leads to a faster recovery and lower post-operative complication rate as compared to other surgeries [8].

The IOP reduction in our study is comparable to that observed in other studies [1] [3] [4] [9]. Also the range of post-op IOP reduction compared with baseline is concordant with our data [1] [3] [4] [7] [9] [10].

Regarding medication reduction, some studies suggest that after surgery there may be a benefit on reducing and/or eliminating preop glaucoma medications [5]. In our series, none of the patients were receiving no medications pre-operatively, which is lower than reported in other studies [3] [5] [11] [12], and may indicate the severity of glaucoma [1]. At the end of follow-up, 32.08% decreased the medication burden compared to preop, although it did not reach statistical significance. The majority of the patients (66.04%) were receiving ≥ 3 medications preop. Several studies have reported that patients receiving more glaucoma medications or more complex medication regimens may have greater difficulty with medication adherence, [11] which may explain our results. In addition, MIGS with the iStent inject is helpful as a safe and minimally invasive add-on treatment to reach a desirable IOP.

As can be expected, there was a significant improvement in CDVA in the combined surgery group compared with preop at all time points ($p < 0.001$) except on the day after surgery. No significant changes in CDVA were observed in the standalone group. Furthermore, 88.63% of the eyes improved or maintained visual acuity compared to preop, reinforcing the evidence that the iStent inject implantation is a safe procedure [1] [10] [13].

The iStent inject causes a positive impact on achieving IOP reduction after 15 - 20 months in more than half of the eyes. These results are compelling, support the MIGS procedure with this device, and show an improved CDVA. This particular MIGS surgery provides an opportunity to decrease complications after surgery through the physiological pathway of the device, reduces costs, since it lessens the financial burden of glaucoma for patients and government, [1] and improves quality of vision and QoL [14].

No glaucoma groups were defined for data evaluation since the number of eyes in the groups is too small compared to the POAG group, which is a limitation of this study. Furthermore, this study was of observational character and did not involve a control group.

5. Conclusion

15 to 20 months data demonstrated a significant decrease in IOP and CDVA after iStent inject implantation. The safety of this device was also guaranteed. Thus, this study supports the effectiveness of iStent inject, improving QoL in

glaucoma patients and provides a useful reference for ophthalmologists and patients who are evaluating their glaucoma treatment options.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper. The author received a research grant for statistical evaluation of the data.

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