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ORIGINAL PAPER

Outcomes of combined gonioscopy-assisted transluminal trabeculotomy and goniosynechialysis in primary angle closure: a retrospective case series

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Abstract

Purpose To evaluate the additional intraocular pressure (IOP) lowering effect of gonioscopy-assisted transluminal trabeculotomy (GATT) to contemporary goniosynechialysis (GSL) in endeavouring to abolish subsequent occlusion after chronic iridotrabecular contact in primary angle closure (PAC) patients.

Methods A retrospective case series of all PAC eyes underwent GATT + GSL with or without phacoemulsification and intraocular lens implantation (PEA + IOL) from December 2016 to May 2018 were recruited. IOP and the number of anti-glaucoma medications were compared pre- and post-operatively by Wilcoxon signed-rank test. Repeated measure ANOVA was used to evaluate the difference in IOP change after the operation between a subgroup of operations (GATT + GSL + PEA + IOL and GATT + GSL) and the arc of cutting of trabeculotomy.

Results Thirty-nine eyes of 30 patients, 37 chronic angle closure glaucoma (CACG), 1 acute primary angle closure (APAC), and 1 plateau iris syndrome were recruited. Mean preoperative IOP was 21.8 ± 5.4 mmHg. Mean post-operative IOP was lowered to 15.1 ± 3.8 mmHg at 1 month, 14.4 ± 1.2 mmHg at 3 months, 14.8 ± 2.1 mmHg at 6 months, 14.5 ± 0.8 mmHg at 1 year, and 15 at 2 years ($P < 0.001$, $P = 0.0012$, $P = 0.001$, $P = 0.028$, and $P = 0.317$ (n = 1), consecutively). Mean of overall post-operative IOP at the last follow-up was 15.1 ± 4.4 mmHg ($P < 0.001$). Mean preoperative number of anti-glaucoma medications was 3.5 ± 1.4. Mean post-operative number of anti-glaucoma medications was reduced to 1.5 ± 1.4 at 1 month, 0.9 ± 0.9 at 3 months, 1.4 ± 1.4 at 6 months, 1.5 ± 0.5 at 1 year, and 2 at 2 years ($P < 0.001$, $P = 0.01$, $P = 0.002$, $P = 0.028$, and $P = 0.317$ ($n = 1$), respectively). Mean of overall post-operative number of anti-glaucoma medications was 1.1 ± 1.2 ($P < 0.001$). There was no significant difference found between the IOP lowering effect in subgroup analysis.

Conclusion GATT + GSL could significantly reduce IOP and number of anti-glaucoma medications from baseline compared to the last follow-up; however, there seemed not to be any superiority to the effects found in previous studies reported about GSL + PEA or PEA alone in PAC patients.

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Introduction

Gonioscopy-assisted transluminal trabeculotomy (GATT) has been studied and reported that it could lower the intraocular pressure (IOP) to approximately 15 mmHg with or without medication in open-angle glaucoma (OAG) patients [1–7]. However, GATT is not a treatment of choice in angle closure patients due to the anatomical difference of anterior chamber angle which blocks the visibility of trabecular meshwork (TM) during surgery, but GATT might have a role in these patients because long-term peripheral anterior synechiae (PAS) causes TM malfunction which leads to aqueous outflow reduction [8].

In this study, we tried to reform the anatomy of anterior chamber angle in patients with primary angle closure (PAC) by combining goniosynechialysis (GSL) before performing GATT and then analysed the surgical outcomes focusing at pre- and post-operative IOP and number of anti-glaucoma medications, and success rate.

Materials and methods

This study was a case series of retrospective medical record review with ethical approval from an institutional review board of Kyoto Prefectural University of Medicine (Kyoto, Japan) and conducted rigorously following the Declaration of Helsinki. Patients in this study were PAC patients who underwent uneventful combined GATT and GSL with or without phacoemulsification and intraocular lens implantation (PEA + IOL) from December 2016 to May 2018 at three surgical centres (Kyoto Prefectural University of Medicine, Baptist Eye Clinic, and Shijo-Karasuma Komuro Eye Clinic) in Kyoto, Japan.

