

DOCTORAL SCHOOL OF MEDICINE

DOCTORAL FIELD: MEDICINE

THESIS

"Strategies in the surgical treatment of neovascular glaucoma"

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INTRODUCTION

Neovascular glaucoma is a secondary form of angle-closure glaucoma with devastating evolution on the eyeball. (1)

The prognosis of this form of glaucoma is unfavorable. It is due to the blocking of the chamber angle by neovascularization, which consequently prevents the drainage of the aqueous humor from the anterior chamber, thus leading to an increase in intraocular pressure to very high values that cannot be reduced by the applied drug treatment. (1)

Thus, the increased value of the intraocular pressure will lead to the loss of vision due to the atrophy of the optic nerve and in an advanced stage to the organic damage of the eyeball, sometimes requiring evisceration due to unbearable pain. (1)

Posterior segment ischemia leads to neovascularization of the chamber angle where a fibro-vascular membrane is formed. In the early phase, this membrane is found only on the trabecular meshwork, when the chamber angle appears open, then it expands to block the angle.

(4)

II. PERSONAL CONTRIBUTIONS

2. GENERAL METHODOLOGY

The study is a descriptive retrospective and prospective one, carried out over 10 years (2009-2019).

Since 2009, 79 cases of neovascular glaucoma have been treated with this method, of which 40 cases operated using the described technique.

The data on the studied cases were collected from the Ophthalmology clinic of the Sibiu County Clinical Hospital and Dr. Stănilă Sibiu Medical Center, then processed and analyzed from a statistical point of view, and the results will be discussed in relation to other current research on neovascular glaucoma.

Statistically significant results were published in specialized journals.

2.1. Development of the treatment algorithm in secondary neovascular glaucoma

Depending on the etiology of GNV, we made a treatment plan that was medical, laser and surgical.

- The first measure we adopted was to assess the patient's condition, performing blood tests and other examinations.
- The general treatment of diabetes and hypertension was initiated after the prior examination of the patient by a cardiologist and a diabetes specialist.
 - To treat NVG patients we developed a treatment algorithm.

3. STUDY ON THE CASES OPERATED BY TRABECULECTOMY

3.1. Purpose and objectives

The purpose of the study involves the analysis of a group of patients with neovascular glaucoma to whom the treatment algorithm was applied and the analysis of a subgroup to whom trabeculectomy was performed. The objectives follow different analysis indicators through which the algorithm is applied.

3.2. Material and method

We performed a retrospective and prospective study on a number of 79 cases hospitalized and treated in the County Clinical Hospital and Dr. Stănilă Medical Center Sibiu, Romania, over a period of 10 years (September 2009 - September 2019) with neovascular glaucoma caused by the following conditions:

- Diabetic retinopathy were 31 cases, patients with long-standing diabetes, proliferative diabetic retinopathy (PDR), especially with neovascularization of the optic disc.
 - Obstructive central vein of the retina or occlusion of the venous branches, 43 cases.
 - Ocular ischemia syndrome, 5 cases.

From the studied group, 40 cases of secondary neovascular glaucoma were selected that were operated on by trabeculectomy.

The etiology of neovascular glaucoma in the studied cases were:

- -occlusion of the central vein of the retina (33.97%);
- -diabetic retinopathy (24.49%);
- central retinal artery occlusion or ocular ischemia syndrome (3.95%).

The study inclusion criteria for patients were:

- 1. NVG was caused by retinal vascular diseases.
- 2. $IOP \ge 24 \text{ mmHg}$.
- 3. Neovascularization of the iris and chamber angle, closed angle.

Data collected included age, history of vascular disease, comorbidities, glaucoma treatment, preoperative and postoperative corrected visual acuity (BCVA), preoperative and postoperative IOP, antimetabolite or antifibrotic used topically.

The amount of IOP reduction after surgery was described as the percentage of IOP reduction from preoperative IOP and IOP after surgery and after three months. IOP measurement was done using I Care tonometer and Aplanotonometer.

