Adal-1 bioadhesive for sutureless recession muscle surgery: a clinical trial

M E Mulet, J L Alió, M M Mahiques, M M Mahiques and J M Martín

doi:10.1136/bjo.2005.076497

Updated information and services can be found at:
http://bjo.bmjournals.com/cgi/content/full/90/2/208

These include:

References
This article cites 19 articles, 3 of which can be accessed free at:
http://bjo.bmjournals.com/cgi/content/full/90/2/208#BIBL

Rapid responses
You can respond to this article at:
http://bjo.bmjournals.com/cgi/eletter-submit/90/2/208

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Topic collections
Articles on similar topics can be found in the following collections

- Ophthalmology (1572 articles)
- Experimental Medicine (521 articles)
- Other ophthalmology (2373 articles)

Notes

To order reprints of this article go to:
http://www.bmjournals.com/cgi/reprintform

To subscribe to British Journal of Ophthalmology go to:
http://www.bmjournals.com/subscriptions/
S trabismus surgery requires suture for the recession or resection of the extraocular muscles of the eye. Several types of suture materials have been used in strabismus surgery such as silk, Dexon, Vicryl, and nylon, each with limitations. One of the most severe complications of the suture technique are scleral perforations, which may be caused by the needles used in the procedures, because of the difficult technique in which the points of suture are occasionally placed retroequatorially. The possibility of intolerance to these materials or induction of granulomas caused by foreign body reaction exists and has been reported. Research into new substances and materials to be used as an alternative to sutures is not new. Adhesives have been used in ophthalmic surgery and in particular in strabismus surgery, with both biological and synthetic adhesives.

Adal-1 bioadhesive for sutureless recession muscle surgery: a clinical trial

M E Mulet, J L Alió, M M Mahiques, J M Martín

Aims: To evaluate the efficacy and biotolerance of the Adal-1 adhesive for muscle sealing in strabismus surgery.

Methods: 27 eyes were included in the study: 17 in the control group and 10 in the study group. Surgery was performed on the recession of the horizontal rectus muscles. In the control group the muscle was joined to the sclera by a Vicryl 7/0 suture. In the study group, the Adal-1 adhesive was used instead. The efficacy of the sealing of the muscle to the sclera and the biotolerance of the surrounding tissues were evaluated.

Results: The muscular recession in the control group was 8.17 (SD 2.38) with displacement of the sealing point of 0.02 (1.7) mm. In the group sealed with adhesive, the muscular recession was 9.09 (3.08) and the displacement was 0.15 (1.56) mm, with no significant differences between the techniques (p<0.05). The infiltration of the surrounding tissues in the immediate postoperative period was greater with the suture technique (p>0.05), but there were no differences in the other postoperative periods (Mann-Whitney U test).

Conclusion: Adal-1 was an effective and safe alternative to sutures in muscle recession for strabismus surgery in this study.

MATERIAL AND METHODS

Following the ethics committee and Spanish Ministry of Health approval, we started an observational, consecutive, prospective randomised clinical trial. In all, 27 eyes were included in the study, with 14 male and 13 female patients with a mean age of 27 years (range 18–76 years). Only one eye and one muscle of each patient was operated. In all cases, informed consent was obtained. Inclusion criteria included patients that required strabismus surgery for the horizontal rectus muscle recession. Fourteen recession surgeries were carried out in the medial rectus and 13 in the lateral rectus muscle.

Material

The study eyes were divided into two groups.

Group I (control group)

The technique within this group was muscle sutured to the sclera with polyglactin 7/0 (Vicryl, Ethicon, Brussels, Belgium) and then suture using the hangback technique (17 eyes).

Group II

The technique within this group was muscle sealed to the sclera using Adal-1 adhesive (10 eyes).

Adal-1 adhesive is a two part adhesive that consists of a mixture of ethyl cyanoacrylate and ethyl carboxyacrylate (fig 1). Ethyl cyanoacrylate was synthesised in three consecutive stages: (1) Knoevenagel reaction between ethyl cyanoacetate and p-formaldehyde in the presence of piperidinium chloride as a base catalyst, (2) depolymerisation by heating with a flame under low pressure, and (3) purification by low pressure distillation.
Ethyl carboxyacrylate is obtained by acid hydrolysis of ethyl cyanoacrylate.

