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Suramin, Genistein and Collagen Matrix (DuraGen) for Delayed Adjustment after Strabismus Surgery: Which One is Best?

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ABSTRACT

Aim: To evaluate the efficacy and safety of suramin, genistein and collagen matrix for the prevention of inflammation, the reduction of fibrosis and the delay in adjustment after strabismus surgery on a rabbit model.

Methods: By using an adjustable suture technique, a recession of the superior rectus muscle (SRM) was made in 36 eyes of 18 rabbits. Three study groups were created using genistein, suramin and collagen matrix ($n = 6$ per group). Two control groups utilized dimethyl sulphoxide (DMSO) ($n = 6$) and balanced salt solution ($n = 12$). The adjustments and measurements were made on days 2, 7, 14. After enucleation was done on day 21, the degree of inflammation was evaluated quantitatively in histopathological sections and immunohistochemical investigations were performed for tissue expression of cytoplasmic vascular endothelial growth factor (VEGF), MAC 387, TGF-β and bFGF.

Results: The adhesions between conjunctiva and SRM were significantly less in the collagen matrix and suramin groups ($p = 0.002$) and adhesions between the sclera and SRM were considerably reduced in the genistein and DMSO groups ($p = 0.006$) on day 7. Force exerted for adjustment was significantly less in the collagen matrix and suramin groups on day 14 ($p = 0.006$). Expression of b-FGF was significantly lower in the conjunctival epithelium in the suramin and genistein groups ($p = 0.0001$ for both). TGF-β was significantly lower ($p = 0.001$) in the suramin group and VEGF expression was totally absent. MAC 387 expression was lower in the genistein and suramin groups ($p = 0.0001$).

Conclusion: Suramin, genistein and collagen matrix successfully reduce adhesions, and facilitate adjustment following recession surgery. Both suramin and genistein effectively suppress growth factor expression, while collagen matrix offers the longest time interval for adjustability after strabismus surgery.

Keywords: Adjustable suture, collagen matrix (DuraGen), genistein, suramin

INTRODUCTION

The adjustable suture surgery for strabismus has been designed to facilitate more accurate ocular alignment. Although this technique minimizes unpredictable results and decreases the need for reoperation, the drift of several prism diopters may occur during the early postoperative period. The investigations on adjustable suture surgery aim to prevent fibrosis and adhesions and, thus, to extend the time interval before the adjustment procedure.[1,2] Delaying the adjustment would provide the surgeon with a better perspective

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to determine how the ocular alignment would subsequently stabilize. In order to enhance delayed adjustment, various materials that hinder the proliferation of subconjunctival fibroblasts and the formation of scar tissue have been utilized, mostly in animal studies. Among these materials are physical barriers such as polytetrafluoroethylene, silicone, oxidized regenerated cellulose, viscoelastic material and biodegradable gel matrix or sheet as well as antiproliferative agents including mitomycin C, 5-fluorouracil and tranilast.[3–8]

Suramin sodium is an aromatic polysulfonated compound which acts as a heparin analog and antagonizes several growth factors *in vitro*. For this reason, it has been used to reduce postoperative fibrosis after trabeculectomy.[9–11] Genistein is a naturally occurring isoflavone inhibiting the proliferation of vascular endothelial cells and tumor cell lines by decreasing the levels of vascular endothelial growth factor (VEGF) and beta-transforming growth factor (TGF-β). As a buffer for dilution and preservation of genistein, dimethyl sulphoxide (DMSO) solution protects tissues from oxidative stress.[12] DuraGen® (Integra Neuroscience, Plainsboro, NJ) is a type 1 collagen matrix graft manufactured from bovine Achilles tendon. This biodegradable graft is usually preferred for duraplasty operations.[13,14]

The present study aims to evaluate the efficacy and safety of suramin, genistein and collagen matrix for the prevention of inflammation, the reduction of fibrosis and the postponement of adjustment after strabismus surgery using a rabbit model.

