

# Quantitative Assessment of Early Postoperative Inflammatory Response Following Micro-incision Phacoemulsification Combined with Minimally Invasive Vitrectomy

Mingxue Ren

National Clinical Research Center for Ocular Diseases, Eye Hospital, Wenzhou Medical University, Wenzhou 325027, Zhejiang Province, China

## Abstract

**Objective** To quantitatively evaluate the early postoperative inflammatory response after micro-incision phacoemulsification combined with minimally invasive vitrectomy, and to compare the differences in postoperative inflammatory responses among three different surgical approaches. **Methods** This prospective, open-label, single-center clinical study enrolled patients who underwent micro-incision phacoemulsification with intraocular lens implantation (phaco group, n=17), minimally invasive 23-gauge vitrectomy (vitrectomy group, n=17), or combined micro-incision phacoemulsification and vitrectomy (combined group, n=30) at our hospital between 2021 and 2022. All patients underwent slit-lamp examination and anterior chamber flare measurement using a laser flare meter (FM-600) preoperatively and at 1 day, 1 week, and 1 month postoperatively. Repeated measures ANOVA was used to assess the time effect of anterior chamber flare values within each group, and one-way ANOVA was used for inter-group comparisons. **Results** There were no significant differences in baseline demographic characteristics among the three groups. The time effect of anterior chamber flare values was statistically significant in the vitrectomy group ( $P=0.04$ ) and the combined group ( $P=0.04$ ), but not in the phaco group ( $P=0.68$ ). Compared with preoperative values, the vitrectomy group showed significant increases in anterior chamber flare at 1 day ( $33.85\pm 53.16$  vs.  $3.93\pm 3.40$  pc/ms), 1 week ( $9.84\pm 13.47$  vs.  $3.93\pm 3.40$  pc/ms), and 1 month ( $5.48\pm 3.94$  vs.  $3.93\pm 3.40$  pc/ms) postoperatively. The combined group showed a significant increase only at 1 day postoperatively ( $24.05\pm 41.36$  vs.  $8.68\pm 15.66$  pc/ms), with values returning to baseline at 1 week and 1 month. No statistically significant differences were observed among the three groups at any time point ( $P=0.39$  preoperatively,  $P=0.23$  at 1 day,  $P=0.90$  at 1 week, and  $P=0.15$  at 1 month). **Conclusion** Both minimally invasive vitrectomy and combined surgery can cause transient blood-aqueous barrier breakdown in the early postoperative period, but recovery to baseline is generally achieved by 1 month. Combined surgery did not significantly increase the postoperative inflammatory response, and its inflammatory profile was similar to that of vitrectomy alone.

## Keywords

Phacoemulsification; Vitrectomy; Combined surgery; Anterior chamber flare; Blood-aqueous barrier; Laser flare photometry.

## 1. Introduction

Cataract and vitreoretinal diseases frequently coexist in middle-aged and elderly populations. With the continuous advancement of phacoemulsification and minimally invasive vitrectomy techniques, combined surgery has become a commonly used clinical strategy [1-3]. Combined surgery avoids a second operation, reduces medical costs, and accelerates visual recovery.

Additionally, it allows for more extensive anterior vitreous removal, thereby reducing the incidence of postoperative proliferative vitreoretinopathy (PVR), and prevents intraoperative lens damage [4-6].

However, intraocular surgical trauma inevitably disrupts the blood-aqueous barrier, leading to protein and inflammatory cell exudation in the aqueous humor, which manifests as postoperative anterior chamber inflammation. Studies have shown that various cytokines (such as BLC, ICAM-1, IL-4, IL-6, and IL-8) are significantly elevated in the aqueous humor after vitrectomy and can persist for up to one year. It is hypothesized that this sustained inflammatory microenvironment may be closely related to the development of secondary glaucoma and complicated cataract after vitrectomy [7-8]. The degree of postoperative inflammatory response is also considered an important risk factor for macular edema following vitrectomy [9]. Therefore, objective and quantitative evaluation of early postoperative inflammatory response after combined surgery is of significant clinical importance for assessing surgical outcomes and optimizing treatment strategies.

