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Research Article

Higher Incidence of Late-Onset Ocular Hypertension Following Vitrectomy with Gas Tamponade for Proliferative Diabetic Retinopathy

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Abstract

Purpose: To compare the incidence of elevation of intraocular pressure before and after vitrectomy between patients with proliferative diabetic retinopathy (PDR) and those with macular hole (MH) or rhegmatogenous retinal detachment (RDD).

Methods: This retrospective observational study included the medical records of consecutive patients who underwent vitrectomy and did not develop postoperative neovascular glaucoma during follow-up for at least 6 months. The patients were divided into three groups according to whether they underwent vitrectomy for PDR (n = 215; 149 men, 66 women; mean age 55.6 ± 11.6 years; mean follow-up duration 22.6 ± 14.9 months), MH (n = 114; 38 men, 76 women; mean age 68.0 ± 7.8 years; mean follow-up duration 20.4 ± 17.1 months), or RRD (n = 41; 25 men, 16 women; mean age 57.8 ± 10.7 years; mean follow-up duration 12.0 ± 5.9 months). Eyes that underwent vitrectomy for PDR were divided according to whether gas tamponade was or was not performed during surgery (PDR tamponade-positive [n = 84] and PDR tamponade-negative [n = 131], respectively). The rate of postoperative elevation of intraocular pressure (IOP) was compared between the PDR tamponade-positive and PDR tamponade-negative subgroups. A significant increase in intraocular pressure (IOP) was defined as an increase of > 4 mmHg from the preoperative IOP or equivalent IOP on antihypertensive medication. A P-value < 0.05 was considered statistically significant.

Results: Thirty-one (36.9%) of 84 eyes were PDR tamponade-positive and 23 (25.1%) of 131 eyes were PDR tamponade-negative. Fifteen (13.2%) of 114 eyes with MH and 11 (26.8%) of 41 eyes with RRD had elevated IOP after vitrectomy. Elevated IOP after vitrectomy was significantly more common in PDR tamponade-positive eyes than in eyes with other diseases. In the PDR group, IOP elevation after vitrectomy was more common in eyes that had gas tamponade than in those that did not and was also more common after vitrectomy for PDR than after vitrectomy for MH or RRD.

Conclusion: Clinicians should follow up patients for late-onset IOP elevation after vitrectomy, especially those with PDR in whom gas tamponade was performed.

Keywords: *Intraocular Pressure; Proliferative Diabetic Retinopathy; Gas Tamponade*

Abbreviations

IOP: Intraocular Pressure; MH: Macular Hole; PDR: Proliferative Diabetic Retinopathy; PPV: Pars Plana Vitrectomy; RRD: Rhegmatogenous Retinal Detachment

Introduction

Pars plana vitrectomy (PPV) is performed for several ophthalmic diseases. Acute elevation of IOP post- vitrectomy has been reported [1], and late-onset glaucoma has also been reported [2-10]. Furthermore, it is also known that vitrectomy using gas tamponade can cause an increase in IOP in the long term [8].

The mechanism of IOP elevation after vitrectomy is not yet clear but might involve oxidative stress in the anterior chamber or inflammation-related damage to the trabecular meshwork [11-14].

IOP elevation after vitrectomy for proliferative diabetic retinopathy (PDR) might contribute to the neovascular of gonio [15]. However, elevated IOP can also occur without neovascular glaucoma after vitrectomy for PDR. The aim of this study was to compare the rate of IOP

elevation after vitrectomy for PDR according to whether gas tamponade was or was not used with that after vitrectomy for macular hole (MH) or rhegmatogenous retinal detachment (RRD).

Materials and Methods

The protocol for this retrospective study was approved by the ethics committee at Toho University Sakura Medical Center (approval number: No. S17005). All study conduct adhered to the tenets of the Declaration of Helsinki. In accordance with the clinical research guidelines of the Japanese Ministry of Health, Labour, and Welfare, the study design was explained to subjects using the hospital's website.

The medical records of consecutive patients who underwent PPV at Toho University Sakura Medical Center between 2011 December and 2016 November and were followed up for at least 6 months after vitrectomy for PDR, MH, or RRD were reviewed. The patients who underwent PDR were divided into two groups according to whether gas tamponade was or was not performed during surgery (PDR tamponade-positive [n = 84] and PDR tamponade-negative [n = 131], respectively). In all cases, the IOP recorded was the mean of three measurements obtained by a non-contact tonometer. Patients with preexisting glaucoma, a preoperative IOP > 22 mmHg, or a history of previous intravitreal or periocular triamcinolone acetonide injections, intraocular inflammation, ocular trauma, or rubeosis iridis were excluded.

