ЦИКЛОДИАЛИЗ *AB EXTERNO* С ИМПЛАНТАЦИЕЙ КОЛЛАГЕНОВОГО ДРЕНЖА В ХИРУРГИЧЕСКОМ ЛЕЧЕНИИ ГЛАУКОМЫ

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Глаукома является актуальной проблемой офтальмологии. Борьба с данной проблемой неотъемлемой частью любой офтальмологической клиники. В России глаукома занимает второе место по частоте среди заболеваний, вызывающих ограничение вида зрения. В Европе глаукома вызывает 3% всех слепот, при этом она является одной из главных причин необратимой слепоты. Хирургическое вмешательство в сочетании с фемтосекундным лазером является одним из самых эффективных методов лечения и улучшает качество жизни пациентов. В данной работе рассмотрено проведение хирургического вмешательства у 26 пациентов (26 глаз) с чередующимися стадиями развития ПОУГ с использованием метода *ab externo*.

**Методы**

Измерения проводились в 26 глазах пациентов. Для оценки эффективности и безопасности проведена оценка диналики ВГД, количества используемых гипотензивных средств, потребности в повторном хирургическом вмешательстве и наличие осложнений. В результате лечения было зарегистрировано снижение ВГД на 34% от исходного уровня (c 29,5 ± 6,8 до 18,8 ± 4,3 мм рт. ст.). Количество используемых гипотензивных средств сократилось с 2,8 ± 0,9 до 0,6 ± 0,9. Успешность проведенного хирургического вмешательства оценивалась по критериям Всемирной глаукомной ассоциации: полный успех достигнут в 73,1% случаев, признанный — в 26,9% случаев. Неудачных исходов от оперативного лечения не зарегистрировано.

**Принципы безопасного хирургического лечения**

Хирургическое вмешательство у пациентов с ПОУГ с использованием метода *ab externo* показывает высокую эффективность и безопасность. В настоящей работе описаны результаты хирургического вмешательства у 26 пациентов, и показано, что метод *ab externo* может быть рекомендован в качестве терапии пациентов с ПОУГ.

**Ключевые слова**: глаукома, хирургическое лечение, *ab externo*, интраокулярное давление, клиническая эффективность, безопасность, концепция и дизайн, исследование, сбор и обработка материала, статистическая обработка, написание и редактирование текста статьи; А. М. Фролов — концепция и дизайн исследования, сбор и обработка материала, статистическая обработка, написание и редактирование текста статьи; А. И. Беззаботнов — концепция и дизайн исследования, сбор и обработка материала; К. А. Абу Заалан — сбор и обработка материала. 

**Соблюдение этических стандартов:** исследование одобрено этическим комитетом медицинского института Российского университета дружбы народов (протокол № 16 от 17 ноября 2016 г.); все пациенты подписали добровольное информированное согласие на участие в исследовании.
Glucoma is one of the main causes of irreversible blindness in the Russian Federation and it is the leading cause of visual impairment among working age population. [1,2]. In 2013, there were 1,180,708 patients registered with this diagnosis in Russian Federation. According to the World Health Organization, there are 60.5 to 105 million people worldwide suffering from glaucoma. The disease turns blind 1 adult person every minute and 1 child every 10 minutes [1].

Glucoma is a multifactorial disease. Today, there is no consensus as to its etiology and pathogenesis. The primary goal of glucoma therapy is to preserve the visual function, which is mainly achieved through persistent normalization of IOP by installation of hypotensive drugs, laser therapy and/or surgery [3, 4]. Some researchers report that in 62 to 82% of patients’ glucoma is at its advanced stages when it is diagnosed for the first time; in such cases local instillation of hypotensive medications is effective only for a short term [5].

Activation of the aqueous humor outflow through natural pathway is probably the most promising surgery aimed to treat POAG [6–9]. These paths are trabecular and uveoscleral outflow pathways (UOP). From the point of view of surgery, UP boasts great potential because of its anatomical and physiological features. Some ophthalmologists believe that there is a link between the uveoscleral outflow path and the eyeball and orbit’s lymphatic system [10]. Current glucoma surgical techniques aimed at activating the UOP imply cyclodialysis with implantation of various types of drainage devices in the supraciliary space. In Russia, the most common implants selected for such surgeries are auto sclera strips [9]. In other countries, surgeons opt for CyPass Micro-Stent (Transcend Medical; USA), iStent Supra (Glaukos; USA), Gold Shunt (SOLX; USA), STARFlo (iSTAR Medical; Belgium), and Aquashunt (OPKO Health Inc.; USA) [11–13].

