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CLINICAL STUDY

Surgical outcomes of trabeculectomy augmented with sub-Tenon injected mitomycin C

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ABSTRACT
BACKGROUND: Recently, trabeculectomy with mitomycin C (MMC) where MMC is applied by injection into the Tenon layer has attracted close attention. However, the data on efficacy and safety of this technique is still limited and more clinical studies are needed. Therefore, the work is aimed at comprehensive evaluation of the effectiveness of trabeculectomy using MMC applied by intra-Tenon injection.
METHODS: A set of 50 eyes in 50 patients underwent trabeculectomy using MMC at concentration of 0.4 mg/ml in a total volume of 0.05 ml. The primary end point was to control intraocular pressure (IOP) on postoperative days 1, 8, 30 and 90 and subsequently at 6 and 12 months after surgery. The secondary end point was to evaluate the changes in various corneal parameters prior to and 90 days after surgical procedure.
RESULTS: The mean preoperative IOP was 32.34 ± 9.45 mmHg. After surgery, the mean IOP significantly decreased to 17.52 ± 4.58 mmHg at the 90-day follow-up, and to 18.14 ± 3.74 and 19.30 ± 3.82 mmHg at 6 and 12 months after the procedure, respectively. The mean BCVA values remained unchanged compared to baseline (0.77 ± 0.23) to the 90-day follow-up (0.80 ± 0.23). The mean number of anti-glaucoma medications significantly reduced from 3.50 ± 0.74 to 0.58 ± 1.03 postoperatively. Similarly, the mean corneal hysteresis and ACD of the eye as well as CECD were significantly changed postoperatively.
CONCLUSIONS: Trabeculectomy using MMC applied by injection is a safe and effective surgical method for the treatment of primary and secondary forms of open-angle glaucoma. It has a significant hypotonising effect and allows a complete discontinuation of antiglaucoma drugs *(Tab. 3, Fig. 3, Ref. 58)*. Text in PDF *www.elis.sk*
KEY WORDS: glaucoma; antiglaucoma surgery; trabeculectomy; cytostatic, mitomycin C.

Introduction

Glaucoma optic neuropathy is the leading cause of blindness in the world; its prevalence increases with age. Africa was found to have the highest prevalence of glaucoma among all continents (1). There are several different types of glaucoma, and they have been classically divided into the categories of primary and secondary open-angle glaucoma (OAG) and primary or secondary angle-closure glaucoma (2). Primary OAG represents the most dominant type of glaucoma damage (2); however, there are several other OAG types, including pigmentary OAG (PIGM) and pseudoexfoliative OAG (PEXG) (3).

Long-term reduction and control of intraocular pressure (IOP) is the mainstay of glaucoma treatment, resulting in the further reduction of glaucomatous optic nerve damage. Apart from topical drug and laser therapy, trabeculectomy has been considered a gold-standard surgical procedure for all types of glaucoma (4). However, the choice of a particular treatment modality depends on the target IOP and must be considered individually.

Trabeculectomy is a well-established surgical procedure for treatment of glaucoma that was introduced in 1968 (5). The procedure is performed by creating a small fistula in the corneoscleral junction which is guarded by a partial-thickness scleral flap, much like a hole is covered by a trapdoor. This trapdoor forms the main resistance for the new outflow of fluid out of the eye. It drains out through the new pathway into the sub-Tenon's space to form a bleb (a pool of aqueous humor under the conjunctiva and tenons). The aqueous humor in the bleb is drained away slowly by the episcleral and conjunctival blood vessels. The tightness of the trapdoor guarding the fistula is modifiable by stitches placed at the time of surgery (6).