Surgical success was defined as IOP <21 mmHg at 3 months after surgery, with or without drug treatment.

The surgical technique we approached was trabeculectomy with application of antimetabolites and antifibrotics on the trabecular meshtwork. The antimetabolite we used was Mitomycin C, 5-Fluorouracil and the antifibrotic agent was Interferon alfa-2b.

After making a trapezoidal scleral flap with a length of 8-10 mm and a width of 4-6 mm, preferably a thickness of about 1/3 of the thickness of the sclera.

I applied the antimetabolite or antifibrotic agent soaked on a cotton pad for 3 minutes.

The trabecular piece was sent for histopathological analysis. The histopathological analysis was done in the department of Sibiu County Clinical Pathological Anatomy Hospital.

Postoperative evolution was favorable in most cases. After surgery, the intraocular pressure normalized, and the eye pain disappeared. Surgical treatment was combined in some cases with anti-VEGF treatment, laser photocoagulation and in some refractory cases transscleral cyclophotocoagulation with the Iridex laser.

3.3. Result

The distribution of the studied group according to the percentages of decrease in eye pressure.

In the studied group, the percentages of decrease in IOP values were high, on average over values of 50-70% decrease compared to the initial value of IOP.

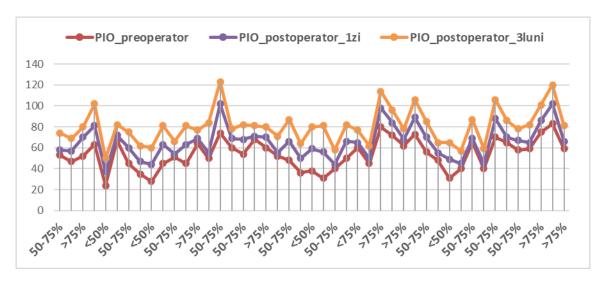


Figure 43. Distribution of the studied group according to the percentages of decrease in eye pressure

Eye pressure values preoperatively, postoperatively and 3 months after the intervention

In the group of 40 cases that were operated by trabeculectomy with antimetabolite application on the scleral bed, we had an oscillation of the IOP values, with very large decreases compared to the initial value. IOP values were lower on the first postoperative day and increased slightly 3 months after the intervention.

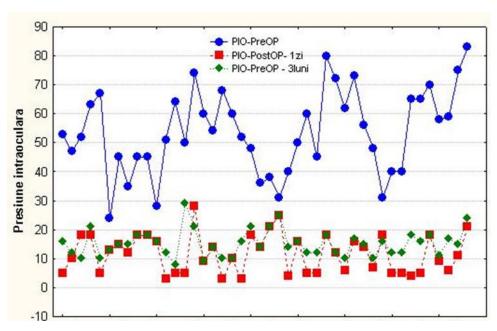


Figure 44. Eye pressure drop values.

Percentages of decrease in eye pressure depend on the substance applied intraoperatively. From the analysis of the studied operated group, it appears that the highest values of percentage decrease in pressure were recorded with the intraoperative use of Mitomycin C, results that also exist in specialized publications. High percentage results were also recorded with the intraoperative use of Interferon alfa-2b, which confirms the effectiveness of its use in GNV filtering surgery due to its anti-inflammatory and anti-fibrotic properties.

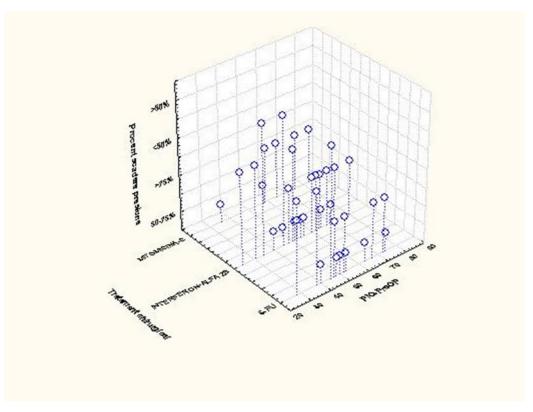


Figure 45. Percentages of decrease in eye pressure depend on the substance applied intraoperatively.

