Protocol of the study "The effectiveness of gonioscopy-assisted transluminal trabeculotomy (GATT) with polypropylene suture in the treatment of pseudoexfoliative glaucoma"

Clinical trial registration This study was registered at Scientific department of Riga East University hospital as a prospective, single-centre clinical trial to determinate the long-term efficacy of GATT method for pseudoexfoliative glaucoma surgical treatment Nr. AP/08-08/22/127 (27.10.2022.).
Ethics approval This research was conducted in accordance with 1964 Declaration of Helsinki. The study received full approval from the University of Latvia Faculty of Medicine Research Ethics Committee Nr. 71-35/61 (24.10.2022).
Consent to participate All patients signed an informed consent form approved by the Research Ethics committee before participating in the study.
Conflict of interest No funding was received for this study.
Investigators The study is led by Dr. Gunta Blezura-Udre (G.B.U.), ophthalmologist at the Riga East University hospital Ophthalmology department (Lielvardes iela 68, Riga, LV1011, Latvia, udreguntab@gmail.com). G.B.U. responsibilities include patient selection, inclusion, performing operations, follow-up, data collection and evaluation of results. The study is supervised by the head of Riga East University hospital Ophthalmology department Assoc. prof. Kristine Baumane (K.B.) (Lielvardes iela 68, Riga, LV1011, Latvia, kbaumane75@gmail.com). K.B. role is supervising of the study.

The study is being conducted by Dr. Gunta Blezura-Udre, ophthalmologist at the Riga East University hospital Ophthalmology Clinic and doctoral student at the University of Latvia. The study will be part of the University of Latvia doctoral program, based on which a doctoral thesis will be developed to obtain a PhD in medical sciences.

Glaucoma is a chronic, progressive degenerative disease of the optic nerve, which results in the destruction of retinal ganglion cells, causing structural and functional damage characteristic of glaucoma. Uncompensated intraocular pressure is one of the main risk factors for disease progression. It has been proven that the "gold standard" surgery, trabeculectomy, effectively reduces intraocular pressure, but it has a relatively high risk of complications[1]. In recent years, the proportion of minimally invasive glaucoma surgery (MIGS) has grown rapidly in relation to traditional glaucoma surgery. The main advantages of MIGS are low risk of complications, rapid recovery, and the possibility of combining it with cataract surgery. For example, according to data from the Medical Service Centre in the US, MIGS increased by 426% between 2012 and 2016 and accounted for 75.5% of glaucoma surgeries in 2017.[2]

GATT with polypropylene suture is one of the MIGS methods, which results in the opening of the natural drainage pathway of the intraocular fluid. GATT can be performed either with the commercially available iTrack system or with polypropylene suture, which is inexpensive. The main reason why MIGS surgery is not so widespread in Latvia is the high cost of the operation. I introduced GATT surgery in Latvia in November 2020. Currently, 120 surgeries have been performed, and the initial results show that the surgery is effective in treating various degrees of glaucoma, including pseudoexfoliative forms. A description of the surgery has been published in the Latvian Medical Journal, and the initial results of the surgery were presented at a meeting of the Latvian Ophthalmologists' Association and at the Best Vol International Conference. Currently, there are two publications available on the effectiveness of GATT in the treatment of pseudoexfoliative glaucoma using the commercially available iTrack catheter[3,4]. There are no data on the treatment of advanced glaucoma using GATT with polypropylene suture, nor are there any publications on changes in ocular hemodynamic after GATT. Changes in the hemodynamic of the optic nerve and retina can be detected using optical coherence tomography angiography (OCTA).

The aim of this study is to prove the long-term effectiveness of GATT with polypropylene suture in the treatment of pseudoexfoliative glaucoma, defining the results as a reduction in eye pressure, the amount of medication used, and the number of complications. To identify risk factors and the impact of comorbidities on the outcome of the surgery. To analyse microvascular changes in the optic nerve and retina after surgery using OCTA.

Working hypothesis: GATT surgery with polypropylene suture effectively reduces intraocular pressure (IOP) and the amount of medication used in cases of early, intermediate, and advanced pseudoexfoliative glaucoma 12 months after surgery.

Research methods. The study will be conducted as a prospective study at the Riga East University hospital (RAKUS) ophthalmology clinic "Bikernieki". The study will be conducted with the approval of the University of Latvia, Life and Medical Sciences Research Ethics Committee and in accordance with the ethical guidelines of the 1975 Helsinki Declaration. The study will include patients who require glaucoma surgery due to uncompensated elevated intraocular pressure despite maximum tolerated glaucoma therapy. A diagnosis of pseudoexfoliative glaucoma will be made by examining the patient with a slit lamp, performing a visual field (VF) test, gonioscopy, intraocular pressure (IOP) and fundus examination. The trial will enrol 66-90 patients who are at least 18 years of age and who will provide their written consent to participate in the study. Patients with pseudoexfoliative glaucoma will be divided into two equal groups depending on the severity of the disease, using the depth of the visual field defect mean deviation (MD) as a criterion. The VF was considered valid if the fixation error was less than 20%, false positive <30% and false negative <30%. Personal data will be pseudonymised, and each patient will be assigned a serial number.

Group 1 – initial and moderate glaucoma with visual field defect MD≤12dB

Group 2 – advanced glaucoma with visual field defect MD>12dB

Study inclusion criteria:

1. Patients diagnosed with pseudoexfoliative glaucoma decompensation with maximum tolerated therapy and requiring antiglaucoma surgery
2. Patient has signed the study informed consent form
3. Over 18 years of age
4. Elevated intraocular pressure >20 mmHg in the study eye
5. The optical parts in the study eye is sufficiently clear to perform diagnostic examinations.

