



## A DISSERTATION FOR THE DEGREE OF MASTER

# Retrospective study of postoperative intraocular pressure and complications in phacoemulsification combined with endoscopic cyclophotocoagulation and phacoemulsification alone in dogs

개에서 내시경 모양체광응고술 병행 및 단독 수정체유화술 후의 안압과 복합증에 대한 후향적 연구

> By Sol Kim

MAJOR IN VETERINARY CLINICAL SCIENCES DEPARTMENT OF VETERINARY MEDICINE GRADUATE SCHOOL SEOUL NATIONAL UNIVERSITY

February, 2023

# Retrospective study of postoperative intraocular pressure and complications in phacoemulsification combined with endoscopic cyclophotocoagulation and phacoemulsification alone in dogs

개에서 내시경 모양체광응고술 병행 및 단독 수정체유화술 후의 안압과 복합증에 대한 후향적 연구

## 지도교수 서 강 문

이 논문을 수의학 석사 학위논문으로 제출함 2022년 10월

## 서울대학교 대학원

수의학과 임상수의학 전공

## 김 솔

## 김 솔의 석사 학위논문을 인준함

### 2022년 12월

위	원	장	(인)
부	위 원	장	(인)
위		원	(인)

## Retrospective study of postoperative intraocular pressure and complications in phacoemulsification combined with endoscopic cyclophotocoagulation and phacoemulsification alone in dogs

Supervised by

**Professor Kangmoon Seo** 

## Sol Kim

Major in Veterinary Clinical Science Department of Veterinary Medicine Graduate School Seoul National University

#### Abstract

This study aimed to investigate the effects of endoscopic cyclophotocoagulation (ECP) on postoperative intraocular pressure (IOP) and complications after phacoemulsification (phaco) in dogs with normal IOP.

Medical records of IOP, conjunctival hyperemia, corneal edema, aqueous flare, posterior synechia, intraocular fibrin, and posterior capsule opacification (PCO) formation in 15 canine eyes that underwent phaco-ECP and 36 eyes that underwent phaco alone were evaluated retrospectively. ECP was applied when either the iridocorneal angle or the ciliary cleft was narrow or closed.

The IOP of the phaco-ECP group persisted within the normal range postoperatively. The phaco-ECP group had a shorter period of dorzolamide use than did the phaco group. PCO was formed earlier in the phaco-ECP group than in the phaco group. The phaco-ECP group showed more severe corneal edema than the phaco group at every follow-up visit. Posterior synechia was more severe in the phaco-ECP group than in the phaco group from two weeks until the last follow-up.

Although ECP might cause more postoperative complications such as corneal edema and posterior synechia, it could effectively reduce the incidence of IOP increase after phaco in dogs with a high risk of postoperative glaucoma.

Keywords: canine, cataract, ciliary body photocoagulation, combined surgery, glaucoma, lasers

Student Number: 2020-29607

## Contents

Introd	uction1
Materi	als and Methods3
1.	Patients and exclusion criteria
2.	Preoperative preparation and surgical technique
3.	Postoperative medication and follow-up7
4.	Statistical analyses
Result	s10
Discus	ssion·····21
Conclu	usion·····26
Refere	nces·····27
Abstra	ct in Korean31

## Introduction

Phacoemulsification (phaco) with intraocular lens (IOL) insertion is the standardized treatment of cataract in veterinary ophthalmology (Michau, 2021). Among the common complications following phaco in dogs, glaucoma is an important cause of failure of phaco because it is vision-threatening and painful (Michau, 2021). Glaucoma constituted 76% of cases in a study describing the histopathologic abnormalities shown in canine eyes eviscerated or enucleated due to complications after phaco (Moore *et al.*, 2003).

Endoscopic cyclophotocoagulation (ECP) was initially introduced in 1986 for the treatment of various refractory glaucomas in humans (Shields, 1986). This cyclodestructive technique ablates ciliary processes under direct visualization using laser photocoagulation, which allows safer and more precise treatment compared with the transscleral approach (Bras and Maggio, 2015). ECP has been broadly used in combination with phaco (phaco-ECP) because the procedure can be performed through the same incision used for phaco to reduce intraocular pressure (IOP) in human patients with glaucoma (Shields, 1986; Lindfield *et al.*, 2012; Clement *et al.*, 2013; Francis *et al.*, 2014; Siegel *et al.*, 2015; Pérez *et al.*, 2018).

Several studies have investigated the efficacy of phaco-ECP in the treatment of glaucoma in humans (Lindfield *et al.*, 2012; Clement *et al.*, 2013; Francis *et al.*, 2014; Siegel *et al.*, 2015; Pérez *et al.*, 2018). Although this is controversial, this procedure has demonstrated a need for fewer glaucoma medications after surgery (Lindfield *et al.*, 2012; Clement *et al.*, 2013; Francis *et al.*, 2014; Siegel *et al.*, 2015; Pérez *et al.*, 2013; Francis *et al.*, 2014; Siegel *et al.*, 2015; Pérez *et al.*, 2013; Francis *et al.*, 2014; Siegel *et al.*, 2015; Pérez *et al.*, 2018). A retrospective study reported that IOP decreased from baseline at all time

points after phaco-ECP and that this decrease was statistically significant with no change in medication (Lindfield *et al.*, 2012). A similarly designed research revealed a mean IOP reduction with the number of hypotensive eyedrops reduced at 12 months postoperatively (Clement *et al.*, 2013). In a prospective study, the phaco-ECP group showed a higher reduction in IOP and had lower number of ocular hypotensive medications than the phaco group after 24 months (Francis *et al.*, 2014). Siegel *et al.* (2015) published a retrospective study confirming that the phaco-ECP group server nedications than the phaco group, although the IOPs of the groups were not significantly different at 36 months follow-up. In a retrospective study of human primary open-angle glaucoma, the phaco-ECP group showed a higher reduction in IOP and had lower number of medications than the phaco group (Pérez *et al.*, 2018). However, the phaco-ECP group was associated with more complications were completely relieved with medical treatment (Pérez *et al.*, 2018).

