

Incidence and risk factors for intraocular pressure rise after transconjunctival vitrectomy

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Purpose: To study the incidence and risk factors of raised intraocular pressures (IOPs) in the follow-up of transconjunctival sutureless vitrectomy (TSV). **Methods:** A retrospective observational study was performed on 635 patients who underwent TSV under a single surgeon. The IOPs were recorded using a calibrated non-contact tonometer at seven postoperative visits, viz., day 1, 7 and 1, 3, 6 months, and 1 day and 1 month following silicone oil removal. **Results:** IOP rise was seen in 24.25% (154) out of the 635 eyes studied. Among patients under 50 years of age, 37.73% had an IOP rise, compared to 21.55% above 50 years (Odds Ratio 2.206). Among males, 30.32% had an IOP rise, as compared to 15.98% females (OR 2.287). In eyes with retinal detachment, 49.16% had raised IOP (OR 5.435), and 24.05% with proliferative diabetic retinopathy (OR 1.780), as opposed to 15.38% with macular hole and 12.32% with epiretinal membrane. This was statistically significant ($P < 0.001$). In eyes with silicone oil, 34.9% developed a rise in IOP (OR 2.738) as compared to 11.94% of other surgeries (OR 0.697). This was statistically significant ($P < 0.001$). **Conclusion:** We observed an increase in IOP postoperatively, more in those under 50 years, males and patients undergoing surgery for RD and PDR.

Key words: Incidence, intraocular pressure rise, postoperative follow up after vitrectomy, risk factors, vitrectomy

Elevated intraocular pressure (IOP) is widely seen as a potential risk factor for optic nerve damage and widely reported postoperatively. The consequences of chronic glaucoma leading to visual field loss are widely acknowledged.^[1] Secondary and transient rises of intraocular pressure after vitreoretinal surgery are well known in literature.^[2-5] Our study is the largest till date on the IOP rise and risk factors after transconjunctival sutureless vitrectomy (TSV). Knowledge about incidence in IOP rise at different intervals and risk factors following TSV can help suspect, identify, and manage IOP rise in the follow-up period. The purpose was to study the incidence and risk factors of IOP rise after TSV and to identify time period involved in IOP rise in the follow-up period.

Methods

A retrospective observational study was performed on 635 patients in a tertiary hospital in South India who underwent transconjunctival sutureless vitrectomy (TSV), 23-gauge type, using the Constellation vitrectomy surgical system. All surgeries were performed by a single surgeon, over a period

of 36 months from years 2013 to 2015. Patient ages ranged from 12 to 95 years and there were 366 males and 269 females in the study. Data was collected from the Electronic Medical Records and Operation Theatre registers. A thorough clinical examination was performed preoperatively. The IOP was measured by a calibrated non-contact tonometer preoperatively and postoperatively on day 1, day 7, 1 month, 3 months, 6 months and 1 day and 1 month following silicone oil removal. Gonioscopy was done if needed.

Indications for TSV included retinal detachment, complications of proliferative diabetic retinopathy, epiretinal membrane, and macular hole. Other causes like a nucleus or intraocular lens drop, vitreous hemorrhage, or asteroid hyalosis were grouped as "Others." Silicone oil, air, or gas was implanted into the vitreous at the end of TSV or other combinations of surgeries, such as phaco fragmentation, or secondary IOL implantation. We did not include 20-gauge surgery in the study as it was not done during this time period.

In surgeries involving gas, 18% SF₆ (sulphur hexafluoride) was used. Silicone Oil was removed about 4--6 months after implantation. IOP less than 20 mm Hg was predefined as normal.

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To exclude pre-existing glaucoma 20 eyes were excluded from the study.

IOPs up to 25 mmHg were observed. Beta-blocker eye drops (timolol maleate 0.5%) was used if IOPs were over 25 mmHg. IOPs over 30 mmHg were treated with topical prostaglandin analogues (latanoprost), topical carbonic anhydrase inhibitors (dorzolamide), and beta-blockers (timolol maleate 0.5%). Oral acetazolamide was added to topical medications if IOPs were over 40 mmHg after ruling out contraindications. A peripheral iridotomy was additionally performed in event of a shallow anterior chamber or pupillary block.

Statistical methods

To obtain the prevalence and percentages of categorical variables, the frequency method was applied. To obtain trends, bar diagrams were applied and for checking associations between categorical variables, the Chi-Square test was applied.

Results

In the given time frame of the study, between 1 day after TSV to 1-month post-silicone oil removal, of the 635 eyes, 24.25% (154) eyes developed an IOP rise above 20 mmHg.