MATERIALS AND METHODS

Study Design

The present study was approved by the Institutional Animal Care and Use Committee and held in accordance with the guidelines issued by the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Ophthalmic and Vision Research.

Eighteen New Zealand white rabbits (six males and twelve females) weighing between 2500 and 4500 g were recruited for the present study. By using an adjustable suture technique, 36 eyes of the recruited rabbits underwent a five mm recession of the superior rectus muscle (SRM). All procedures were performed under general anesthesia using an intramuscular administration of 40 mg/kg of ketamine hydrochloride and 5 mg/kg of xylazine hydrochloride. Topical anesthesia was maintained with oxybuprocaine hydrochloride. After surgical antisepsis was provided with povidone iodine, a limbal peritomy was performed from 10 to 2 o'clock. The SRM was isolated with a Jameson hook and the intermuscular connections were dissected. The superior oblique tendon was disinserted and allowed to retract from the surgical field to make the SRM movements freer in further adjustments. A double-armed 6–0 vicryl suture was placed close to the insertion point of the superior rectus tendon and the muscle was removed from the globe with Westcott scissors. The muscle was recessed 5 mm from the insertion and an adjustable suture was tied temporarily with a single throw and locked with a half bow. After closing the edge of the conjunctival peritomy with 8–0 vicryl sutures, tobramycin eye ointment was applied topically.

The suramin group consisted of six eyes among which suramin solution (250 mg/ml) was applied over and under the surface of the SRM with a soaked cellulose sponge for 5 min. Later the surgical area was irrigated thoroughly with 10 ml of balanced salt solution (BSS). The genistein group similarly consisted of six eyes among which genistein (0.5 mg/ml) was administered over and under the surface of the SRM with a soaked cellulose sponge for 5 min. The collagen matrix group consisted of six eyes in which DuraGen® barrier matrix (1 cm × 0.5 cm × 0.2 cm) was placed between the SRM and the sclera and also between the SRM and the conjunctiva. Two control groups were made for comparison and named the DMSO and BSS groups. The DMSO group was made up by six eyes which were the contra laterals of the six eyes that received genistein. The DMSO solution was administered over and under the whole surface of the SRM with a soaked cellulose sponges for 5 min. The BSS group consisted of 12 eyes which were the contra laterals of the suramin and collagen matrix groups. Approximately 10 ml of BSS was administered over and under the surface of the SRM with a soaked cellulose sponges for 5 min.

Adjustments and measurements were made by the same researcher (C.O.) on days 2, 7 and14 during the postoperative period. The researcher was blinded to both the grouping and to the treatments administered on the ocular tissue. The necessary force for adjustment was measured with the help of a push pull gauge (Gpp-8, Jonard Industrial, NY) (Figure 1). Initially, a loop handle was prepared at the end of the suture which was put over the SRM. Then, the push pull gauge was used to grasp the loop handle and the SRM was moved as close as possible to the original insertion area by applying tangential force (Figure 2). Meanwhile the adhesions between the SRM, the sclera and the conjunctiva were graded on a scale of 0–4; namely, 0 = no adhesions, 1 = filmy adhesions which are easily separated with blunt dissection, 2 = mild and moderate adhesions which are freely dissected, 3 = moderate and dense adhesions which are separated with difficulty and 4 = severe adhesions which cannot be dissected. The muscle was replaced in its recessed position at the end of each adjustment session. In the collagen matrix

group the original matrix was laid again over and under the muscle. No complications occurred in any of the rabbit eyes recruited for the present study.

Histopathological Evaluation

On the 21st postoperative day, all animals were sacrificed by intravenous injection of 10 ml sodium pentothal and all eyes were enucleated. Tissues containing the SRM, adjacent sclera and conjunctiva were placed into 10% formaldehyde solution for histopathological and immunohistochemical investigation. All samples were stained with a standard hematoxylin–eosin (HE) technique and were evaluated using standard light microscopy under ×40 magnification.