PAC patients in this study were classified into three groups, including chronic angle closure glaucoma (CACG), acute primary angle closure (APAC), and plateau iris syndrome. Patients were excluded if they had any history of ocular trauma or any other ocular diseases which might have caused secondary glaucoma in the operated eye and/or affected patients' vision other than cataract.

Subgroup analysis was created by type of the operation, which were GATT + GSL + PEA + IOL and GATT + GSL without PEA + IOL, and by the degree of cutting arc which was $\geq 180°$ and $< 180°$.

IOP less than or equal to 15 mmHg with or without anti-glaucoma medication post-operatively was considered successful as the number could be expected from the previous study [3].

t-test or Mann–Whitney *U* test for independent continuous variables and paired *t*-test or Wilcoxon signed-rank test for dependent continuous variables were used as seen suitably. Chi-square was used to analyse categorical variables. P-value < 0.05 was considered statistically significant.

Surgical technique

All surgeries were performed by one surgeon (KM). Before the operation, levofloxacin hydrate (Cravit® Ophthalmic Solution 1.5%, Santen Pharmaceutical Co. Ltd., Osaka, Japan) was prescribed four times a day for three days and on the day of operation, oxybuprocaine hydrochloride (Benoxil® Ophthalmic Solution 0.4%, Santen, Osaka, Japan) and adrenaline solution (Bosmin®, Daiichi Sankyo, Tokyo, Japan) were administered five times twice, respectively. Additionally, for PEA + IOL patients, combined tropicamide/phenylephrine hydrochloride (Mydrin-P® ophthalmic solution, Santen Pharmaceutical Co Ltd, Osaka, Japan) was also applied for pupillary dilatation.

Lidocaine (Xylocaine® 2%, Aspen Japan, Tokyo, Japan) of 3 ml was applied at inferotemporal quadrant for subtenon anaesthesia right before the operation started, then 0.81-mm wound was first created at 2 o'clock of peripheral cornea, then ophthalmic viscoelastic device (Healon®, Johnson and Johnson Vision, Tokyo, Japan or Opelead®, Senju Pharmaceutical Co. Ltd., Osaka, Japan) was injected into the anterior chamber to stabilise it, and then two (or three in combined PEA + IOL) more 0.81-mm wounds were made at 12 o'clock (10 o'clock for PEA main port and 9 o'clock for capsulorhexis in combined PEA + IOL) and 8 o'clock. Goniosynechialysis was done by pressing all the PAS as much as possible down gently with a spatula (Mori-goniospatula®, Handaya Co Ltd, Tokyo, Japan, Fig. 1a); after that, 5–0 nylon

(Chin-trabeculotomy nylon suture®, Handaya Co Ltd, Tokyo, Japan) was then put in the anterior chamber through the 8 o'clock wound to around 6 o'clock area of the angle just to be ready for the next procedure. Afterwards, double-mirror goniolens (Ocular Mori Upright Surgical Gonio Lens® or Ocular Upright 1.3X Surgical Gonioprism®, Ocular Instruments, Bellevue, WA, USA) was used to evaluate and visualise the intraocular surgical site throughout the surgery. 27-gauge needle was then introduced via the 12 or 10 o'clock wound to make an approximately 2-mm linear horizontal incision at pigmented TM to expose Schlemm's canal (Fig. 1b) so that the 5–0 nylon could be inserted into the Schlemm's canal with 25-gauge intraocular forceps (MAXGrip® forceps, Alcon Japan, Tokyo, Japan) at around 6 o'clock angle (Fig. 1c). The suture would be passed through the Schlemm's canal anti-clockwise to approximately 12 o'clock angle to make 180° cut or as far as it could go in case that there were any obstacles before it reached the target point. Capsulorhexis was done at this step in eyes with PEA + IOL, and then another 0.81-mm wound was made at the cornea opposite to where the tip of 5–0 nylon was. After that, 27-gauge needle was used again