Incidence of rise of IOP >20 mm of Hg

It was seen that in 55.19% of 154 eyes, an IOP rise occurred within 1 month of TSV. In 21.42% of eyes, the IOP rise occurred between 1 and 3 months of TSV and in 23.37% of eyes, the IOP rise occurred 3 months onwards of TSV.

At 1 day postoperatively, 17.21% of eyes showed a higher IOP. By the 1st week postoperatively, 38.41% showed higher IOP. By 1 month postoperatively, it fell to 27.81% which further declined to 9.93% by 3 months. However, by 6 months postoperatively, 13.24% showed increased IOP. At 1 day after silicone oil removal postoperatively, only 3.97% showed IOP rise which increased to 11.92% 1 month after silicone oil removal.

In the calculation of incidence of IOP rise in the seven-time periods, three patients were excluded as numerical data was not appropriately documented.

Risk factors for the rise of IOP >20 mm of Hg

Males had a significantly increased risk compared to females [Odds ratio 2.287 with Confidence Interval (95% CI) of Lower and Upper limit 1.545--3.415]. Of the total males (366), 30.32% (111) eyes had a rise in IOP as compared to 15.98% (43) eyes of the total females (269), Chi-Square Test, $P < 0.001$ [Fig. 1].

Patients less than 50 years of age had a significantly increased risk of developing IOP rise compared to those above 50 years of age (Odds ratio 2.206 with 95% CI of 1.415--3.44). Among the total patients aged less than 50 years (106), 37.73% (40) eyes had a rise in IOP as compared to 21.55% (114) eyes of the patients aged more than 50 years (529) of the total sample of 635 (Chi-Square Test, $P < 0.001$) [Fig. 2].

Patients operated for retinal detachment (RD) had a significantly increased risk of having raised IOPs compared to other groups (Odds ratio 5.435) as did patients operated for complications from PDR (Odds ratio 1.780). Among the 120 eyes with RD, 49.16% (59) of 120 eyes (Odds ratio 5.435 with 95% CI

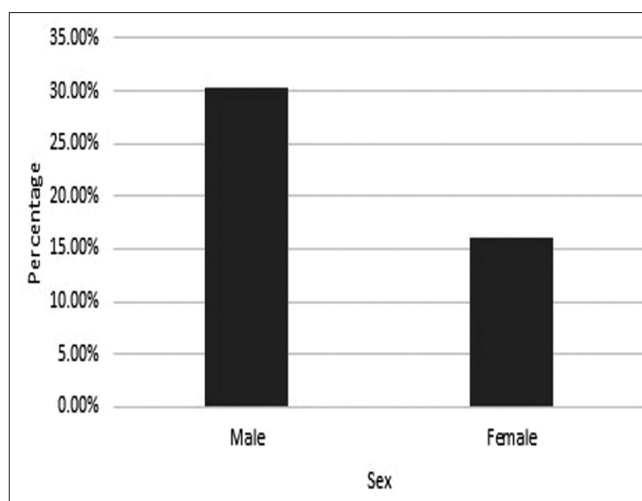


Figure 1 (original): Percentage of IOP rise by sex distribution. 30.32% of males had an IOP rise more than 20 mmHg of 635 patients. 15.98% of female had an IOP rise more than 20 mmHg of 635 patients. ($P < 0.001$)

of 3.024--9.767) developed a rise in IOP. Of the 212 eyes with proliferative diabetic retinopathy (PDR), 24.05% (51) developed high IOP (Odds ratio 1.780 with 95% CI of 1.016--3.119). Among the 91 eyes with macular hole (MH), 15.38% (14) and of 73 eyes with epiretinal membrane (ERM) 12.32% (9) eyes developed a rise in IOP. The IOP rise among different etiological diagnosis for surgery were statistically significant (Chi-Square Test, $P < 0.001$) [Fig. 3].

Patients with silicone oil injected in the eye had a significantly increased risk of having increased IOP. Out of 635 eyes, 34.9% (111 eyes) of the 318 eyes with silicone oil implanted developed a rise in IOP (Odds ratio 2.738 with 95% CI of 1.590--4.712). However, only 11.94% (24 eyes) of the 201 eyes with air or gas implanted developed a rise in IOP (Odds ratio 0.697 with 95% CI of 0.361--1.327), and 16.37% or 19 eyes of the remaining 116 eyes without any tamponade also developed a rise in IOP. This difference between the tamponade agents to cause IOP rise was statistically significant (Chi-Square Test, $P < 0.001$) [Fig. 4].