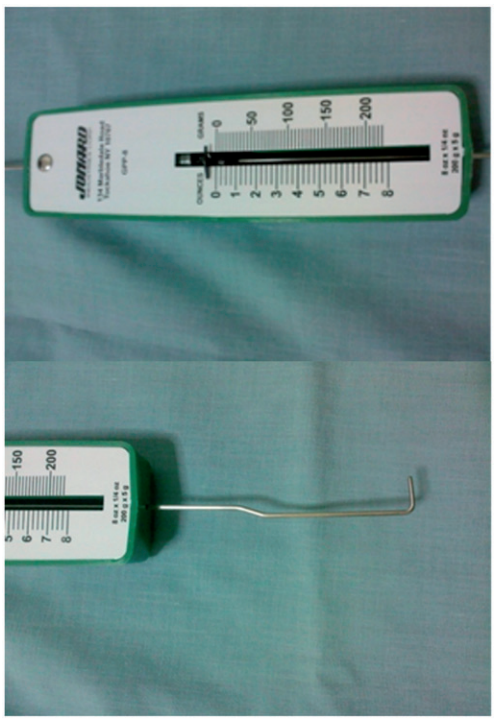

FIGURE 1 Jonard Gpp-8 push pull gauge.

The presence of inflammation and the number of multinucleated giant cells in striated muscle were noted.

Immunohistochemical Assessment

Immunolabeling was performed in paraffin-embedded plugs using monoclonal antibodies as a part of the avidin–biotin–peroxidase system. Each subject was defined according to the following criteria:

(1) Cytoplasmic VEGF antibody-3 expression was determined in the most vascularized area, inflammatory infiltrate within the muscle and conjunctival epithelium.
(2) Cytoplasmic MAC 387 (monoclonal antibody to macrophages) expression was assessed in the macrophages within the muscle tissue.
(3) Cytoplasmic CD105 (transforming growth factor-beta 1/3 receptor, endoglin) expression was evaluated in vascular endothelial cells, conjunctival epithelium and the lymphocytes within the inflammatory infiltrate of the muscles.
(4) Cytoplasmic b-FGF (basic fibroblast growth factor) expression was specified in vascular endothelial cells, conjunctival epithelium and the lymphocytes within the inflammatory infiltrate of the muscles.

Statistical Analysis

Collected data were analyzed with the Statistical Package for Social Sciences version 11 (SPSS Inc, Chicago, IL). Mann–Whitney *U* and Wilcoxon Signed-Rank tests were used to detect any differences between the groups. Whenever statistical significance was identified, Kruskal–Wallis Variance Analysis and Friedman Variance Analysis were performed to find the different group. $p \leq 0.05$ was accepted to be statistically significant.

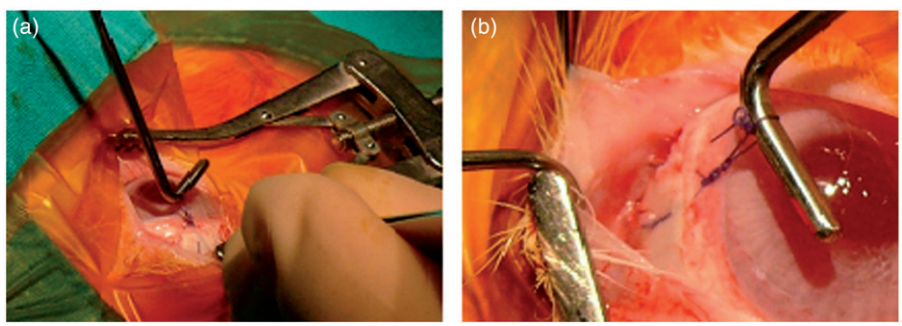

FIGURE 2 (a) A loop handle was prepared at the end of the suture which was put over the superior rectus muscle. (b) The push pull gauge was used to grasp the loop handle and the superior rectus muscle was moved as close as possible to the original insertion area.