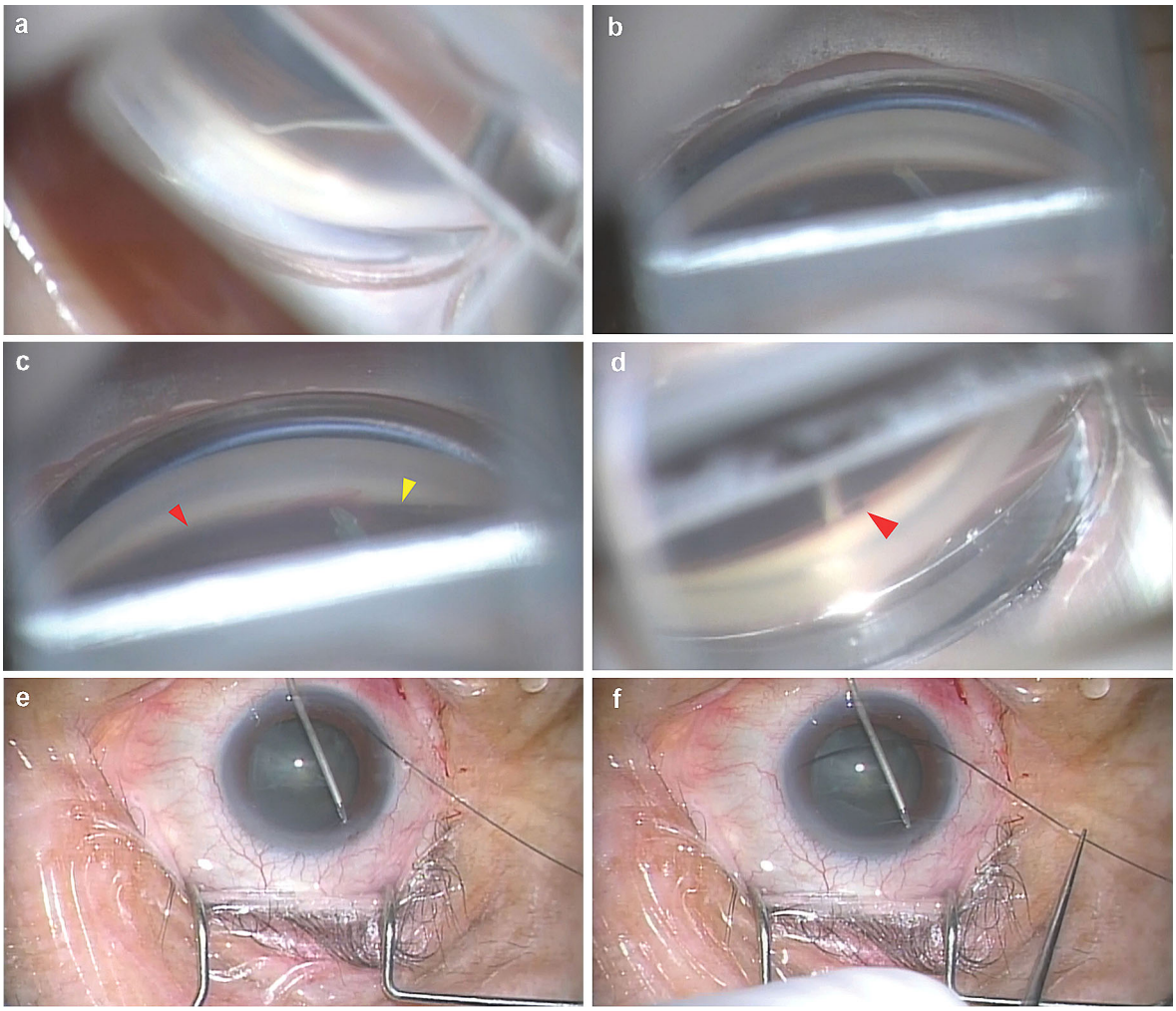

Fig. 1 Goniosynechialysis and gonio-assisted transluminal trabeculotomy procedure. **a** Goniosynechialysis by using a spatula. **b** Pigmented trabecular meshwork cutting by a 27-gauge needle. **c** 5–0 nylon trabeculotomy suture insertion (yellow arrow; suture outside Schlemm's canal in black line, red arrow; suture inside Schlemm's canal in faint black shadow. **d** Cutting at the distal end of the trabeculotomy suture (red arrow; the tip of a suture in Schlemm's canal). **e** Grasping tip of a suture with 25-gauge intraocular forceps. **f** Pulling at the proximal end to cut trabecular meshwork along the length of the suture inside Schlemm's canal

Table 1 Demographic data of patients

Age (years)	73.6 ± 9 (53–86)
Sex (male/female)	7:22
Laterality (right/left, eyes)	19:20
Type of glaucoma (CACG/APAC/plateau iris syndrome, eyes)	37:1:1
Mean preoperative BCVA (logMAR)	0.2 ± 0.6
Mean preoperative IOP (mmHg)	21.8 ± 5.4 (14–36)
Mean number of preoperative anti-glaucoma medications	3.5 ± 1.4 (0–6)
Mean preoperative visual field MD (dB)	− 11.3 ± 7.6[a]
Type of operations (GATT + GSL + PEA + IOL/GATT + GSL, eyes)	35:4
Degree of cutting arc of GATT	160.4 ± 36.1 (60–270)
Mean post-operative BCVA (logMAR)	0.1 ± 0.5*
Mean post-operative follow-up period (months)	6.3 ± 4.8 (1–23)
Post-operative hyphema (% of cases)	100
Mean duration of post-operative hyphema (days)	15.6 ± 20.7