Anterior chamber cells and flare are important indicators of anterior chamber inflammation. Although the traditional SUN grading system is widely used, it is somewhat subjective and exhibits considerable inter-evaluator variability [10]. Anterior chamber flare values measured by laser flare photometry are considered an objective and sensitive indicator for assessing blood-aqueous barrier disruption, and have been widely used to evaluate postoperative inflammatory responses following various surgeries, including minimally invasive vitrectomy, phacoemulsification, and trabeculectomy [11-13]. To date, no studies have utilized laser flare photometry to quantitatively assess the inflammatory response after combined micro-incision phacoemulsification and minimally invasive vitrectomy. This prospective study aimed to use laser flare photometry to quantitatively evaluate and compare early postoperative inflammatory responses among three surgical approaches, providing evidence-based guidance for clinical treatment decisions.

## **2. Subjects and Methods**

### **2.1. Study Design and Participants**

This prospective, open-label, single-center clinical study was approved by the hospital ethics committee, and all patients provided written informed consent. Patients hospitalized and undergoing surgical treatment at the ophthalmology department of our hospital between July 2021 and June 2022 were enrolled and divided into three groups: the phaco group (micro-incision phacoemulsification with intraocular lens implantation, n=17), the vitrectomy group (minimally invasive 23-gauge vitrectomy, n=17), and the combined group (combined micro-incision phacoemulsification and 23-gauge vitrectomy, n=30).

The inclusion criteria were as follows: age between 18 and 80 years; diagnosis of age-related cataract, complicated cataract after vitrectomy, idiopathic epiretinal membrane, idiopathic macular hole, or vitreous opacification; no other ocular surgery within the past six months; no topical or systemic corticosteroid use within the past three months; and ability to provide written informed consent. Patients were excluded if they had coexisting ocular diseases such as uveitis, glaucoma, ocular hypertension, diabetic retinopathy, retinal vein occlusion, or iris neovascularization; a history of ocular trauma; systemic autoimmune diseases; pregnancy or lactation; neurological or psychiatric disorders precluding informed consent or follow-up; or inability to cooperate with examinations.

### **2.2. Examinations**

All patients underwent slit-lamp examination (assessing the cornea, lens, anterior chamber exudation, vitreous cavity, and fundus), measurement of uncorrected and best-corrected visual

acuity (BCVA), intraocular pressure (IOP) assessment, and anterior chamber flare measurement using the FM-600 (Kowa, Tokyo, Japan) preoperatively and at 1 day, 1 week, and 1 month postoperatively. Anterior chamber flare values were expressed as photon counts per millisecond (pc/ms).

### 2.3. Surgical Procedures

In the phaco group, standard micro-incision phacoemulsification with posterior chamber intraocular lens implantation was performed. In the vitrectomy group, standard three-port 23-gauge minimally invasive vitrectomy was performed, with retinal laser photocoagulation, gas, or silicone oil tamponade as clinically indicated. In the combined group, micro-incision phacoemulsification with intraocular lens implantation was performed first, followed by 23-gauge vitrectomy. All surgeries were performed by the same experienced vitreoretinal surgeon.

### 2.4. Statistical Analysis

SPSS statistical software was used for data analysis. Continuous variables were expressed as mean  $\pm$  standard deviation ( $\bar{x}\pm s$ ). Repeated measures ANOVA was used to assess the time-dependent trend of anterior chamber flare values within each group. One-way ANOVA was used for inter-group comparisons at each time point. Non-parametric tests were applied when data did not follow a normal distribution. A P-value  $<0.05$  was considered statistically significant.

## 3. Results

### 3.1. Baseline Characteristics

There were no statistically significant differences in age, sex, or systemic comorbidities (hypertension, diabetes) among the three groups (Table 1).

Table 1 Baseline demographic characteristics of the three groups

Group	Phaco(n=17)	Vitrectomy(n=17)	Combined(n=30)
Age(years)	68.06 $\pm$ 11.34	54.65 $\pm$ 18.45	64.20 $\pm$ 9.96
Sex (male/female)	7/10	5/12	6/24
Hypertension (n)	6/17	3/17	4/30
Diabetes (n)	2/17	1/17	0/30

### 3.2. Anterior Chamber Flare Values

Changes in anterior chamber flare values among the three groups at each time point are presented in Table 2.