There is no long-term comparative data on phaco-ECP versus phaco alone in dogs. This study aimed to elucidate the prophylactic effect of ECP on postoperative glaucoma development and to compare postoperative complications between phaco-ECP and phaco alone in dogs. In this study, phaco-ECP was performed for prophylactic purposes of postoperative glaucoma in dogs with narrow iridocorneal angle or ciliary cleft.

### **Materials and Methods**

#### 1. Patients and exclusion criteria

A retrospective chart review was performed of canine patients who visited the Veterinary Medical Teaching Hospital at Seoul National University between January 2019 and December 2021. Informed owner consent was obtained for the possible postoperative complications of each procedure prior to surgery. The medical records of canine patients who underwent phaco-ECP or phaco alone for cataracts with IOL implantation were evaluated. Information collected from medical records included breed, sex, age, operated eve (right or left), diabetic status, stage of cataract (immature, mature, or hypermature), preoperative gonioscopy, ultrasound biomicroscopy (UBM) before surgery, IOP, presence of uveitis, follow-up period, and postoperative complications. Gonioscopy and UBM findings were recorded as open, narrow, and closed iridocorneal angle and ciliary cleft, respectively, based on descriptions in the clinical records. Gonioscopy was classified according to the width of the iridocorneal angle, and the ratio of the width of the anterior opening of the ciliary cleft and the distance from the origin of the pectinate ligaments to the anterior surface of the cornea was greater than 0.45 was classified as "open," 0.15 to 0.45 as "narrow," and less than 0.15 as "closed (Ekesten B and Narfström K, 1991)." In the case of UBM, the ciliary cleft was defined as the hypoechoic space between the ciliary body and the sclera, and it was classified as "open" if it was clearly identified, "closed" if it was collapsed, and "narrow" otherwise.

ECP was applied when either the iridocorneal angle or the ciliary cleft was narrow

or closed. All patients with and without diabetes who received phaco-ECP or phaco alone with IOL placement during the study period were included. Intraoperative capsular tension ring (CTR) implantation and/or anterior vitrectomy were also included in the study. Canine patients were required to have at least 6 months postoperative follow-up period. The exclusion criteria were as follows: 1) eyes with ocular hypertension or glaucoma preoperatively that were untreated or treated with ocular hypotensive medication, 2) eyes with lens capsule rupture before surgery and 3) eyes that had undergone intraocular surgery, such as Ahmed gonioimplantation and retinopexy.

#### 2. Preoperative preparation and surgical technique

Prior to surgery, all dogs underwent a thorough ophthalmic and physical examination including Schirmer tear test-1 (Schirmer Tear Test Strips, Merck Animal Health, USA), IOP measurement using rebound tonometry (iCare<sup>®</sup> Tonovet, iCare Finland Oy, Finland), neuro-ophthalmic examinations, slit-lamp biomicroscopy (SL-D7, Topcon, Japan) at 10x magnification, binocular indirect ophthalmoscopy (Vantage Plus<sup>®</sup>, Keeler, UK), UBM with 50 MHz transducer (MD-320W, Meda, China), gonioscopy (Pan Retinal<sup>®</sup> 2.2, Volk, USA; Genesis-D, Kowa, South Vermont, USA) (Bedford, 1973), electroretinography (Reti-port<sup>®</sup>, Roland Consult, Germany) and fluorescein staining (Fluorescein paper, Haag-streit diagnostics, Switzerland) by board-certified veterinary ophthalmologists including two diplomates of the Asian College of Veterinary Ophthalmologists (AiCVO). The B-scan ocular ultrasonography was performed by a radiologist.

Carprofen 2.2 mg/kg per oral (PO) twice a day (BID) (Rimadyl<sup>®</sup>, Zoetis, Brazil) and 0.2% cyclosporine ophthalmic ointment BID (Optimmune<sup>®</sup>, Merck Animal Health, USA) were administered for 1 week until the night before surgery as preoperative medications. Topical neomycin/polymyxin B/dexamethasone (NPD) ophthalmic solution (Maxitrol<sup>®</sup>, Novartis, Belgium), 0.03% flurbiprofen sodium ophthalmic solution (Bausch & Lomb, USA), and 1% tropicamide ophthalmic solution (Mydriacyl<sup>®</sup>, Alcon, USA) were administered 2 h before surgery every 15 min. Topical 0.5% tropicamide/0.5% phenylephrine hydrochloride (Mydrin-P<sup>®</sup>, Santen, Japan) was added every 30 min 1 h before surgery.

General anesthesia was performed, and a non-depolarizing neuromuscular blocker (rocuronium bromide 0.2–0.5 mg/kg, Hana Pharm, Korea) was administered intravenously to enhance central eye positioning. Patients were mechanically ventilated and placed in dorsal recumbency. The eyes and eyelids of the patients were aseptically prepped. Routine phacoemulsification (Stellaris<sup>®</sup>, Bausch & Lomb Incorporated, USA) was performed by two board-certified veterinary ophthalmologists. A CTR (An-CTR<sup>®</sup>, An-vision Inc., USA) was placed in the capsule to enhance capsular stability when zonular laxity was observed during surgery. A 41D foldable soft acrylic one-piece IOL (An-lens<sup>®</sup>, An-vision Inc., USA) was inserted in all eyes with no concurrent or preexisting contraindications to placement. Anterior vitrectomy was performed when vitreous was present within the anterior chamber and pupil.