Continuous data are shown as mean ± standard deviation

CACG chronic angle closure glaucoma; *APAC* acute primary angle closure; *BCVA* best-corrected visual acuity; *IOP* intraocular pressure; *MD* mean deviation; *GATT* gonioscopy-assisted transluminal trabeculotomy; *GSL* goniosynechialysis; *PEA + IOL*, phacoemulsification + intraocular lens implantation

[a]9 missing data of standard automated perimetry

* Statistical difference between pre- and post-operative BCVA, *P*-value = 0.031, Wilcoxon signed-rank test

Table 2 Comparison of intraocular pressure between pre- and post-operation

Post-operative follow-up	IOP (mmHg) (A/B)	*P*-value*	Percent reduction from baseline (%)	Eyes (A/B)
Baseline	21.8 ± 5.4			39
	(21.6 ± 5.4:23.6 ± 5.7)			(35:4)
1 month	15.1 ± 3.8	< 0.001	31.7 ± 25.2	35
	(14.8 ± 3.4:18 ± 1)			(33:2)
3 months	14.4 ± 1.2	0.012	38.1 ± 27.5	9
	(14.4 ± 1.2:n/a)			(9:0)
6 months	14.8 ± 2.1	0.001	37.6 ± 25.7	16
	(14.5 ± 1.9:16.5 ± 3.5)			(13:3)
1 year	14.5 ± 0.8	0.028	38.1 ± 18.3	6
	(14.4 ± 0.9:15[a])			(5:1)
2 years[a]	15	0.317	31.2	1
	(15:n/a)			(1:0)
Overall final IOP at last follow-up	15.1 ± 4.4	< 0.001	30.1 ± 29.8	39
	(14.6 ± 4.1:16.5 ± 2.4)			(35:4)

Continuous data are shown as mean ± standard deviation

A, GATT + GSL + PEA + IOL; B, GATT + GSL

n/a not applicable; *IOP* intraocular pressure

[a]Number of patients at the time point = 1; standard deviation cannot be calculated.

