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PhD THESIS
SUMMARY

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CANALOPLASTY AND VISCOCANALOSTOMY IN THE OPEN ANGLE GLAUCOMA TREATMENT

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Personal Research Part

1. Introduction

The interest in nonpenetrating glaucoma surgery has increased in recent years mainly because it doesn't open the anterior chamber, thus avoiding the risks associated with hypotony and overfiltration. Nonpenetrating glaucoma surgery aims the site of maximal resistance to aqueous humor outflow, namely the internal wall of Schlemm's canal and the juxtacanalicular connective tissue. Nonpenetrating surgical techniques described so far are deep sclerectomy, viscocanalostomy and canaloplasty. The common denominator of these techniques is the deep sclerectomy with a trabeculo-descemetic window dissection that allows gradual filtration of aqueous humor from the anterior chamber. Viscocanalostomy adds localized dilation of Schlemm's canal using a high molecular weight viscoelastic material and canaloplasty achieves circumferential dilation of Schlemm's canal using a tension suture.

This study presents a comparison between canaloplasty and viscocanalostomy, both performed in the County Emergency Hospital of Piatra Neamț, Romania, from 2012 to 2017, in patients with open angle glaucoma. Enclosed information regarding either the surgical technique or the presional results may be a matter of further interest.

2.The purpose of the study

Nonpenetrating glaucoma techniques have been developed in order to improve the safety profile of conventional penetrating procedures. The goal of nonpenetrating surgical procedures is intraocular pressure (IOP) lowering by increasing aqueous humor outflow through natural pathways (collector channels, aqueous veins, episcleral veins). This is accomplished by reducing the resistance to aqueous humor outflow at the level of the internal wall of Schlemm's canal and the juxtacanalicular connective tissue. The common part of these techniques is the internal trabeculum preservation, thus being a viable alternative to conventional trabeculectomy. The core element of these techniques is the avoidance of eyeball opening with elimination of iridectomy and prevention of early

glaucoma and any form of angle-closure glaucoma. Eyes with previous ocular surgery (cataract extraction with intraocular lens placement) were not excluded from the study.

Preoperative evaluation included ocular and systemic history and complete ocular examination. Patients were evaluated one day after the surgical procedure and then one month, 3, 6, 12, 18, 24 , 30 and 36 months. Topic antiglaucomatous medication was interrupted after surgery and recommenced if IOP values needed it.

All surgical procedures were performed under local anesthesia, using the transconjunctival retrobulbar anesthesia described by Martinez Toldos and Ezequiel Campos[1]. Preoperative antisepsy of ocular surface was done according to the guidelines of the European Society of Cataract and Refractive Surgery about prevention of endophthalmitis after cataract surgery[2]. The reference point for needle pathway was the inferior portion of lateral rectus muscle insertion. The needle entrance was in the herniated adipose tissue under the inferior tarsal plate, in Eisler's pocket. The needle was introduced just posterior of the inferior tarsal plate through this pocket, with the eye in primary position. Thus the needle pathway is anterior and lateral of posterior lamella of capsulopalpebral fascia, so the entrance of the anesthetic drugs in the orbit rarely produces chemosis. Often in this region there is a herniation of the orbital septum[3].

Canaloplasty was performed using the surgical technique described by Gabor Scharioth, MD, PhD, using the Glaucolight microcatheter from D.O.R.C. [4], and viscocanalostomy was performed using the surgical technique described by Robert Stegmann, MD[5]. The first surgical steps are the same for both procedures. In both procedures the adequate exposure of superior limbus using a intracorneal traction suture. After superior limbic peritomy I performed superficial scleral flap delineation, about 5×5 mm, using a special marker. In both techniques using the bipolar cautery is avoided in order to preserve the integrity of the collector channels. After superficial scleral flap dissection I performed deep scleral flap delineation, 1 mm inside superifial scleral flap margins. Deep sleral flap dissection into clear cornea is accompanied by unroofing of Schlemm's canal and trabeculo-descemetic window delineation, which displays intense percolation of aqueous humor. In canaloplasty I used Glaucolight microcatheter to dilate and to place a tension suture inside the Schlemm's canal. In viscocanalostomy I performed localized dilation of Schlemm's canal through its surgical created orifices and scleral lake maintenance using high molecular weight viscoelastic material. Thus the diameter of Schlemm's canal in juxtaorificial portion increased from 25-30 μm in physiologic conditions to about 230 μm[6]. In postoperative period the patients received topical medication for 4 weeks, a fixed combination of antibiotic and cortizon. The