RESULTS

Mechanical Evaluation

Adhesions between the Conjunctiva and the SRM
For all of the suramin, genistein, collagen matrix, DMSO and BSS groups, the number and severity of the adhesions between the conjunctiva and the SRM increased progressively throughout the study period. For all of these groups, the severity of the adhesions between the conjunctiva and the SRM was significantly higher at day 7 than at day 2. The adhesions between the conjunctiva and the SRM were significantly fewer in the collagen matrix and suramin groups (Table 1).

Adhesions between the Sclera and the SRM
For all of the study groups, the number and severity of the adhesions between the sclera and the SRM increased progressively throughout the study period. For all of these groups, the severity of the adhesions between the sclera and the SRM was significantly higher at day 7 than at day 2. The adhesions between the sclera and the SRM were significantly fewer in the genistein and DMSO groups (Table 2).

Assessment of Adjustability
The SRM could be adjusted in all groups on day 2 and day 7, and it was possible to make adjustments in all the eyes except one eye in the genistein group on day 14. All of the study groups were statistically similar in the aspect of the force exerted for adjustment on day 2 and day 7. However, the force exerted for adjustment was statistically lower in the suramin and collagen matrix groups on day 14 (Table 3).

Histopathological Findings

HE staining revealed that all of the study groups were statistically similar in the aspect of inflammation ($p = 0.148$). The genistein group had the least number of giant cells, and among all the groups, only this group revealed a statistically significant difference with respect to the BSS group in the aspect of giant cells (1.3 ± 1.5 versus 4.0 ± 5.3; $p = 0.007$).

Immunohistochemical Findings

Expression of Basic Fibroblast Growth Factor
Expression of basic fibroblast growth factor (b-FGF) was significantly lower in conjunctival epithelium of the suramin and genistein groups ($p = 0.0001$ and $p = 0.0001$, respectively) compared with the BSS, DMSO and collagen matrix groups. Compared with the BSS, DMSO, collagen matrix and suramin groups, the expression of b-FGF was significantly lower in the vascular endothelium and stromal infiltrate of the genistein group ($p = 0.0001$) (Table 4) (Figure 3).

Expression of VEGF
Expression of VEGF was completely absent in the conjunctival epithelium of the suramin group. The DMSO, genistein, BSS and collagen matrix groups revealed statistically similar VEGF expressions ($p = 0.608$). Compared with the BSS, DMSO and collagen matrix groups, VEGF expression was significantly lower in the vascular endothelium of the genistein and suramin groups ($p = 0.0001$). The stromal infiltrate of the genistein group also showed a significantly lower expression compared with the DMSO, BSS, suramin and collagen matrix groups ($p = 0.008$) (Table 4) (Figure 4).

Expression of Beta-Transforming Growth Factor
Expression of transforming growth factor-β (TGF-β) was significantly lower in the conjunctival epithelium of the suramin group compared with the collagen matrix, DMSO, genistein and BSS groups ($p = 0.001$). The vascular endothelium of the collagen matrix group disclosed a significantly lower expression compared with the DMSO, BSS, suramin and genistein groups ($p = 0.05$). The collagen matrix, BSS, genistein, suramin and DMSO groups revealed similar TGF-β expressions within the stromal infiltration tissues ($p = 0.734$) (Table 4).

TABLE 1 Adhesions between conjunctiva and superior rectus muscle.

Groups	Mean adhesion scores			p^b
	Day 2	Day 7	Day 14	
Collagen matrix ($n = 6$)	0.83 ± 0.40	1.50 ± 0.83	2.66 ± 0.81	0.017*
Suramin ($n = 6$)	0.80 ± 0.44	2.20 ± 0.44	3.40 ± 0.54	0.033*
Genistein ($n = 6$)	1.16 ± 0.40	3.10 ± 0.75	3.66 ± 0.51	0.006*
Balanced salt solution ($n = 12$)	1.75 ± 0.62	2.75 ± 0.62	3.58 ± 0.51	0.0001*
Dimethyl sulphoxide ($n = 6$)	1.33 ± 0.51	3.0 ± 0.0	3.33 ± 0.51	0.004*
p^a	0.007*	0.002*	0.104	

[a]Kruskal–Wallis variance analysis was performed.
[b]Friedman variance analysis was performed.
*$p < 0.05$ was accepted to be statistically significant.

