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# TWO-STAGE OR SINGLE-STAGE VITREORETINAL SURGERY WITH PHACOEMULSIFICATION IN PATIENTS WITH ADVANCED PROLIFERATIVE DIABETIC RETINOPATHY?

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 $\Rightarrow$  The literature review compares the combined (vitreoretinal surgery with silicone tamponade and phacoemulsification of incipient cataract with intraocular lens implantation) and two-stage (phacoemulsification with intraocular lens implantation as a second step, simultaneously with the silicon oil removal, after vitreoretinal surgery) surgical treatment of patients with advanced proliferative diabetic retinopathy and complicated incipient cataract. Modern concepts of treatment tactics of this disease, its efficacy are analyzed. Benefits and drawbacks of each of the discussed surgical treatment methods are specified.

*Keywords:* proliferative diabetic retinopathy; vitreoretinal surgery; phacoemulsification; diabetes mellitus.

## ДВУХЭТАПНАЯ ИЛИ ОДНОМОМЕНТНАЯ ВИТРЕОРЕТИНАЛЬНАЯ ХИРУРГИЯ С ФАКОЭМУЛЬСИФИКАЦИЕЙ У ПАЦИЕНТОВ С ДАЛЕКОЗАШЕДШЕЙ СТАДИЕЙ ПРОЛИФЕРАТИВНОЙ ДИАБЕТИЧЕСКОЙ РЕТИНОПАТИИ?

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◆ Данный обзор литературы посвящён сравнению комбинированного (витреоретинальная хирургия с силиконовой тампонадой и факоэмульсификация начальной катаракты с имплантацией интраокулярной линзы) и двухэтапного (факоэмульсификация начальной катаракты с имплантацией интраокулярной линзы вторым этапом одновременно с удалением силиконового масла, после витреоретинальной хирургии) методов хирургического лечения пациентов с далекозашедшей стадией пролиферативной диабетической ретинопатии и с осложнённой начальной катарактой. Рассмотрены современные представления о тактике лечения данной патологии, её эффективности, а также перечислены преимущества и недостатки каждого из рассматриваемых методов оперативного вмешательства.

♦ Ключевые слова: пролиферативная диабетическая ретинопатия; витреоретинальная хирургия; факоэмульсификация; сахарный диабет.

The advanced stage of proliferative diabetic retinopathy (PDR) is one of the most serious complications of diabetes mellitus (DM), and is the primary cause of vision loss and disability in this category of patients [1]. According to recent data from the International Diabetes Federation, there are approximately 425 million patients aged between 20

and 79 years old with diabetes worldwide. Moreover, approximately every third diabetic patient has various stages of diabetic retinopathy, and an advanced stage threatening vision loss develops in every tenth patient [2]. In addition, it is known that this group of patients often has concomitant lenticular opacity. Cataracts have been proven to occur in diabetic patients 2 to

5 times more commonly than in non-diabetics. The risk of developing cataracts is 15 to 25 times higher in diabetic patients under the age of 40 years [3].

Vitreoretinal surgery (VRS) is currently the "gold standard" for surgical treatment of patients with advanced PDR.[4] However, when planning such surgeries, the question is often when to remove the initial cataract: during VRS or later, when it progresses further? In some cases, phacoemulsification (PE) with an intraocular lens (IOL) implantation is offered to such patients as a first stage surgery, with VRS to follow later. Such decisions are based on the cases in which the authors noted that cataracts often developed or progressed after VRS. According to some reports, this is true in 12.5% to 80% of cases [5, 6].

The causes for this development and progression include mechanical damage to the lens during VRS, the adverse effects of irrigation solutions, and the use of an air-gas mixture or silicone oil (SO) as the endotamponade [7]. In their 2016 study, Singh et al recorded the presence of cataracts in 18.8% of patients with tamponade of the vitreous cavity with an air-gas mixture for 3 months after surgery [8]. According to Casswell (1987), a clinically significant cataract occurs in 60% of patients after VRS with silicone tamponade, and progression of already existing lens opacity is registered in 85% of cases [9]. In 2008, Zeitz revealed that cataract development occurred in 89.2% of cases with SO tamponade of the vitreous cavity for a period of more than 3 months [10]. It should be noted that vitrectomy with induced posterior vitreous detachment and removal of its anterior sections also increases the risk of lens opacities [11].

The high risk of cataract development and progression after VRS induced the introduction of combined VRS and PE in clinical practice [12, 13]. The results of the simultaneous performance of VRS and PE were presented by Koenig for the first time in 1990 [14]. Later, the development and improvement of the phacovitrectomy technique increased the number of supporters of this approach for the surgical treatment of patients with vitreoretinal pathology.