Regarding natural crystalline lens status, in the CAN group there were 32 phakic eyes and 8 pseudophakic eyes, with posterior chamber intraocular lens placed in the capsular bag. Among the phakic eyes, there were 8 hypermetropic, 14 myopic and 4 emmetropic. In 6 eyes there was no objective refraction measurement due to the opacification of the natural crystalline lens. Visual acuity testing in CAN group revealed that most of the eyes had visual acuity between 0.2 and 0.5 and the lowest level of visual acuity was recorded in eyes with relative afferent pupillary defect (RAPD). Standard automated perimetry has been performed in 3 eyes, in a private setting. Optic nerve head evaluation has been done at the slit lamp using the 90 diopter lens, vertical C/D ratio ranging from 0.7 to 0.9 at all the eyes from the CAN group. Eyes with RAPD had vertical C/D ratio of 0.9. Also these eyes had the highest IOP levels. In all the eyes of CAN group gonioscopy showed an opened anterior chamber angle (grade 3 or 4, Shaffer grading system) with trabecular pigmentation in PEXG eyes.

IOP has been measured with Goldmann applanation tonometer, after a few drops of local anesthetic. The mean preoperative IOP in CAN1 subgroup was 30,429±10,009 mm Hg. The mean preoperative IOP in CAN2 subgroup was 31,000±7,652 mm Hg. Preoperative medication in both subgroups consisted of 2, 3 or 4 antiglaucomatous drugs. In most cases 3 drugs were used, either a prostaglandin analogue with a fixed combination, betablocker and carbonic anhydrase inhibitor, or a fixed combination of a prostaglandin analogue and betablocker together with carbonic anhydrase inhibitor. 2 eyes, 1 in CAN1 subgroup and 1 in CAN2 subgroup, had 4 preoperative antiglaucomatous drugs. The 4th drug was an alpha$_2$ receptor agonist.

4.1.2. Postoperative IOP in CAN group

Postoperative IOP was measured one day after sugery (D1), one month (M1), 3, 6, 12, 18, 24, 30 and 36 months (M3, M6, M12, M18, M24, M30, M36). The measurement method was the same, applanation tonometry using Goldmann applanation tonometer. The IOP level at each follow-up moment was assigned to one of the following grups:

Complete success: IOP $\leq$ 2 1 mm Hg without medication, with several subgroups:

- A1: 19 mm Hg $\leq$ IOP $\leq$ 21 mm Hg
- A2: 16 mm Hg $\leq$ IOP $\leq$ 18 mm Hg
- A3: IOP $\leq$ 15 mm Hg

Qualified success, IOP $\leq$ 21 mm Hg with medication

Surgical failure, IOP > 21 mm Hg.

reduction), with 16 eyes in A3 IOP subgroup, 10 eyes in A2 and 1 eye in A1. In CAN2 subgroup (12 eyes) the mean postoperative IOP was 17,250±4,330 mm Hg (44,35% reduction), with 4 eyes in A3 IOP subgroup, 6 in A2, 1 in A1 and 1 whose IOP value required antiglaucomatous medication. In M24 the mean postoperative IOP in CAN1 subgroup (27 eyes) was 15,519±1,949 mm Hg (48,99% reduction), with 11 eyes in A3 IOP subgroup, 15 eyes in A2 and 1 eye in A1. In CAN2 subgroup (10 eyes) the mean postoperative IOP was 17,200±2,098 mm Hg (44,51% reduction), with 1 eye in A3 IOP subgroup, 6 eyes in A2, 2 eyes in A1 and 1 eye in B IOP subgroup (qualified success). In M30 the mean postoperative IOP in CAN1 subgroup (20 eyes) was 15,300±2,319 mm Hg (49,71% reduction), with 8 eyes in A3 IOP subgroup and 12 eyes in A2. In CAN2 subgroup (7 eyes) the mean postoperative IOP was 17,571±2,820 mm Hg (43,31% reduction), with 1 eye in A3 IOP subgroup, 4 eyes in A2, 1 eye in A1 and 1 eye in B IOP subgroup. The complete success rate was 85,71%. In M36 the mean postoperative IOP in CAN1 subgroup (17 eyes) was 15,125±2,754 mm Hg (50,29% reduction), with 7 eyes in A3 IOP subgroup, 9 eyes in A2 and 1 eye in A1. In CAN2 subgroup (6 eyes) the mean postoperative IOP was 17,667±2,658 mm Hg (43% reduction) with 1 eye in A3 IOP subgroup, 3 eyes in A2, 1 eye in A1 and 1 in B IOP subgroup. The complete success rate was 83,33%.