Table 2 Comparison of anterior chamber flare values among the three groups (pc/ms,  $\bar{x}\pm s$ )

Group	Preoperative	Postoperative 1d	Postoperative 1w	Postoperative 1m	P
Phaco	7.06 $\pm$ 5.48	10.43 $\pm$ 9.71	8.63 $\pm$ 7.54	7.41 $\pm$ 5.08	0.68
Vitrectomy	3.93 $\pm$ 3.40	33.85 $\pm$ 53.16*	9.84 $\pm$ 13.47*	5.48 $\pm$ 3.94*	0.04
Combined	8.68 $\pm$ 15.66	24.05 $\pm$ 41.36*	8.68 $\pm$ 6.43	8.17 $\pm$ 4.49	0.04
Pb	0.39	0.23	0.90	0.15	-

Repeated measures ANOVA for time effect; \* Significantly different from preoperative value (P $<0.05$ ); b One-way ANOVA for inter-group comparison

Repeated measures ANOVA showed no significant change in anterior chamber flare values over time in the phaco group (P=0.68). In contrast, the time main effect was significant in both the vitrectomy group (P=0.04) and the combined group (P=0.04). Post-hoc analysis revealed that the vitrectomy group had significantly higher anterior chamber flare values at 1 day, 1 week, and 1 month postoperatively compared with preoperative values. The combined group showed

a significant increase only at 1 day postoperatively, with values returning to baseline at 1 week and 1 month.

One-way ANOVA showed no statistically significant differences in anterior chamber flare values among the three groups at any time point ( $P=0.39$  preoperatively,  $P=0.23$  at 1 day,  $P=0.90$  at 1 week, and  $P=0.15$  at 1 month).

## 4. Discussion

This prospective study used laser flare photometry to quantitatively evaluate the early postoperative inflammatory response after combined micro-incision phacoemulsification and minimally invasive vitrectomy. The results showed that both minimally invasive vitrectomy and combined surgery caused transient blood-aqueous barrier breakdown in the early postoperative period, as evidenced by elevated anterior chamber flare values. However, inflammatory responses in all groups had essentially returned to preoperative levels by 1 month. Notably, combined surgery did not exhibit a more severe inflammatory response than vitrectomy alone, and no statistically significant inter-group differences were observed at any time point.

### 4.1. Inflammatory Characteristics After Cataract Surgery and Vitrectomy Alone

In this study, anterior chamber flare values in the phaco group showed no significant fluctuation across time points, suggesting that micro-incision phacoemulsification causes minimal disruption to the blood-aqueous barrier with rapid recovery. This finding is consistent with previous reports [12]. In contrast, the vitrectomy group showed a significant increase in anterior chamber flare at 1 day postoperatively, and although values gradually declined at 1 week and 1 month, they remained significantly above preoperative baseline. This result supports the findings of Jiang et al [7], who reported sustained elevation of inflammatory cytokines in the aqueous humor after vitrectomy, indicating that blood-aqueous barrier repair requires a longer time. The relatively severe inflammatory response after vitrectomy may be attributed to longer surgical duration, mechanical and chemical irritation from intraocular irrigation solutions, and phototoxic damage from the light fiber and operating microscope [13-14].

### 4.2. Inflammatory Characteristics After Combined Surgery

The combined group showed a significant increase in anterior chamber flare at 1 day postoperatively, but values returned to baseline by 1 week, indicating a faster recovery than the vitrectomy-alone group. This finding is clinically significant because, despite the increased number of procedural steps and longer surgical duration, combined surgery did not result in more severe sustained inflammation. Several factors may explain this observation. First, combined surgery avoids the additional trauma of a second operation, thereby reducing cumulative surgical stress. Second, following cataract removal, the surgeon can perform vitrectomy with a clearer and wider field of view, which reduces anterior segment manipulation and the number of instrument entries into the eye, thereby minimizing mechanical irritation to the iris and ciliary body. Third, the application of micro-incision techniques, including 23-gauge vitrectomy and micro-incision phacoemulsification, further reduces intraocular tissue disturbance.

Previous studies evaluating postoperative inflammation after combined surgery have relied primarily on slit-lamp observations, including anterior chamber exudation, posterior synechiae, and endophthalmitis rates, lacking objective quantitative data [4,6,15]. This study provides objective quantitative evidence through laser flare photometry, supporting the safety of combined surgery in terms of inflammatory control.

### 4.3. Clinical Implications and Future Perspectives

Postoperative inflammatory response is recognized as an important risk factor for macular edema and secondary glaucoma after vitrectomy [9,16]. Our results indicate that early postoperative inflammation after combined surgery is transient and generally resolves by 1 month, providing evidence-based support for surgeons considering combined surgery. However, the follow-up duration in this study was only 1 month, which is insufficient to assess the long-term effects on macular edema, glaucoma, or cataract progression. Future studies with longer follow-up periods and aqueous humor cytokine analysis are needed to further elucidate the long-term impact of different surgical approaches on the intraocular microenvironment.