Study exclusion criteria:

1. Acute inflammation of the anterior or posterior segment of the eye
2. Aphakia
3. Significant dislocation of the intraocular lens
4. Closed-angle glaucoma
5. History of fistulizing glaucoma surgery, laser trabeculoplasty
6. Patient refuses to participate in the study.

Examinations performed in the study:

1. Obtaining anamnesis on the duration of the disease, medications used, hypertension, diabetes
2. Blood pressure measurement before surgery (Digital Blood Pressure Monitor, Senso Advance, Japan)
3. Vision test with the best corrected visual acuity in the decimal system
4. Biomicroscopy - to assess the degree of lens opacity, pseudoexfoliative syndrome in the eye
5. Gonioscopy - to determine the degree of pigmentation, Sampolesi line
6. Intraocular pressure measurement using Goldman tonometry (average of 2 measurements)
7. Corneal pachymetry (Konon Cell Check 20 (Konan Medical, Inc., Japan)
8. Corneal endothelium analysis (Konon Cell Check 20 (Konan Medical, Inc., Japan)
9. Computerized visual field 24-2, SITA (Carl Zeiss Meditec, Dublin)
10. Optic nerve and macula OCT, OCTA (Optovue Solix Full Range with AngioVue Expert, (Optovue Inc. Freemont CA, USA)).

The examination plan is shown in the table.

Examinations	Before operation	Day after operation	7-10 Days	1 Month	3 Months	6 Months	12 Months
Anamnesis	X						
Blood pressure	X						
Visual acuity	X		X	X	X	X	X
IOP	X	X	X	X	X	X	X
Number of medications	X			X	X	X	X
Biomicroscopy	X	X	X	X	X	X	X
Gonioscopy	X						X
Pachymetry	X						X
Endothelial cells	X						X
VF	X				X		X
OCTA	X			X		X	X
OCT	X			X		X	X
Hyphema		X	X	X	X	X	X
Complications		X	X	X	X	X	X

Surgery protocol.

All patients will undergo GATT with polypropylene suture 360° as standalone or on combination with cataract surgery under local anaesthesia. Premedication is prescribed before surgery, Sol. Pilocarpine, Sol. Levofloxacin in the eye to be operated on. Disinfection of the surgical field. Eye speculum. Two paracenteses 1.2 mm, corneal incision 2.2 mm. Sol. Lidocaine 0.3 mm in the anterior chamber, DiscoVisc (Alcon) will be administered. Thermally blunted polypropylene suture 5.0. prepared. Under Jacob-Swan gonioprism control 2 mm goniotomy in the nasal quadrant. Introduction of polypropylene suture into Schlemm's canal using microsurgical forceps and will be guided 360-degree. The end of the thread will be grasped and pulled it out of the anterior chamber. Irrigation – aspiration using bimanual instruments. Determination of venous pulse using the Fellman method. Filling of the anterior chamber with Sol. ProVisc (Alcon). Hydration of wounds. Instillation of Sol. Levofloxacin. Bandage. The course of the operation will be recorded on a data carrier.

After surgery, patients will be prescribed antibiotic and glucocorticoid drops 4 times a day for 14 days, and non-steroidal anti-inflammatory drops for 6 weeks. Pilocarpine drops will be prescribed to all patients after surgery for 4 weeks, depending on the pressure on the following day (if IOP on the first postoperative day was <17 mmHg, then once daily, if ≥17 mmHg twice daily). Others glaucoma medications were stopped on the first day after surgery. If IOP was elevated, additional glaucoma medications were prescribed, with preference given to carbohydrase inhibitors.

Work results.

All data obtained from the participants was evaluated and analysed in R version 4.4.1. Kaplan–Meier estimation with log-rank tests was used to estimate the cumulative surgical success. The statistical significance level was accepted as $p < 0.05$.

Reference:

[1]Gedde SJ, Feuer WJ, Shi W, Lim KS, Barton K, Goyal S, Ahmed IIK, Brandt J; Primary Tube Versus Trabeculectomy Study Group. Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 1 Year of Follow-up. Ophthalmology. 2018 May;125(5):650-663. doi: 10.1016/j.ophtha.2018.02.003. Epub 2018 Feb 21. PMID: 29477688.

[2]Birnbaum FA, Neeson C, Solá-Del Valle D. Microinvasive Glaucoma Surgery: An Evidence-Based Review. Semin Ophthalmol. 2021 Nov 17;36(8):772-786. doi: 10.1080/08820538.2021.1903513. Epub 2021 Jul 23. PMID: 34297650.
[3]Bozkurt E, Yenihayat F, Olgun A, Yazıcı AT, Şahbaz İ. The efficacy of gonioscopy-assisted transluminal trabeculectomy combined with phacoemulsification. Int Ophthalmol. 2021 Jan;41(1):35-43. doi: 10.1007/s10792-020-01550-x. Epub 2020 Aug 31. PMID: 32869109.
[4]Sharkawi E, Lindegger DJ, Artes PH, Lehmann-Clarke L, El Wardani M, Misteli M, Pasquier J, Guarnieri A. Outcomes of gonioscopy-assisted transluminal trabeculotomy in pseudoexfoliative glaucoma: 24-month follow-up. Br J Ophthalmol. 2021 Jul;105(7):977-982. doi: 10.1136/bjophthalmol-2020-315954. Epub 2020 Jul 29. PMID: 32727734; PMCID: PMC8237193.

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