Expression of MAC 387

The expression of MAC 387, an indicator of macrophages within the muscle tissue, was significantly lower in the genistein and suramin groups compared with the BSS, DMSO and collagen matrix groups (52.5 ± 39.3 versus 28.5 ± 17.1 versus 25.8 ± 7.8 versus 28.5 ± 17.1 versus 12.6 ± 9.9 versus 10.6 ± 2.5; $p = 0.0001$ for all groups) (Figure 4).

DISCUSSION

The findings in the present study show a significantly delayed ocular wound closure with suramin, genistein and collagen matrix in an in vivo model. This rabbit study, which closely resembled the adjustable suture technique used in strabismus surgery, showed that all three had potential value for adoption in strabismus surgery by means of postponing adjustment.

There is still ongoing research to find the ideal anti-adhesive and anti-fibrotic material that would enable the surgeon to delay adjustment as long as possible until the edema and inflammation were resolved, so that alignment was further stabilized after strabismus surgery. In the present study, in an attempt to investigate and compare the efficacy of suramin, genistein and collagen matrix (DuraGen®), the healing and scarring process following the superior rectus recession in rabbits has been demonstrated. After subsequent re-adjustments were made, the adjustability of the SRM, the force exerted for adjustment and the adhesions between the SRM and the conjunctiva or sclera were evaluated.

Several studies have investigated different types of chemical agents that can be used for delayed adjustment after strabismus surgery. Mitomycin-C and 5-fluorouracil are two antiproliferative agents which have been used to control the healing process after strabismus surgery. Hwang and Chang demonstrated that the combination of polytetrafluoroethylene and 5-fluorouracil or the addition of viscoelastic agent would allow the delay of adjustment for up to 4 weeks after surgery in 80% of experimental eyes.[3] Significant reduction was observed in the fibroblasts and the proliferation of collagen fibers after applying mitomycin-C at the surgical area during the recession of the SRM.[4]

In contrast to these highly toxic drugs, the present study investigates the efficacy of suramin and genistein. Suramin has been frequently used for trabeculectomy and recently has been demonstrated to decrease the amount of collagen type I and collagen type III.[9–11] Genistein is a natural flavonoid and the major component of soybean. This particular molecule exerts varying effects at different concentrations,

TABLE 2 Adhesions between sclera and superior rectus muscle.

	Mean adhesion scores			
Groups	Day 2	Day 7	Day 14	p^b
Collagen matrix ($n = 6$)	0.83 ± 0.40	1.50 ± 0.83	1.83 ± 0.75	0.040*
Suramin ($n = 6$)	0.80 ± 0.44	2.00 ± 0.70	1.60 ± 0.54	0.025*
Genistein ($n = 6$)	0.16 ± 0.40	0.83 ± 0.40	2.50 ± 1.37	0.011*
Balanced salt solution ($n = 12$)	1.00 ± 0.60	1.83 ± 0.71	2.33 ± 1.07	0.022*
Dimethyl sulphoxide ($n = 6$)	0.16 ± 0.40	0.66 ± 0.51	1.16 ± 0.40	0.002*
p^a	0.010*	0.006*	0.113	

[a]Kruskal–Wallis variance analysis was performed.
[b]Friedman variance analysis was performed.
*$p < 0.05$ was accepted to be statistically significant.

TABLE 3 Force exerted for adjustment.