A surgical UOP activation technique implying cyclodialysis ab externo with implantation of NACI in the supraciliary and suprachoroidal spaces has been developed. The implant is usually used to prolong the hypotensive effect after non-penetrating deep sclerectomy.

Purpose. To evaluate the effectiveness and safety of a novice glucoma surgical technique implying valve cyclodialysis ab externo with implantation of NACI supraciliary space in moderate and severe POAG patients.

METHODS

A total of 26 patients (26 eyes) aged 54 to 87 years (mean age 73.0 ± 8.3; 12 male and 14 female), exhibiting severe POAG were operated upon and under observation. Seventeen patients (65.4%) exhibited severe POAG and 9 (34.6%) — terminal stage of glucoma.

The inclusion criteria were: POAG; concomitant pathology (POAG and cataract); medically uncontrolled IOP informed consent to participate in the study. The exclusion criteria were narrow-angle glucoma, secondary glucoma, patients exhibiting acute attack of glucoma, and congenital glucoma. Neither previous cataract surgery nor previous glucoma surgery substantiated exclusion of participants from the study. The post-surgery follow-up period was 12 months.

Eighteen patients (69.2%) had undergone simultaneous surgery for concomitant pathology. Thirty patients (50%) were suffering from pseudoexfoliation syndrome. Eleven (42.3%) patients had previously undergone glucoma surgery. The mean number of previous surgeries associated with glucoma was 1.6.

Before surgery, all glucoma patients were instilling one or a combination of two or more hypotensive drugs. Two (7.7%) patients were instilling 1 drug, 5 (19.2%) patients — a combination of 2 hypotensive drugs, 15 (57.7%) patients — 3 drugs and 4 (15.4%) patients — a combination of 4 drugs. Despite the local hypotensive therapy, the average IOP level before surgery was 29.5 ± 6.8 mmHg.

All patients underwent the following standard ophthalmological examination before surgery: visual acuity checkup, tonometry (used Maklakov method with 10.0 g), biomicroscopy, ophthalmoscopy, gonioscopy, ultrasound biomicroscopy (UBM), B-scanning and optical coherence tomography (OCT). The cyclodialysis cleft (CC) was monitored with the help of a single-mirror goniolens, B-scanning and UBM (Marvel B-scan with UBM, Appasamy medical equipment (P) ltd; India) with the sensor operating at 50 MHz and 30 MHz and up to 30 dB, and OCT (Visante OCT, Zeiss; Germany).

The patients were examined on 1st day, 1 week, 1, 3 and 6 months and 1 year after surgery. Each examination included gonioscopy, tonometry, visual acuity testing. The anterior chamber angle (ACA), CC condition and position of the implant were registered with the AIA 11 slit lamp (Appasamy associates, India) and its built-in Canon digital camera (Canon; China). The main efficacy criteria were IOP dynamics, number of hypotensive drugs used, number of intra- and postoperative complications, and need for a repeat surgery. Descriptive statistical methods were applied to analyze the results of the study: mean, 95% confidence interval (CI) and standard deviation were calculated; Student’s test was used to determine the significance (P). Statistical processing of the digital data was performed with the help of SPSS Statistics (IBM) 22.0 (USA) for Windows 10.

Nesterov–Vurgaf–Kiselev–Tanyashina’s table [14] was used to convert tonometry IOP data into true IOP (P°). Surgical outcomes were evaluated as per World Glaucoma Association recommendations [15]. It was considered a complete success if P° was ≤15 for moderate glucoma patients and ≤12 mmHg for severe glucoma patients or when the IOP decrease was by more than 30% against baseline, and P° was >6 mmHg.

Further, a complete success was registered when the target pressure was achieved without hypotensive medication; in case additional hypotensive medications were required to achieve the target IOP, the success was considered as partial. Criteria for a failure were inability to achieve the target pressure even with additional hypotensive medications and the need for a repeat surgical intervention.