The success of trabeculectomy is often affected by the formation of a subconjunctival scar at the site of the filtering bleb due to a wound-healing reaction (7). To minimize a failure of trabeculectomy, anti-fibrotic agents such as 5-fluorouracil and mitomycin C (MMC) have been widely used to improve the outcomes of the procedure (8-10). Although, minimal invasive glaucoma surgery is a promising procedure in OAG patients, trabeculectomy with MMC still remains the best option in certain patient populations (11, 12). The use of MMC increases the efficacy of trabeculectomy due to its

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potent antiproliferative effect, which prevents fibrosis of the filter pad, while consequently reducing the risk of filtration failure (13). On the other hand, perioperative use of MMC during trabeculectomy is associated with a higher incidence of complications such as hyphema, bleb avascularity, postoperative hypotension, chorioid ablation, shallow anterior chamber (AC), filtration failure, or hyperfiltration of the surgical wound. The most feared complication is endophthalmitis (14, 15). Another concern with the use of MMC is the lack of the consensus on concentration that should be used (16). However, recent studies have shown that employing different concentrations of MMC, namely 0.2 mg/ml or 0.4 mg/ml, did not result in a significant difference in the efficacy and safety rates of trabeculectomy. Nevertheless, the higher concentration of MMC demonstrated a tendency towards greater efficacy (16). In addition, other studies suggest that values of IOP were lower when MMC was used in concentration of 0.5 mg/ml, rather than 0.2 mg/ml (17).

Various methods of applying MMC during trabeculectomy surgery such as the traditional sponge method and intra-Tenon injection have been studied (18-22). However, there are some concerns with the use of sponges, including loss and retention of MMC-soaked sponges, damage to the conjunctiva during sponge manipulation and the limited efficacy to treat a large area of sclera with sponges (23). A recent national survey of intraoperative MMC employment during trabeculectomy surgery in the UK revealed that MMC-soaked sponges are clearly preferred by 94 % of surgeons versus 6 % of surgeons who preferred the sub-Tenon injection of MMC (24). The authors of this study recommended the injection form of delivering MMC in order to reduce and minimize the chance of retention of the MMC-soaked swab. Therefore, injection of MMC into the Tenon's capsule may attract more attention among surgeons. In fact, there has been a trend to perform the trabeculectomy augmented with a lower dosage of sub-Tenon injected MMC rather than employing the MMC-onlay (25). On the other hand, the data on efficacy and safety of this popular technique are still limited and more clinical studies are needed (26).

As a result, the aim of the current study was to investigate the efficacy and safety of MMC when applied at a higher concentration, namely at 0.4 mg/ml by means of intra-Tenon injection in patients with different type of glaucoma (POAG, PIGM and PEXG). The primary end-point was to follow up IOP on postoperative days 1, 8, 30 and 90 and postoperative months 6 and 12. The secondary end point was to evaluate the changes in the value of corneal hysteresis, the depth of the anterior chamber (ACD) of the eye, and the value of the best corrected visual acuity (BCVA) before the surgical procedure and 90 days thereafter. Furthermore, the central corneal endothelial cell count (CECD) and coefficient of variation in cell area (CV) were also evaluated before trabeculectomy and 90 days and 12 months thereafter.

Methods

Study design and subjects

This observational study was conducted at the Department of Ophthalmology of Slovak Medical University and University Hospital in Bratislava, Slovakia from January 2019 to June 2020. This study followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients prior to surgery. Selection criteria included patients with OAG who did not undergo previous ophthalmic surgery, were older than 20 years and were not allergic to MMC. Patients had medically uncontrolled glaucoma as indicated by high IOP (over 21 mmHg), worsening of visual field, or optic nerve head changes. Exclusion criteria were applied to patients with previous glaucoma surgery, chronic or recurrent uveitis, pathologic myopia, iris neovascularization, and unwillingness or inability to give consent. Only one eye of each eligible patient was included.

Preoperative assessment

All patients underwent a baseline ophthalmologic examination before surgery, including the measurements of IOP and corneal hysteresis by means of Goldmann applanation tonometer (Keeler Ltd, Windsor, UK) and Ocular Response Analyser (ORA, Reichert Inc., NY, USA), respectively, as well as BCVA measurements, central visual acuity evaluation using ETDRS optotypes, and measurement of ACD using a Visante OCT (Carl Zeiss, Germany). Measurements of the IOP and corneal hysteresis were performed before any application of topical medication and always between 8:00 am and 11:00 am, in order to exclude the effect of diurnal rhythm on IOP.

CECD and CV were fully automatically measured using a non-contact specular microscope (Perseus, CSO, Italy) preoperatively.

