Effect of ADCON-L on adjustable strabismus surgery in rabbits

Mi Young Choi, Soo-Jae Auh, Dong Gyu Choi, Bong Leen Chang

Abstract

**Background/aims**—In search of a way to prevent postoperative adhesion after strabismus surgery, an animal study was performed to assess the effect of a gel consisting of a polyglycan ester in a gelatin matrix (ADCON-L).

**Methods**—Bilateral recessions of superior rectus muscle (SR) were performed on 16 rabbits. ADCON-L was applied beneath and over the SR in the right eyes of all rabbits, while the operative fields in the left eyes were irrigated with a balanced salt solution (BSS). The adjustment was performed on each SR at 4 and 7 days postoperatively on the same eye. The length and force of the adjustment and the degree of adhesion were recorded. At 3 weeks postoperatively, disinsertional force was measured in several of the eyes, and the other eyes were enucleated.

**Results**—The length of the adjustment was longer and the force of the adjustment was less in the ADCON-L group than in the BSS treated group at 4 and 7 days postoperatively (p=0.00). A significant reduction (p=0.00) in the degree of adhesion was noted in eyes treated with ADCON-L. There was no significant difference in disinsertional force between the two groups. Histopathological evaluation of the muscle revealed decreased fibrosis of perimuscular connective tissue in eyes treated with ADCON-L at 3 weeks postoperatively.

**Conclusion**—This study suggests that ADCON-L helps to prevent postoperative adhesion in rabbits and enables adjustment twice within 7 days postoperatively without complications.

Focus on the text. The present study was conducted to assess the efficacy of ADCON-L in inhibiting adhesion and to evaluate the safety of using the product in situations involving strabismus surgery.

Subjects and methods

Sixteen white rabbits of both sexes, weighing 2.0–2.5 kg, were selected for the study. The care and handling of the rabbits were in accordance with the Association for Research in Vision and Ophthalmology Resolution on the Use of Animals in Research and the policies in the “Guidelines for the Care and Use of Laboratory Animals” (National Institute of Health publication No 85–23, as revised in 1985). Each rabbit was anaesthetised with an intramuscular injection of ketamine HCl (20 mg/kg, Ketara, Yukan, Kunpo, Korea) and xylazine (2 mg/kg, Rompun, Bayer Korea, Seoul, Korea).

Surgery

Surgical antisepsis with polyvinylpyrrolidone-iodine (Betadine) was applied to the eyelids before each operation. After a limbal peritomy from 10 o’clock to 2 o’clock, the superior rectus muscle (SR) was isolated on a Jameson hook and intermuscular connections were dissected. The SR was then placed on a double armed 6–0 polyglactin suture (Vicryl, Ethicon, Somerville, NJ, USA) close to the insertion site and disinserted from the globe. The SR in both eyes was recessed 5 mm using a hangback...
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Figure 1. Photograph shows the procedure by which ADCON-L is injected after recession of superior rectus.

technique and the two sutures were tied together to make pole sutures. This technique enables easy evaluation of adhesion between the muscle and the sclera. A loop handle of 6–0 polyglactin suture was made around the pole sutures for future traction. ADCON-L of about 1 ml was applied around SR in the right eyes (Fig 1) and the same amount of a balanced salt solution (BSS, Alcon, Fort Worth, TX, USA) was irrigated around the SR in the left eyes. The edges of the conjunctival peritomy were approximated with two simple interrupted 6–0 polyglactin sutures. At the end of each procedure, ofloxacin ointment was applied topically and 2 mg of gentamicin was injected in the thigh muscle.

POSTOPERATIVE PROCEDURES

Adjustment

Four days postoperatively, the animals were reanaesthetised and operated on for adjustment in a randomised, masked fashion. A wide limbal peritomy from 8 o’clock to 4 o’clock was performed and each SR was adjusted. A dial tension gauge (DT-50, Teclock, Japan) or push-pull gauge (PP-705, 5 g, 500 g, Teclock, Japan) was used to grasp the loop handle of the sutures connected to the muscle. The SR was moved anteriorly as much as possible, and the necessary force was measured with the gauge. A Castroviejo caliper was used for measurement of the length of adjustment. The length of adjustment was defined as the advanced distance from the recessed site. After the force and length of the adjustment were recorded each advanced SR was repositioned to the recessed site. The edges of the conjunctival peritomy were approximated with two simple interrupted 6–0 polyglactin sutures.

Seven days postoperatively, the rabbits were reanaesthetised and each SR was adjusted with the same procedure. The force and length of the adjustments were recorded. After the muscle was advanced, the separated pole sutures were tied together to permanently secure the muscle. The edges of the conjunctival peritomy were approximated with two simple interrupted 6–0 polyglactin sutures. Postoperative care consisted of a daily application of ofloxacin ointment for 3 days after each procedure.

Evaluation of adhesions

At the times of adjustment, adhesion between the muscle, sclera, and conjunctiva was evaluated and recorded. The adhesion was classified as SR/C (SR/conjunctiva) if it was located above the SR and SR/S (SR/sclera) when located below the SR. The severity of the adhesion was scored on a scale from 0 to 4, where 0 = no adhesion, 1 = adhesion easily separable with blunt dissection with cotton tip applicator, 2 = mild adhesion with freely dissectible plane, 3 = dense adhesion with difficult dissection, and 4 = non-dissectible plane.

Measurement of disinsertional force

Three weeks postoperatively, 4–0 black silk was threaded through the SR close to the new insertion point and grasped by the push-pull gauge in 13 rabbits. The push-pull gauge was used to pull the 4–0 black silk until disinsertion of the SR from the sclera was achieved. Disinsertional force, defined as the force necessary to disinsert the SR, was measured and recorded.