	Force exerted for adjustment (g/mm)			
Groups	Day 2	Day 7	Day 14	p^b
Collagen matrix ($n = 6$)	23.16 ± 7.70	31.41 ± 7.90	29.68 ± 8.31	0.065
Suramin ($n = 6$)	17.00 ± 3.46	25.50 ± 5.25	32.75 ± 8.53	0.016*
Genistein ($n = 6$)	13.20 ± 4.14	36.88 ± 7.50	58.16 ± 25.08	0.015*
Balanced salt solution ($n = 12$)	16.58 ± 6.31	29.33 ± 10.36	53.44 ± 16.42	0.0001*
Dimethyl sulphoxide ($n = 6$)	15.00 ± 4.00	35.16 ± 9.78	41.54 ± 6.96	0.006*
p^a	0.070	0.056	0.006*	

[a]Kruskal–Wallis variance analysis was performed.
[b]Friedman variance analysis was performed.
*$p < 0.05$ was accepted to be statistically significant.

TABLE 4 Immunohistochemical findings.

Tissue expression of growth factors	Immunohistochemical findings					p^a
	DuraGen	Suramin	Genistein	Balanced salt solution	Dimethyl sulphoxide	
b-FGF						
Conjunctiva epithelium	15.8 ± 9.7	3.9 ± 7.3	1.0 ± 2.3	23.9 ± 8.3	18.7 ± 10.5	0.0001*
Vascular endothelium	37.2 ± 11.3	27.3 ± 7.6	17.5 ± 7.7	62.4 ± 11.8	54.1 ± 16.5	0.0001*
Stroma	20.0 ± 7.0	18.1 ± 12.3	14.3 ± 2.7	48.4 ± 18.5	26.3 ± 4.8	0.0001*
VEGF						
Conjunctiva epithelium	14.9 ± 11.8	00 ± 00	21.04 ± 15.5	18.8 ± 10.8	26.4 ± 15.1	0.608
Vascular endothelium	53.1 ± 15.8	19.7 ± 12.3	20.6 ± 6.2	63.4 ± 23.9	59.7 ± 21.2	0.0001*
Stroma	13.5 ± 8.1	16.3 ± 17.9	11.3 ± 5.0	25.5 ± 8.7	28.0 ± 14.2	0.008
TGF-β						
Conjunctiva epithelium	19.0 ± 6.9	0.6 ± 1.7	17.6 ± 9.0	10.7 ± 6.1	18.7 ± 8.1	0.001*
Vascular endothelium	33.6 ± 10.4	40.8 ± 26.9	40.6 ± 19.6	57.9 ± 22.3	70.1 ± 20.1	0.05
Stroma	16.0 ± 2.2	13.6 ± 8.9	14.3 ± 8.5	15.9 ± 6.0	12.5 ± 3.9	0.734

[a]Kruskal–Wallis variance analysis was performed.
*$p < 0.05$ was accepted to be statistically significant.

