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Treatment Outcomes of Mitomycin C-Augmented Trabeculectomy, Sub-Tenon Injection versus Soaked Sponges, after 3 Years of Follow-up

A Randomized Clinical Trial

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Purpose: To report the 3-year outcome of trabeculectomy with mitomycin C (MMC)-soaked sponges versus intra-Tenon injection of MMC in eyes with uncontrolled primary open-angle glaucoma.

Design: Randomized clinical trial.

Participants: Eighty-two consecutive patients with uncontrolled primary open-angle glaucoma.

Methods: Participants were randomized either to intra-Tenon injection of 0.1 ml of 0.01% MMC (TI group) or 0.02% subconjunctival application of MMC-soaked sponges (TS group). Patients were followed up for 3 years after surgery. The data for 73 eyes were included in the final analysis.

Main Outcome Measures: The primary outcome measure was the surgical success, defined as intraocular pressure (IOP) more than 5 mmHg and <21 mmHg, and IOP reduction of 20% or more from baseline, no reoperation for glaucoma, and no loss of light perception vision. Secondary outcome measures were IOP, glaucoma medications, best-corrected visual acuity (VA), bleb morphologic features according to the Indiana Bleb Appearance Grading Scale, complications, and endothelial cell count changes.

Results: The cumulative probability of success at 3-year follow-up was 72.2% in the TI group and 65.1% in the TS group ($P = 0.30$). Uncontrolled IOP was the most common reason for failure. The mean preoperative IOP was 22.4±4.6 mmHg with an average of 3.1±1.0 medications. At 3 years, final IOP was 15.3±3.7 mmHg in the TI group and 16.4±3.5 mmHg in the TS group ($P = 0.55$). Mean glaucoma number of medications was 0.9±1.1 and 1.1±1.1 in the TI and TS groups, respectively ($P = 0.54$). Blebs tended to be more diffuse ($P = 0.032$), less vascularized ($P = 0.013$), and more shallow ($P = 0.012$) after intra-Tenon injection. Visual outcomes and endothelial cell changes were similar in both groups ($P = 0.47$ and $P = 0.94$, respectively).

Conclusions: Although the success rate and IOP reduction were comparable with both techniques, bleb morphologic parameters were more favorable after intra-Tenon injection of 0.1 ml of 0.01% MMC. *Ophthalmology Glaucoma 2018;1:66-74 © 2018 by the American Academy of Ophthalmology*

Trabeculectomy is the most common procedure performed to reduce intraocular pressure (IOP) and prevent further glaucomatous optic nerve head damage.[1] Modifications such as titratable scleral flap sutures and intraoperative antimetabolites, as well as postoperative interventions such as suture removal or lysis and bleb needling with or without antimetabolites, have improved the efficacy and safety profile of the primary procedure introduced by Cairns in 1968.[2–4]

Despite antimetabolite efficacy, their side effects are worrisome because they lack cell specificity in their cytotoxic effect.[5] Early and late complications such as bleb leakage, hypotony, corneal decompensation, flat anterior chamber, cataract, choroidal effusion, suprachoroidal hemorrhage, hypotony maculopathy, blebitis, and endophthalmitis have led investigators to scrutinize their application in trabeculectomy. Although the type, concentration, and contact time of antimetabolites are discussed extensively in the literature,[6–8] the method of delivering antimetabolite to the trabeculectomy site has not been evaluated thoroughly.

This study was designed to compare prospectively the safety and efficacy of intra-Tenon injection of mitomycin C (MMC; TI group) and subconjunctival application of MMC-soaked sponges (TS group).[9] In a previous study, although the 6-month outcomes of both groups were comparable regarding IOP control, those in the TI group tended to have more diffuse and low-lying blebs.[9] The goal of this study