Incidence of peak IOP rise

The 154 eyes of patients with high IOP after TSV were followed up to see when was the highest peak of IOP during follow-up. We found that 15.89% of patients had the peak of their IOP rise on the first day itself and thereafter it fell. The highest number of eyes, that is, 33% had their peak by the first week, followed closely by 26.49% of eyes who had their peaks by 1st month. Only 5.29% of patients had their peak of IOP rise during the third month as opposed to 9.93% at 6 months following surgery. Thus, the maximum rise in IOP was seen between the first week to first month following TSV.

Only a miniscule 1.32% of eyes had their peak rise of IOP on the first-day post-silicone oil removal. One month following SOR, 7.94% of eyes had their peak rise of IOP. In the calculation of peaks of IOP, three patients were excluded as numerical data was not appropriately documented.

In 89.09% of eyes, IOP normalized at 6 months after TSV.

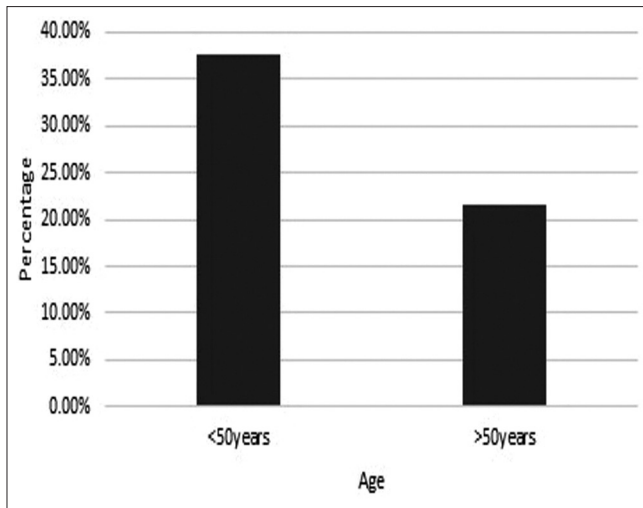


Figure 2 (original): Percentage of IOP rise by age distribution. 37.73% of patients less than 50 years had an IOP rise more than 20 mmHg of 635 patients. 21.55% of patients more than 50 years of age had an IOP rise more than 20 mmHg of 635 patients. ($P < 0.001$)

Peak rise of IOP among various etiologies undergoing TSV

In eyes with RD, 51.56% had a rise in IOP by 1 month, 21.87% between 1 and 3 months and 21.87% from 3 months after TSV. In eyes with complications from PDR, 41.66% had a rise in IOP by 1 month, 15% between 1 and 3 months and 30% from 3 months after TSV. In eyes with MH, 53.33% had the rise in IOP by 1 month, 33.33% between 1 and 3 months and 6.6% from 3 months after TSV. In eyes with ERM, 50% had the rise in IOP by 1 month, 30% between 1 and 3 months and 10% from 3 months after TSV. Thus, across all the etiologies for which TSV was done, the peak of IOP rise was seen in the first month itself.

Peak rise of IOP in different tamponading agents

In eyes that underwent silicone oil implantation, 46.82% had a rise in IOP by 1 month, 18.25% between 1 and 3 months and 25.39% from 3 months after TSV. Likewise in eyes with air/gas implantation, 57.69% had the rise in IOP by 1 month, 30.76% between 1 and 3 months and 3.8% from 3 months onwards of TSV. In eyes with other VR procedures without tamponade, 50% had the rise in IOP by 1 month, 18.18% between 1 and 3 months and 18.18% from 3 months after TSV. Thus again, whatever be the tamponading agent used, the peak IOP was always seen in the first month itself.

Causes of IOP rise after TSV

There were six eyes with steroid-induced glaucoma that showed glaucomatous disc changes. A total of four eyes that underwent silicone oil injection had glaucomatous changes by the time of SOR. Steroids were tapered early and antiglaucoma agents added in these cases.

There were three eyes with neovascular glaucoma among the 154 eyes where NVA was the cause of IOP rise. They had undergone anti-VEGF injection, panretinal photocoagulation, and medical management. There were nine eyes with IOP rise in the sixth month with emulsification of oil at the angles although not gross emulsification in the vitreous.