Surgical procedure

The surgeries were performed either under general anaesthesia or under local retrobulbar anaesthesia, using a fixed combination of adrenaline and articaine, in a volume of 2.0 ml. All surgeries were performed by a single microsurgeon (Nora Majtanova).

After the patient´s eye was prepped and draped, the limbal-based conjunctival peritomy was performed at the superior quadrant, followed by blunt dissection of the Tenon capsule. The diathermocoagulation of the episcleral veins was used to prevent perioperative bleeding. Balanced saline solution on a blunt cannula was used to irrigate the eye. A corneoscleral flap was marked out with shallow incisions demarcating three sides of a 5-mm square, with the free limbs extending backwards radially from the limbus. The preparation of the partial-thickness corneoscleral flap was made using a crescent knife, followed by excision of a portion of the trabecular meshwork, and Schlemm's canal. The anterior chamber was entered underneath the scleral flap with a keratome. Peripheral iridectomy was performed using Vannas scissors. The scleral flap was closed with two releasable sutures. The conjunctiva was closed with 10-0 nylon suture. Dexamethasone was injected into the inferior conjunctival fornix.

MMC was injected approximately 8-9 mm posterior to the limbus in an area away from the superior rectus muscle in the sub-Tenon space using a 30-gauge needle. It was used in the last step of the operation as a subconjunctival injection into the surrounding area of the surgical wound. The concentration of MMC used was 0.4 mg/ml and the total volume delivered was 0.05 ml.

Postoperative assessment

Postoperatively, all eyes received topical antibiotics (levofloxacin 0.5 %) and a topical steroid (prednisolone acetate 1 %), both four times daily. The subjects were followed up on postoperative days 1, 8, 30 and 90. The postoperative data included BCVA, IOP, number of glaucoma medications and complications. In addition, the postoperative IOP was further monitored in all patients after 9 and 12 months. Postoperative CECD and CV were measured in all patients after 3 and 12 months.

Trabeculectomy with MMC was considered a complete success when the postoperative IOP was 21 mmHg or lower with at least 20 % reduction from baseline without the use of antiglaucoma medications and need for additional glaucoma surgery. Qualified success was defined as meeting the criteria for complete success, while not requiring an increase in the number of medications compared to the pre-surgery regimen, along with no need for additional surgery.

Complete failure was defined as a requirement for additional glaucoma surgery (except for needling procedures).

Statistical analysis

All statistical analyses were performed using R (programming language R) and GraphPad Prism (GraphPad Software Inc., La Jolla, CA, USA). The Shapiro-Wilk test of normality was used to determine the data distribution. In this analysis, a paired Wilcoxon test and unpaired Mann Whitney test were used, when data were not normally distributed. For normally distributed data, the t-test was used. Value of $p < 0.05$ was considered statistically significant. Kaplan-Meier survival analysis was used to evaluate the success of surgery.

We calculated the number of study patients according to IOP mean value. In a previous study (27), the mean and standard deviation (SD) of IOP values at 12 months after trabeculectomy using MMC at a concentration ranging from 0.2 to 0.5 mg/mL were 12.2 mmHg and 3.9 mmHg, respectively. We assumed that the mean value of IOP in the group of patients where MMC was used at a concentration of 0.4 mg/mL was 2 mmHg lower than the mean value of IOP in the published study. With 90 % power and type I error of 5 %, the estimated sample size was 44.

Results

Subjects

The data on 50 eyes of 50 patients gathered from a 90-day follow-up were analyzed. Additionally, the analysis of IOP values was carried out based on data acquired from a 12-month observation. Baseline demographics and clinical characteristics of participants are shown in Table 1. All participants were of Caucasian ethnicity with a mean age of 57.5 ± 16.4 years and 60 % were men.

In terms of distribution of individual types of glaucoma in which trabeculectomy was performed, POAG clearly dominated (54 % of patients), followed by PEXG (24 % of patients) and PIGM (22 % of patients). We divided the patients into two groups. The first group consisted of 23 phakic patients (46 %), while the second group consisted of 27 pseudophakic patients (54 %).

Tab. 1. Demographics and preoperative characteristics of patients who went underwent trabeculectomy with mitomycin C applied by intra-Tenon injection.