Simultaneous performance of VRS and CPE is justified by the need for better visualization of the fundus during surgical procedure [12], reduction of the patient rehabilitation period, reduction of the total number of surgeries, and reduction of risks and costs associated with a second surgery [13]. Improvement of the fundus visualization after PE, as a stage of combined surgery, optimizes retinal sanitation and

allows laser coagulation at the extreme periphery in PDR patients, which, according to the authors, reduces the risk of complications such as secondary neovascular glaucoma (NVG), recurrence of vitreous hemorrhage, and retinal detachment [15].

Supporters of the combined approach note that PE on the avitreal eye is associated with certain difficulties, namely mobility of the lens capsule, instability of the anterior chamber depth, weakness of zonules, and pupil rigidity during surgery [16-20]. Cataract surgery under such conditions increases the risk of damage to the posterior capsule and of displacement of the lens masses into the vitreous cavity [6]. Thus, in 2016 Elhousseini et al. reported that the frequency of iatrogenic damage to the posterior capsule during VRS on the avitreal eye was 3.7% (52 out of 1399 cases); in 11% of cases (5 of 45), rupture of the posterior capsule during subsequent PE was registered in this group of patients [21]. However, the development of technical methods aimed at reducing the risks of PE on avitreal eyes significantly optimized the results. Thus, Malyugin et al. (2013) analyzed the aspects of the altered anatomical parameters of the anterior chamber of the avitreal eve and proposed a reasonable technology for performing PE. It is characterized by a special geometry of the formed corneal tunnel, an increase in the distance of the phacoemulsification needle relative to the irrigation sleeve, and a decrease in the angle of inclination of the working part of the chopper. The surgery is completed with the formation of a window using a vitreophage in an indurated posterior capsule after IOL implantation. Using this technique, the authors operated on 45 avitreal eyes and received positive results without complications in all cases [22].

A similar technique was described by Tahchidi et al (2009), with an original aspect being their use of a modified chopper with an angle of inclination of the working part of 70–75° [17]. Sachedev et al (2009) suggested modifying the phaco chop technique by lowering the parameters of irrigation-aspiration, which enabled reduction of the load on the zonules and breaking the nucleus safely, especially under myosis conditions [23]. Joshi (2018) reported on the successful experience of performing PE on avitreal eyes using a modified silicone sleeve, which helped maintaining the depth of the anterior chamber while reducing the risk of intraoperative complications [16]. To prevent the pupil narrowing and maintain the necessary mydriasis throughout the surgery, injection of epinephrine solution into the anterior chamber or use of iris refractors was proposed [6]. Yu et al (2018) reported that the increased depth of the anterior chamber along with lack of vitreous allows the lens to be removed in the anterior chamber, maintaining a safe distance to the corneal endothelium and reducing the risk of damage to the posterior capsule [24]. Thus, the use of the above technical methods avoids the specific complications characteristic of PE on eves with lack of vitreous and justifies PE as a second stage alternative surgery after VRS during rehabilitation of PDR patients. This choice is also supported by the fact that, when performing PE during combined VRS in PDR patients, surgeons note difficulties in performing capsulorrhexis due to the absence or weakening of the red fundus reflex because of vitreous hemorrhage, as well as undesirable prismatic effects during VRS caused by implanted IOL [25].

Another special aspect of VRS in patients with advanced PDR is the need to perform the second stage of surgical treatment due to silicone tamponade of the vitreous cavity. Along with an initial cataract, this enables PE to be delayed until the planned removal of SO. The use of viscoelastic gel and an intracapsular ring during PE in eyes with silicone tamponade optimizes such surgery and reduces its risks [26].

In 2013, M. Shishkin et al proposed a sparing option for removing SO through one port after PE in eyes with cataract and partial exit of oil into the anterior chamber. The presence of a defect in the anterior hyaloid membrane allows the infusion solution to be delivered through a cannula mounted in the anterior chamber. According to the authors, such an approach allows for more sparing of the anatomical structures and reduces the risk of local proliferation in the area of the sclerostome [27]. Zhu et al (2017) reported the efficacy and safety of a combination of transpupillary removal of SO with PE and IOL implantation [28].