For phaco-ECP, after the placement of the IOL, viscoelastic material (1% sodium hyaluronate, An-vision Inc., USA) was injected again between peripheral anterior lens capsule and posterior iris to visualize the ciliary processes by inflating sulcus, with the pupil still dilated. A laser endoscope (E4 MicroProbe<sup>®</sup>, Endo Optiks, USA) was inserted through the corneal incision and pupillary space to approach the ciliary processes. Under direct visualization, the epithelium of the ciliary process was whitened and contracted using a connected 810-nm diode laser (OcuLight<sup>®</sup>, Iridex Corporation, USA) ranged 200–350 mW with 1,000 ms duration and 1,000 ms repeat interval. The treatment was applied at an average of 210° to the ciliary processes. Overtreatment, represented by "popping" or tissue explosion, was avoided. At treatment completion, the viscoelastic material was thoroughly eliminated from the eye using irrigation and aspiration. The corneal incision was closed in a double continuous suture pattern with 9-0 polyglactin 910 (Coated Vicryl<sup>®</sup>, Ethicon, USA).

#### 3. Postoperative medication and follow-up

All canine patients received standardized postoperative medication of tropicamide q12 h, 0.5% moxifloxacin (Vigamox<sup>®</sup>, Alcon, USA) q4-6 h, 1% prednisolone acetate (Pred Forte<sup>®</sup>, Allergan, USA) q4-6 h, NPD q4-6 h, 0.3% sodium hyaluronate (Hyalein<sup>®</sup>, Santen, Japan) PRN, and 1.2% hyaluronate lubricating gel (An-HyPro<sup>®</sup>, An-vision Inc., USA) q6-12 h. In addition, 2% dorzolamide (Trusopt<sup>®</sup>, Merck, USA) was administered for several weeks at q6-12 h until the IOP stabilized under 15 mmHg. In addition, all canine patients were administered amoxicillin/clavulanic acid 12.5 mg/kg PO BID (Augmentin<sup>®</sup>, IlSung, Korea) and carprofen 2.2 mg/kg PO BID for 1 week.

Ophthalmic examinations were scheduled for the next day and at 1 week, 2 weeks, 1 month, 3 months, 6 months, and thereafter postoperatively. In this study, medical records for up to 6 months were analyzed. Nevertheless, the actual re-examination schedule was adjusted in accordance with each patient's healing progress, concurrent ophthalmic diseases, or any complications requiring a schedule change. The frequency and dosage of medications were gradually reduced or discontinued according to the patients' ophthalmic examination findings. At each follow-up time point, the following were evaluated: conjunctival hyperemia, corneal edema, aqueous flare, and posterior synechia (all scored on a scale of 0-3, where 0 = none, 1 = mild, 2 = moderate, and 3 = severe). Specifically, conjunctival hyperemia was 0 when the bulbar conjunctiva is normal (small, pale pink vessels mainly observed at or near the limbus), 1 when pink-red bulbar conjunctival vessel with branches extending at least 1-3 mm posteriorly from the limbus to the fornix, 2 when prominent red bulbar conjunctival vessels with several branches extending from the

limbus to the fornix, and 3 when red-dark red congested bulbar conjunctival vessels with extensive branches extending from the limbus to the fornix (Yang *et al.*, 2021). In case of corneal edema, if there was none, it was scored as 0. Cases with slightly increased corneal thickness and clear iris details were scored as 1, cases with increased stromal thickness and blurred iris details were scored as 2, and cases with the corneal thickness was markedly increased and the iris details were not visible were scored as 3 (Kausar *et al.*, 2015; Tsaousis *et al.*, 2015). Aqueous flare was 0 if none, 1 if the details of the iris and lens were clear, 2 if the details of the iris and lens were hazy, and 3 if they were fixed and coagulated with considerable fibrin (Hogan *et al.*, 1959). Posterior synechia was scored as 0 for no posterior synechia, 1 for less than 120 degrees, 2 for less than 240 degrees, and 3 for more than 240 degrees (Zhao *et al.*, 2020). In addition, IOP, intraocular fibrin, posterior capsule opacification (PCO), intraocular hemorrhage, and retinal detachment (RDT) were assessed at every follow-up.

If fibrin was observed in the anterior chamber upon re-examination,  $25 \ \mu g$  of tissue plasminogen activator was administered intracamerally in severe cases. Canine patients were diagnosed with vision loss if the visual placing and menace responses were negative.

#### 4. Statistical analyses

The collected data were commissioned to the Seoul National University Statistical Research Institute for statistical analysis. R statistical software (version 4.1.1, R foundation) was used for the statistical analyses. The Shapiro-Wilk test was used to test the normality of the data (p > 0.05). The level of statistical significance was established at p < 0.05. Fisher exact test was used to evaluate the statistical differences in categorical variables between the phaco-ECP and phaco groups. Statistical differences in continuous variables between both groups were assessed using the Wilcoxon rank sum test and two sample *t*-test. To analyze the IOP according to the two groups and time points, log transformation was taken to satisfy normality.

## Results

The clinical records of 15 eyes (11 dogs, 7 unilateral, 4 bilateral) that underwent phaco-ECP and 36 eyes (26 dogs, 16 unilateral, 10 bilateral) that underwent phaco alone were evaluated in this study. The signalment, breed distribution, surgery variables, and preoperative measurements of the two groups are described in Table 1. There were no significant differences between the groups in terms of signalment, breed distribution, diabetic status, gonioscopic grade, surgical variables, baseline IOP, conjunctival hyperemia, and aqueous flare. Cataract stage was higher and ciliary cleft represented by UBM was narrower in the phaco-ECP group (p = 0.024and p = 0.010, respectively).

