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REVIEW

Risk Factors and Management of Intraocular Pressure Elevation After Vitrectomy Combined with Silicone Oil Tamponade

Lexin Ge*, Na Su*, Wen Fan, Songtao Yuan

Department of Ophthalmology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, 210029, People's Republic of China

*These authors contributed equally to this work

Correspondence: Songtao Yuan, Department of Ophthalmology, The First Affiliated Hospital of Nanjing Medical University, No. 300 Guangzhou Road, Nanjing, 210029, People's Republic of China, Email songtaoyuan@njmu.edu.cn

Abstract: Silicone oil has emerged as the common option for intraocular tamponade during complicated retina vitrectomy. However, the postoperative elevation of intraocular pressure (IOP), influenced by numerous factors, remains a significant and frequently encountered complication that poses a potential threat to vision. Extensive research has been conducted to investigate the risk factors associated with elevated IOP following silicone oil tamponade, including silicone oil viscosity, preoperative high IOP, diabetes, and lens status. This comprehensive review aims to gather and summarize the current research findings regarding the risk factors contributing to IOP elevation following silicone oil tamponade, as well as the optimal management strategies for secondary glaucoma. The analysis includes the physicochemical properties of silicone oil, preoperative and intraoperative risk factors, and the effective management of secondary glaucoma. Enhancing our understanding of the primary factors associated with silicone oil-induced IOP elevation will facilitate the guidance of timely and appropriate interventions.

Keywords: intraocular pressure, silicone oil, ocular hypertension, pars plana vitrectomy, secondary glaucoma

Introduction

Silicone oil (SO) is a collective term for a series of hydrophobic polymeric and monomeric chemicals made of silicon-oxygen linkages, known as organosiloxane.[1] It was first implemented in vitreoretinal surgery by Cibis[2] in 1962, due to its stability and convenient storage, silicone oil has become increasingly popular as a commonly used filling material in vitrectomy.

In recent years, combining vitrectomies with silicone oil tamponade has become the mainstream approach for managing complex vitreoretinopathy. Silicone oil exhibits stability, transparency, non-toxicity, and remarkable biocompatibility within the ocular environment, allowing for effective monitoring of retinal healing after operation.[3,4] Its high interfacial tension enables silicone oil to act as a tamponade agent, sealing retinal defects and preventing the ingress of vitreous fluid into the subretinal space through the retinal break.[5] Furthermore, silicone oil restricts the free diffusion of proliferating cells and biochemical substances in the vitreous cavity while serving as a space-filling material.[6,7] In cases of severe proliferative vitreoretinopathy, giant rhegmatogenous retinal de-tachment, ocular trauma with retinal detachment, proliferative diabetic retinopathy combined with traction retinal detachment, silicone oil filling remarkably enhances retinal reattachment rates and postoperative visual acuity.[8–14] It has become an essential component of modern vitreous surgery, greatly improving the success rates of complex retinal detachment repair through rapid advancements in vitreous microsurgery.

Although silicone oil has been successfully used as a filler by retinal surgeons for decades, several studies have now found that silicone oil can cause a variety of complications, including cataracts, keratopathy, intraocular pressure (IOP) elevation, hypotony, silicone oil emulsification, iritis, endophthalmitis, and anterior dislocation.[15–17] Notably, elevated IOP stands out as the most frequently encountered complication. Soon after widespread adoption of silicone oil filling for complex retinal detachment surgery, cases of elevated intraocular pressure were reported. Various prevalence percentages

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have been reported in several studies, varying from 2.2% to 56%.[18–20] However, recent statistics indicate a decreasing incidence of postoperative hypertension, falling between 3% and 30%.[21–23] This improvement can be attributed to the use of high-viscosity silicone oil and advancements in surgical techniques and in clinical practice, such as inferior peripheral iridectomy, postoperative administration of corticosteroids, and the adoption of lateral or prone positioning. These factors contribute to enhanced outcomes and reduced complications in vitreoretinal surgery. Due to policy constraints in public hospitals in our country, silicone oil filling is the predominant choice for patients who undergo vitrectomy combined with intraocular filling. Consequently, there is a significant prevalence of eyes filled with silicone oil in China, which requires an analysis of the factors contributing to increased intraocular pressure after silicone oil filling. Despite these advancements, the mechanism underlying the development of high IOP following silicone oil filling remains unknown. Maintaining intraocular pressure continues to be one of the important goals during the postoperative period. Understanding the risk factors and pathogenesis associated with the development of high IOP after silicone oil filling can effectively prevent and reduce its occurrence, ultimately minimizing the impact on visual function.