Considerable attention in the recent literature has also been given to the presence of refractive errors after phacovitrectomy [29, 30]. These errors are caused by a number of factors, such as vitreous body replacement, changes in keratometry data, errors in measuring the anteroposterior axis of the eye when calculating the IOL power, difference between the actual and planned IOL positions, and presence of vitreoretinal pathology in the macular region, such as diabetic macular edema and retinal detachment [31]. It is worth noting that difficulties arise when calculating the IOL power in eyes with SO tamponade of the vitreous cavity. Measurement of the anteroposterior axis in such eyes is a complex procedure, because the refractive index of SO is higher than that of the vitreous body. Accordingly, the speed of ultrasound in SO varies. However, despite this, there are studies demonstrating that measuring the anteroposterior axis in eyes with silicone tamponade is not only possible, but also quite reliable when using modified ultrasound biometry at an ultrasound speed of 1000 m/s and IOL-Master optical biometry in the Silicone Filled Eye mode [32].

Performing PE as the second stage after VRS in patients with initial cataract and PDR (or refraining from prophylactic removal of a clear lens during VRS) avoids significant damage to the blood-ocular barrier and reduces the risk of specific complications such as NVG, recurrence of vitreous hemorrhage, and cystoid macular edema [33–35].

At the same time, the development of postoperative complications is also noted by supporters of a combined approach to surgical treatment of this category of patients, focusing on the need for more extensive studies to determine the safest terms for performing PE [36–38]. Thus, in a retrospective study, Zheng et al (2010) noted that the most common change in the anterior segment in the postoperative period was posterior capsule fibrosis, which occurred in 17.5% of cases [37]. One of the most severe complications that could lead to an irreversible loss of visual function is NVG. It is believed that neovascularization of the iris and anterior chamber angle develops in response to retinal ischemia, trauma, or the inflammatory process [39]. The mechanisms of NVG development after simultaneous VRS and PE include the destruction of the barrier between the anterior and posterior segments of the eye, which leads to anterior diffusion of vasoproliferative substances, such as VEGF (vascular endothelial growth factors) and inflammatory cytokines [40]. In a retrospective study, Chung et al (2002) compared the efficacy of combined and sequential surgery (PE after VRS) and found that NVG occurred only after phacovitrectomy in DM patients (15.4%) [41]. In this case, the prescription of a IOP-lowering drug regimen is often insufficiently effective in the treatment of NVG, which necessitates additional surgical procedure. Kwon et al (2017) demonstrated that NVG developed in 11.8% of PDR patients after phacovitrectomy, 46.6% of whom required additional surgery in the form of glaucoma

surgery with implantation of Ahmed drainage device [36].

Many researchers note that cystoid macular edema is one of the most common complications of PE, especially when complicated cataracts are removed in DM patients [42]. Moreover, there is evidence that combined VRS and PE also leads to more frequent development of cystoid macular edema [34, 35]. Although the mechanism of its development after PE is still not fully understood, it is known that the inflammatory response plays a significant role in its pathogenesis [43]. Lahey et al (2003) report that postoperative inflammation in the anterior chamber was more pronounced after combined surgery compared with VRS alone [16]. In their study, Rivas-Aguino et al (2009) also noted the development of a diffuse fibrinoid reaction of the anterior chamber after simultaneous VRS and PE in 32.1% of PDR patients [35].

Another common complication of combined surgery is ocular hypertension. Park et al revealed that the percentage of increased IOP was significantly higher in the phacovitrectomy group than in the VRS alone group (60% versus 30%, respectively) [44]. This complication often leads to the necessity of earlier removal of SO from the vitreous cavity, which, in turn, is often accompanied by recurrence of vitreous hemorrhage and retinal detachment [45].

At present, there is no consensus on the need to remove the initial cataract (or clear lens) during VRS in patients with advanced PDR. Although the apparent advantage of phacovitrectomy is the reduction in the total number of surgical interventions, it should be noted that many patients in this category require the second stage of surgical treatment because of silicone tamponade of the vitreous cavity [14]. This then allows PE to be delayed until the planned removal of SO. In addition, simultaneous VRS and PE procedure increases the duration of the first stage of surgical treatment. A larger amount of surgical aid increases the risk of postoperative complications, which often lead to the need for additional surgical treatment [34-36]. This represents a certain risk in patients with long-term DM, severe comorbidity, and high risk of cardiovascular complications.

In this regard, the question remains unresolved if the existing approach — performing PE simultaneously with VRS — is the most favorable in patients with advanced PDR. A few cases monitored by various authors indicate the feasibility of PE as the second stage after VRS. It is also possible that under certain conditions, lens removal as the first stage after preliminary preparation using nonsteroidal antiinflammatory drugs is reasonable. Thus, a study on the safety and the efficacy of staged PE and VRS in patients with advanced PDR is relevant.

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