Hiroshima J. Med. Sci.
Vol. 72, No. 3·4, 27~31, December, 2023
HIMJ 72–5

Preliminary outcomes of cataract surgery with iStent inject® W

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ABSTRACT

This study was performed to investigate the preliminary outcomes and complications of patients with glaucoma who underwent cataract surgery with iStent inject® W implantation. The study involved 32 eyes of 27 patients (mean age, 69.2 ± 10.0 years) who underwent cataract surgery with an iStent inject® W from November 2020 to June 2021 at Kyorin University Hospital and were followed up for at least 3 months. Intraocular pressure (IOP), mean number of medications, and postoperative complications were retrospectively reviewed from the medical records. The mean number of medications was represented by a score of 1 point for a single eye drop for glaucoma and 2 points for a combination drug. Thirty-one eyes had primary open-angle glaucoma and one had exfoliation glaucoma. The preoperative and 1-month postoperative IOP was 17.1 ± 3.0 and 16.4 ± 2.6 mmHg, respectively, with no significant difference (p = 0.6183). Three months postoperatively, however, the IOP significantly decreased to 14.7 ± 2.4 mmHg (p = 0.0020). The mean number of medications preoperatively and 1 and 3 months postoperatively was 3.4 ± 1.1, 1.8 ± 1.0, and 2.1 ± 1.2, respectively, showing a significant decrease after 1 and 3 months ($p < 0.0001$ for both). Postoperative complications included stent occlusion by the iris in two eyes, anterior chamber hemorrhage in one eye, and temporary IOP elevation in two eyes. Temporary IOP elevation and anterior chamber hemorrhage resolved within approximately one week of postoperative follow-up. Cataract surgery with the iStent inject® W showed no serious intraoperative or postoperative complications. It is useful for lowering the IOP and reducing the number of medications in patients with glaucoma.

Key words: *iStent Inject® W*, *Open-angle Glaucoma*, *Cataract Surgery*, *Postoperative Complications*

INTRODUCTION

Implant surgery has recently become widespread in glaucoma treatment. In the field of minimally invasive glaucoma surgery (MIGS), cataract surgery combined with titanium intraocular stent implantation has become the world's first outflow tract reconstruction combined with instrument placement. The first version of this titanium intraocular stent device was called the iStent® Trabecular Micro-Bypass Stent System (Glaukos Corp., Aliso Viejo, CA, USA; hereinafter referred to as the iStent®)[3,6]. The iStent® is an L-shaped device that is placed in the trabecular meshwork. It was inserted into Schlemm's canal using a special inserter. This product was approved in Japan in 2016. The shape of the iStent® device thereafter improved, resulting in development of the iStent inject® Trabecular Micro-Bypass Stent System (hereinafter referred to as the iStent inject®), a second-generation intraocular drain for combined cataract surgery[2,5]. The iStent inject® was approved for use in Europe in 2012 and in the United States in 2018. However, the iStent inject® was not approved in Japan; only the iStent inject® W, described below, can be used in this country. In addition to improvements in shape, the maximum number of devices that can be inserted has also increased. With the iStent®, the number of devices that can be inserted is one per inserter, but with the iStent inject® and iStent inject® W, it is now possible to insert up to two devices per inserter. As a result, two devices can be inserted in a single procedure when using the iStent inject® and iStent inject® W. A retrospective study comparing cataract surgery with the iStent® versus iStent inject® showed that both the rate of intraocular pressure (IOP) reduction and the efficacy of eye drop reduction at 12 months were significantly better in the iStent inject® group, and there was no difference in the rate of complications[7]. Notably, because the iStent® involves one insertion per procedure while the iStent inject® involves two insertions per procedure, it is possible that a higher number of device insertions may provide superior surgical efficacy. However, it is difficult to compare these results owing to the different types of devices used.