Materials and Methods

The primary objective of this review is to assess the risk factors contributing to elevated intraocular pressure subsequent to pars plana vitrectomy (PPV) combined with silicone oil tamponade. The evaluation will consider various aspects, including the physicochemical characteristics of silicone oil, preoperative, intraoperative, and postoperative risk factors, as well as the management of secondary glaucoma.

Extensive literature research was conducted using the Medline database through the PubMed interface. The search involved various combinations of terms including but not limited to: "vitrectomy", "silicone oil", "intraocular pressure elevation" or "secondary glaucoma", "surgical treatment" and "vitreous substitutes". Articles that provided relevant information on the prevalence and pathophysiology of high IOP or glaucoma associated with silicone oil tamponade were included. Additional references were obtained from the reference lists of the included studies. We excluded articles that were not in English, as well as editorials, letters to the editor, reviews, conference presentations, and articles that were not relevant to the topic. A final total of 91 articles from the period 1962 to 2023 were included in the final analysis.

Pathogenesis

After the utilization of SO in retinal surgical procedures, various mechanisms have been proposed to account for the occurrence of IOP elevation and even late-stage glaucoma in the postoperative period. These mechanisms encompass the migration of SO into anterior chamber, which can potentially obstruct the trabecular meshwork with emulsified particles of SO,[24] chronic inflammatory response,[25] angle closure from synechiae, rubeosis irides,[26] and pre-existing glaucoma[27] are also involved. The most prevalent mechanism contributing to persistent elevation of postoperative IOP is considered to be secondary open-angle glaucoma triggered by obstruction of the trabecular meshwork.[27,28] The diminished outflow of aqueous humor is thought to result from permeation and intraocular inflammation caused by surgical manipulation and emulsified particles of SO, leading to chronic trabeculitis. Previous studies have shown that inflammatory factors may instigate the development of glaucoma,[29,30] increased concentrations of the inflammatory mediators Interleukin-17 (IL-17), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) in the aqueous humor of patients with SO filling, especially those with secondary glaucoma, supporting the hypothesis of inflammation involvement in the pathogenesis of glaucoma.[31,32] A reciprocal relationship may exist between inflammation and emulsified SO, whereby emulsified SO triggers an immune response while inflammatory proteins act as surfactants, promoting further emulsification.

Risk Factors

Numerous studies have investigated the risk factors associated with the development of intraocular pressure elevation following vitrectomy combined with silicone oil filling. Depending on the timing of occurrence, cases can be categorized into early postoperative ocular hypertension and late-onset SO-induced glaucoma.[33] There are various pathological mechanisms that can contribute to early IOP elevation, including potential causes related to angle closure. Furthermore, pre-existing glaucoma exacerbation, intraocular inflammation, adverse reactions to postoperative steroid therapy, pupillary block, or mechanical obstruction of the trabecular meshwork by emulsified silicone oil particles can also lead to early IOP elevation.[21,34–38] If early IOP elevation is not adequately controlled, it can progress into late-onset glaucoma, which may result in irreversible visual impairment or even blindness. Several factors have been identified as potential contributors to IOP elevation, including preoperative factors such as myopia, diabetes, lens status, and preoperative high IOP. Additionally, the physicochemical properties of silicone oil and the use of intraoperative laser may also impact the development of postoperative IOP elevation.

Physico-Chemical Properties of Silicone Oil

Silicone oil exhibits favorable biocompatibility with the human eye. Due to its stable buoyancy and high surface tension, silicone oil maintains the bonding between retinal neuroepithelium and pigment epithelium, contributing to retinal reattachment. Adverse reactions, including silicone oil emulsification and inflammatory responses, may occur depending on factors such as the viscosity of the silicone oil and the duration of its filling, potentially leading to elevated intraocular pressure after surgery.