The new Adal-1 adhesive formulation contains a new acrylic derivative, ethyl carboxyacrylate, which acts as a plastifer improving flexibility and producing less exothermal reaction and reduced toxicity. Polymerisation is relatively short, it provides good immediate adhesion to eye tissues, and the adhesive mixture is not as stiff as ethyl cyanoacrylate.

The adhesive mixture should be prepared within 1 hour of application onto the tissues. If this time is exceeded, the adhesive properties of the product may be modified with a resulting reduction in adhesive capacity and in the strength of tissue sealing.

For preservation, it is important to keep the two acrylic compounds in separate containers, out of light, free from humidity and, ideally, in a temperature range of between 5°C and 15°C.

**Surgical technique**

Following peribulbar anaesthesia with a 5 ml mixture of bupivacaine 0.75% and lidocaine 2%, a conjunctival dissection was carried out with Wescott scissors (Moria, France) and muscular capture was performed with a rectus muscle hook (Moria). Following calculation for recession measurement, the recession of the muscle was carried out with recession of the Tenon layer. Given that this procedure was experimental, and in order to guard against inadvertent loss of the muscle, we devised a technique that utilised a “safety handle.” This safety procedure was carried out to avoid muscular retraction to the muscular cone, where recapture would be very difficult or even impossible, in case the adhesive did not achieve sufficient sealing. This safety handle was 10 mm longer than the corresponding retroinsertion to be performed and was created with polyglyactin 7/0 (Vicryl) suture at the edge of the muscle, and was sutured to the sclera (hangback technique)

In order to attach the rectus muscle to the sclera, we carefully dried the scleral area and one drop of the Adal-1 adhesive was applied to both the sclera and the tip of the sectioned muscle with a 25 gauge cannula (Steriseal, UK) (fig 2). The two parts were then joined and pressed against each other for approximately 30 seconds until the start of the prepolymerisation was observed and minimal residue appeared around the side of the muscle when the adhesive was pressed (fig 3). At the site of the junction of the muscle to the sclera, one nylon 10/0 stitch (Alcon, Fort Worth, TX, USA) was placed in the centre of the end of the muscle and could be seen through the conjunctiva.

In the suture group the corresponding retroinsertion was performed with polyglyactin 7/0 suture at the edge of the muscle, and was sutured to the sclera (hangback technique), without a safety handle. At the site of the junction of the muscle to sclera, in the centre of the muscle, one nylon 10/0 stitch was placed and the distance of the nylon suture knot to limbus was intraoperatively measured by callipers (Asico, AE-1500 Germany) (fig 4).

We evaluated muscle sealing to the sclera and also the presence of muscular displacement from the initial sealing area. We measured this distance in all postoperative visits. The presence of conjunctival ulceration caused by the polymerised spicules of the adhesive, and inflammation (conjunctival injection, oedema, erosion, and secretion) were observed on all visits (table 1). Fundus ophthalmoscopy was carried out to ascertain the presence of areas of retinal whitening or scleral burns and/or needle perforation. The eyes were followed up for 3 months after the procedure.

In the immediate postoperative period, 1% dexamethasone drops were applied three times a day for 15 days. Ocular
surface inflammation was graded according to an ocular surface inflammatory index previously published by Alio et al. Values for this index were obtained at 1–3 days, 1 month, and 3 months after the procedure. The clinical follow up was evaluated by an independent observer who applied the bioadhesives or performed the suture in the strabismus surgery.

The results were analysed using SPSS 10.1 non-parametric Mann-Whitney U test. Statistical significance was considered when p ≤ 0.05. A normal distribution test was carried out in each group. In order to measure relevance, the Mann-Whitney statistics and the related confidence interval (CI) were used to compare different groups. A two sided 95% CI was chosen in this study design.

RESULTS

In group I, 17 eyes (11 medial rectus and six lateral rectus) were included. The mean muscular recession was 8.17 (2.38) mm ranging between 5.5 mm and 13 mm. In group II, a total of 10 eyes were included (three cases of medial rectus surgery and seven cases of lateral rectus surgery). The mean muscle recession in this group was 9.9 (3.08) mm, ranging between 5 mm and 14 mm.