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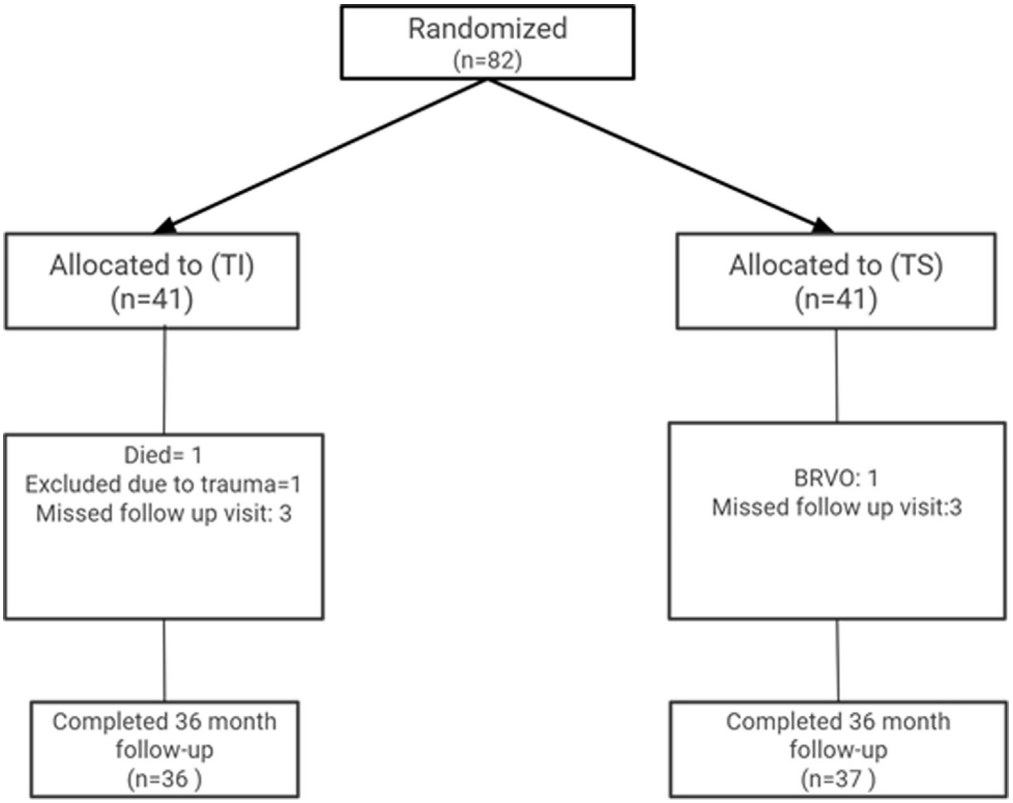

Figure 1. Diagram showing study design and patient retention. BRVO = branch retinal vein occlusion; TI = intra-Tenon mitomycin C injection; TS = subconjunctival application of mitomycin C-soaked sponges.

was to report the outcomes of treatment during 3 years of follow-up.

Methods

The design and methods of the study were described previously in detail[9] and are summarized here. The protocol of this study was approved by the institutional review board of the Shahid Beheshti University of Medical Science, Tehran, Iran. Our research adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from each participant. This randomized clinical trial is registered at clinicaltrials.gov (identifier, NCT02385370) according to the standards set by the International Committee of Medical Journal Editors and the World Health Organization.

Patients with uncontrolled primary open-angle glaucoma receiving maximum medical treatment who were older than 25 years were enrolled in this study. Exclusion criteria included history of prior ocular surgery and manipulation of the conjunctiva; necessity for a combined cataract procedure; ocular or systemic comorbidities that could affect the procedure and outcomes of the study, such as iridocorneal endothelial syndrome, active neovascularization, or uveitis; epithelial or fibrous downgrowth; immunodeficiency; connective tissue disease; uncontrolled diabetes; pregnant or nursing women; need for combined surgery; or anticipation of another surgery in future. Only 1 eye of each eligible patient was included.

Randomization was performed on the day of the surgery. Assignments were generated by a computer program using a random permuted block algorithm with block sizes of 2, 4, and 6. Randomization was performed by a biostatistician, and the sequence was concealed from the investigators. Patients and clinicians who visited the patients and collected the data were masked to the assignment during follow-up.

Surgical Technique

All surgeries were performed by 2 experienced glaucoma surgeons (M.P. and H.E.). Anesthesia was achieved by injecting intravenous sedation and local peribulbar injection of 2 ml of lidocaine 2% (Lignidic 2%; Caspian Tamin Pharmaceutical Co., Rasht, Iran). After lid speculum insertion and cul-de-sac irrigation with povidone−iodine and normal saline solution, 0.1 ml of 0.01% MMC (Mitomycin C Kyowa; Kogyo Company, Tokyo, Japan) was injected into the sub-Tenon space in the superior cul-de-sac and was spread diffusely with a blunt spatula over the superior conjunctiva; a Weck-Cel sponge (XOMED Surgical Products, Inc., Jacksonville, FL) was used to prevent anterior migration of the MMC, and it was limited to the area covered by the upper lid, avoiding the interpalpebral area. The fornix-based conjunctival peritomy was performed at the superior to superonasal quadrant for 1.5 to 2 clock hours, followed by blunt dissection of Tenon's capsule 1 minute after MMC injection. The operation field was irrigated copiously with a balanced salt solution, and diluted MMC was drawn out of Tenon's capsule by muscle hook during dissection. A 3.0×4.0-mm trapezoidal half-thickness scleral flap was created using a crescent knife followed by lamellar dissection of the scleral flap 1 mm into the clear cornea. After fashioning a sideport, the anterior chamber was entered underneath the scleral flap with a keratome and the incision was squared off with the sideport knife. A block of the clear cornea was removed by Kelly punch (ASICO, LLC, Westmont, IL) and peripheral iridectomy was performed using Vannas scissors (Ambler Surgical, Exton,