**P*-value analysed by Wilcoxon signed-rank test and compared to baseline

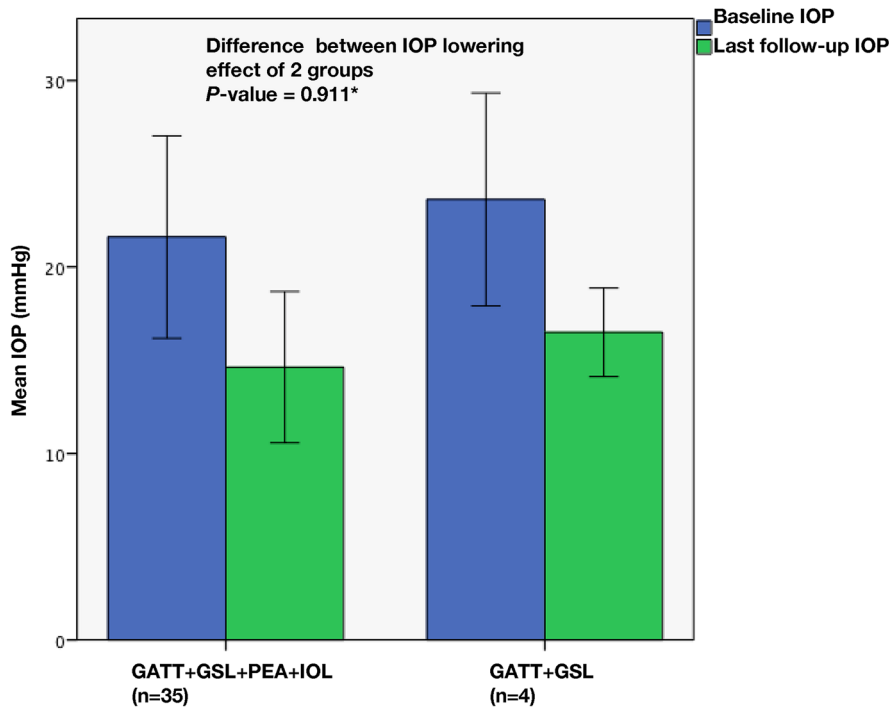

Fig. 2 The difference from baseline of last follow-up IOP between a type of operation. Baseline IOP; GATT + GSL + PEA + IOL = 21.6 ± 5.4 mmHg, GATT + GSL = 23.6 ± 5.7 mmHg; *P*-value = 0.546, Mann–Whitney *U* test. Last follow-up IOL; GATT + GSL + PEA + IOL = 15.6 ± 4.1 mmHg, GATT + GSL = 16.2 ± 2.4 mmHg; *P*-value = 0.092, Mann–Whitney *U* test. **P*-value analysed by Mann–Whitney *U* test. IOP, intraocular pressure; GATT, Gonioscopy-assisted transluminal trabeculotomy; GSL, goniosynechialysis; PEA + IOL, phacoemulsification + intraocular lens implantation

through the wound to cut the TM (Fig. 1d) in order to use 25-gauge intraocular forceps for grasping the tip of suture (Fig. 1e). After pinching the suture tightly, the tail of suture was pulled back to cut the TM along its length in the Schlemm's canal (Fig. 1f). Standard PEA + IOL procedure would be done from this time on in the eyes needed. Ultimately, the anterior chamber was irrigated, the PEA main port was sutured by 10–0 nylon, and 0.4 ml subconjunctival betamethasone sodium phosphate (Rinderon®ophthalmic solution 0.4%, Shionogi, Osaka, Japan) was injected regarded as the end of the operation.

The operation's details could be changed according to anatomical variability of the patients' eyes, for example, the site of suture insertion and the passing suture's direction.