Surgery technique

The surgical field was prepared with 0.5% chlorhexidine (ethanol) solution and 5% aqueous povidone–iodine solution (Betadine, EGIS; Hungary), followed by instillation of local anesthetic (proxymethacaine 0.5% solution, Alcaine) (Alcon; USA) in conjunctival sac. A fixation suture was placed at 6 o’clock at the limbus (7–0 polypropylene). Two paracenteses were made at 7–8 hours or 4–5 hours. The AC was irrigated with 0.2 ml of 0.01% carbachol solution to constrict pupil followed by irrigation with 1.4% hyaluronic acid to maintain AC depth during surgery and, to avoid post-operative hypotony and hyphema. A conjunctivotomy was performed parallel to the limbus running from 10 to 13 hours. A 5 mm long conjunctival flap was dissected. Minimal diathermocoagulation of the superficial scleral vessels was performed when needed. Five mm away from the limbus, a 1/2 thickness rectangular scleral flap measuring 3 × 2 mm, was dissected with its base to the limbus (Fig. 1A). In the next step, 4.0 mm away from the posterior
border of the surgical limbus and parallel to it an incision up to the ciliary body was made through remaining deep layers of sclera. (Fig. 1B). At the extreme points of this incision, 2 vertical cuts (1mm long) were made towards limbus on either side to create a valve. (Fig. 1C). A spatula was inserted through paracentesis into the AC and cyclodialysis ab interno under visual control was performed till its distal end appeared in the incision (Fig. 1D). The spatula was withdrawn and cyclodialysis was completed ab externo through the scleral incision (Fig. 1E). The thus created cyclodialysis tunnel (CT) was filled with 0.1–0.2 ml of cohesive viscoelastic (1.4% hyaluronic acid). Through the scleral incision an angled long suture tying forceps with closed tying platforms was inserted through the tunnel until its ends were visible in the anterior chamber angle. At this stage the arms of the forceps were released to widen the cleft as wide as the incision in the sclera (Fig. 1F). Cyclodialysis was further advanced under the back lip of the incision in the sclera to expand it towards the suprachoroidal space. Next, using the same angled forceps the NACI (pre-moistened in a balanced salt solution) was captured between the tying platforms in such a way that distal 0.5mm of tying platforms remained free (Fig. 1G). Under visual control, the forceps with NACI was inserted through the incision in the sclera and pushed forward until the distal ends of the forceps and the NACI appeared in the AC’s angle. After this, the forceps was opened and withdrawn carefully leaving the implant in the tunnel. The posterior end of the implant was inserted under the back lip of the incision into the suprachoroidal space (Fig. 1H). The NACI's position in the tunnel was checked (Fig. 1I). Once satisfied, the superficial scleral flap was put back in its place and sutured with 2 interrupted sutures (10–0 nylon). Conjunctiva was sutured to the limbus using the same suture material. The corneal incisions were sealed with corneal stromal hydration. At the end of the operation, 0.2 ml of dexamethasone solution was injected under the conjunctiva. Antibacterial ointment in the conjunctival cavity and a sterile aseptic dressing were applied to the eye. Conjunctival sutures were removed on 7th day after surgery.

Thus, the technique allowed to create a CT of sufficient width to enable reliable communication between AC and the supraciliary space that, in turn, communicates with the suprachoroidal space, which is the key to the aqueous humor outflow via UP.

The Xenoplast implants used in this study were customized as per needs. Its dimensions were changed to 6.0 × 1.0 × 0.5 mm instead of the standard 4.0 × 1.0 × 0.5 mm. This length was necessary to have the implant reaching the suprachoroidal space with 1 mm being left behind in the AC angle.

RESULTS

The mean baseline IOP was 29.5 ± 6.8 mmHg. (95% CI 26.6–32.3). Twelve months after surgery, the mean IOP was 18.8 ± 4.3 mmHg. (95% CI 16.9–20.6; p ≤ 0.01). The decrease in IOP was by 33.8 ± 18.8% against the baseline. Figure 2 shows the IOP dynamics at different follow-up visits.

A significant decrease in IOP was registered in postoperative period. As compared to baseline IOP, at 1, 3, 6 and 12 months after surgery the decrease was by 37.6 ± 16.4%, 33.6 ± 10.7%, 32.1 ± 13.0% and 33.8 ± 18.8%, respectively.

The mean number of hypotensive medications used before the surgery was 2.8 ± 0.9 (95% CI 2.5–3.2). Twelve months after surgery this reduced to 0.6 ± 0.9 (95% CI 0.2–0.9) (p < 0.01), a reduction by more than 80%. Figure 3 shows use of hypotensive medications at different follow-up visits.