The clinical findings in group I (Vicryl 7/0 sutures) showed a mean displacement of 0.02 (SD 1.7) mm (5 mm less than desired and 2 mm more than desired) from the nylon 10/0 suture (Alcon, Forth Worth, TX, USA) that was used as a reference. In all cases, the operated muscles were correctly attached to the sclera by Vicryl suture. No eyes showed suture breaking.

The degree of inflammation was evaluated in the immediate postoperative period, at 1–3 days, 1 month, and 3 months. In group I, the complications included the appearance of a granuloma caused by the suture in three cases (17.6%), one in the nasal sector and two in the temporal sector. In the three cases of granuloma, the patients reported a significant degree of discomfort during the postoperative period (table 1).

In group II (Adal-1 tissue adhesive), in 100% of the muscles, the adhesive was effective in fixing the muscles to sclera in the desired position. There was a mean displacement from the reference nylon suture of 0.15 (1.56) mm. The range was from 2 mm less than desired to 2.5 mm more than desired. Two cases of granuloma were observed. These were caused by the protrusion of the Vicryl safety suture and not by foreign body sensation and there were no cases of pain (table 1).

The degree of displacement of the muscles between the two groups was not statistically significant, p = 0.459 (Mann-Whitney U test).

There were no statistically significant differences between the groups regarding the degree of inflammation, which is more likely to be as a result of the surgery than to the sealing technique or the sealing of the muscle to the sclera. There were differences in the immediate postoperative period, with a greater degree of conjunctival irritation in the control group (p = 0.040), at 1 month (p = 0.868) and at 3 months (p = 0.089). There were no statistically significant differences between the two groups in the other inflammatory parameters studied (oedema, secretion, ulceration) during the periods studied. There were no cases of scleral perforation, whitening, or scleral or retinal burn in the Adal adhesive group.

DISCUSSION

Strabismus surgery is one of the most frequent surgeries that takes place in the paediatric age group. In most eyes, the surgical technique includes muscle resection/recession together with suturing of the muscle(s) usually with reabsorbable sutures. The use of sutures in strabismus surgery results in complications related to the suture material itself. In cases in which the shortening and thus the

<table>
<thead>
<tr>
<th>Table 1 Inflammatory index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td><strong>Group 1</strong></td>
</tr>
<tr>
<td>Sutured</td>
</tr>
<tr>
<td>Not sutured</td>
</tr>
<tr>
<td>Displaced</td>
</tr>
<tr>
<td>Conjunctival injection</td>
</tr>
<tr>
<td>Abs-mild</td>
</tr>
<tr>
<td>Mild-mod</td>
</tr>
<tr>
<td>Mod-sev</td>
</tr>
<tr>
<td>Conjunctival oedema</td>
</tr>
<tr>
<td>Abs-mild</td>
</tr>
<tr>
<td>Mild-mod</td>
</tr>
<tr>
<td>Mod-sev</td>
</tr>
<tr>
<td>Ulceration</td>
</tr>
<tr>
<td>Secretion</td>
</tr>
<tr>
<td>Complications</td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
</tr>
<tr>
<td>Adal-1</td>
</tr>
<tr>
<td>1–3 days</td>
</tr>
<tr>
<td>Sealed</td>
</tr>
<tr>
<td>Displaced</td>
</tr>
<tr>
<td>Conjunctival injection</td>
</tr>
<tr>
<td>Abs-mild</td>
</tr>
<tr>
<td>Mild-mod</td>
</tr>
<tr>
<td>Mod-sev</td>
</tr>
<tr>
<td>Conjunctival oedema</td>
</tr>
<tr>
<td>Abs-mild</td>
</tr>
<tr>
<td>Mild-mod</td>
</tr>
<tr>
<td>Mod-sev</td>
</tr>
<tr>
<td>Ulceration</td>
</tr>
<tr>
<td>Secretion</td>
</tr>
<tr>
<td>Discomfort</td>
</tr>
<tr>
<td>Complications</td>
</tr>
</tbody>
</table>
Neither anterior nor posterior scleral whitening was observed, confirming the minimal degree of exothermal reaction produced by the adhesive mixture. Adal-1 was previously tested on an animal model.\textsuperscript{5} In addition, a small amount of the adhesive was applied in the procedures.\textsuperscript{5, 10} Efficacy was 100% in both groups and in all cases of interoperative sealing. The muscle-sclera junction created with Adal-1 was able to withstand greater or equal tensile strength (for different ocular movements) than sutures.\textsuperscript{5, 12} A minimum contact time between the adhesive and the muscle-sclera junction was necessary to imitate prepolymerisation for it to be effective.