Post-operative management

After the operation, all of the eyes were given a levofloxacin hydrate four times a day, betamethasone sodium phosphate 0.1% four times a day, and bromfenac sodium hydrate (Bronuck® ophthalmic solution 0.1%, Senju Pharmaceutical Co. Ltd., Osaka, Japan) twice a day regardless the type of operation for one month. All of the anti-glaucoma medications were stopped and would be restarted as necessary if the IOP was not on target and if the IOP could not be controlled with medications, other surgical interventions would be considered.

Patients were followed up at 1 day, 1 week, 1 month, then every month until 6 months, 1 year, and 2 years, but data were collected at 1 month and so on.

Result

Patient characteristics

Thirty-nine eyes of 30 PAC patients were included in this study with a diagnosis of CACG in 37 eyes, APAC

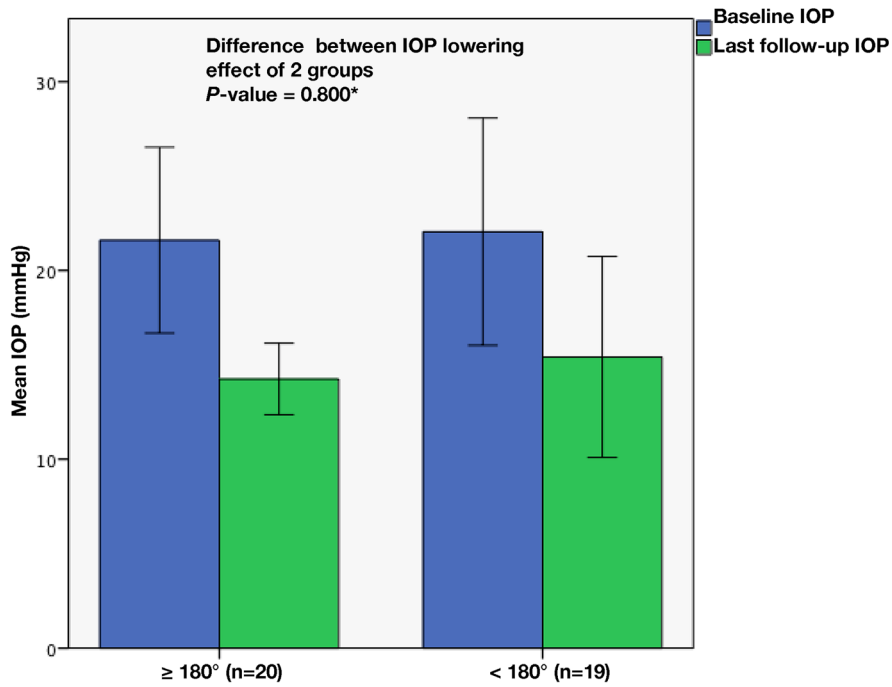

Fig. 3 The Difference from baseline of last follow-up IOP between the degree of arc of gonioscopy-assisted transluminal trabeculotomy. Baseline IOP; ≥ 180° = 21.6 ± 4.9 mmHg, < 180° = 22.1 ± 6 mmHg; *P*-value = 0.955, Mann–Whitney *U* test. Last follow-up IOL; ≥ 180° = 14.5 ± 1.9 mmHg, < 180° = 15.4 ± 5.3 mmHg; *P*-value = 0.932, Mann–Whitney *U* test. **P*-value analysed by Mann–Whitney *U* test. IOP, intraocular pressure.

in 1 eye, and plateau iris syndrome in 1 eye. Thirty-five eyes underwent GATT + GSL + PEA + IOL and 4 eyes with GATT + GSL with PEA + IOL that had been done previously. Mean preoperative IOP, the number of anti-glaucoma medications, and follow-up period were 21.8 ± 5.4 mmHg, 3.5 ± 1.4, and 6.3 ± 4.8 months, respectively (Table1).