Complete success was registered in 84.6% of cases (22 patients) at 1 and 3 months after surgery, in 80.8% of cases (21 patients) — at 6 months and in 73.1% of cases (19 patients) — at 12 months. Partial success was in 15.4% (4 patients), 15.4% (4 patients), 19.2% (5 patients) and 26.9% (7 patients) of cases at 1, 3, 6 and 12 months, respectively. There were no failures.
registered in this clinical study: up to 1 year after the surgery all the participating patients had their IOP normalized.

In patients with partial success hypotensive drugs were prescribed (1% and 2% pilocarpine, 0.5% timolol, 0.005% latanoprost, 2% dorzolamide and their combinations), which brought the IOP down to the target values and below.

In most of the cases, during surgery there was intraoperative mild hemorrhage in the area of cyclodialysis. To prevent further possible complications, the AC was irrigated with balanced salt solution before hydrating the corneal incisions.

Post-operative follow-up

Early postoperative period. Filtration bleb. A flat bleb was registered in 7 (27%) patients on the first day after surgery, in 4 (15%) patients it developed during the 1st week. In 1 patient (4%) the bleb lasted for a period of 1 month. After 3 months there were no filtering blebs noticed in any of the patients.

Hyphema. Through the entire follow-up period there was only one case of hyphema. Its level measured less than 1 mm; it self-resorbed within 3–5 days without any additional medication. There were another 2 cases with some blood elements in aqueous humour. In both cases it resolved without interventions.

Hypotension and shallow AC. P° below 6 mmHg was considered hypotension; this value corresponds to 14.5 mmHg IOP value measured with a tonometer following the Maklakov method with a weight of 10.0 g. The minimum IOP value registered after surgery was 15 mmHg, i.e. there were no cases of hypotension. One patient had shallow AC; in this case, a combined surgery was performed for a concomitant pathology. An iris-claw intraocular lens (Appasamy associates, India) was implanted in the retro pupillary space. The patient had a pupillary block that needed laser iridectomy. After iridectomy the block was resolved, and AC deepened.

There were no complications registered in the late post-operative period. Gonioscopically, NACI was stable and maintained its position in CT, no shift or total dislocation was observed (Fig. 4). Also, there were no obvious signs of inflammation observed.

Imaging of the formed outflow paths. To assess state of the created CT and position of the implant in the tunnel ultrasound B-scanning and UBM of the surgery zone, as well as longitudinal and transverse OCT of the anterior segment of the eye, were done (Fig. 5), (Fig. 6). Integrity of the CT at 12 months post-operatively was confirmed. The NACI was in the supraciliary and suprachoroidal spaces, which were expanded.

DISCUSSION

Today, there are many surgical techniques aimed at activating aqueous humor outflow through natural paths [6–9, 11, 13]. The most interesting of them imply activation of the UOP [6, 9, 11, 13]. The majority of UOP activation surgeries include elements of cyclodialysis [16–18]. Some Russian
ophthalmologists suggested using autologous sclera as drainage device in the context of the UOP outflow surgery [19].

Two-year observation of 55 refractory glaucoma patients that underwent cyclodialysis ab externo and had Gold Shunt drainage device implanted revealed that the IOP level stabilized in 67.3% of cases aided by additional hypotensive medication. Only 3 patients (5.5%) did not need supplementary therapy to have the IOP level reach the target values. The registered post-surgery complications were ciliochoroidal detachment, corneal edema, and excessive filtering. The main factor that makes Gold Shunt implants inefficient is formation of a thin fibrous membrane that obliterates the front end of the drainage device [20].

There is a report [21] that states Gold Shunt inefficiency in patients with advanced stages of glaucoma: 77% of cases required repeat hypotensive surgery due to high IOP. Examination of the 5 explanted Gold Shunt implants revealed that the reason of their failure is the fibrous tissue that prevented aqueous humor outflow through the CC and the implant’s slits [22].

In case of well-known CyPass Micro-Stent, which was implanted in the supraciliary space ab interno while treating a concomitant pathology secured, only a 14% reduction of IOP at 12 months post-surgery [23]. The surgery lead to complications, such as temporary hypotension, transient IOP increase and microshunt slit obstruction. Other researchers also reported CyPass Micro-Stent slit obstruction and CC obliteration as the main cause of IOP decompensation [24]. Some ophthalmic surgeons used a YAG laser to reopen the drainage; the procedure allowed restoring of fluid outflow through the microshunt and normalizing IOP [25]. Recently, Alcon discontinued its CyPass microshunt due to significant loss of endothelial cells 5 years after implantation.