Variables	Phaco-ECP	Phaco	<i>p</i> -value
No. of eyes (No. of patients)	15 (11)	36 (26)	
Age (yr)			$0.876^{a}$
	$8.2\pm2.9$	$8.4\pm3.4$	
Sex			$0.099^{b}$
Male castrated	11 (73.3)	14 (38.9)	0.077
Female spayed	3 (20.0)	13 (25.0)	
Female	1 (6.7)	9 (36.1)	
Male	0(0.0)	0 (0.0)	
Breed			0.477 <sup>b</sup>
Poodle	6 (40.0)	8 (22.2)	0.477
Maltese dog	4 (26.7)	5 (14.0)	
Mongrel	2 (13.3)	4 (11.1)	
Bichon Frise	0 (0.0)	5 (13.9)	
Spitz	0 (0.0)	4 (11.1)	
Yorkshire Terrier	0 (0.0)	4 (11.1)	
Cocker Spaniel	1 (6.7)	2 (5.6)	
Miniature Pinscher	1 (6.7)	1 (2.8)	
Shih Tzu	1 (6.7)	1(2.8) 1(2.8)	
Boston Terrier	0(0.0)	1(2.8) 1(2.8)	
Pomeranian dog	0 (0.0)	1(2.8) 1(2.8)	
¥			0.542
Eyes	10(667)	20(55.6)	0.543 <sup>b</sup>
OD OS	10 (66.7)	20 (55.6)	
OS	5 (33.3)	16 (44.4)	
Diabetic status			$1.000^{b}$
Non diabetics	7 (46.7)	17 (47.2)	
Diabetics	8 (53.3)	19 (52.8)	
Stage of cataract			0.024 <sup>bc</sup>
Immature	2 (13.3)	2 (5.6)	
Mature	6 (40.0)	28 (77.8)	
Hypermature	7 (46.7)	6 (16.7)	
Gonioscopy			0.184 <sup>b</sup>
Open	4 (26.7)	16 (44.4)	
Narrow	10 (66.7)	20 (55.6)	
Closed	1 (6.7)	0 (0.0)	

**TABLE 1.** Comparison of signalment, surgery variables and preoperative measures between the phaco-ECP and phaco groups

UBM			0.010 <sup>bc</sup>
Open	2 (13.3)	20 (55.6)	
Narrow	11 (73.3)	15 (41.7)	
Closed	2 (13.3)	1 (2.8)	
CTD			1.000 <sup>b</sup>
CTR	10 (66 7)	22(62.0)	1.000
No	10 (66.7)	23 (63.9)	
Yes	5 (33.3)	13 (36.1)	
Vitrectomy			0.297 <sup>b</sup>
No	13 (86.7)	25 (69.4)	
Yes	2 (13.3)	11 (30.6)	
Preoperative IOP (mmHg)			$0.418^{a}$
	$11.7 \pm 4.1$	$12.9\pm4.5$	0.110
Preoperative hyperemia <sup>d</sup>			0.254 <sup>b</sup>
0	8 (53.3)	25 (69.4)	
1	5 (33.3)	10 (27.8)	
2	2 (13.3)	1 (2.8)	
3	0 (0.0)	0 (0.0)	
Preoperative aqueous flare <sup>d</sup>			0.343 <sup>b</sup>
0	12 (80.0)	33 (91.7)	
1	3 (20.0)	3 (8.3)	
2	0 (0.0)	0 (0.0)	
3	0 (0.0)	0 (0.0)	
Volues are presented as mean + S	· · ·	0 (0.0)	

Values are presented as mean  $\pm$  SD or number (%).

Phaco, phacoemulsification; ECP, endoscopic cyclophotocoagulation; SD, standard deviation; OD, oculus dexter; OS, oculus sinister; UBM, ultrasound biomicroscopy; CTR, capsular tension ring; IOP, intraocular pressure.

<sup>a</sup>Wilcoxon rank sum test; <sup>b</sup>Fisher exact test; <sup>c</sup>p < 0.05; <sup>d</sup>Preoperative conjunctival hyperemia and aqueous flare scored on a scale of 0–3, where 0 = none, 1 = mild, 2 = moderate, and 3 = severe. The comparative mean IOP of phaco-ECP versus phaco alone from baseline to six months is shown in Table 2. In the phaco group, IOP tended to increase until the first postoperative week and thereafter, decreased. At 1 week postoperatively, the mean IOP was significantly higher in the phaco group than in the phaco-ECP group (p = 0.011). The IOP of the phaco-ECP group persisted within the normal range after surgery. However, 6 months postoperatively, the mean IOP was significantly higher in the phaco group.

Time ——	Mean IOP ± S	<i>p</i> -value	
	Phaco-ECP group	Phaco group	p-value
Baseline	$11.7 \pm 4.1$	$12.9 \pm 4.5$	0.154
1 day	$14.9\pm8.8$	$15.0 \pm 10.6$	0.565
1 wk	$11.7 \pm 4.0$	$16.3 \pm 8.1$	0.011 <sup>a</sup>
2 wk	$11.2 \pm 4.5$	$12.6 \pm 3.2$	0.101
1 mon	$10.4 \pm 5.0$	$11.3 \pm 4.4$	0.191
3 mon	$10.0 \pm 4.4$	$11.1 \pm 4.0$	0.131
6 mon	$14.0\pm2.9$	$11.9 \pm 3.8$	0.974

**TABLE 2.** Comparative mean IOP of phaco-ECP group versus phaco group from baseline to 6 months

IOP, intraocular pressure; Phaco, phacoemulsification; ECP, endoscopic cyclophotocoagulation; SD, standard deviation.

Two sample *t*-test of the log value of mean IOP, log transformation was taken to satisfy normality;  ${}^{a}p < 0.05$ .