HISTOLOGICAL EXAMINATION

One rabbit was sacrificed at postoperative 4 days, 7 days and 3 weeks and eyeballs including SR and conjunctiva were enucleated. The eyeball was examined microscopically using haematoxylin and eosin staining. Masson’s trichrome staining was also performed to evaluate the degree of fibrous proliferation.

STATISTICAL ANALYSIS

A statistical analysis was performed to determine the effect of ADCON-L in preventing adhesion and delaying adjustment. The length of advancement, the force necessary for adjustment, and the disinsertional force were analysed using Student’s $t$ test. The severity of the adhesions was analysed using Wilcoxon rank sum test.

Results

ADJUSTABILITY

At 4 days postoperatively, an adjustment was possible in all eyes treated with ADCON-L or BSS. At 7 days postoperatively, an adjustment was possible in all eyes treated with ADCON-L but in only six out of 13 eyes treated with BSS (Table 1).

FORCE AND LENGTH FOR ADJUSTMENT

At 4 days postoperatively, the average force and length of the adjustments were 70.30 g and 1.75 mm, respectively, in eyes treated with BSS, and 48.00 g and 4.34 mm, respectively, in eyes treated with ADCON-L (Table 1, Fig 2). At 7 days postoperatively, the average force and length of the adjustments were 145.00 g and 1.00 mm, respectively, in eyes treated with BSS, and 79.10 g and 3.18 mm, respectively, in eyes treated with ADCON-L (Table 1, Fig 2). There were statistically significant differences in the average force and length of the adjustments between eyes treated with BSS and eyes treated with ADCON-L at 4 and 7 days postoperatively ($p=0.00$).

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Degree of adhesion

In the eyes treated with ADCON-L, the mean score for adhesion between the conjunctiva and the muscle was 0.75 at 4 days postoperatively and 1.87 at 7 days postoperatively. In the eyes treated with BSS, the mean score for adhesion between the conjunctiva and the muscle was 2.19 at 4 days postoperatively and 3.79 at 7 days postoperatively (Table 1). The mean score for adhesion between the muscle and the sclera was 0.88 at 4 days postoperatively and 2.33 at 7 days postoperatively in eyes treated with ADCON-L and 1.75 and 3.71, respectively, in eyes treated with BSS (Table 1). These results suggest that ADCON-L helped to reduce postoperative adhesion (p = 0.00).

Disinsertional force

Disinsertional force was greater in eyes treated with ADCON than in eyes treated with BSS (Fig 3, mean (SD): 431 (198) in ADCON-L group, 373 (174) in BSS treated group). However, the difference was not statistically significant (p=0.50).

Histological examination

Histological examination by light microscopy revealed less fibrosis and inflammation and no abnormality of the sclera or underlying ciliary body in eyes treated with ADCON-L (Table 1). ADCON-L could not be demonstrated in ADCON-L group.

Discussion

Adhesion following strabismus surgery often affects the postoperative outcome and makes adjustment and dissection difficult in cases of reoperation. Although Howard and Smith have been able to delay the final adjustment up to 1 week postoperatively without additional materials, a variety of materials have been used in attempts to prevent postoperative adhesion following strabismus surgery in animal studies. Among these materials are silicone, supramid, polypeptide sleeve, viscoelastics, interceed, polyglactin 910 mesh, polytetrafluoroethylene (PTFE), mitomycin-C (MMC), and 5-fluorouracil (5-FU). However, it is yet to be definitely demonstrated that these materials reduce adhesion in humans, although findings...
from one clinical study with sodium hyaluronic acid suggest that it reduces the amount of force necessary to adjust a muscle. Furthermore, occurrences of serious complications related to 5-FU after glaucoma surgery have been reported. Similarly, there are reports of severe complications after the use of MMC as a medical adjunct to pterygium and glaucoma surgery. And the marked forward migration of the muscle fibre at the later stage in MMC migration of fibroblasts in vitro. It is therefore the present study to evaluate the establishment of an inhibitory barrier to invading fibroblasts in vivo. ADCON-L contains a carbohydrate polymer that has been shown to block the migration of fibroblasts in vitro. It is therefore possible that ADCON-L acts in vivo by establishing an inhibitory barrier to invading fibroblasts, which results in less adhesion.

The precise mechanism by which ADCON-L reduces adhesion remains unclear. It has been shown that the glycosaminoglycan moiety of certain proteoglycans can establish boundaries for cellular migration both in vitro and in vivo. ADCON-L contains a carbohydrate polymer that has been shown to block the migration of fibroblasts in vitro. ADCON-L acts in vivo by establishing an inhibitory barrier to invading fibroblasts, which results in less adhesion.

Although there was no statistical difference, disinsertional force was greater in the disinsertional group at 3 weeks postoperatively whereas ADCON-L remained in the operative field at 4 days postoperatively whereas ADCON-L was found to be effective and safe adjunct to adjustable strabismus surgery. Therefore, we performed a readjustment to assess its ability to facilitate adjustment in the same eye at 7 days postoperatively. However, we can not extrapolate the results of this study to those of an experiment in which the first adjustment had been performed at 7 days postoperatively.

Rabbits have little subconjunctival connective tissue, so the original recession surgery was performed with little bleeding. It therefore seems quite possible that the operative procedures in rabbit eyes would induce less adhesion postoperatively than in human eyes after strabismus surgery. In humans, it is essential to achieve complete haemostasis before applying ADCON-L to obtain its maximum effect.

In conclusion, ADCON-L is of potential value in the prevention of adhesion and may be used as a means of providing two adjustments without complication for as long as 1 week after extraocular muscle surgery in rabbits.

Supported in part by a grant from the Chungbuk National University Hospital Research Fund, 2000.


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*Br J Ophthalmol* 2001 85: 80-84
doi: 10.1136/bjo.85.1.80

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