Both the iStent® and iStent inject® have a common IOP-lowering mechanism, and when placed in Schlemm's canal, a bypass between the anterior chamber and Schlemm's canal is formed. As a result, IOP

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is lowered because the anterior chamber fluid flows through the stent into Schlemm's canal, avoiding the trabecular meshwork, which has strong outflow resistance[7]. Cataract surgery with the iStent inject® was also found to reduce the number of glaucoma eye drops compared with preoperatively[7]. In another study, cataract surgery with the iStent® versus iStent inject® was retrospectively compared[11]. There was no difference in the frequency of complications, and the cataract surgery with the iStent inject® was significantly superior in terms of the IOP reduction rate and glaucoma eye drop reduction[11]. The flange portion of the iStent inject® that remains in the anterior chamber is 230 μm in diameter. The iStent inject® W, which was approved in Japan in 2019, has a wider flange that expands the flange portion to 360 μm in diameter.

Similar to the iStent®, the iStent inject® W is approved in Japan only for use in combination with cataract surgery. The second edition of the criteria for the use of intraocular drains in combination with cataract surgery was published in 2020. According to this guideline, the glaucoma types for which cataract surgery combined with iStent® and iStent inject® W implantation is indicated are primary open-angle glaucoma and exfoliation glaucoma. In this study, we examined the postoperative outcomes and postoperative complications of patients with glaucoma who underwent cataract surgery with the iStent inject® W.

MATERIALS AND METHODS

This study involved 32 eyes of 27 patients who underwent cataract surgery with iStent inject® W implantation from November 2020 to June 2021 at Kyorin University Hospital in Japan and were followed up for at least 3 months. Patients were selected from their medical records, and a retrospective study was conducted. Patients who were taking oral IOP-lowering medications preoperatively or postoperatively, had active uveitis, or had undergone a previous intravitreal injection or intraocular surgery were excluded. The 32 eyes were divided into three groups: all-stage, early to-moderate-stage, and advanced-stage. The study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the Ethics Committee of Kyorin University Hospital (approval no. 1861). Informed consent was obtained from all patients. The authors declare no conflict of interest.

The study was performed within three months preoperatively. Using the 30-2 or 24-2 Swedish Interactive Thresholding Algorithm-Standard, a mean deviation of −6 dB or more was defined as early, between −12 dB and −6 dB as moderate, and below −12 dB as advanced[11].

The basic surgical procedure used in this study was as follows. All surgical cataract incisions were made using an upper clear corneal incision. After cataract surgery and insertion of the intraocular lens, the anterior chamber was filled with an ophthalmic viscosurgical device. A gonioscope was used to observe the nasal trabecular meshwork, and two iStent inject® W devices were inserted. If the surgeon determined that it was technically difficult to insert two devices, the surgery was terminated after the insertion of one device. The anterior chamber was washed, and wound closure was confirmed. All preoperative glaucoma eye drops were discontinued on the day of surgery. Preoperative prostanoid receptor-related drug-containing preparations were sequentially resumed according to IOP. The outcome measures were the mean number of medications, the IOP at 1 and 3 months postoperatively, and postoperative complications within 3 months. JMP® Pro 16 was used for the statistical analysis. The Tukey–Kramer honest significant difference (HSD) test was used to compare data over time (specifically, by comparing means at three or more time points). Statistical significance was set at $p < 0.05$.

RESULTS

This study involved 27 patients and 32 eyes (5 patients underwent surgery in both eyes). No patients were excluded during the follow-up period.

The glaucoma stage was early in six eyes, moderate in eight, and advanced in 18. The patients' age (mean ± standard deviation) was 69.2 ± 10.0 years, and 17 and 15 eyes belonged to male and female patients, respectively (Table 1). Thirty-one eyes had primary open-angle glaucoma and one eye had exfoliation glaucoma. The preoperative IOP was 17.1 ± 3.0 mmHg, and the mean number of medications before surgery was 3.4 ± 1.1. Two stents were in 29 eyes and 1 in 3 eyes. The mean IOP of all patients was 17.1 ± 3.0 mmHg preoperatively, 16.4 ± 2.6 mmHg at 1 month postoperatively (4.1% decrease from preoperatively), and 14.7 ± 2.4 mmHg at 3 months postoperatively (14.0% decrease from preoperatively). The *p*-value of the mean IOP compared with the preoperative IOP was 0.6183 at 1 month postoperatively, but significantly decreased to 0.0020 at 3 months postoperatively (Tukey–Kramer HSD test) (Table 2). One month postoperatively, the mean number of medications was 3.4 ± 1.1 preoperatively, 1.8 ± 1.0 at 1 month postoperatively, and 2.1 ± 1.2 at 3 months postoperatively. There was a significant decrease in the mean number of medications from the preoperative period to 1 and 3 months postoperatively ($p < 0.0001$).