In one eye, air displacement contributed to pupillary block and one eye had a bleed under the silicone oil and this displaced

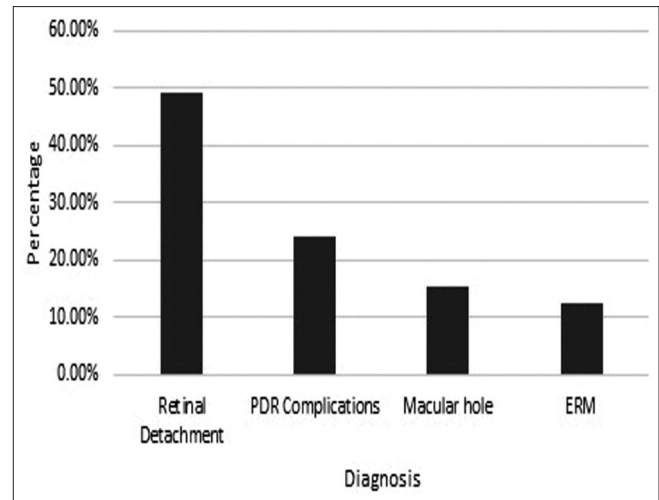


Figure 3 (original): Percentage of IOP rise by diagnosis distribution. Of 635 patients 49.16% with retinal detachment (RD) had an IOP rise of more than 20 mmHg. 24.05% with complications from proliferative diabetic retinopathy (PDR) had an IOP rise of more than 20 mmHg. 15.38% with macular hole had an IOP rise of more than 20 mmHg. 12.32% with epiretinal membrane (ERM) had an IOP rise of more than 20 mmHg of 635 patients. ($P < 0.001$)

the lens anteriorly contributing to pupillary block. Peripheral iridotomy was done for both these cases.

Secondary open-angle glaucoma was the most common cause of rise of IOP. Of 154 eyes with IOP rise, none needed surgical intervention.

Discussion

IOP rise after vitreoretinal surgery is well known. However, incidence and risk factors are not studied in great detail. Literature is contradictory concerning associations between vitrectomy and raised IOP [Table 1].^[6] However, it is often agreed that there is a good response to medical therapy for IOP rise following vitrectomy. In most of the studies, a mix of 20, 23, and 25 gauge vitreous surgeries were studied. We, however, studied 23-gauge TSV, as it is the commonest vitreous surgery done in India nowadays.

Wu *et al.* reviewed the IOP of 198 patients who underwent vitrectomy and demonstrated that the incidence of high IOP (≥ 24 mmHg) or increased IOP (≥ 5 mmHg) was greater in vitrectomized eyes than in control eyes.^[7] Fujikawa *et al.* reported that in eyes with MHs, the mean IOP increased after vitrectomy.^[8]

In contrast, Yu *et al.* could not demonstrate any statistically increased risk between ocular hypertension (OHT) or glaucoma after vitrectomy.^[9] Similarly, Lalezary *et al.* reported that the incidence of increased IOP levels exceeding 4 mm Hg was not significant between operated eyes (15%) and fellow eyes (14%) in eyes that underwent vitrectomy for vitreous hemorrhage, ERM, or MH in patients with diabetes.^[10]

Our study showed the highest incidence of IOP rise occurring within 1 month. The maximum frequency of peaks of IOP occurred between 1 week and 1 month postoperatively after TSV. Thus, follow-up visits with IOP monitoring are

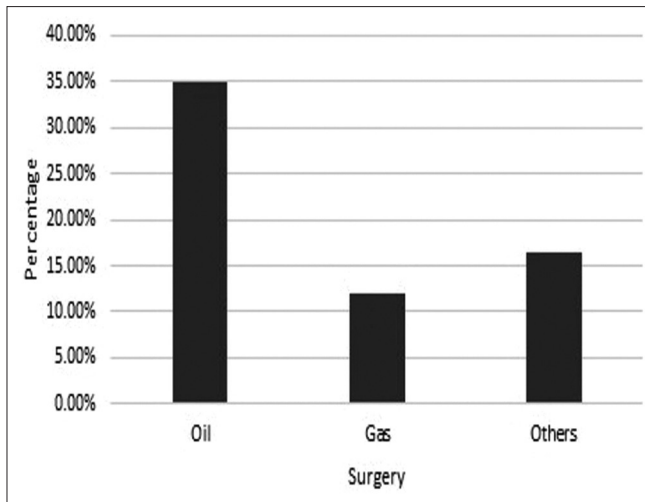


Figure 4 (original): Percentage of IOP rise by tamponade distribution. 34.9% with oil tamponade had an IOP rise more than 20 mmHg of 635 patients. 11.94% with air or gas tamponade had an IOP rise more than 20 mmHg of 635 patients. 16.37% of other surgeries had an IOP rise more than 20 mmHg of 635 patients. ($P < 0.001$)

required at 1 week and 1 month following vitreoretinal surgery to detect an IOP rise and for early management.