The time to discontinuation of dorzolamide was shown in Table 3. The average duration of medication in the phaco-ECP group was  $14.1 \pm 8.3$  days and that of the phaco group was  $24.2 \pm 14.0$  days. The phaco-ECP group had a significantly shorter period of IOP-lowering drug use than the phaco group (p = 0.007). The difference between the two groups in the time to fibrin formation was not significant; however, postoperative PCO formation occurred significantly earlier in the phaco-ECP group ( $9.5 \pm 5.2$  days) than in the phaco group ( $38.1 \pm 33.3$  days) (p = 0.000, Table 3).

## TABLE 3. Comparison of the time to dorzolamide discontinuation, fibrin and PCO formation

Variables —	Mean ± S	- <i>p</i> -value		
variables	Phaco-ECP group	Phaco group	- p-value	
Discontinuation of 2% dorzolamide	$14.1 \pm 8.3$	$24.2\pm14.0$	$0.007^{a}$	
Fibrin formation	$4.7\pm7.6$	$5.0\pm 8.2$	0.582	
PCO formation	$9.5 \pm 5.2$	$38.1\pm33.3$	0.000 <sup>a</sup>	

PCO, posterior capsule opacification; SD, standard deviation; Phaco, phacoemulsification; ECP, endoscopic cyclophotocoagulation.

Wilcoxon rank sum test;  ${}^{a}p < 0.05$ .

The incidence of postoperative complications in the phaco-ECP and phaco groups are shown in Table 4. There were no significant differences between the two groups with regard to the incidence of corneal ulceration, hypopyon, fibrin formation, PCO formation, intraocular hemorrhage, and RDT. Intraocular hemorrhage occurred in some cases in both groups. In the phaco group, two patients had vitreal hemorrhage, two patients had retinal hemorrhage, and one patient had vitreal and retinal hemorrhage. However, in the phaco-ECP group, one patient had vitreal hemorrhage. RDT was identified in one patient in the phaco group.

Complications	Phaco-ECP group	Phaco group	<i>p</i> -value
Corneal ulceration	3 (20.0)	3 (8.3)	0.343
Hypopyon	3 (20.0)	0 (0.0)	-
Fibrin formation	7 (46.7)	14 (38.9)	0.757
PCO formation	15 (100.0)	36 (100.0)	1.000
Intraocular hemorrhage	1 (6.7)	5 (13.9)	0.657
Retinal detachment	0 (0.0)	1 (2.8)	-

**TABLE 4.** Comparison of the incidence of postoperative complications between the phaco-ECP and phaco groups

Values are presented as number (%).

The *p*-values for missing values are unreliable and are marked with dashed line.

Phaco, phacoemulsification; ECP, endoscopic cyclophotocoagulation; PCO, posterior capsule opacification.

Fisher exact test;  ${}^{a}p < 0.05$ .

Conjunctival hyperemia, corneal edema, aqueous flare, and posterior synechia were compared between the phaco-ECP and phaco groups at different time points (Table 5). Conjunctival hyperemia was more severe in the phaco-ECP group than in the phaco group only 1 week after surgery (p = 0.008). The phaco-ECP group showed significantly more severe corneal edema than the phaco group at all time points (1 day, p = 0.005; 1 week, p = 0.006; 2 weeks, p = 0.000; 1 month, p =0.000; 3 months, p = 0.002; 6 months, p = 0.011). In the case of aqueous flares, there was no difference at any time point between the two groups postoperatively. However, posterior synechia was more severe in the phaco-ECP group than in the phaco group 2 weeks, 1 month, 3 months, and 6 months postoperatively (2 weeks, p = 0.005; 1 month, p = 0.048; 3 months, p = 0.002; 6 months, p = 0.041). This meant that the degree of postoperative posterior synechia did not differ between the two groups until one week immediately after surgery, depending on whether ECP was used in conjunction with cataract surgery, but started to differ from two weeks after surgery, and this difference persisted until the last follow-up.

Time	Conjunctival hyperemia			Corneal edema		Aqueous flare		Posterior synechia				
	Phaco-ECP group	Phaco group	<i>p</i> -value	Phaco-ECP group	Phaco group	<i>p</i> -value	Phaco-ECP group	Phaco group	<i>p</i> -value	Phaco-ECP group	Phaco group	<i>p</i> -value
Baseline	$0.6\pm0.7$	$0.3\pm0.5$	0.254				$0.2\pm0.4$	$0.1\pm0.2$	0.343			
1 day	$1.2\pm0.4$	$1.1\pm0.5$	0.750	$2.1\pm0.5$	$1.4\pm0.7$	0.005ª	$2.5\pm0.7$	$2.0\pm0.9$	0.110	$0.0\pm0.0$	$0.0\pm0.2$	1.000
1 wk	$1.1\pm0.3$	$0.7\pm0.5$	$0.008^{a}$	$1.1\pm0.7$	$0.5\pm0.7$	0.006ª	$1.1\pm0.3$	$0.9\pm0.5$	0.208	$0.1\pm0.4$	$0.1\pm0.4$	0.443
2 wk	$0.9\pm0.7$	$0.5\pm0.5$	0.106	$1.0\pm0.7$	$0.1\pm0.4$	$0.000^{a}$	$0.9\pm0.5$	$0.7\pm0.6$	0.225	$0.9 \pm 1.1$	$0.1 \pm 0.4$	0.005 <sup>a</sup>
1 mon	$0.8\pm0.4$	$0.5\pm0.5$	0.110	$0.8\pm0.7$	$0.0\pm0.2$	$0.000^{a}$	$0.8\pm0.7$	$0.7\pm0.6$	0.808	$1.0 \pm 1.2$	$0.3\pm0.7$	$0.048^{a}$
3 mon	$0.2\pm0.4$	$0.3\pm0.5$	0.502	$0.6\pm0.8$	$0.0\pm0.2$	0.002 <sup>a</sup>	$0.4\pm0.5$	$0.4\pm0.5$	1.000	$1.2\pm0.9$	$0.4\pm0.7$	0.002 <sup>a</sup>
6 mon	$0.3\pm0.5$	$0.2\pm0.6$	0.239	$0.6\pm0.9$	$0.1\pm0.3$	0.011 <sup>a</sup>	$0.2\pm0.4$	$0.4\pm0.6$	0.850	$1.2\pm1.0$	$0.5\pm0.8$	0.041 <sup>a</sup>

TABLE 5. Comparison at different time points for conjunctival hyperemia, corneal edema, aqueous flare and posterior synechia

All scored on a scale of 0-3, where 0 =none, 1 =mild, 2 =moderate, and 3 =severe.