The 32 eyes were divided into two groups: the early-to-moderate stage group (14 eyes) and the advanced stage group (18 eyes) (Table 2). The mean IOP was not significantly different preoperatively and 1 month postoperatively; however, it significantly decreased at 3 months postoperatively. The mean number of medications was significantly lower at 1 and 3 months postoperatively than preoperatively. These trends were similar across all the stages. Postoperative complications included stent occlusion by the iris in two eyes (6.3%), anterior chamber hemorrhage in one eye (3.1%), and transient elevation of IOP (> 10 mmHg above the preoperative IOP) in two eyes (6.3%). One eye with anterior chamber hemorrhage was also the eye that subsequently developed stent occlusion. No other eye had any complications. Both eyes with stent occlusion underwent the insertion

Table 1 Patient characteristics

Age	69.2 ± 10.0 years
sex (male/female)	17/15 eyes
Glaucoma type	
primary open-angle glaucoma	31 eyes
exfoliation glaucoma	1 eye
Glaucoma stage	
Early stage (MD value −6 dB or more)	6 eyes
Moderate stage (MD value −12 dB or more and less than −6 dB)	8 eyes
Advanced stage (MD value less than −12 dB)	18 eyes
Pre-operative IOP	17.1 ± 3.0 mmHg
Pre-operative mean number of medications	3.4 ± 1.1
Number of stents inserted	
2	29 eyes
1	3 eyes

Table 2 IOP and mean number of medications by glaucoma stage

	IOP (mmHg)	*P* value#	mean number of medications	*P* value#
all stages				
Pre-op	17.1 ± 3.0		3.4 ± 1.1	
1 M follow up	16.4 ± 2.6	0.6183	1.8 ± 1.0	< 0.0001
3 M follow up	14.7 ± 2.4	0.0020	2.1 ± 1.2	< 0.0001
Early to moderate stage				
Pre-op	17.9 ± 2.8		3.3 ± 1.0	
1 M follow up	17.1 ± 2.2	0.6515	1.5 ± 0.7	< 0.0001
3 M follow up	15.4 ± 2.4	0.0376	1.7 ± 1.0	0.0002
Advanced stage				
Pre-op	16.4 ± 2.9		3.5 ± 1.1	
1 M follow up	16.0 ± 2.8	0.8722	2.0 ± 1.1	0.0011
3 M follow up	14.1 ± 2.2	0.0402	2.4 ± 1.2	0.0260

#: *P* values at 1 M follow up and 3 M follow up are compared with Pre-op by Tukey-Kramer HSD test for each glaucoma stage

of two stents, only one of which became occluded. The transient IOP elevation and anterior chamber hemorrhage resolved within one week postoperatively with conservative follow-up. These were the only complications identified, and no serious postoperative complications occurred.

DISCUSSION

The two types of glaucoma included in this study were primary open-angle and exfoliation glaucoma. The IOP was significantly lower at 3 months postoperatively than preoperatively in all eyes, in eyes with early to moderate stage glaucoma, and in eyes with advanced stage glaucoma; the mean number of medications was also reduced. The frequency of anterior chamber hemorrhage was lower than that in MIGS combined with other cataract surgeries. As described later, the frequency of anterior chamber hemorrhage ranges from 16.7% to 18.2% in cataract surgery with the Kahook Dual Blade (New World Medical, Rancho Cucamonga, CA, USA) and microhook ab interno trabeculotomy. No significant post-operative complications were observed.