Specific Gravity of Silicone Oil

Specific gravity, also known as density, is a fundamental physical property that quantifies the ratio between the density of a given substance and that of a reference substance, typically water. In the context of silicone oil, specific gravity plays a crucial role in determining its buoyancy or propensity to float within the eye.[39] In clinical practice, silicone oils are commonly categorized into two types based on their density: standard silicone oil (SSO) and heavy silicone oil (HSO). SSO, which is in liquid form, exhibits a lighter density than water and provides robust support for the superior retina. In contrast, HSO is a compound composed of semi-fluorinated and silicone oil, possessing a higher density than water and a lower viscosity than SSO, enabling effective filling of the inferior quadrant after surgery.[6,7,28,29,40] However, it is worth noting that HSO is more prone to causing postoperative elevation of intraocular pressure,[41,42] the presence of hemifluoride makes the compound unstable, accelerating the emulsification process and triggering more inflammatory response, consequently leading to increased IOP.

Viscosity of Silicone Oil

The viscosity of silicone oil plays a significant role in determining the occurrence of postoperative elevated intraocular pressure (IOP) following vitrectomy combined with silicone oil tamponade. Silicone oils with lower viscosity are more likely to induce elevated IOP. The viscosity of silicone oils commonly used in clinical practice today ranges from 1000 to 5000 cSt. Silicone oil with lower viscosity tends to emulsify more rapidly, leading to the formation of microdroplets that can obstruct the trabecular meshwork or Schlemm's canal, thereby contributing to increased IOP. On the other hand, higher viscosity silicone oil exhibits enhanced biocompatibility and greater resistance to emulsification.[43] Due to its lower tendency for emulsification, many surgeons prefer to use higher viscosity silicone oil, such as 5000 cSt, for intraoperative tamponade, particularly in patients re-quiring long-term or permanent silicone oil filling for complex retinal detachments. An increase in viscosity leads to increased surface tension and reduced emulsification rates, as demonstrated by in vitro studies.[18,44]

Duration and Volume of Silicone Oil Tamponade

In clinical practice, for patients with more severe conditions such as complex retinal detachment, the volume or duration of silicone oil filling is increased appropriately to maximize retinal reattachment. Excessive filling of the vitreous cavity will cause anterior displacement of the iris septum of the lens, peripheral iris bulge or anterior synechia, pupil block and shallowness of the anterior chamber, and the risk of postoperative ocular hypertension will increase; at the same time, due to the complexity of the operation and severe postoperative inflammatory reaction, there is a possibility of choroidal edema, which can result in relatively excessive silicone oil filling. Overfilling with silicone oil is a frustrating issue that cause an immediate increase in IOP, it can be managed by removing a small quantity of SO. Extending the duration of silicone oil filling in the eye accelerates the emulsification process, imposes a chronic toxic effect on the outflow pathway of aqueous humor, and ultimately hinders the function of the trabecular meshwork, resulting in increased intraocular pressure.[21]

Preoperative Influencing Factors

Preoperative High Intraocular Pressure

Studies[23,45] have found that patients with preoperative preexisting glaucoma are more susceptible to postoperative IOP elevation. Jabbour et al found that high preoperative IOP was associated with a high risk of developing IOP elevation, for a relative risk of 1.12. Furthermore, patients with late-onset IOP elevation tend to have higher preoperative IOP values compared to those with early-onset IOP elevation.[45] This increased vulnerability to postoperative IOP elevation among glaucoma patients may be attributed to anatomical factors related to glaucoma, such as a flat anterior chamber, narrow anterior chamber angle, impaired trabecular meshwork function, and other relevant factors. These factors raise the risk of elevated intraocular pressure following silicone oil tamponade, surpassing that of individuals without glaucoma-related conditions.