Surgical techniques

All patients underwent lens removal via phacoemulsification or PPV. An intraocular lens was implanted in the posterior chamber when phacoemulsification was performed. PPV was performed using a 20G, 23G, or 25G three-port vitrectomy system (Accuras® or Constellation®, Alcon, Inc., Fort Worth, TX). Following vitrectomy, fibrovascular proliferative membranes were removed and retinal neovascularization was cauterized to create a posterior vitreous detachment as peripherally as possible in the eyes with PDR. The vitreous base was then shaved by scleral compression, and pan-retinal photocoagulation was performed if needed using an intraocular laser at the vitreous base with scleral depression. Retinal tamponade was achieved with gas (air, 20% SF6, or 12% C3F8) with a retinal detachment or a surgically created retinal tear. The type of tamponade was selected according to the extent and estimated duration of retinal detachment. Betamethasone drops were instilled 4times per day for about one month after vitrectomy.

Statistical analysis

The IOP at the final visit was compared with that at the preoperative visit. A postoperative increase in IOP of > 4 mmHg was defined as a significant elevation. The rate of IOP elevation was compared between the study groups. All statistical analyses were performed using Statcel software (OMS, Saitama, Japan). The Kruskal-Wallis test was used to compare the rate of IOP elevation between the gas tamponade cases. The chi-squared independence test was used to compare the rate of IOP elevation between the PDR tamponade-positive and PDR tamponade-negative groups. A P-value < 0.05 was considered statistically significant.

Results and Discussion

Lensectomy was performed during vitrectomy in 38 (92.7%) of 41 eyes with RRD, 103 (90.4%) of 114 eyes with MH, 108 (82.4%) of 131 PDR tamponade-negative eyes, and in 70 (83.3%) of 84 PDR tamponade-positive eyes.

The mean preoperative IOP was 13.5 ± 3.4 mmHg in the PDR tamponade-positive eyes, 13.8 ± 3.0 mmHg in the PDR tamponade-negative eyes, 12.0 ± 3.1 mmHg in the eyes with RRD, and 14.2 ± 3.1 mmHg in the eyes with MH; the respective mean postoperative IOP values were 14.7 ± 3.8 mmHg, 14.5 ± 3.6 mmHg, 13.7 ± 2.6 mmHg, and 14.1 ± 3.5 mmHg.

IOP was found to be elevated after vitrectomy in 31 (36.9%) of the 84 PDR tamponade-positive eyes, 23 (25.1%) of the 131 PDR tamponade-negative eyes, 15 (13.2%) of the 114 eyes with MH, and 11 (26.8%) of the 41 eyes with RRD. The rate of IOP elevation was significantly higher after vitrectomy in the PDR tamponade-positive eyes than in those that had undergone vitrectomy for RRD or MH (P = 0.016). In the PDR group, elevation of IOP was significantly more common in the tamponade-positive eyes than in the tamponade-negative eyes (P = 0.0014).

The incidence of IOP elevation after vitrectomy has been reported to be 2% - 19.5% [2-10,16]. IOP elevation post-vitrectomy was more common in eyes with PDR than in the previous reports, but not in the eyes with MH or RRD. These inconsistent findings may reflect differences in the inclusion and exclusion criteria, duration of follow-up, and definition of IOP elevation used in the different studies. In a previous study, significant post-vitrectomy IOP elevation was found in eyes with RRD but not in eyes with RRD, epiretinal membrane, or

	PDR tamponade-positive	PDR tamponade-negative	RRD	MH
Cases, n	84	131	41	114
Age, years	53.4 ± 11.1	57.0 ± 11.7	57.8 ± 10.7	68.0 ± 7.8
Male sex	69.5%	69.0%	61.0%	33.3%
Preoperative IOP	13.5 ± 3.4	13.8 ± 3.0	12.0 ± 3.1	14.2 ± 3.1
Postoperative IOP	14.7 ± 3.8	14.5 ± 3.6	13.7 ± 2.6	14.1 ± 3.5
Lensectomy during vitrectomy	83.3%	82.4%	92.7%	73.0%
Rate of IOP elevation	36.9%	25.1%	26.8%	13.2%
Duration of follow-up, months	22.9 ± 15.0	22.4 ± 14.9	12.0 ± 5.9	20.4 ± 17.1
Gas tamponade	Air, n = 19; SF_6, n = 53; C_3F_8, n = 12		Air, n = 0; SF_6, n = 37; C_3F_8, n = 4	Air, n = 1 SF_6, n = 109; C_3F_8, n = 4

Table 1: *Patient demographic and ocular characteristics in each case.*

IOP: Intraocular Pressure; MH: Macular Hole; PDR: Proliferative Diabetic Retinopathy; RDD: Rhegmatogenous Retinal Detachment.