Phaco, phacoemulsification; ECP, endoscopic cyclophotocoagulation.

Fisher exact test;  ${}^{a}p < 0.05$ .

## Discussion

Glaucoma is a serious complication of phaco surgery, ultimately leading to vision loss in many cases (Michau, 2021). ECP for glaucoma in dogs has been conducted since 2004, and studies have shown encouraging outcomes for the treatment of primary and secondary glaucoma (Bras *et al.*, 2005; Lutz *et al.*, 2013). However, long-term comparative data of phaco-ECP versus phaco alone in dogs are rare. This study aimed to compare the effects of ECP on postoperative IOP and complications, and it could effectively reduce the incidence of IOP increase after phaco in dogs with a high risk of postoperative glaucoma, although corneal edema and posterior synechia were more severe.

Based on the results of this study, the IOP in the phaco group tended to increase until the first week after surgery and thereafter, decreased. First week after surgery, the IOP was significantly higher in the phaco group than in the phaco-ECP group. The IOP of the phaco-ECP group persisted within the normal range postoperatively. In a previous study that defined glaucoma as an elevation in IOP, which was irreconcilable with the function and health of the optic nerve and retina, 16.8% of eyes developed glaucoma postoperatively with a median follow-up of 5.8 months (Biros *et al.*, 2000). In this present study, even though ECP was applied to patients with a high predisposition to postoperative glaucoma (patients with narrow or closed ciliary cleft), the postoperative IOP persisted within the normal range, it is considered that the application of ECP has IOP maintenance effect after surgery. Unlike in previous human studies, ECP was used for the prevention of postoperative glaucoma in dogs with normal IOP in this study, and it was not applied to canine glaucoma patients. Further studies on the effects of lowering IOP and reducing ocular hypotensive medications after ECP in dogs with glaucoma would be required.

The IOP was significantly higher in the phaco-ECP group than in the phaco group at 6 months postoperatively. The ciliary cleft on the UBM in the phaco-ECP group was significantly narrower than that in the phaco group in this study, suggesting high predisposition to postoperative glaucoma and more severe posterior synechia was observed in the phaco-ECP group than in the phaco group from the second week postoperatively, which were considered the reasons for the increase in IOP in the phaco-ECP group 6 months after surgery. IOP might have been increased immediately after surgery, if ECP was not applied in the phaco-ECP group, and it was thought to have a short-term effect of lowering the increase in IOP. In addition, although there was a significant difference from that of the phaco group, the IOP of the phaco-ECP group at 6 months postoperatively was within the normal range, which might also be due to the effect of ECP.

Dorzolamide was instilled as postoperative management until IOP was stabilized to 15 mmHg in this study. The mean duration of administration in the phaco-ECP group was  $14.1 \pm 8.3$  days, and that in the phaco group was  $24.2 \pm 14.0$  days. Considering that the period of ocular hypotensive eye drops use was significantly shorter in the phaco-ECP group, the ECP procedure was considered to keep the IOP low postoperatively. This result was consistent with those of previous studies showing a decrease in the use of hypotensive medications after ECP application (Clement *et al.*, 2013; Francis *et al.*, 2014; Siegel *et al.*, 2015; Pérez *et al.*, 2018).

The cataract stage and UBM showed significant differences between the phaco-ECP and phaco groups before surgery. The ciliary cleft narrows as the cataract stage increased (Rose *et al.*, 2008). The incidence of postoperative glaucoma and preoperative cataract stage is controversial (Biros *et al.*, 2000; Sigle *et al.*, 2006; Klein *et al.*, 2011). Despite the higher cataract stage and narrower ciliary cleft in the phaco-ECP group in this study, postoperative IOP persisted within the normal range, thus helping ECP maintain IOP after phaco surgery.

The incidence of fibrin formation after phaco surgery in dogs was 4.55–34% (Michau, 2021). The incidence of fibrin formation in this study was 46.7% in the phaco-ECP group and 38.9% in the phaco group. There was no significant difference between the two groups; however, the phaco-ECP group showed a higher incidence than that of the previous study. Furthermore, intraocular fibrin formation occurred 1–3 weeks after surgery (Michau, 2021), and the results of this study was consistent with those of previous studies, with an average of  $4.7 \pm 7.6$  and  $5.0 \pm 8.2$  days in the phaco-ECP group and phaco group, respectively. The difference between the two groups in the time points of fibrin formation was not significant; therefore, the time points of fibrin formation were independent of ECP during surgery. However, the time of PCO formation was significantly earlier in the phaco-ECP group  $(9.5 \pm 5.2)$ days) than in the phaco group  $(38.1 \pm 33.3 \text{ days})$ . It is known that contact with IOL and surgical invasion stimulates residual lens epithelial cells to produce numerous cytokines, possibly affecting lens epithelial cells and leading to fibrous proliferation and collagen production to form PCO (Hayashi et al., 2004). Although it is not known exactly how ECP affects PCO formation, the application of ECP accelerated PCO in this study.

In a previous study comparing the outcomes of transscleral cyclophotocoagulation and ECP in humans, the postoperative incidence of corneal edema was more severe in the ECP group (Beardsley *et al.*, 2017). Similarly, corneal edema was significantly more severe in the phaco-ECP group at all time points up to the last follow-up in this study. Based on the results of the above studies, ECP was considered to affect the corneal endothelium.