Although the mechanism is not fully understood, cataract surgery alone lowers IOP even in eyes with open-angle glaucoma. The Ocular Biomechanics Study Group reported a significant 25.0% reduction in IOP from preoperatively to 3 months postoperatively in eyes with open-angle glaucoma treated with cataract surgery alone (15.2 ± 4.3 to 11.4 ± 2.7 mmHg, $p < 0.05$)[14]. Qassim et al[10]. also reported IOP values after cataract surgery alone for primary open-angle glaucoma using longitudinal data. The data showed a mean IOP reduction of 2.22 mmHg (13.2%) from a preoperative value of 16.7 mmHg ($p < 0.001$). A prospective study of cataract surgery with the iStent inject® also showed a significant reduction in IOP compared with cataract surgery alone[12]. In the present study, with the iStent inject® W, there was a significant IOP reduction of 14.0% at 3 months postoperatively compared with preoperatively.

Previous studies that demonstrated the IOP-lowering effects of cataract surgery alone were conducted without changing the number of glaucoma eye drops. In the present study, glaucoma eye drops were discontinued at the time of surgery and were gradually increased. Consequently, IOP reduction from the preoperative period and a decrease in glaucoma eye drops were achieved simultaneously. Because the IOP-lowering effect of cataract

surgery with the iStent inject® W compared with cataract surgery alone is almost identical, we believe that this technique is suitable for patients who expect to see a reduction in the number of glaucoma eye drops. In the future, it would be desirable to examine the rate of IOP reduction after matching the conditions of cataract surgery alone as well as the patients' eye drops. The iStent®, iStent inject®, and iStent inject® W are devices used in MIGS in which the instrument is implanted in the trabecular meshwork. Another type of MIGS involves the use of an instrument to incise the trabecular meshwork. The Trabectome® (NeoMedix Corp., Tustin, CA, USA), Kahook Dual Blade (New World Medical), TrabEx+ device (MicroSurgical Technology, Redmond, WA, USA), microhook trabeculotomy device, and 360° suture trabeculotomy device are applicable to this procedure. These procedures can be performed alone or in combination with cataract surgery. Whether MIGS involving incision of the trabecular meshwork or cataract surgery combined with iStent inject® W implantation is more appropriate for some patients can be difficult to determine. Yousef et al[13]. reported the results of cataract surgery combined with use of the Trabectome®. In their study, the mean IOP decreased from 18.3 ± 5.1 mmHg before surgery to 13.1 ± 3.2 mmHg at 1 month after surgery, and it decreased by 27.9% (to 13.2 ± 3.3 mmHg) 3 months after surgery. IOP was significantly lower at all postoperative time points than during the preoperative period. The mean number of medications decreased from 2.7 ± 1.2 before surgery to 2.1 ± 1.6 at 3 months after surgery (a decrease of 22.2%)[8]. The Kahook Dual Blade Goniotomy Study Group reported the results of cataract surgery mainly performed with the Kahook Dual Blade[8]. In their report, the IOP decreased from 18.2 mmHg before the operation to 14.1 mmHg at 1 month after the operation, and it decreased by 26.4% (to 13.4 mmHg) 3 months after the operation. IOP was significantly lower at all postoperative time points than during the preoperative period. The mean number of medications decreased by 75.2% from 1.45 before surgery to 0.36 at 3 months after surgery ($p < 0.001$)[8]. As noted above, in the present cataract surgery combined with iStent inject® W implantation, the mean IOP decreased by 14.0% at 3 months postoperatively (from 17.1 mmHg preoperatively). Cataract surgery combined with the Trabectome® reduced the mean IOP by 27.9% at 3 months postoperatively (from 18.3 mmHg preoperatively), and the cataract surgery with the Kahook Dual Blade reduced the mean IOP by 26.4% at 3 months postoperatively (from 18.2 mmHg preoperatively). Therefore, cataract surgery with MIGS involving incision of the trabecular meshwork may have a stronger IOP-lowering effect than cataract surgery with iStent inject® W implantation. Aoki et al[1]. reported the long-term outcomes of cataract surgery using a Kahook Dual Blade. The preoperative IOP was 23.2 ± 5.4 mmHg, which decreased by 28.7% to 15.8 ± 3.3 mmHg at 6 months postoperatively and to 16.7 ± 2.1 mmHg at 12 months postoperatively. IOP was significantly lower at all postoperative time points than during the preoperative period. The mean number of medications also significantly decreased from 3.3 ± 1.2 preoperatively to 1.0 ± 1.4 at 6 months postoperatively and to 1.1 ± 1.4 at 12 months postoperatively. The mean number of medications was significantly lower at all postoperative time points than that during the preoperative period. In this report, anterior chamber hemorrhage was observed in 18.2% of the patients who underwent cataract surgery with the Kahook Dual Blade.