Demographics	n (%)
Age (years)	
Mean ± SD	57.5 ± 16.4
Min-Max	22–89
Gender	
Male	30 (60)
Female	20 (40)
Eye	
Right	26 (52)
Left	24 (48)
Diagnosis	
POAG	27 (54)
PEXG	12 (24)
PIGM	11 (22)

POAG – primary-open angled glaucoma; PIGM – pigmentary glaucoma; PEXG – pseudoexfoliation glaucoma

Changes in IOP values

The mean IOP value prior to the scheduled surgical procedure was 32.34 ± 9.45 mmHg. In patients who underwent right-eye surgery, IOP preoperative values ranged from 18 to 55 mmHg, with a mean of 31.3 ± 8.7 mmHg. IOP values associated with left-eye procedure ranged from 21 to 53 mmHg, with a mean value of 33.5 ± 10.2 mmHg.

At all postoperative time points, the mean IOP value followed a decreasing trend in all patients (Fig. 1). On the first day of surgery, the average value of IOP was 9.68 mmHg. On the eighth postoperative day, the mean IOP value was 15.44 mmHg, but with a wide variation among individual patients (ranging from 5 mmHg to 40 mmHg). The mean IOP value decreased compared to the preoperative value of 32.34 ± 9.45 mmHg to 17.52 ± 4.58 mmHg on the 90th postoperative day, accounting for a decrease of more than 46 %. A similar trend of decrease in postoperative IOP values was also observed after 9 and 12 months, where average decreases of 44 % and 40 % were observed, respectively (Fig. 1). As to individual types of glaucoma, the measurement of IOP at

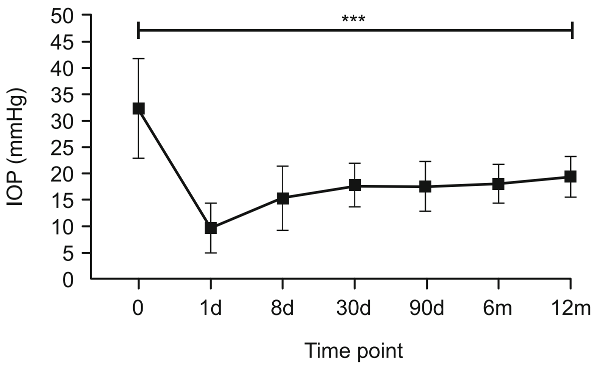

Fig. 1. Graph showing intraocular pressure (IOP) at baseline and during follow-up. The data are expressed as the mean values with SD. *** $p < 0.001$. Baseline vs. 12 -month comparison within the group of patients who underwent trabeculectomy with MMC, based on paired Wilcoxon's single-rank test.

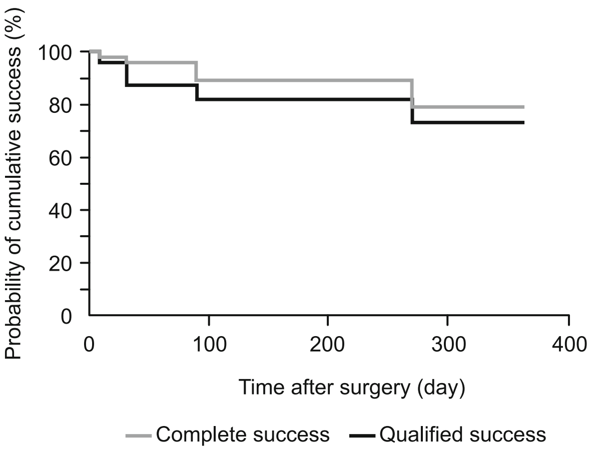

Fig. 2. Kaplan-Meier plot showing the cumulative probability of the complete and qualified success rates in patients based on the following criteria: IOP ≤ 21 mmHg and IOP reduction ≥20.

12 months showed that compared to its perioperative values, the average values of the IOP decrease in groups with POAG, PEXG and PIGM were 38.0 %, 45.6 % and 38.5 %, respectively. A statistically significant decrease in postoperative IOP during the whole follow-up period was present in every glaucoma group of patients (data not shown). However, no differences were found between these groups in IOP trends from baseline to postoperative month12 (data not shown).

