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To Study the Long Term Effects on Corneal Endothelial Cell Density with Mitomycin C Augmented Trabeculectomy Vs Trabecuelectomy without Mitomycin C in Primary Glaucoma: A Comparative Study

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Abstract: ***Purpose: To study the long term effects of Mitomycin C (MMC) assisted trabeculectomyin patients with primary glaucoma on the corneal endothelial cells. Methods: In this study, 60 eyes underwent standard trabeculectomy with mitomycin c (Group I) and 60 eyes of patients underwent standard trabeculectomy without mitomycin c (Group II). Specular microscopy was performed at 1 month, 3 month and 6 month postoperatively. The variable included was corneal endothelial cell density(CECD). Results: Overall, the mean preoperative corneal endothelial cell density was 2572.37 +/-245.82mm2 , postoperatively at 1 month, 3 month and 6 month the cell density was significantly reduced to 2388.71 +/- 283.54 mm2 , 2332.43 +/- 244.66 mm2 and 2265.53 +/- 238.58 mm2 respectively.(p <0.05). Conclusion: With the use of Mitomycin C in trabeculectomy, there occurs significant corneal endothelial cell loss. Most of the endothelial cell count loss occurs intra-operatively, or in the early postoperative period. Hence it can be said that the corneal endothelial cells are vulnerable to the use of Mitomycin - C agent and thus may lead to future corneal decompensation in extremely compromised eyes.***

Keywords: MMC, Trabeculectomy, CECD

1. Introduction

Glaucoma is a leading cause of irreversible blindness worldwide and is second only to cataract as the most common cause of blindness overall(1).

Trabeculectomy as the standard procedure in penetrating anti-glaucoma surgery was introduced by Cairns in 1968.[2]Wound healing and scar formation causing fibrosis and the obstruction of aqueous outflow remain the most common reason for the failure of trabeculectomy[3], [4].

Adjunctive antifibrotic agents, such as 5-fluorouracil (5-FU) or Mitomycin-C (MMC), are commonly used to increase the success rate of glaucoma filtering surgery.[5][6].

MMC is an antitumor, antibiotic derived from Streptomyces caespitosus with its alkylating properties,which has an inhibitory effect on fibrosis of the tissue and vascular growth both of which play important roles in tissue remodelling, healing and scar formation. It is used as an anti-metabolite during trabeculectomy. However, it is frequently accompanied by short- and long-term complications such as hypotony, bleb leaks, cataract formation, avascular filtering blebs, thinning of the conjunctiva, subsequent blebitis, and endophthalmitis.

In trabeculectomy, MMC may also penetrate into the adjacent ocular tissues, beyond its application site.[7] Since the corneal endothelial cells lack division capacity hence possible damage to the endothelium are irreparable and cell density may diminish gradually.[8][9].

Specular microscopy is the investigation of choice for evaluating the condition of the corneal endothelium or detect any damage to the cells that may have been caused by the disease or surgery itself. [10,11] The mentioned study was undertaken to evaluate and compare the effect of Mitomycin-C on the corneal endothelial cells in Mitomycin-C augmented trabeculectomy and trabeculectomy without the use of Mitomycin C in primary glaucoma.

2. Methods

This prospective randomised comparative study was conducted in compliance with the tenets of declaration of Helsinki and Institutional ethical committee approval had been obtained ahead of the study. The study was held at the department of ophthalmology, SMS medical college & hospital, Jaipur. 120 patients were selected for the study who suffered from primary glaucoma. After explaining the need of the study, surgical procedures to be followed and possible complications, an informed consent was obtained from the patients and they were assigned into two groups;

Group I (n = 60) patients who underwent trabeculectomy with intraoperative application of 0.2 mg/ml Mitomycin C for 120 seconds

Group II (n = 60) patients who underwent trabeculectomy without the use of Mitomycin C.

Eligibility Criteria

Inclusion criteria
Patients with an IOP >20 mmHg with maximal tolerated anti glaucoma drugs, Patients having intolerable side effects of anti glaucoma drugs, Patients with POAG and having poor compliance for anti glaucoma drug use, Patients who couldn't afford anti glaucoma medicines, Patients willing for surgery, Patients willing for follow ups were included in study.

Exclusion criteria
Age less than 18 years, Any glaucoma other than primary glaucoma, Recent ocular infection or inflammation, Previous intraocular surgery, anterior segment laser surgery, History of IOP altering events such as retinal detachment or prolonged corticosteroid administration, Corneal or retinal pathology, History of presence of uveitis, Those who were not willing to participate, Those who were not able to come for the follow up were excluded.

Pre-operative evaluation
Baseline information, was gathered such as, age, gender, number of anti-glaucoma medications and medical history were noted. All the patients received a complete preoperative examination, including best corrected visual acuity measurement (BCVA)on the Snellen's chart, slit lamp examination, applanation tonometry (Goldmann applanation tonometry), gonioscopy, dilated fundus evaluation, Humphrey visual field (24-2, or 30-2) examination, and specular microscopy was performed.