4.1.3. Postoperative medication

Canaloplasty had an important IOP lowering effect in all eyes, both in POAG and PEXG eyes. Postoperative antiglaucomatous medication was not necessary, most of the eyes being assigned in A postoperative IOP group (complete success) at each follow-up moment. There is only 1 PEXG eye with IOP 30 mm Hg in M18 that needed postoperative medication. The IOP was below 21 mm Hg with medication afterwards.In this eye gonioscopy showed thickening of trabeculo-descemetic window and absence of the intracanalicular suture.

4.1.4. Intra- and postoperative complications

There were no intraoperative complications in eyes with canaloplasty, either in POAG or in PEXG eyes. Postoperative complications were early and late. Early postoperative complications were noticed in D1 and consisted of: hyphema (6 eyes from CAN1 and 1 eye from CAN2); hematic Tyndall of anterior chamber (1 eye of CAN1 and 2 eyes of

mean 5,00±2,58 days. The hospital admission time in VCS2 subgroup ranged from 3 to 13 days, mean 5,50±2,90 days.

Regarding natural crystalline lens status, in the VCS group there were 28 phakic eyes and 12 pseudophakic eyes, with posterior chamber intraocular lens placed in the capsular bag. Among the phakic eyes, there were 9 hypermetropic, 11 myopic and 3 emmetropic. In 5 eyes there was no objective refraction measurement due to natural lens opacification.Visual acuity testing in VCS group revealed that most of the eyes had visual acuity between l.p (light perception) and 0.1 and the lowest level of visual acuity was recorded in eyes with relative afferent pupillary defect (RAPD). Standard automated perimetry has been performed in 2 eyes in a private setting. Optic nerve head evaluation has been done at the slit lamp using the 90 diopter lens, vertical C/D ratio ranging from 0.7 to 0.9 at all the eyes from the VCS group. In all the eyes of CAN group gonioscopy showed an opened anterior chamber angle (grade 3 or 4, Shaffer grading system, with trabecular pigmentation in PEXG eyes).

IOP has been measured with Goldmann applanation tonometer, after a few drops of local anesthetic. The mean preoperative IOP in VCS1 subgroup was 32,821±7,029 mm Hg. The mean preoperative IOP in VCS2 subgroup was 34,667±5,774 mm Hg. Preoperative medication in both subgroups consisted of 2, 3 or 4 antiglaucomatous drugs. Eyes with 2 preoperative topical drugs (9 eyes, 3 from VCS1 and 6 from VCS2) had a prostaglandin analogue and a betablocker, in separate admninictration (1 eye) of in a fixed combination (6 eyes, 3 from VCS1 and 3 from VCS2). 2 eyes from VCS1 had preoperative administration of prostaglandin analogue and carbonic anhydrase inhibitor. There were 28 eyes with 3 preoperative topic drugs, 23 from VCS1 and 5 from VCS2. There were used either a prostaglandin analogue with a fixed combination, betablocker and carbonic anhydrase inhibitor (18 eyes from VCS1 and 5 eyes from VCS2), or a fixed combination of a prostaglandin analogue and betablocker together with carbonic anhydrase inhibitor (5 eyes of VCS1). There were 2 eyes from VCS1 subgroup with 4 preoperative antiglaucomatous drugs. The 4th drug was an alpha$_2$ receptor agonist.