Figure 2 plots the results of the Kaplan-Meier survival analysis at 1-year follow-up. Based on the success criteria, the cumulative rates of complete success were 100 %, 95.7 %, 82.9 %, 75.7 %, 51.4 % and 51.4 % at postoperative days1, 8, 30, and 90, and months 9 and 12, respectively. In the analysis of qualified success, the cumulative success rates were 100 %, 96.5 %, 87.7 %, 82.5 %, 73,7 % and 73.7 % at postoperative days 1, 8, 30, and 90, and months 9 and 12, respectively.

Changes in visual acuity, corneal hysteresis, ACD, CECD and CV after surgical procedure

In the study group of patients, the minimum value of BCVA before surgery was 0.2 and the maximum value was at the level of 1.0, with an average value of 0.78. On the 90th postoperative day, the average value of the best corrected visual acuity was 0.8. In total, up to 15 patients achieved the value of the best corrected visual acuity after undergoing trabeculectomy with MMC. The data did not show a statistical improvement in the BCVA after the antiglaucoma filtration procedure (Tab. 2).

Corneal hysteresis and ACD and their changes were monitored before surgery and on postoperative day 90. The mean value of corneal hysteresis before surgery was 8.71 mmHg (with minimum of 4.2 mmHg and maximum of 11.6 mmHg). At day 90 after trabeculectomy, the mean value of corneal hysteresis was 9.52 mmHg (with minimum of 7.2 mmHg and maximum of 12.4 mmHg), representing a statistically significant postoperative increase of 0.81 mmHg (an increase of almost 10 % compared to the start value) (Tab. 2).

After trabeculectomy, we also observed a change in the ACD. The average depth before the filtration operation was at the level of 3.20 mm, but after the operation, it decreased to an average value of 3.11 mm (a loss of 0.09 mm) (Tab. 2).

Table 3 shows the CEDC over the course of the study in 3 types of glaucoma diagnosed in patients. Overall, there was a significant decrease in CECD from the baseline value of 2126 ± 312.6 to 1980 ± 290.3 at 3 months and 1961 ± 288.3 cells/mm^2 at 12 months after surgery in all patients. The rates of cell loss from baseline to postoperative months 3 and 12 were 6.9 % and 7.8 %, respectively. A significant reduction in CECD was documented in each diagnosed type of glaucoma (Tab. 3).

Similarly, significant changes in CV values were documented. The mean CV was 26.82 ± 3.60 before surgery while at 3 and 12 months after surgery, they were 27.74 ± 3.43 and 28.22 ± 3.44 %, respectively.

Tab. 2. Baseline characteristics and outcome 90 days after trabeculectomy with mitomycin C applied by intra-Tenon injection.

Parameter	Time point		p
	Baseline	90th day	
IOP			
Mean±SD	32.34±9.45	17.52±4.58	<0.001[a]
Median (range)	30 (18–55)	18 (8–34)	
BCVA			
Mean±SD	0.77±0.23	0.80±0.23	0.129[a]
Median (range)	0.9 (0.2–1.0)	0.9 (0.1–1.0)	
Corneal hysteresis			
Mean±SD	8.71±1.58	9.52±1.22	<0.001[b]
Median (range)	8.85 (4.20–11.60)	9.60 (7.20–12.40)	
ACD			
Mean±SD	3.20±0.41	3.11±0.40	<0.001[b]
Median (range)	3.12 (2.32–4.05)	3.06 (2.30–3.99)	
Antiglaucoma drugs			
Mean±SD	3.50±0.74	0.58±1.03	<0.001[a]
Median (range)	4 (1–4)	0 (0–4)	

[a] – Wilcoxon's single-rank test, [b] – paired t-test

Tab. 3. Comparison of preoperative and postoperative CECD and CV measurements in 3 types of glaucoma in patients who underwent trabeculectomy with mitomycin C applied by intra-Tenon injection.