MH [10]. The results of our present study indicate that elevation of IOP is more likely after vitrectomy in patients with PDR in whom gas tamponade is performed than in patients with MH or RRD.

The mechanism of IOP elevation is thought to involve oxidative or inflammatory stress in the trabecular meshwork [11-14]. Generally, more vitreous is removed when vitrectomy is performed for RRD and PDR than when it is performed for MH. The oxidative stress is higher in eyes with RRD or PDR than in eyes with MH. In a previous study of development and worsening of open-angle glaucoma post-vitrectomy found that the mean IOP was significantly higher in the eyes that underwent surgery, especially those that were pseudophakic or aphakic, than in the fellow eyes [8]. The pathogenesis was assumed to be increased partial pressure of oxygen in the vitreous cavity post-vitrectomy that might cause oxidative stress in the trabecular meshwork, particularly in the absence of a crystalline lens. Most of the eyes in our study were pseudophakic, so we could not compare the rate of IOP elevation according to the status of the lens. Further research is needed to determine if such a relationship exists.

Generally, the severity of intraocular inflammation after vitrectomy is considered to be higher in order MH, RD, PDR. Vitrectomy for RRD is known to cause more inflammation because of dispersion of pigment granules from the retinal pigment epithelium. Therefore, the IOP elevation could be caused by a clogging of the trabecular meshwork by retinal pigment epithelial cells [11-14]. However, vitrectomy for PDR is considered to cause more inflammation because of hemorrhage resulting from retinal neovascularization and the operating time required to remove the fibrovascular membrane is longer than that for other vitreous disorders. In the present study, rate of IOP elevation was significantly higher in eyes that underwent vitrectomy for PDR with gas tamponade than in those that underwent vitrectomy for RRD and MH.

It is possible that the inflammatory stress in the anterior chamber is higher when gas tamponade is used because of prone positioning [8]. The increased inflammation in the anterior chamber in response to the inflammatory cytokines released during gas tamponade would also increase the stress on the trabecular meshwork. This caused the inflammation of PDR with gas tamponade to IOP elevation after vitrectomy for long-time relative to PDR without gas tamponade.

In this study, we could not examine the duration of gas tamponade in all patients. The effects of factors such as type of gas used for tamponade and duration of the presence of intraocular gas on control of IOP after vitrectomy need to be investigated further. Future studies of inflammation after vitrectomy should obtain measurements using a flare meter if inflammation in the anterior chamber is considered to be the cause of IOP elevation after vitrectomy and compare of difference of gauze of vitrectomy that contribute to inflammation after vitrectomy. Further studies that compare IOP elevation between less inflamed eyes with epiretinal membrane in which gas tamponade has not been performed and eyes with PDR in which gas tamponade has been used would be informative.

We should consider the contribution of triamcinolone acetonide to increased IOP. Triamcinolone acetonide was reported to disappear rapidly in the rabbit eye with lensectomy and vitrectomy after 6.5 days [17]. It is possible that triamcinolone acetonide affects the trabecular meshwork during diapering TA, the use of triamcinolone acetonide during vitrectomy might not less responsible for late-onset IOP elevation.

This study has several limitations that should be kept in mind when interpreting its findings, First, the follow-up duration may not have been long enough to detect all cases of late-onset IOP elevation. Second, the possibility that elevation of IOP may have been unrelated to vitrectomy was not considered. Third, in eyes with PDR, the missing of tinny neovascular of gonio is considered. Fluorescein angiography of the iris is needed in eyes with PDR so as not to miss neovascular of gonio.

Conclusions

Clinicians should be aware of the risk of late-onset IOP elevation after vitrectomy. This risk appears to be higher in eyes with PDR in which gas tamponade is used than in eyes with PDR in which it is not performed, eyes with MH, and eyes with RD.

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Conflicts of Interest

The authors declare no conflicts of interest.

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