3. Surgical Technique

All the surgeries were performed by the same surgeon under peribulbar anesthesia. In group I, The eye was prepared with Povidone Iodine 5% solution.Controlled gentle digital massage with the hand was given**.** Superiorrectus bridle suture was placed, Trabeculectomy was performed in the superotemporal or superonasal quadrant trying to avoid sites of perforating scleral vessels. A fornix based conjunctival flap was prepared . Haemostasis was achieved by adequate wet field cautery. Subconjunctival Mitomycin C 0.2 mg/ml was applied for 120 seconds with 3 merocel sponges. Subconjunctival space copiously irrigated with 30 ml Ringer Lactate. A 4 x 4 mm triangular scleral flap one third of the thickness dissected to within 1 mm of clear cornea with a Bard Parker knife.After creating a paracentesis opening, inner sclerostomy block was dissected out with the blade in the dimensions 2mm × 3 mm,at the base of the hinge of the superficial scleral flap. Peripheral iridectomy performed through the inner sclerostomy with a vannas scissor and a single toothed fine forceps. Scleral flap reapproximated with an apical 10-0 nylon suture and one releasable suture. Conjuctival flap closed water tight by 10-0 nylon suture.

Group II patients underwent the above mentioned procedure without the use of intra-operative application of MMC

Postoperatively, the patients were prescribed a combination of antibiotic-steroid (tobramycin 0.3% + dexamethasone 0.1%) eye drops every 2 hours for 1 week which tapered over the following 5 weeks. Cycloplegic-mydriatic drops (homatropine 2%) eye drops or atropine 1% eye drops were used when signs of early inflammation appeared and shallow A/C or hypotony was observed.

Follow up examination was conducted 1st and 3rd day, 1 week and 2 week ,1 month, 3month and 6 month postoperatively with specular microscopy being done at 1st, 3rd and 6th month postoperatively. Four specular photographs were taken at every examination, and the mean data were considered for statistical analysis. Four specular photographs were taken at every examination, and the mean data were considered for statistical analysis.

Statistical analysis
The statistical analysis was thereby performed using the Statistical Package for Social Sciences software version 23 (SPSSInc., Chicago, Illinois, USA). Analysis of variance (ANOVA) was used to analyze intragroup changes in continuous variables pre and postoperatively. In cases of Normal distribution of data , mean and SD were used while in cases variable are not normally distributed then median were used. The Mann Whitney U test was used to compare mean values of intergroup continuous variables. Categorical data was evaluated using the Chi square test. For all measurements, a two tailed test was used, and $P < 0.05$ was considered as significant for measured variables.

4. Results

120 eyes of 120 patients were evaluated in our study with the aim to study and evaluate the corneal endothelial cell density in patients undergoing trabeculectomy with Mitomycin C and trabeculectomy without Mitomycin C

The study observes the postoperative status of the corneal endothelium after trabeculectomy with and without the use of Mitomycin C and compares the 2 groups. In our study, the mean age was observed to be 56.10± 8.921 years in Group I and 55.83± 9.851 years in Group II. There were no significant differences in terms of mean age (P =0.93). No significant difference was observed according to gender i.e groups were comparable according to gender. (P = 0.466). No significant difference were observed in CECD i.e groups were comparable.

The study assessed the endothelial cell count, using specular microscopy post-operatively at intervals of 1 month, 3 month and 6month and observed that the patients falling under Group I, the mean endothelial cell count dropped to 2388.71 +/- 283.54 mm2 , 2332.43 +/- 244.66 mm2 and 2265.53 +/- 238.58 mm2 respectively.($p < 0.05$) at 1, 3 and 6 months

In Group II, the mean corneal endothelial cell count dropped to 2466.85± 266.65/mm^2 at 1 month and 2442.37 ± 269.80 /mm^2 at 3 months and 2335.44±258.88/mm2 at 6 month . It was observed that pre-operatively there was no significant difference in the endothelial cell counts between the two groups, but the mean endothelial cell count loss was significantly higher in group I as compared to group II at each follow up. (P=0.004).

5. Discussion

The corneal endothelium, is primarily a non-replicative tissue. In event of an acute insult to the tissue, it responses to a loss of endothelial cells, the residual cells enlarge and slide in an attempt to cover the posterior corneal surface, and this is reflected in a short term increase in the cell size associated with decrease in the percentage of hexagonal cells. There was no difference in endothelial cell count preoperatively in both the groups. The evaluation of the endothelial cell count was performed post-operatively at the intervals of 1 month, 3 month and 6 months.

It was then observed that the mean endothelial cell loss was significantly higher in group 1 as compared to group 2 at each follow up. (P=0.004).
The endothelial cell density or count is an acceptable and widely used parameter for the status of the cornea after surgery. The decrease in cell density demonstrates the surgical trauma itself, whereas the morphological change in the cells reflects the process of repair.

The patient selection is very important as the humancorneal endothelium is vulnerable to Mitomycin C and the endothelial loss resulting from the surgical trauma itself may result in the corneal decompensation.

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