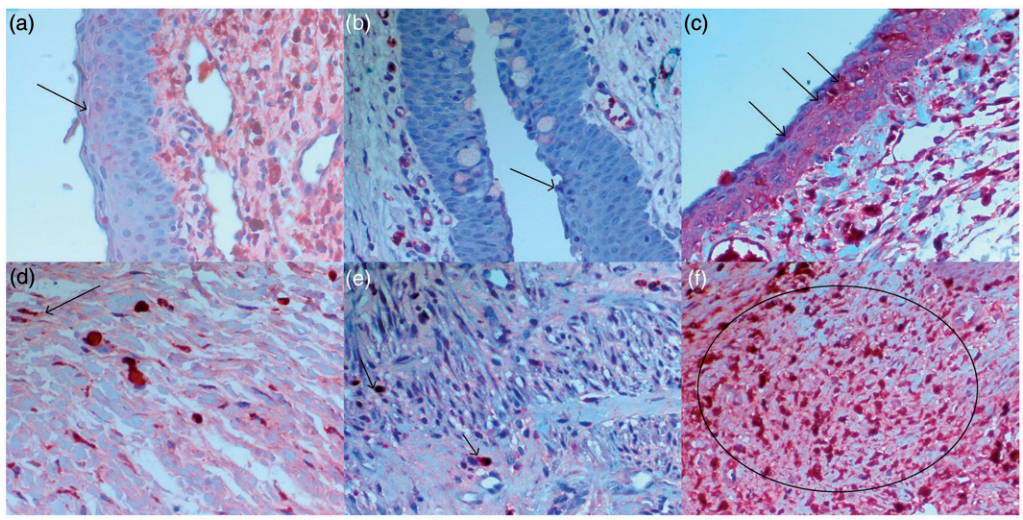

FIGURE 3 The expression of b-FGF was indicated by black arrows and ring. (a) The expression of b-FGF in conjunctival epithelium in suramin group. (b) The expression of b-FGF in the conjunctival epithelium in the genistein group. (c) The expression of b-FGF in the conjunctival epithelium in the BSS group. (d) The expression of b-FGF in the stromal infiltrate of the suramin group. (e) The expression of b-FGF in the stromal infiltrate of the genistein group. (f) Diffuse b-FGF expression in the stromal infiltrative cells in the BSS group.

including the inhibition of angiogenesis, phosphorylation of tyrosine kinase, DNA synthesis and cell cycle arrest at the S phase.[12]

The findings of the present study indicate a statistically significant reduction in the number and severity of adhesions between the conjunctiva and the SRM in the suramin group. A similarly significant decrease was noted for the adhesions between the sclera and the SRM in the genistein group and the number of giant cells was significantly less in rabbit eyes that received genistein. Flavonoids and isoflavonoids impair migration and proliferation and three dimensional orientation of vascular endothelial cells due to non-specific inhibition of tyrosine kinases. The induction of apoptosis as well as cell cycle arrest that has been shown for genistein may play a role for reducing scleral adhesions.[12] Suramin specifically inhibits the production of collagen synthesis by Tenon's capsule and collagen matrix acts as a physical barrier between the conjunctiva and the muscle, so these two agents were more effective in decreasing the conjuntival adhesion.[15]

Dimethyl sulfoxide is a highly polar organic liquid that is widely used as a chemical solvent. Because of its ability to penetrate biological membranes, it is used as a vehicle for the topical application of pharmaceuticals.[16] Dimethyl sulfoxide also shows a range of pharmacological activity, including analgesia and anti-inflammation.[17] Several studies have documented DMSO use with soft tissue damage, local