Regarding the risk factors, vitrectomy for ERM is considered to be the least surgically invasive among the various vitrectomy procedures and showed the least IOP rise among all etiologies. The Kaplan–Meier survival analysis with the log-rank test between ERM and MH showed that the eyes in the MH group had a higher risk of IOP increase than those with ERM.^[8]

In our study, patients with RD were strongly associated, with an over five times risk, to develop an IOP rise in comparison with simple vitrectomy. Management of RD also included scleral buckle in some cases (4), cryotherapy, barrage laser, delimiting laser, and silicone oil injected in all cases. A scleral buckle constricts the vortex veins and also compresses the eye, thereby increasing the IOP. Cryotherapy and laser photocoagulation increase inflammation and choroidal congestion making the eye susceptible to secondary open and closed angle glaucoma. Silicone oil is incompressible and does not allow for any room when choroidal congestion occurs post laser and cryotherapy. However, we did not see any eye with angle-closure glaucoma among the eyes with RD. All the cases

Table 1: Other studies on IOP changes after vitrectomy

Study	Definition of high IOP	Incidence of high IOP	Number of cases	Type of cases and type of surgery
1. L. Wu, M. H. Berrocal, F. J. Rodriguez <i>et al.</i>	IOP ≥ 24 mmHg or an increase of ≥ 5 mmHg in the IOP	19.2%(12-106 months)	38 of the 198	Pars plana vitrectomy for an idiopathic epiretinal membrane
2. Y. Hasegawa, F. Okamoto, Y. Sugiura <i>et al.</i>	>25 mm Hg	approximately one-quarter of cases within 1 day	52 of 228 (22.8%)	All types of VR surgery 20 gauge
3. M. Fujikawa, O. Sawada, M. Kakinoki, <i>et al.</i>	IOP increase of 4 mmHg	ERM (5.3%) at 12 months, (7.0%) at end; MH (3.3%) at 12 months (8.2%) at end	ERM $n=57$; 3 at 12 months, 4 at end, MH $n=61$; 5 at 12 months, 10 at end	Vitrectomy for ERM and Macular Hole
4. A. L. Yu, W. Brummeisl, M. Schaumberger <i>et al.</i>	IOP ≥ 22 mmHg with optic disk changes and/or visual field defects consistent with glaucoma.	4.31% with postoperative OAG and 4.31% with postoperative ocular hypertension	19 vitrectomized eyes with postoperative OAG, and 19 vitrectomized eyes with postoperative ocular hypertension.	Pars plana vitrectomy with a 20-gauge for all cases
5. Lalezary M, Kim SJ, Jiramongkolchai K <i>et al.</i>	1) incidence of open-angle glaucoma 2) increase in IOP of >4 mmHg	Incidence of increased IOP >4 was 7% at 4 years and 34% at 8 years	52 of 101 eyes	Non emergent vitrectomy
6. Yog Raj Sharma, Archana Pruthi, Raj Vardhan Azad <i>et al.</i>	IOP ≥ 30 mmHg at day 1	20.5%	15 out of 73 cases	Pars plana vitrectomy (PPV) for proliferative diabetic retinopathy (PDR)
7. Ki-I Y, Yamashita T, Uemura A, Sakamoto T	IOP of treated eye/ IOP of fellow eye of more or equal to 1.2	8.2% of eyes at baseline, 7.1% at 3 months, 15.9% at 6 months, 16.9% at 12 months, 27.8% at 24 months, 11.8% at 36 months, 27.8% at 48 months, and 30.8% at 60 months	(7/85 eyes) at baseline, (6/84) at 3 months, (13/82) at 6 months, (14/83) at 12 months, (15/54) at 24 months, (4/34) at 36 months, (5/18) at 48 months, and (4/13) at 60 months	Combined phacoemulsification, intraocular lens implantation, and vitrectomy procedure for macular hole or epiretinal membrane

Contd...

Table 1: Contd...