4.2.2. Postoperative IOP in VCS group

Postoperative IOP was measured one day after sugery (D1), one month (M1), 3, 6, 12, 18, 24, 30 and 36 months (M3, M6, M12, M18, M24, M30, M36). The measurement method was the same, applanation tonometry using Goldmann applanation tonometer. The IOP level at each follow-up moment was assigned to one of the following grups:

reduction), with 6 eyes in A1 subgroup and 3 in A2. 1 eye restarted antiglaucomatous medication due to IOP > 21 mm Hg, 1 eye had IOP > 21 mm Hg under medication (surgical failure) and 1 eye had IOP < 21 mm Hg with medication (B group of IOP). So the complete success rate in PEXG eyes at 6 months was 75% and the qualified success rate was 83,33%. In M12 the mean postoperative IOP in VCS1 subgroup (28 eyes) was 19,143±3,472 mm Hg (40,69% reduction) with 1 eye in A3 IOP subgroup, 14 eyes in A2 and 6 in A1 IOP subgroup. 5 eyes had IOP > 21 mm Hg and restarted antiglaucomatous medication, 1 eye is in B IOP subgroup and 1 eye has IOP > 21 mm Hg with medication (surgical failure). The complete success rate at 12 months in POAG eyes was 75%. In VCS2 subgroup (12 eyes) the mean postoperative IOP was 19,333±4,250 mm Hg (40,69% reduction), with 2 eyes in A3 IOP subgroup, 4 eyes in A2, 2 eyes in A1, and 2 eyes in B IOP group. 1 eye required antiglaucomatous medication and 1 eye is in C IOP group (surgical failure). The complete success rate in PEXG eyes was 66,66% and the qualified success rate was 83,33%. In M18 the mean postoperative IOP in VCS1 subgroup (28 eyes) was 19,286±2,800 mm Hg (40,25% reduction), with 1 eye in A3 IOP subgroup, 12 eyes in A2 and 5 eyes in A1, 6 eyes in B, 1 eye in C (surgical failure) and 3 eyes required antiglaucomaous recommencement due to IOP > 21 mm Hg. In VCS2 subgroup (12 eyes) the mean postoperative IOP was 19,417±3,753 mm Hg (43,98% reduction), with 5 eyes in A2 IOP subgroup, 5 in B, 1 in C and 1 whose IOP value required antiglaucomatous medication. In M24 the mean postoperative IOP in VCS1 subgroup (27 eyes) was 18,407±2,576 mm Hg (42,97% reduction), with 14 eyes in A2 IOP subgroup, 1 eye in A1 and 9 eyes in B, 1 eye in C IOP group and 2 eyes whose IOP value required antiglaucomatous medication. The complete success rate in POAG eyes at 24 months was 55,55% and the qualified success rate was 88,88%. In VCS2 subgroup (11 eyes) the mean postoperative IOP was 17,818±2,523 mm Hg (48,60% reduction), with 3 eyes in A2 IOP subgroup, 1 eye in A3, 6 eyes in B and 1 eye in C IOP subgroup. In M30 the mean postoperative IOP in VCS1 subgroup (16 eyes) was 18,407±2,576 mm Hg (42,97% reduction), with 1 eye in A1 IOP subgroup, 4 eyes in A2 and 11 eyes in B IOP subgroup. In VCS2 subgroup (7 eyes) the mean postoperative IOP was 18,714±2,058 mm Hg (46,01% reduction), with 3 eyes in A IOP subgroup and 4 eyes in B. In M36 the mean postoperative IOP in VCS1 subgroup (13 eyes) was 17,846±1,519 mm Hg (44,71% reduction), with 8 eyes in B IOP subgroup and 5 eyes in A2. In VCS2 subgroup (5 eyes) the mean postoperative IOP was 17,200±1,304 mm Hg (50,38% reduction) with 2 eyes in A2 IOP subgroup, and 3 in B IOP subgroup. The complete success rate at 36 months was 38,46% in POAG eyes and 40 % in PEXG eyes.

4.3. Comparison of the two nonpenetrating surgical techniques considering the IOP result and the clinical form of glaucoma