5. FINAL CONCLUSIONS

- Neovascular glaucoma is a very difficult pathology and is very difficult to manage;
- To avoid irreversible visual loss, treatment must start very early;
- The use of retinal photocoagulation and intravitreal injections in addition to surgery can reduce anterior and posterior pole neovascularization and normalize IOP;
- The management of neovascular glaucoma must be done according to a good treatment algorithm;
- The mean preoperative IOP was 52.17 mmHg, postoperative IOP 11.6 mm Hg and 3 months after surgery it increased to 15.05 mmHg;
- The mean IOP before surgery was very high and decreased by 40.57 mmHg after surgery at 3 days and remained the same at 3 months;
- Surgery with antimetabolites and antifibrotic agents is important to avoid fibrosis of the filtering bleb, and in most cases, IOP was maintained for a long time.

- Interferon alfa-2b applied under the scleral flap during trabeculectomy can be a good solution in filtering surgery from GNV;
- Uncontrolled IOP is the main risk factor involved in ocular surface distress. Long-term maintenance of normal intraocular pressure is important in the management of NVG, but also in protecting the ocular surface;
- Transscleral micropulsed laser cyclophotocoagulation can be used as an alternative treatment in patients with uncontrolled IOP;
- The prognosis of the disease is reserved, GNV is considered in the literature "malignant glaucoma", due to the often-disabling evolution towards vision loss;
- Repeated checks, management of vascular diseases can improve the quality of life of patients with GNV.

6. ORIGINALITY OF THE THESIS

The doctoral thesis is the result of the study on a very complicated and difficult to treat pathology, often with unfavorable and disabling evolution of an advanced age group and with multiple associated pathologies.

The observation period of patients with this pathology was very long because the condition is quite rare.

The originality regarding the use of Interferon alfa-2b in glaucoma surgery is a novelty in specialized literature.

The motivation regarding the use of a substance due to its properties is due to the research of specialized literature as well as financial needs. The interferon was obtained through collaboration with the Hematology Department, with the availability of unused vials. The amount of substance used, being very small, could only be supplied at the time of the surgical intervention. Practically, the use of Interferon was without financial costs compared to the use of Mitomycin C or 5-Flurouracil, which involve high costs that sometimes patients cannot bear.

The personal contribution in the thesis was through the research of the specialized literature on the properties of Interferon, its use, but also the development of a treatment algorithm to help us manage this pathology as effectively as possible.

The conclusions of the paper identify possible approaches to neovascular glaucoma through the prism of personal clinical experience but also in collaboration with specialists from the Sibiu County Hospital, OftaTotal Clinic Sibiu and "Lucian Blaga" University Sibiu.

SELECTIVE BIBLIOGRAPHY

- 1. NA Liao, Chaohong Li, Huilv Jiang, Aiwu Fang, Shengjie Zhou, and Qinmei Wang, Neovascular glaucoma: a retrospective review from a tertiary center in China, BMC Ophthalmol. 2016; 16: 14. Published online 2016 Jan 27. doi: 10.1186/s12886-016-0190-8
- Senthil S, Dada T, Das T, Kaushik S, Puthuran GV, Philip R, Rani PK, Rao H, Singla S, Vijaya L. Neovascular glaucoma A review. Indian J Ophthalmol. 2021 Mar;69(3):525-534. doi: 10.4103/ijo.IJO_1591_20. PMID: 33595466; PMCID: PMC7942095
- 3. Dumbrăveanu L, Cușnir V, Bobescu D. A review of neovascular glaucoma. Etiopathogenesis and treatment. Rom J Ophthalmol. 2021 Oct-Dec;65(4):315-329.
- 4. Putera I, Suryono AN, Artini W. Challenging Management of Neovascular Glaucoma to Achieve the Best Visual Outcome. Case Rep Ophthalmol. 2020 Feb 19;11(1):85-91.