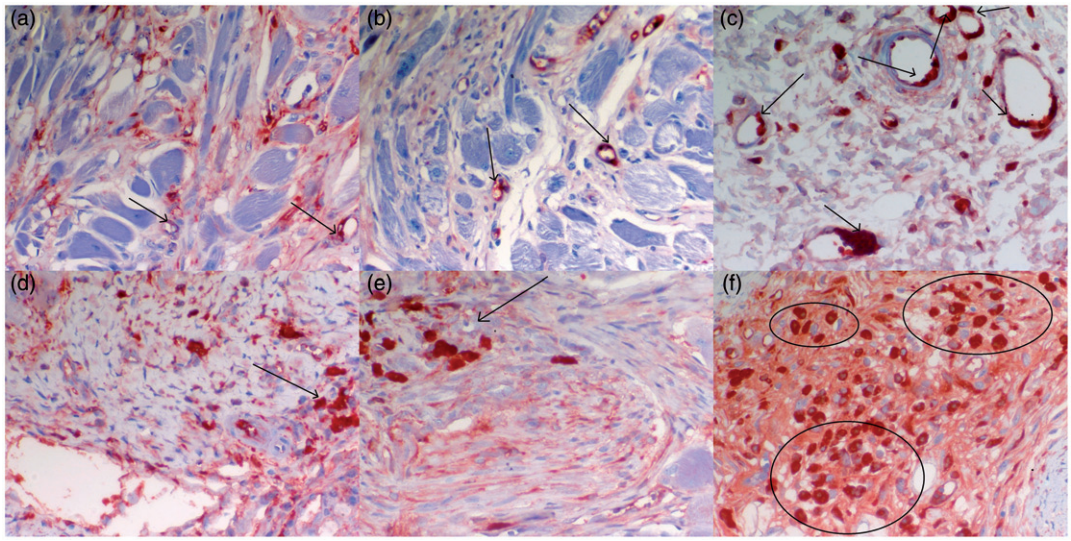

FIGURE 4 The expression of VEGF and MAC 387 was indicated by black arrows and rings. (a) VEGF expression in the vascular endothelium of the suramin group. (b) VEGF expression in the vascular endothelium of the genistein group. (c) VEGF expression in the vascular endothelium of the BSS group. (d) The expression of MAC 387 in the suramin group. (e) The expression of MAC 387 in the genistein group. (f) Diffuse expression of MAC 387 in the BSS group.

tissue death, skin ulcers and burns.[18] DMSO reduces inflammation by several mechanisms. It is an antioxidant, a scavenger of the free radicals that gather at the site of injury.[19] Therefore, the dimethyl sulfoxide group is not only a control group, but it has also been investigated for its anti-inflammatory properties.

Immunohistochemically, there was considerably less expression of b-FGF, VEGF, TGF-β and MAC 387 in both the suramin and genistein groups. These findings imply that suramin and genistein hinder the fibrosis and scarring process by affecting the cytokines. However, long-term mechanical results did not support the clinical effectiveness of the anti-fibrotic effects of genistein.

Choi and co-workers applied a gel consisting of polyglycan ester in a gelatin matrix (ADCON-L®) and it was found that adjustment was possible in all eyes at day 4 and day 7 after surgery.[5] Kim and colleagues showed that polyurethane film with and without sustained release dexamethasone could delay adjustment for up to six weeks after strabismus surgery.[6] Choung and Hwang claimed that a synthetic polylactide and polyglycolide copolymer membrane (SurgiWrap®) could successfully prevent adhesions.[7] Lee et al. reported that slow-releasing tranilast in polytetrafluoroethylene/polylactide-co-glycolide laminate provided a five-week-long delay in adjustment in rabbits undergoing adjustable suture surgery.[8]

Similarly, the present study questions whether collagen matrix can be used to prevent fibrosis and scarring in ocular tissue after strabismus surgery. In the DuraGen group, the adhesions between the conjunctiva and the SRM were reduced significantly and it was significantly easier to achieve adjustability. However, apart from the decrease in the expression of TGF-β, no significant alterations could be detected in the histopathological and immunohistochemical characteristics of the rabbit eyes treated with collagen matrix. Thus, it can be hypothesized that collagen matrix prevents postoperative adhesions, probably by mechanical inhibition of the fibroblastic migration.

The findings of the present study are limited by the relatively small number of rabbit eyes that were treated with suramin, genistein and collagen matrix, stemming from unsuitable laboratory conditions that precluded the inclusion of more animals in the study. Also for this reason, adjustments were made subsequently within the same ocular tissue and, thus, the scores and measurements were biased by the previous interventions. During study intervention, serial measurements were made on days 2, 7 and 14 after surgery. The adhesions were assessed and broken down at each time point and the muscle adjusted in the same eyes. This meant that the healing process effectively started again after each time point, but probably with increased inflammation because of the repeated tissue disruption caused by the intervention. Nevertheless, a statistically significant reduction in the number and severity of adhesions between surgically involved tissues was noted with all three agents.

In conclusion, the results of our studies suggest that suramin, genistein and collagen matrix successfully inhibit postoperative adhesions and facilitate adjustment following recession surgery. Both suramin and genistein effectively hinder fibrosis and scarring at the surgical area and collagen matrix offers the longest time interval for adjustability after strabismus surgery. To the best of our knowledge, this is the first animal study held to evaluate mechanical,

histopathological and immunohistochemical findings simultaneously so that the efficacy and safety of certain agents could be identified for adjustability after strabismus surgery. Further research is warranted to clarify the efficacy of suramin, genistein and collagen matrix using adjustable sutures for strabismus surgery.

DECLARATION OF INTEREST

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

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