The comparison between the two groups, CAN and VCS, was done using the t test. One can notice that preoperative IOP values are much higher than postoperative IOP values in both groups and the mean preoperative IOP doesn't differ significantly between the two groups ($p=0,128$). At each follow up moment the mean postoperative IOP is lower than the mean preoperative IOP ($p<0,05$). ANOVA test was used to analyse subgroups in the entire follow-up period. Comparing the CAN 1 and CAN2 subgroups one can notice that there are statistically significant differences only in M24 and in M30. So the mean postoperative IOP after canaloplasty is not significantly different between eyes with POAG and eyes with PEXG, except in M24 and in M30, being lower in eyes with POAG. Comparing the VCS1 and VCS2 subgroups one can notice that there is no statistically significant difference in mean postoperative IOP between the two subgroups at any follow-up moment. One can assume that the IOP result after viscocanalostomy doesn't differ significantly in POAG from PEXG eyes. Speaking about the eyes with POAG, if we compare the mean postoperative IOP after canaloplasty with mean postoperative IOP after viscocanalostomy (CAN1 and VCS1 subgroups) we can see that canaloplasty produces a significantly lower mean IOP than viscocanalostomy in every follow-up moment, in eyes with POAG. Speaking about the eyes with PEXG (CAN2 and VCS2 subgroups) we can see that canaloplasty produces lower mean postoperative IOPs than viscocanalostomy, but this is statistically significant only in M3, M6 and M12.

The success probability of each surgical technique was appreciated with Kaplan-Meyer survival analysis. The predefined IOP postoperative levels were used in order to estimate success probability to reach a certain IOP level in a follow-up time. So, in CAN group the success probability to obtain a IOP value less than 21, 18 or 15 mm Hg in 6 months is 100%, 89,12% and 53,62%, respectively. In 12 months success probabilities are 100%, 79,43% and 50,11%, respectively. In VCS group the success probability to obtain a IOP value less than 21, 18 or15 mm Hg in 6 months is 100%, 50,11% and 35,48% respectively. In 12 months success probabilities are 63,09%, 31,62% and 19,95% respectively.

eyes in M3, 6 eyes in M6, 1 eye in M18. Recommencement of antiglaucomatous medication was required in 1 eye in M3, in 5 eyes in M12, in 3 eyes in M18 and in 2 eyes in M24. 1 eye from VCS1 subgroup was assigned as a surgical failure and attended no longer the follow-up from M24. The complete success rate in this subgroup was as follows: 100% in L1, 96,42% in L3, 92,85% in L6, 75% in L12, 64,28% in L18, 55,55% in L24, 31,25% in L30 and 38,46% in L36. The qualified success rate was as follows: 96,42% in M6, 78,57% in M12, 85,71% in M18, 88,88% in M24, and 100% in M30 and in M36 (due to reduction of the number of patients attending the follow-up exams)

In VCS2 subgroup the number of eyes assigned in A3 postoperative IOP subgroup diminuated in time, only 1 eye had IOP < 15 mmHg in M24. The earliest moment of antiglaucomatous medication restarting was M1 and 1 eye was assigned as a surgical failure in M3. The case attended follow-up visits till M24, and then was scheduled for penetrating surgery (trabeculectomy) in a tertiary center.

The complete success rate in this subgroup was as follows: 83,33% in M1 and M3, 75% in M6, 66,66% in M12, 41,66% in M18, 36,36% in M24, 42,85% in M30 and 40% in M36 (due to reduction of the number of patients attending the follow-up exams).

5.3.Comparison of the two nonpenetrating surgical procedures

The only study published by now regarding the safety and efficacy of canaloplasty and viscocanaloplasty was done by Koerber, in 30 eyes from 15 patients with POAG, in whom he performed canaloplasty in one eye and viscocanaloplasty in the congener eye[9]. In the current study I designed a comparative analysis of canaloplasty and viscocanalostomy with particular reference to IOP-lowering effect, number of postoperative antiglaucomatous medication still required and intra- and postoperative complications. The mean postoperative IOP was significantly reduced than mean preoperative IOP, both in CAN and in VCS group. The mean postoperative IOP after canaloplasty is not significantly different between eyes with POAG and eyes with PEXG, except in M24 (p=0,029)and in M30 (p=0,045), being lower in eyes with POAG. The IOP result after viscocanalostomy doesn't differ significantly in POAG from PEXG eyes. Comparing the presional result of the two surgical procedure in each clinical form of glaucoma, we can notice that canaloplasty produced mean IOP values significantly lower than viscocanalostomy in eyes with POAG (p<0,05). Speaking about the eyes with PEXG I found that canaloplasty produces lower mean postoperative IOPs than viscocanalostomy, but this is statistically significant only in M3, M6 and M12 (p<0,05). Also, there are

platinum standard of glaucoma surgery in the XXIst century, knowing that trabeculectomy is the gold standard of antiglaucomatous surgery in the XXth century.

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