Study	Definition of high IOP	Incidence of high IOP	Number of cases	Type of cases and type of surgery
8. Al-Jazzaf AM, Netland PA, Charles S	IOP more or equal to 21 mm Hg and sustained rise for 6 weeks or more	11%	51 of 450 eyes	Pars plana vitrectomy and silicone oil injection
9. Our Study	IOP more than 20 mHg	24.25%	154 of 635	Indications for surgery included retinal detachment, complications from proliferative diabetic retinopathy (PDR), epiretinal membrane (ERM), macular hole (MH) and others. Silicone oil, air or gas was implanted during the surgery or combined surgeries done

where IOP increased after TSV for RD had secondary open angle glaucoma. Steroid response also may have contributed to the rise in IOP in these cases. A late rise in IOP was seen when there was emulsified oil in the angles.

Patients with proliferative diabetic retinopathy were also significantly associated, with over one and a half times the risk of a simple vitrectomy. All patients completed PRP before silicone oil injection. It is likely that extensive PRP caused significant choroidal congestion which compresses the incompressible silicone oil which in turn transmits this pressure to raise the IOP. There may be an anterior shift of lens iris diaphragm also because of silicone oil compression. There was one pupillary block due to anterior shift of the lens iris diaphragm due to postoperative bleeding under oil. Steroid response also may have contributed to IOP rise. There were 3 cases where neovascular glaucoma was the cause of IOP rise.

Al-Jazzaf AM *et al.* found chronic IOP elevation occurs in a minor number of eyes (11%) treated with silicone oil. Most are effectively managed with antiglaucoma medications.^[11] In our series, 10.91% had elevated IOP at 6 months.

Our study showed patients who underwent silicone oil implantation appeared to be strongly associated with over two and a half times likelihood the risk, in comparison with their counterparts, to develop an IOP rise. Our explanation is, in cases which required silicone oil implantation, extensive laser photocoagulation and cryotherapy, were applied, which may lead to inflammatory congestion and edema of choroidal vasculature which may in turn cause compression of silicone oil and IOP rise in the initial month period. Emulsification of oil and migration of emulsified oil into the anterior chamber would be the cause of rise in IOP in later cases.

Patients below 50 years of age were seen to be at twice the risk of developing raised IOP. Younger patients have heightened inflammatory response following surgery and so increased incidence of trabeculitis and anterior chamber inflammation may be the cause of IOP rise in younger age groups.

With regard to possible mechanisms of intraocular rise at day 1 postoperatively, trabeculitis, pupillary membrane from post-surgical inflammation leading to seclusio and oclusio pupillae, forward push mechanism of the lens iris diaphragm

from choroidal congestion secondary to laser photocoagulation and ciliary body rotation, secondary angle-closure glaucoma and a scleral buckle which may cause compression of the vortex veins by volume effect and increased episcleral pressure were possible causative factors for IOP rise.

At 1 week postoperatively, trabeculitis, pupillary membrane from post-surgical inflammation leading to seclusio and oclusio pupillae, expansion of gas, steroid response, secondary angle-closure glaucoma and a scleral buckle which may cause compression of the vortex veins by volume effect and increase of episcleral venous pressure may be causes of IOP rise.

At 1 month postoperatively, steroid-induced glaucoma, forward push mechanism of the lens iris diaphragm from choroidal congestion secondary to laser photocoagulation and ciliary body rotation, secondary angle-closure glaucoma and a scleral buckle which may cause compression of the vortex veins by volume effect and increased episcleral pressure may be the causes of IOP rise.

At 3 months and 6 months postoperatively, steroid-induced glaucoma and early emulsification of silicone oil were possible causes of IOP rise.

Post 1 day after silicone oil removal postoperatively, air bubble or gas expansion induced pupillary block mechanism and inflammation may be causes of IOP rise. Post 1 month after silicone oil removal, already emulsified oil in the angle, steroid-induced glaucoma and inflammation were causes of IOP rise.

The high association in the RD and proliferative diabetic retinopathy case series and silicone oil implantation series show there is an increased risk of IOP rise in these eyes and it is necessary to measure the IOP in these cases regularly, to detect a potential rise.

The pattern of highest incidence of IOP rise and maximum frequency of peak of IOP rise between 1 week and 1 month postoperatively suggests that follow-up visits and IOP monitoring are required the most between the first week and first month postoperatively to detect an IOP rise.

Conclusion

Knowledge of incidence, risk factors, and mechanism of IOP rise following TSV is crucial in the follow-up and management

of patients after surgery. After TSV there is higher IOP rise in males, those younger than 50 years and in cases where RD and proliferative diabetic retinopathy are managed, especially with silicone oil. Highest IOP peaks occurred between first week and first month and non-adherence to IOP monitoring during this period may lead to loss of sight to a potentially blinding glaucoma.

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Conflicts of interest

There are no conflicts of interest.

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