Post-operative intraocular pressure

Post-operatively, IOP was 15.1 ± 3.8 mmHg at 1 month, 14.4 ± 1.2 mmHg at 3 months, 14.8 ± 2.1 mmHg at 6 months, 14.5 ± 0.8 mmHg at 1 year, and 15 at 2 years. IOP reduction from the baseline was statistically significant in all follow-up time point except at 2 years ($P < 0.001$, $P = 0.0012$, $P = 0.001$, $P = 0.028$, and $P = 0.317$, consecutively, Table2). In a subgroup analysis categorised by type of the operation, there was no statistically significant difference found in IOP lowering effect between GATT + GSL + PEA + IOL group, 6.7 ± 5.1 mmHg, and GATT + GSL group, 7.1 ± 4.8 mmHg, during baseline and the last follow-up ($P = 0.911$, Fig. 2). Also in a subgroup of the degree of cutting arc ≥ 180° and < 180°, no statistically significant difference found in IOP lowering effect during baseline and in the last follow-up it was 6.9 ± 4.4 mmHg and 6.6 ± 5.7 mmHg, respectively ($P = 0.800$, Fig. 3).

Post-operative anti-glaucoma medications

Anti-glaucoma medications were diminished significantly from 3.5 ± 1.4 before the surgery to 1.5 ± 1.4 at 1 month, 0.9 ± 0.9 at 3 months, 1.4 ± 1.4 at 6 months, 1.5 ± 0.5 at 1 year, and 2 at 2 years ($P < 0.001$, $P = 0.01$, $P = 0.002$, $P = 0.028$, and $P = 0.317$, respectively, Table 3).

Success rate

According to the criteria of success of IOP less than or equal to 15 mmHg (calculated from mean baseline IOP) with or without anti-glaucoma medication, the success rate was 71.8% (28 eyes; $P = 0.006$, X^2) at the

Table 3 Comparison of number of anti-glaucoma medications between pre- and post-operation

Post-operative follow-up	Number (A/B)	*P*-value*	Eyes (A/B)
Baseline	3.5 ± 1.4		39
	(3.5 ± 1.4:3.8 ± 0.5)		(35:4)
1 month	1.5 ± 1.4	< 0.001	35
	(1.5 ± 1.4:1.7 ± 1.2)		(33:2)
3 months	0.9 ± 0.9	0.01	9
	(0.9 ± 0.9:n/a)		(9:0)
6 months	1.4 ± 1.4	0.002	16
	(1 ± 1.2:2.5 ± 0.7)		(13:3)
1 year	1.5 ± 0.5	0.028	6
	(1.4 ± 0.6:2[a])		(5:1)
2 years[a]	2	0.317	1
	(2:n/a)		(1:0)
Overall final number of anti-glaucoma medication at last follow-up	1.1 ± 1.2	< 0.001	39
	(1 ± 1.3:1.3 ± 1)		(35:4)

Continuous data are shown as mean ± standard deviation

A, GATT + GSL + PEA + IOL; B, GATT + GSL

n/a not applicable; *IOP* intraocular pressure

[a]Number of patients at the time point = 1; standard deviation cannot be calculated.

**P*-value analysed by Wilcoxon signed-rank test and compared to baseline

last follow-up visit. Among 28.2% of failed cases (11 eyes), two CACG patients both underwent GATT + GSL + PEA + IOL who needed the second operation, trabeculectomy + mitomycin C, in order to control the IOP at fifth and seventh months. Their IOP at the last visit was 28 mmHg and 29 mmHg, respectively, with 4 anti-glaucoma medications.

Complication

Hyphema occurred in all cases, and all of them spontaneously resolved in 15.6 ± 20.7 days after the surgery without any serious sequelae. One post-operative IOP spike was found in 1 CACG patient after GATT + GSL + PEA + IOL, from 22 mmHg preoperation to 35 mmHg on day 1 follow-up but could be treated by anti-glaucoma medications without any further surgical intervention and IOP was reduced to 20 mmHg at 1 week post-operation.