Myopia

Previous studies have indicated a higher likelihood of glaucoma in individuals with myopia, particularly in eyes with a diopter greater than −6.00D. The incidence of optic nerve injury in glaucoma is significantly higher in these eyes compared to others.[46] Additionally, there is a significant and positive correlation AL and the degree of SO emulsification.[47] However, the exact mechanism behind this correlation remains unclear. One possible explanation could be the larger volume of silicone oil injected into the vitreous cavity in myopic eyes compared to normal eyes.[48] This increased volume results in greater buoyancy of the silicone oil, leading to increased stress between the lens and iris. Consequently, anterior displacement is facilitated, causing a narrowing of the chamber angle and subsequent elevation of intraocular pressure.

Lens Status

Numerous studies have extensively investigated the impact of lens status on the elevated IOP following silicone oil tamponade, but the conclusions drawn from these studies remain controversial. Aphakia is considered a significant risk factor for the occurrence of open-angle glaucoma (OAG) with SO filling, with a 10-fold increase in risk.[49] Due to the absence of the lens, the anterior and posterior chambers communicate with each other, leading to the accumulation of silicone oil droplets near the iris pupillary margin. Consequently, aqueous humor circulation is impeded, resulting in pupil blockage. It is worth noting that aphakic patients with older age and poor general health conditions, who are unable to maintain a prolonged prone position after surgery, have a higher possibility of silicone oil entering the anterior chamber. This further obstructs the chamber angle and subsequently leads to elevated intraocular pressure. Avitabile found that postoperative SO emulsification is more likely to develop in patients with aphakic eyes, while it is rare or even absent in phakic eyes.[24] Individuals with pseudophakic who receive silicone oil tamponade have a lower risk of both IOP elevation and corneal endothelial cell loss compared to those with aphakic eyes.[50] Meanwhile recent research suggested that presence of lens is a protective factor and may delay the development of OAG.[51]

Although the influence of pseudophakic eyes on postoperative high intraocular pressure is relatively smaller compared to aphakic eyes, it still poses a risk factor.[45,52] This may be due to the relatively low anterior chamber pressure after silicone oil filling. The small volume of the intraocular lens and its weak barrier effect allow the silicone oil in the posterior chamber and vitreous cavity to easily enter the anterior chamber through the suspension ligament when patients change their positions abruptly. As a result, secondary ocular hypertension may occur due to the pressure difference. Moreover, the vitreous oxygen gradient is present in normal eyes, but after vitrectomy this gradient is eliminated due to a significant increase in intravitreal oxygen concentration,[53] It is speculated that this increase in oxygen concentration may enter the anterior chamber and trabecular meshwork in pseudophakic eyes, causing oxidative damage as pseudophakic eyes lack the ability to consume oxygen.[54]

Diabetes Mellitus

The association between diabetes mellitus and ocular hypertension following silicone oil tamponade has been a subject of conflicting reports. Whether diabetes is a risk factor for intraocular hypertension after silicone oil filling is still controversial. deCorral et al[55] have demonstrated that diabetes had no impact on IOP elevation. However, Honavar et al,[56] through their univariate analysis, observed a significant correlation between diabetes mellitus and silicone oil glaucoma. Their multivariate analysis further identified diabetes as an independent risk factor, increasing the risk of secondary glaucoma by 6-fold. They argue that persistent retinal ischemia and hypoxia caused by long-term hyperglycemia lead to continued synthesis of vascular endothelial growth factor (VEGF) by retinal endothelial cells. This triggers neovascularization, resulting in elevated permeability, increased inflammation, and trabecular edema, ultimately leading to blockage of the trabecular network by inflammatory particles and ghost cell glaucoma, and subsequent high intraocular pressure. Henderer et al[57] also insist that patients with diabetes, especially those with proliferative diabetic retinopathy, face a significant risk of postoperative IOP elevation compared to patients with proliferative vitreoretinopathy alone. The risk of elevated intraocular pressure is greatly influenced by high blood sugar levels in patients with diabetes, contributing to a more severe postoperative inflammatory response. However, a recent study by Jabbour et al[45] has shown diabetic patients had a lower incidence in the risk of intraocular hypertension in diabetic patients following silicone oil tamponade. Diabetes is considered to be a protective factor to prevent postoperative ocular hypertension. The authors propose that compared to non-diabetic patients, diabetic patients experience more severe retinal ischemia and hypoxia, resulting in a lower oxygen ratio to the trabecular meshwork after surgery. This leads to weaker oxidative stress and a lower incidence of high intraocular pressure.