Postoperative inflammation after cataract surgery is inevitable, and the occurrence of inflammation often involves complications such as aqueous flare, iris adhesions, and postoperative glaucoma, which often immediately affect the outcome of following surgery (Zhao et al., 2020). The most usual postoperative progress of ECP was intraocular inflammation, which was minimal for the first 2 days after surgery and worsened on the 3rd day after surgery, causing moderate inflammation for 3-5 days after surgery and gradually disappearing over the next 2 weeks (Bras et al., 2005). In this study, conjunctival hyperemia, which suggested intraocular inflammation, was significantly greater in the phaco-ECP group than in the phaco group at 1 week after surgery, consistent with the results of previous studies (Bras et al., 2005). In the case of aqueous flare, which reflected the severity of intraocular inflammation, there was no difference between the two groups at all time points postoperatively. However, posterior synechia following surgery was more severe in the phaco-ECP group than the phaco group at 2 weeks, 1 month, 3 months, and 6 months after surgery. Posterior synechia is known to be caused by an increase in inflammatory substances in the aqueous humor and is strongly related to aqueous flare (Hendrix et al., 2021). Although there was a strong association between aqueous flare and posterior synechia, the two postoperative outcomes had different tendencies.

This study had some limitations, mainly due to its retrospective nature. There was

a difference in the number of eyes between the phaco-ECP and phaco groups because the number of eyes satisfying the inclusion criteria during the study period was not controlled. The effect of ECP on the postoperative IOP after cataract surgery was investigated; however, since ECP was applied when either the iridocorneal angle or the ciliary cleft was narrow or closed, the iridocorneal angle (expressed as UBM and gonioscopy), which might be a factor highly related to postoperative glaucoma, was not controlled. Further studies on the effect of ECP under the same iridocorneal angle condition would be needed. Furthermore, the surgical procedures were conducted by two different ophthalmic surgeons who might have had slight differences in surgical techniques. In addition, when both eyes of one subject were included in a study, it was recommended to assess the correlation between the eyes (Armstrong, 2013); however, but due to the small sample size, both eyes were independently viewed and analyzed. Studies with larger sample sizes and longer follow-up periods are warranted.

To date, studies on ECP in dogs have reported long-term control of IOP and reduced need for topical glaucoma medications in approximately 80% of treated cases 12 months after surgery, and maintenance of vision in approximately 70% of cases (Plummer *et al.*, 2021). This study investigated the effects of ECP on postoperative IOP and complications after phaco in dogs with normal IOP but narrow iridocorneal angle or ciliary cleft.

## Conclusion

In conclusion, although ECP might cause more postoperative complications, such as corneal edema or posterior synechia after phaco surgery than phaco alone, it would be an additional option in consultation with an owner for the prevention of IOP increase in the early postoperative period in patients with a high risk of postoperative glaucoma, which is a major postoperative complication that would cause vision loss.

## References

- Armstrong RA. Statistical guidelines for the analysis of data obtained from one or both eyes. Ophthalmic and Physiological Optics: the Journal of the British College of Ophthalmic Opticians (Optometrists) 2013;33(1):7-14.
- Beardsley R, Law SK, Caprioli J, et al. Comparison of Outcomes between Endoscopic and Transcleral Cyclophotocoagulation. Vision (Basel) 2017;1(4):24.
- Bedford PG. A practical method of gonioscopy and goniophotography in the dog and cat. *J Small Anim Pract* 1973;14(10):601-606.
- Biros DJ, Gelatt KN, Brooks DE, et al. Development of glaucoma after cataract surgery in dogs: 220 cases (1987–1998). Journal of the American Veterinary Medical Association 2000;216(11):1780-1786.
- Bras D, Maggio F. Surgical Treatment of Canine Glaucoma: Cyclodestructive Techniques. *The Veterinary clinics of North America. Small Animal Practice* 2015;45(6):1283-1305.
- Bras ID, Robbin TE, Wyman M, et al. Diode endoscopic cyclophotocoagulation in canine and feline glaucoma. Veterinary Ophthalmology 2005;8(6):449.
- Clement CI, Kampougeris G, Ahmed F, *et al.* Combining phacoemulsification with endoscopic cyclophotocoagulation to manage cataract and glaucoma. *Clinical and Experimental Ophthalmology* 2013;41(6):546-551.

- Ekesten B, Narfström K. Correlation of morphologic features of the iridocorneal angle to intraocular pressure in Samoyeds. *Am J Vet Res* 1991;52(11):1875-1878.
- Francis BA, Berke SJ, Dustin L, et al. Endoscopic cyclophotocoagulation combined with phacoemulsification versus phacoemulsification alone in medically controlled glaucoma. Journal of Cataract and Refractive Surgery 2014;40(8):1313-1321.
- Hayashi Y, Kato S, Fukushima H, et al. Relationship between anterior capsule contraction and posterior capsule opacification after cataract surgery in patients with diabetes mellitus. Journal of Cataract and Refractive Surgery 2004;30(7):1517-1520.
- Hendrix DVH, Thomasy SM, Gum GG. Physiology of the eye. In: Gelatt KN, Ben-Shlomo G, Gilger BC, Hendrix DVH, Kern TJ, Plummer CE. Veterinary Ophthalmology. New Jersey: Wiley-Blackwell; 2021;140.
- Hogan MJ, Kimura SJ, Thygeson P. Signs and symptoms of uveitis. I. Anterior uveitis. *American Journal of Ophthalmology* 1959;47(5 Pt 2):155-170.
- Kausar A, Farooq S, Akhter W, et al. Transient Corneal Edema After Phacoemulsification. Journal of the College of Physicians and Surgeons Pakistan 2015;25(7):505-509.
- Klein HE, Krohne SG, Moore GE, et al. Postoperative complications and visual outcomes of phacoemulsification in 103 dogs (179 eyes): 2006–2008. *Veterinary Ophthalmology* 2011;14(2):114-120.