Type of glaucoma	Time point			p
	Baseline	3rd month	12th month	
POAG (n=27)				
CECD (cells/mm^2)	2178±352.7	2028±327.4	2009±325.0	<0.001[a]
CV (%)	26.59±3.84	27.41±3.59	27.89±3.68	<0.001[a]
PEXG (n=12)				
CECD (cells/mm^2)	1926±237.3	1794±218.4	1775±219.1	<0.001[a]
CV (%)	28.42±3.58	29.33±3.55	29.75±3.31	<0.001[a]
PIGM (n=11)				
CECD (cells/mm^2)	2218±170.0	2065±161.8	2044±156.8	<0.001[a]
CV (%)	25.64±2.50	26.82±2.48	27.36±2.58	<0.001[a]

[a] – Wilcoxon's single-rank test

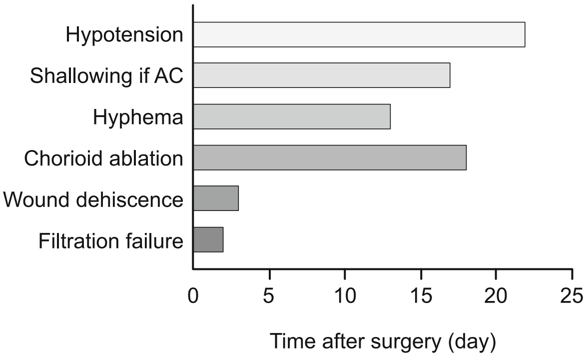

Fig. 3. Early and late post-trabeculectomy complications.

Antiglaucoma drugs and postoperative complications

From the patients' perspective, the number of regularly administered antiglaucoma drugs is a significant factor influencing their quality of life. Therefore, we evaluated the effect of filtration surgery on the number of drugs used before and after surgery, specifically on the 90th postoperative day. The average number of drugs used before surgery per patient was 3.5. On the 90th day after the operation, this value dropped significantly to 0.58 (Tab. 2). Of the total number of patients, 35 (70 %) did not require any drug therapy postoperatively.

Trabeculectomy, like any other surgery procedure, has postoperative complications. We documented early complications (< 1 month), such as postoperative hypotension in 22 patients (44 %), shallowing of the anterior chamber of at least 1 mm in 17 patients (34 %), chorioid ablation in 18 patients (36 %) and hyphema in 13 patients (26 %). Late complications (≥ 1 month) included surgical wound dehiscence in 3 patients (6 %) and filtration failure in 2 patients (4 %) (Fig. 3).

Discussion

A significant hypotonising effect of trabeculectomy augmented with sub-Tenon injected MMC at a concentration of 0.4 mg/ml was demonstrated, resulting in a postoperative decrease in the IOP value in each patient. The measured values indicate that IOP tends to increase during the postoperative period, mainly within the first 7 days after surgery, followed by stabilization within one to three months. A reduction of 46 % and 40 % in the average preoperative value of IOP was documented on the 90th postoperative day and at 12 months, respectively. The postoperative decrease in IOP enabled a significant reduction in the number of antiglaucoma drugs, to values as low as 0.58. Of the total number of patients, 35 (70 %) did not require any postoperative anti-glaucoma therapy. Despite the complexity of the surgical procedure, there was no statistically significant decrease in BCVA after trabeculectomy. On the contrary, an increase in BCVA from its preoperative value of 0.78 to the value of 0.8 was recorded on the 90th postoperative day. There was an increase in the value of corneal hysteresis postoperatively by 0.81 mmHg (almost 10 % increase compared to the original value), which we attribute to the significant decrease in postoperative IOP. We observed an opposite effect when evaluating ACD of the eye. After the operation, it shallowed to an average value of 3.11 mm, which represents a decrease of 0.09 mm compared to the average value before the operation. The trabeculectomy surgery alters corneal biomechanical characteristics and anterior segment parameters (28). Several studies have shown that ACD begins to increase gradually, reaching almost 90 % of its preoperative values after 2 weeks (29–31). On the other hand, some studies have demonstrated that ACD is not affected by trabeculectomy, at least a few weeks after surgery (32, 33). Furthermore, ACD in patients who underwent trabeculectomy was higher at third postoperative month in comparison to the preoperative mean value (34).