Surgical Factors

Muether et al[58] found that when pars plana vitrectomy was combined with panretinal photocoagulation (PRP) and silicone oil tamponade for the treatment of proliferative diabetic retinopathy with tractional retinal detachment, particularly in patients who underwent intraoperative PRP and silicone oil tamponade, there was a significant increase in postoperative intraocular pressure compared to patients treated with PPV and silicone oil tamponade alone. This observation raises speculations that PRP exacerbates the postoperative inflammatory response, interferes with venous blood reflux in the choroid, and induces changes in local hemodynamics and opening of the capillary bed. These factors contribute to choroidal and ciliary body edema and exudation,[59] as well as forward movement of the iris root, narrowing of the anterior chamber angle, obstruction of aqueous humor outflow pathways, and subsequent elevation of intraocular pressure.[60,61] Meanwhile, the study[45] also found that patients undergoing membrane segmentation during surgery appear to have a lower risk of increased intraocular pressure. Wide relaxing retinotomy is associated with a higher risk factor for silicone oil emulsification, which can occur earlier than expected, even as early as two months post-operation.[62]

Post-Operative Influencing Factors

Silicone Oil Emulsification

Emulsification is the process of dispersing silicone oil into droplets over a period of several weeks to months. Various factors can contribute to the emulsification of silicone oil, encompassing the quality and viscosity of the oil itself, inflammatory and hemorrhagic conditions, the presence of shear forces, and turbulence induced by saccadic eye movements. de Silva et al[63] have suggested more complete silicone oil fill, along with the effect of indentation from an encircling band, can reduce silicone oil emulsification by minimizing the movement of silicone oil and water and the resulting shear forces. Silicone oil emulsification is the main cause of delayed ocular hypertension. The time of silicone oil emulsification after surgery ranging from 5 to 24 months.[64] With the prolongation of the filling time, the emulsified silicone oil droplets can directly enter the anterior chamber with the aqueous humor. This can lead to the obstruction of the anterior chamber angle or penetration into the trabecular meshwork, resulting in the collapse of the trabecular meshwork and scleral sclerosis, the outflow of aqueous humor, and secondary ocular hypertension.[65]

Silicone Oil Migration into Anterior Chamber

The migration of silicone oil into the anterior chamber is recognized as the primary risk factor for secondary high intraocular pressure and even glaucoma after silicone oil filling.[66] Silicone oil bubbles can mechanically obstruct the trabecular network and impede the outflow of aqueous humor, resulting in elevated intraocular pressure.[67] Pupillary block is the primary mechanism of angle-closure glaucoma associated with SO tamponade.[68] When SO migrates anteriorly, it displaces the aqueous humor, causing it to accumulate inferiorly in the posterior chamber. This displacement leads to the anterior pushing of the iris, resulting in irido-trabecular contact. Additionally, it allows for more SO to enter the anterior chamber (AC), eventually filling both the AC and the pupil, while accumulating superiorly in the posterior chamber.[69] In some cases, the migration of a large SO bubble can cause iridolenticular block, particularly when heavy SO is used in patients who adopt prolonged supine positioning.[22,70] Pupillary block is most commonly observed in aphakic eyes. However, this complication has also been reported in phakic and pseudophakic eyes.[34,71,72]