Okada et al[9]. reported the long-term results of cataract surgery combined with microhook trabeculotomy. The incision range of the trabecular meshwork was divided into 120° and 180° incision groups. In the 120° incision group, the preoperative IOP was 16.9 ± 7.6 mmHg, decreased by 18.8% to 12.5 ± 2.7 mmHg at 6 months after the operation, and decreased by 29.5% to 10.9 ± 2.7 mmHg at 12 months after the operation. IOP was significantly lower at all postoperative time points than during the preoperative period. In the 180° incision group, the preoperative IOP was 17.1 ± 7.0 mmHg, decreased by 15.3% to 12.9 ± 2.4 mmHg at 6 months after the operation, and decreased by 24.1% to 12.1 ± 3.2 mmHg at 12 months after the operation. To reiterate, IOP was significantly lower at all postoperative time points than during the preoperative period. Cataract surgery combined with MIGS to incise the trabecular meshwork has also been reported to reduce IOP for 6 months or longer. Future studies should examine the long-term course of cataract surgery combined with iStent inject® W implantation. Okada et al[9]. reported that hyphema forming a fluid surface was observed in 16.7% of patients in the 120° incision group and 18.2% of patients in the 180° incision group. Dorairaj et al[4]. reported residual hyphema in 3.8% of patients 1 week after cataract surgery using the Kahook Dual Blade. In contrast, in the present study, hyphema resolved spontaneously within one week in one eye (3.1%). The rate of hyphema was lower in this study of cataract surgery with the iStent inject® W than in previous reports of MIGS, which involves incision of the trabecular meshwork. Therefore, cataract surgery with the iStent inject® W may be suitable for patients who wish to undergo MIGS but want to prevent hyphema to the greatest extent possible. In this study, IOP was not significantly reduced at 1 month postoperatively but was significantly reduced at 3 months postoperatively. Possible reasons for the IOP-lowering effect appearing relatively late after surgery include the appearance of the IOP-lowering effect of cataract surgery alone at 3 months postoperatively and a gradual increase in the amount of aqueous humor outflow from the device lumen into the Schlemm's canal. However, the results of the present study did not allow us to clearly determine this mechanism. In all reports of cataract surgery with iStent injection, there was a downward trend in IOP 1 month postoperatively compared to preoperatively, as in the present study. There was also a downward trend at three and six months postoperatively. However, the Kahook Dual Blade Goniotomy Study Group's report on cataract surgery with the Kahook Dual Blade showed that IOP continued to decrease 1 month postoperatively. Among the cataract surgeries with MIGS described so far, only

the report of cataract surgery with a Trabectome® by Yousef et al[13]. showed no tendency of IOP to decrease even after 1 month postoperatively. However, the reason these surgeries showed no tendency for IOP to decrease 1 month postoperatively remains unclear. In cataract surgery with MIGS, follow-up is recommended because of the possibility of IOP reduction even one month postoperatively. Based on comparisons with other surgeries, cataract surgery with the iStent inject® W should be performed when IOP control is achieved with eye drops. It should also be performed when glaucoma eye drops need to be reduced or when cataract surgery is required. Moreover, it should be performed when the patient wishes to undergo glaucoma surgery but wants to minimize the frequency and severity of complications to the greatest extent possible.

The main limitation of this study was its retrospective, single-institution design. This study design resulted in a high dropout rate, short follow-up period, and a small number of patients.

Acknowledgment

We thank Angela Morben, DVM, and ELS from Edanz (https://jp.edanz.com/ac) for editing a draft of the manuscript.

(Received December 12, 2022)
(Accepted April 27, 2023)

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