### 4.4. Limitations

This study has several limitations. First, as a single-center, open-label study with a relatively small sample size (64 cases), the statistical power may be limited, particularly for inter-group comparisons. Second, aqueous humor cytokine analysis was not performed, precluding mechanistic insights at the molecular level.

## 5. Conclusion

Micro-incision phacoemulsification combined with minimally invasive vitrectomy causes transient blood-aqueous barrier breakdown in the early postoperative period, but recovery to baseline is generally achieved by 1 month. Combined surgery did not significantly increase the postoperative inflammatory response, and its postoperative inflammatory profile was similar to that of vitrectomy alone. Laser flare photometry is an objective and effective tool for quantitatively evaluating postoperative inflammatory responses after combined surgery.

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## References

- Lahey, J. M., Francis, R. R., & Kearney, J. J. (2003). Combining phacoemulsification with pars plana vitrectomy in patients with proliferative diabetic retinopathy: A series of 223 cases. *Ophthalmology*, *110*(7), 1335–1339.
- Chaudhry, N. A., Cohen, K. A., Flynn, H. W., et al. (2003). Combined pars plana vitrectomy, lens removal and intraocular lens implantation for complications of diabetic retinopathy. *Seminars in Ophthalmology*, *18*(3), 132–141.
- Lahey, J. M., Francis, R. R., Kearney, J. J., et al. (2004). Combining phacoemulsification and vitrectomy in patients with proliferative diabetic retinopathy. *Current Opinion in Ophthalmology*, *15*(3), 192–196.
- Lahey, J. M., Francis, R. R., Fong, D. S., et al. (2002). Combining phacoemulsification with vitrectomy for treatment of macular holes. *British Journal of Ophthalmology*, *86*(8), 876–878.
- Chung, T. Y., Chung, H., & Lee, J. H. (2002). Combined surgery and sequential surgery comprising phacoemulsification, pars plana vitrectomy, and intraocular lens implantation: Comparison of clinical outcomes. *Journal of Cataract and Refractive Surgery*, *28*(11), 2001–2005.
- Mochizuki, Y., et al. (2006). Surgical results of combined pars plana vitrectomy, phacoemulsification, and intraocular lens implantation. [Journal name missing], *16*(2), 279–286.

- Gu, R., Zhou, M., Jiang, C., et al. (2016). Elevated concentration of cytokines in aqueous in post-vitreotomy eyes. *Clinical & Experimental Ophthalmology*, 44(2), 128–134.
- Saari, K. M., Guillén-Monterrubio, O. M., Hartikainen, J., et al. (1997). Measurement of protein concentration of aqueous humour in vivo: Correlation between laser flare measurements and chemical protein determination. *Acta Ophthalmologica Scandinavica*, 75(1), 63–66.
- Kim, S. J., et al. (2009). Incidence of postvitrectomy macular edema using optical coherence tomography. *Ophthalmology*, 116(8), 1531–1537.
- Jabs, D. A., et al. (2005). Standardization of uveitis nomenclature for reporting clinical data. *American Journal of Ophthalmology*, 140(3), 509–516.
- Bernasconi, O., Papadia, M., & Herbort, C. P. (2010). Sensitivity of laser flare photometry compared to slit-lamp cell evaluation in monitoring anterior chamber inflammation in uveitis. *International Ophthalmology*, 30(5), 495–500.
- Shah, S. M., & Spalton, D. J. (1994). Changes in anterior chamber flare and cells following cataract surgery. *British Journal of Ophthalmology*, 78(2), 91–94.
- Agarwal, A., Joshi, D., Katoch, D., et al. (2019). Application of laser flare photometry in the quantification of blood-aqueous barrier breakdown after micro-incision vitrectomy. *Ocular Immunology and Inflammation*, 27(4), 651–657.
- Oshika, T. (1990). Aqueous protein concentration in rhegmatogenous retinal detachment. *Japanese Journal of Ophthalmology*, 34, 63–71.
- Chung, T. Y., et al. (2002). Combined surgery and sequential surgery... *Journal of Cataract and Refractive Surgery*.
- Federman, J. L., & Schubert, H. D. (1988). Complications associated with the use of silicone oil in 150 eyes after retina-vitreous surgery. *Ophthalmology*, 95(7), 870–876.