Management of Postoperative High Intraocular Pressure

If IOP rises after intraocular tamponade with silicone oil, in most cases it can be controlled by medications alone.[73] Al-Jazza found that 40 of 51 eyes (78%) with elevated intraocular pressure were treated only with glaucoma medicines.[74] The most common IOP-lowering medications used for treating ocular hypertension secondary to vitrectomy are beta-blockers,[27] which can suppress aqueous humor production. Cycloplegics and corticosteroids are used for drug treatment to reduce inflammation, and aqueous suppressants are used to reduce aqueous humor production to control intraocular pressure.[67] At the same time, selective laser trabeculoplasty can be utilized as an adjunct treatment for glaucoma to help control intraocular pressure.[75] When medical therapy fails to adequately control IOP, the next consideration is silicone oil removal. However, insufficient duration of silicone oil tamponade may contribute to recurrent retinal detachment. Several studies[22,76–78] have demonstrated that re-moving silicone oil leads to reversible intraocular pressure changes in most patients. However, Flaxel et al[79] reported that IOP elevation persisted even after the removal of silicone oil. Budenz et al[80] have shown that patients who underwent silicone oil removal alone to control IOP tended to be more prone to persistent postoperative IOP elevation and may require additional surgeries for secondary glaucoma. On the other hand, patients who also underwent silicone oil removal combined with glaucoma surgery were more probable to develop hypotony.

Surgical treatment becomes necessary for patients who do not achieve IOP control with medication and silicone oil removal. The decision for surgical treatment should consider factors such as visual function, the degree of elevated intraocular pressure, gonioscopic evaluation, conjunctival status, fundus condition, and systemic condition. Due to the limited success rate of traditional filtering surgery in the management of secondary glaucoma, the use of glaucoma drainage implants and ciliary body destruction surgeries are considered superior options.[74,81]

In order to decrease the incidence of IOP elevation postoperatively, Ando[35] performed inferior peripheral iridectomy during vitrectomy in aphakic and pseudophakic patients. This technique aims to inhibit the forward migration of silicone oil and minimize the risk of pupillary obstructive glaucoma. Currently, there are four main surgical approaches employed for the treatment of persistent glaucoma after silicone oil removal: trabeculectomy, deep sclerectomy, Ahmed valve, and Ex-Press minishunt. El Saied et al[82] conducted a comparison of these surgical approaches and found that the Ex-Press minishunt exhibited the highest success rate in controlling persistent glaucoma after silicone oil removal, followed by the Ahmed valve, trabeculectomy, and deep sclerectomy in descending order of efficacy.

Future Directions

The intraoperative introduction of fillers, such as inert gas or silicone oil, into the vitreous cavity can disrupt the structural and physiological stability of the eye.[83] An ideal vitreous replacement should possess similar characteristics to the natural vitreous humor, including transparency, biocompatibility, volume retention, elasticity, and the absence of negative properties like age-related liquefaction and biodegradation.[84] On one hand, substances with a molecular structure resembling that of the vitreous humor can serve as fillers, preserving the elasticity and pressure of the eye. On the other hand, structural molecules with chemical and physiological properties conducive to the diffusion of metabolites and gases, facilitating drug perfusion, and promoting positive interactions with intraocular structures are sought after.[85,86] Current research has focused on developing a hydrophilic alternative to silicone oil as the side effects associated with silicone oil filling are primarily attributed to its hydrophobic nature. Efforts are now directed towards the creation of a hydrophilic vitreous substitute that exhibits fewer toxic side effects. Hydrogels have emerged as a potential alternative, representing a class of hydrophilic polymers with desirable attributes such as transparency, biocompatibility, and viscoelastic properties similar to that of the vitreous humor, thus capable of emulating its biological functions.[87–89] Notably, smart hydrogels have garnered attention for their ability to respond to environmental and external physical stimuli.[90] However, these fillers have the potential to elicit an immune response and induce inflammation.[91]

Conclusions

Postoperative elevation of intraocular pressure is a common complication that occurs following vitrectomy combined with silicone oil tamponade. The increase in intraocular pressure subsequent to silicone oil filling is the result of various interacting factors. The key risk factors include the physicochemical properties of silicone oil, preoperative high intraocular pressure, lens state, myopia, diabetes and intraoperative PRP. Although removal of SO after an average of 2–3 months and maybe antiglaucoma medication are the only necessary steps in the large majority of cases of intraocular hypertension secondary to silicone oil. If the intraocular pressure remains uncontrolled and progresses to secondary glaucoma, it will lead to irreversible damage to the vision of patient. Therefore, meticulous monitoring of intraocular pressure is essential during silicone oil tamponade, particularly in individuals with associated risk factors. Medication or even surgical interventions should be considered to manage intraocular pressure effectively if necessary.

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Disclosure

The authors report no conflicts of interest in this work.

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