Discussion

The results of this retrospective case series showed that GATT + GSL with or without PEA + IOL could reduce the post-operative IOP and number of anti-glaucoma medications significantly; however, GATT + GSL alone seemed to be slightly superior to GATT + GSL + PEA + IOL in the mean IOP change from preoperation (7.1 ± 4.8 mmHg and 6.7 ± 5.1 mmHg, respectively) without statistical significance. The reason for this difference might be because of the dissimilarity of the number of cases between these two groups since there were only four cases in GATT + GSL group. Unfortunately, post-operative IOP and number of anti-glaucoma medications in this study were not obviously better than the previous studies about surgical management in PAC patients without GATT [9–16] (Table 4). GATT was chosen to be an additional procedure in this study to overcome the possibility of residual glaucoma, but these results did not comply to our hypothesis that there would be a Schlemm's canal endothelial damage and subsequent occlusion after chronic iridotrabecular contact [8] supporting by recent analytical studies that could not show the significant benefit of GSL + PEA + IOL over PEA + IOL alone in PAC patients [17, 18]. Possible explanations to our results are the pathology mentioned above did not occur equally throughout 360° of Schlemm's canal and by choosing to do only 180° of GATT because there was no significant difference in post-operative IOP between complete and partial trabeculotomy [19, 20] might not cover all of the PAS area and could affect the negative results of this study. The other important disadvantage of the study was that the loss ratio of the follow-up cases was very high. This could be explained by the medical system in Japan that the patients whose clinical were improved and stable after surgery would be referred back from the University or tertiary care hospitals to the local doctors and the follow-up continued at the local hospitals. However, we believe that our study could be the first step for the future studies with better GATT procedures which covers all 360° or the PAS area which might be able to answer our question about the additional effect of GATT in eliminating subsequent occlusion in PAC patients more distinctly.

In conclusion, GATT + GSL could reduce the IOP and number of anti-glaucoma medications to the level

Table 4 Result comparison with previous studies

	Preoperative IOP (mmHg)	Post-operative IOP (mmHg)	Preoperative anti-glaucoma medications	Post-operative anti-glaucoma medications	Operation	Diagnosis (*n*)
Harasymowycz et al. [9]	40.7	15.5	3.8	1.7	GSL + PEA	APAC (21)
Fakhraie et al. [10]	34.3	17.5	3.7	0.6	GSL + PEA	APAC (24)
Razeghinejad et al. [11]	39.4	13.4	3.8	0.4	GSL + PEA	APAC (11)
Teekhasenee et al. [12]	29.7	13.2	2.4	0.1	GSL + PEA	CACG (52)
Razeghinejad et al. [13]	20.9	14.8	2.7	1.0	GSL + PEA	CACG (56)
Maeda et al. [14]	37.7	12.2	-	-	GSL + PEA	PAC (19)
Lai et al. [15]	19.7	15.5	1.9	0.5	PEA	PAC (21)
Tham et al. [16]	24.2	16.1	3.3	1.7	PEA	PAC (27)
This study	21.8	15.1	3.5	1.1	GATT + GSL + PEA + IOL/ GATT + GSL	PAC (39)

IOP intraocular pressure; *CACG* chronic angle closure glaucoma; *APAC* acute primary angle closure; *PAC* primary angle closure; *GATT* gonioscopy-assisted transluminal trabeculotomy; *GSL* goniosynechialysis; *PEA + IOL* phacoemulsification + intraocular lens implantation

of satisfaction in PAC patients but compared to the contemporary treatment in the previous studies such as GSL, GSL + PEA or even PEA alone, GATT could not show the benefit over those operations. However, this was only a retrospective case series; a better-designed analytical study is necessary to verify the usefulness of GATT in PAC patients.

Compliance with ethical standards

Conflict of interest Kazuhiko Mori, MD, PhD, is the inventor of Ocular Mori upright surgical gonio lens, who receives a share from the profit of products' commerce.

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