Sub-Tenon injection of MMC during trabeculectomy offers several advantages compared to the traditional surgical procedure with MMC applied in the form of sponge (19). The injection of MMC has a much more predictable dose of delivery, which may minimize adverse effects (35). The injection of MMC significantly reduces application time (30 s for injection vs. 3-5 min for sponge), delivers the exact amount of MMC and reduces the complication of losing or retaining the sponge. Several randomized clinical studies have been conducted in order to compare the outcomes of MMC delivered by intra-Tenon injection vs. sponge application during trabeculectomy surgery at different postoperative endpoints (18–20, 23, 36, 37). Overall, the sub-Tenon injection of MMC is considered to be a safe and effective alternative to the conventional soaked sponge method. This method may produce more favourable bleb morphology after trabeculectomy (20, 38). On the other hand, little information is available regarding the concentration and dosage of MMC applied using intra-Tenon injection. In our study, MMC was used at a concentration of 0.4 mg/ml in a total fixed volume of 0.05 ml for each patient who underwent trabeculectomy. Similarly, a few studies reported the use of MMC at a fixed concentration and volume. In a very recent study, patients received a sub-Tenon injection of 0.15 ml of MMC at a concentration of 0.1 mg/ml (20). The same concentration of MMC but applied in a volume of 0.1 ml was used in the study by Esfandiari et al (18). On the other hand, several studies reported that the concentration of MMC was determined by the surgeon based on characteristics of the individual patient and risk of bleb failure determined preoperatively. MMC was used in a concentration ranging from 0.05 to 0.5 mg/ml and the total volume delivered was 0.1 ml (19, 27).

The short application time (30 s) for MMC after its sub-Tenon injection during trabeculectomy reduces its potential cytotoxicity in comparison to the traditional 5-min application of MMC. MMC exhibits cytotoxic effects and can induce the damage of the corneal endothelium (39). Interestingly, fibroblasts exposed to sublethal doses of MMC may still affect the growth and activity of untreated fibroblasts which may explain why scarring after filtration surgery occurs despite MMC treatment (40). A very recent study by Park et al (2021) reported that lidocaine, a frequently used local anaesthetic agent in filtration surgery for glaucoma, increases the cytotoxicity after its combination with MMC (0.2 mg/ml) (41). Therefore, utilizing sub-Tenon injection of MMC seems to be a more suitable method of providing MMC, while reducing potential cytotoxicity owing to its brief application time.

A population of patients with homogeneous ethnicity (Caucasian) participated in our study. The most prevalent diagnosis was POAG, followed by PEXG and PIGM. A recent study assessed the differences in efficacy and safety of trabeculectomy with MMC soaked in sponges (0.2 mg/ml) between patients with POAG and those with primary angle closure glaucoma (PACG) (42). A significant decrease in postoperative IOP was demonstrated in both groups. As compared to the group with PACG, the group of patients with POAG yielded a more significant decrease in IOP from the mean preoperative value of 31.4 ± 10.5 mmHg to the value of 10.5 ± 3.4 mmHg measured on the 90th postoperative day. Complications of surgical procedures were not common. The authors reported postoperative hypotension (1.8 %), chorioid ablation (2.8 %), filter pad cystic transformation (2.8 %) and wound hyperfiltration (1.8 %) (42).

In our study, at all points of follow up, no significant differences were recorded between POAG, PEXG and PIGM groups of patients regarding the IOP mean values. Similarly, Duzgan et al (2017) showed no statistically significant differences in IOP values between POAG and PEXG groups of patients; however, the decrease in IOP values in the PEXG group was found to be lower compared to the POAG group (43).