There are also reports describing the effect of phacoemulsification on IOP in the early and late postoperative periods in patients with POAC [27, 28]. Some authors noted a 3–3.5 mmHg increase in IOP in the early post-operative period (up to 2 weeks). By the end of the first month after surgery the IOP level returned to its pre-surgery values. At 3 months authors noted a mean decrease in IOP by 3.1 mmHg from the baseline [27]. Another study reported a decrease in IOP level by 1.7 ± 3.1 mmHg from the baseline at 12 months after surgery [28]. In our study, 18 (69.2%) patients presented concomitant pathologies that were treated simultaneously with the main disease. The IOP level decreased by 11 ± 7.3 mmHg from the baseline at 12 months after surgery. The significant IOP decrease at 12 months after surgery proves more marked hypotensive effect by our technique than by phacoemulsification alone.

In this study cyclodialysis ab externo with implantation of NACI has been advocated for severe glaucoma patients. The surgery aims to activate outflow through UOP by forming a CT connecting AC to the supraciliary and suprachoroidal spaces. Implantation of the NACI in the CT ensures lasting and effective opening of the tunnel, thus activating aqueous outflow through UOP and secures persistence of the hypotensive effect. Watertight closure of scleral incisions helps avoiding filtration under the conjunctiva, which is unnatural. The surgery is
minimally traumatic. Sciera was sectioned between two rectus muscles so that the eyeball’s mobility remained undisturbed. Cyclodialysis ab interno was necessary to avoid any descemet’s membrane detachment, while detaching the ciliary body from the scleral spur. This is a common complication occurred if the approach is ab externo. In our ab interno — ab externo combined approach, a limited amount of ciliary body is detached from the scleral spur ab interno, thus creating a shallow cleft, which is then enlarged by ab externo approach. The scleral valve facilitates insertion of instruments through the scleral incision into suprachoroidal space, thus reduces trauma to the ciliary body. The valve is also an eyeball anchor point, which facilitates manipulations in the suprachoroidal space.

The NACI “Xenoplast” implanted into suprachoroidal and suprachoroidal spaces was selected because of its high biocompatibility with the eye tissues and lack of a pronounced inflammation after implantation due to the material being non-toxic and non-immunogenic [29]. The implant is available in dry form; when wetted, it swells no more than 0.1%. Its porous structure (pore size 200–700 µm) allows the fluid flow through the entire structure. A large number of studies implying non-penetrating deep sclerectomy with NACI implantation in the intrascleral space demonstrate the high efficiency of this implant. The authors reported a persistent decrease of the IOP level 1.5 years after surgery in patients with advanced glaucoma: the IOP reached 13.0 ± 0.5 mmHg without hypotensive medication [30].

In this series over the entire follow-up period not a single failure case was registered. Obvious signs of inflammation, hypotension, reactive syndromes, NACI dislocation was not observed, which confirm safety of the suggested surgical technique. There was only one case of hyphema, which resolved within 5 days.

Twelve months after valve cyclodialysis ab externo with NACI implantation the mean IOP decreased by 33.8 ± 8.8% from the baseline and equaled to 18.8 ± 4.4 mmHg (p ≤ 0.01), which proves the high hypotensive efficacy of the suggested modality. Another proof thereof is the 80.1% reduction in the use of hypotensive medication (from 2.8 ± 0.9 to 0.6 ± 0.9) (p ≤ 0.01) at 12 months after surgery, which improves the patients’ quality of life and significantly reduces their expenses on medicine purchase. It should be noted that through the follow-up period all cases ended in a overall success: complete success in 73.1% of cases (19 patients), partial — in 29.9% of cases (7 patients).

CONCLUSION

Valve cyclodialysis ab externo with implantation of the Xenoplast NACI in the suprachoroidal space proved to be a highly effective and safe way to decrease IOP and the amount of hypotensive medications used in the advanced stage POAG patients; the number of complications associated with the surgery is minimal.

Thus, the suggested valve cyclodialysis ab externo with implantation of Xenoplast NACI is a highly effective and safe surgery for advanced staged POAG.

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