- Lindfield D, Ritchie RW, Griffiths MF. 'Phaco-ECP': combined endoscopic cyclophotocoagulation and cataract surgery to augment medical control of glaucoma. *BMJ Open* 2012;2(3):e000578.
- Lutz EA, Webb TE, Bras ID, *et al.* Diode endoscopic cyclophotocoagulation in dogs with primary and secondary glaucoma: 292 cases (2004–2013). *Veterinary Ophthalmology* 2013;16(6):40.
- Michau TM. Surgery of the lens. In: Gelatt KN, Ben-Shlomo G, Gilger BC, Hendrix DVH, Kern TJ, Plummer CE. Veterinary Ophthalmology. New Jersey: Wiley-Blackwell; 2021;1410-1431.
- Moore DL, McLellan GJ, Dubielzig RR. A study of the morphology of canine eyes enucleated or eviscerated due to complications following phacoemulsification. *Veterinary Ophthalmology* 2003;6(3):219-226.
- Pérez Bartolomé F, Rodrigues IA, Goyal S, et al. Phacoemulsification plus endoscopic cyclophotocoagulation versus phacoemulsification alone in primary open-angle glaucoma. European Journal of Ophthalmology 2018;28(2):168-174.
- Plummer CE, Komáromy AM, Gelatt KN. The Canine Glaucoma. In: Gelatt KN, Ben-Shlomo G, Gilger BC, Hendrix DVH, Kern TJ, Plummer CE. Veterinary Ophthalmology. New Jersey: Wiley-Blackwell; 2021;1237.
- Rose MD, Mattoon JS, Gemensky-Metzler AJ, *et al.* Ultrasound biomicroscopy of the iridocorneal angle of the eye before and after phacoemulsification and intraocular lens implantation in dogs. *American Journal of Veterinary*

Research 2008;69(2):279-288.

- Shields MB. Intraocular cyclophotocoagulation. *Transactions of the Ophthalmological Societies of the United Kingdom* 1986;105(Pt 2):237-241.
- Siegel MJ, Boling WS, Faridi OS, et al. Combined endoscopic cyclophotocoagulation and phacoemulsification versus phacoemulsification alone in the treatment of mild to moderate glaucoma. Clinical and Experimental Ophthalmology 2015;43(6):531-539.
- Sigle KJ, Nasisse MP. Long-term complications after phacoemulsification for cataract removal in dogs: 172 cases (1995–2002). Journal of the American Veterinary Medical Association 2006;228(1):74-79.
- Tsaousis KT, Panagiotou DZ, Kostopoulou E, *et al.* Corneal oedema after phacoemulsification in the early postoperative period: A qualitative comparative case-control study between diabetics and non-diabetics. *Annals of Medicine and Surgery* (Lond) 2015;5:67-71.
- Yang VY, Miller PE, Keys DA, et al. Effects of 0.02% netarsudil ophthalmic solution on intraocular pressure of normotensive dogs. *Veterinary Ophthalmology* 2021;24(Suppl 1):87-95.
- Zhao Y, Deng X, Chang P, et al. Expression Profiles of Inflammatory Cytokines in the Aqueous Humor of Children after Congenital Cataract Extraction. *Translational Vision Science & Technology* 2020;9(8):3.

## 국문 초록

## 개에서 내시경 모양체광응고술 병행 및 단독 수정체유화술 후의 안압과 복합증에 대한 후향적 연구

## 지도교수 서 강 문

### 김 솔

서울대학교 대학원

수의학과 임상수의학 전공

본 연구는 정상 안압 개에서 수정체유화술 후 안압과 복합증에 대해 내시경 모양체광응고술이 미치는 영향을 조사하는 것을 목적으로 하였다. 내시경 모양체광응고술 병행 수정체유화술을 시행한 15개의 눈과 단독 수정체유화술을 시행한 36개의 눈에서 안압, 결막 충혈, 각막 부종, 방수 흐림, 홍채 후방 유착, 안내 섬유소 및 수정체 후낭 혼탁 형성의 의료 기록을 후향적으로 평가하였다. 내시경 모양체광응고술은 우각 또는 모양체틈새가 좁거나 폐쇄된 경우에 적용하였다. 내시경 모양체광응고술 병행 수정체유화술을 시행한 군의 수술 후 안압은 정상 범위 내에서 지속되었다. 내시경 모양체광응고술 병행 수정체유화술을 시행한 군은 단독 수정체유화술을 시행한 군보다 dorzolamide 사용 기간이 더 짧았다. 수정체 후낭 혼탁은 내시경 모양체광응고술 병행 수정체유화술을 시행한 군에서 더 일찍 형성되었다. 추적 관찰 시 내시경 모양체광응고술 병행 수정체유화술을 시행한 군이 단독 수정체유화술을 시행한 군보다 더 심한 각막 부종을 보였다. 홍채 후방 유착은 2주부터 마지막 추적 관찰 시까지 내시경 모양체광응고술 병행 수정체유화술을 시행한 군이 단독 수정체유화술을 시행한 군보다 더 많이 발생하였다.

내시경 모양체광응고술은 각막 부종 및 홍채 후방 유착과 같은 술 후 복합증을 더 유발할 수 있으나 수정체유화술 후 녹내장의 위험이 높은 개에서 안압 증가의 발생을 효과적으로 감소시킬 수 있을 것으로 사료된다.

**주요어:** 개, 녹내장, 레이저, 모양체광응고술, 백내장, 병행 수술 **학 번:** 2020-29607

32