Corneal hysteresis is a corneal biomechanical parameter which characterizes viscoelasticity. There is evidence that values of corneal hysteresis are significantly lower in eyes with glaucoma compared to normal eyes (44). The influence of trabeculectomy using MMC on the corneal biomechanical properties including corneal hysteresis has been described in several studies (45–48). Overall, the data obtained from clinical studies showed that mean values of corneal hysteresis significantly increased after trabeculectomy with MMC. When, comparing different types of open-angle glaucoma, corneal hysteresis was found to be preoperatively lower in patients with PEXG than in patients with POAG (48). Postoperatively, there was a statistically significant increase in corneal hysteresis values in both groups of patients. However, a more significant difference before and after trabeculectomy was determined in patients with PEXG. These observations of a significant difference in mean corneal hysteresis before and after trabeculectomy with MMC are consistent with our results. Therefore, corneal hysteresis represents a valuable and useful measure in the management of glaucoma after trabeculectomy (49). On the other hand, contrary to our results and aforementioned studies, Pillunat et al showed that corneal hysteresis values were not significantly changed in 35 eyes before and after trabeculectomy with MMC (46). Despite continuous improvements in trabeculectomy, shallow or flat AC remains a common postoperative complication. In the present study, the shallowing of AC and choroid ablation, the most prevalent complications in patients who underwent trabeculectomy, were reported in 17 (34 %) and 18 (36 %) patients, respectively. A similar prevalence of the shallowing of AC was reported in a recent study by Sharma et al (50), where the shallowing of AC was found in 39 % of patients who underwent trabeculectomy with MMC at a concentration of 0.4 mg/ml. On the contrary, other studies reported that flat AC was present in less than 10 % of patients who had undergone trabeculectomy regardless of the form of MMC application (18, 51). Potential risk factors for the shallowing of AC after trabeculectomy are patient age over 60 years, neovascular glaucoma and preoperative intraocular pressure above 50 mmHg (51). Nie analyzed the causes of shallow AC after glaucoma surgery in 183 patients (218 eyes). AC shallowing occurred in 42 eyes (19.3 %) and the most common cause was excessive filtration (52).

In this study, we also analyzed the endothelial cell loss and compared variations in cell size after trabeculectomy using MMC applied by intra-Tenon injection. Trabeculectomy may cause various changes in the CECD; a decrease of 3.2 – 18.2 % has been reported for CECD (53–56). One of the major risk factors for decreasing CECD after trabeculectomy is MMC (57). Very few clinical studies investigated the effect of intra-Tenon injection of MMC on endothelial cell count (18–20, 38). Overall, no differences in endothelial cell count between MMC-soaked sponge group and intra-Tenon injection of MMC group were found. Moreover, the authors of these studies did not find any significant differences between the mean preoperative and postoperative values of CECD in the intra-Tenon injection group at 6 and 12 months after the surgery. Contrary to these findings, our results showed significant CECD decreases of 6.9 % and 7.8 % at postoperative months 3 and 12. Another risk factor of postoperative complications after the filtration antiglaucoma procedure using MMC is the development of an infection. An extensive, prospective observational cohort study was conducted in order to report on the 5-year incidence of bleb-related infection after MMC-augmented glaucoma filtering surgery (58). The study included 1,098 patients (1,098 eyes) who underwent trabeculectomy using MMC (916 eyes) or phaco-trabeculectomy with artificial intraocular lens implantation (182 eyes). Patients with different types of glaucoma were included in the study group. In total, 21 patients (2.5 %) developed an infectious complication after surgery, 2 (1.6 %) of which were after phaco-trabeculectomy and 19 (2.8 %) after trabeculectomy. The intensity of inflammatory manifestations varied. In 10 patients, postoperative blebitis developed, with a mild inflammatory reaction in the anterior chamber; in 6 patients, the inflammatory reaction was localized in the anterior chamber, while in 5 patients, the maximum inflammatory reaction was present in the vitreous area. The mean length of time from antiglaucoma surgery to inflammatory manifestations was 27.3 ± 15.9 months. Among patients who developed an infectious postoperative complication, 8 (10.3 %) experienced an insufficient conjunctival wound healing.

The main limitations of our study lie in the relatively short follow-up and absence of a control group comprising patients who underwent trabeculectomy with MMC applied in the form of a sponge. A longer follow-up would help us compare the rates of long-term success complications more effectively.

Conclusions

Taken together, in the study group, a significant hypotonising effect of trabeculectomy with MMC was observed. The correct indication, timing and performance of the filtration procedure in patients resulted in a reduction in the number of antiglaucoma drugs, improved visual acuity, and enhanced the quality of life of patients. In order to investigate the effect of trabeculectomy on IOP, postoperative complications and their impact on patients' quality of life, it is necessary to conduct further prospective studies with a longer follow-up period.

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