A second surgery was required in three eyes of the bioadhesive group as a result of undercorrection. Fibrosis, muscle structural changes, or an alteration of the surrounding tissues were not observed when the conjunctiva was retracted to start the surgery. Muscle dissection was easy and no remnants of the polymerised adhesive were seen 3 months after the initial surgery, confirming the total macroscopic absorption of the adhesive.\textsuperscript{10, 11, 19, 21}

This is the first study carried out on humans and confirms the good results of the previous experimental studies on animal models,\textsuperscript{5, 11} such as its good biotolerance in the surrounding tissues and minimal tissue toxicity,\textsuperscript{19} proving that Adal-1 adhesive is an effective and safe alternative to suture in strabismus surgery. Moreover, it facilitates the surgical technique of recession surgery and shortens surgical time. Tissue adhesives can also be used in cases of intolerance to suture materials. Further studies are needed to ascertain the effectiveness of the new bioadhesive in muscle resection strabismus surgery.

Authors’ affiliations
M E Mulet, J L Alió, Ophthalmology Department, Miguel Hernández University, Alicante, Spain
M E Mulet, J L Alió, M M Mahiques, Research and Development Department, Vissum Instituto Oftalmologico de Alicante, Spain
M M Mahiques J M Martin, Biomaterials Department, Alicante University, Alicante, Spain

This study has been financed in part by an IBEROEA/FIS 95/1.487 grant from the Spanish Ministry of Health, Instituto de Salud Carlos III and the Red Temática de Investigación Cooperativa en Oftalmologia, Subproyecto de Superficie Ocular, (C03/13).

The authors have no financial interest in any of the issues contained in this article and have no proprietary interest in the development or marketing of the products or medical equipment used in this study.

REFERENCES
Clinical Evidence—Call for contributors

Clinical Evidence is a regularly updated evidence-based journal available worldwide both as a paper version and on the internet. Clinical Evidence needs to recruit a number of new contributors. Contributors are healthcare professionals or epidemiologists with experience in evidence-based medicine and the ability to write in a concise and structured way.

Areas for which we are currently seeking contributors:

- Pregnancy and childbirth
- Endocrine disorders
- Palliative care
- Tropical diseases

We are also looking for contributors for existing topics. For full details on what these topics are please visit www.clinicalevidence.com/ceweb/contribute/index.jsp

However, we are always looking for others, so do not let this list discourage you.

Being a contributor involves:

- Selecting from a validated, screened search (performed by in-house Information Specialists) epidemiologically sound studies for inclusion.
- Documenting your decisions about which studies to include on an inclusion and exclusion form, which we keep on file.
- Writing the text to a highly structured template (about 1500-3000 words), using evidence from the final studies chosen, within 8-10 weeks of receiving the literature search.
- Working with Clinical Evidence editors to ensure that the final text meets epidemiological and style standards.
- Updating the text every 12 months using any new, sound evidence that becomes available. The Clinical Evidence in-house team will conduct the searches for contributors; your task is simply to filter out high quality studies and incorporate them in the existing text.

If you would like to become a contributor for Clinical Evidence or require more information about what this involves please send your contact details and a copy of your CV, clearly stating the clinical area you are interested in, to CECommissioning@bmjgroup.com.

Call for peer reviewers

Clinical Evidence also needs to recruit a number of new peer reviewers specifically with an interest in the clinical areas stated above, and also others related to general practice. Peer reviewers are healthcare professionals or epidemiologists with experience in evidence-based medicine. As a peer reviewer you would be asked for your views on the clinical relevance, validity, and accessibility of specific topics within the journal, and their usefulness to the intended audience (international generalists and healthcare professionals, possibly with limited statistical knowledge). Topics are usually 1500-3000 words in length and we would ask you to review between 2-5 topics per year. The peer review process takes place throughout the year, and our turnaround time for each review is ideally 10-14 days.

If you are interested in becoming a peer reviewer for Clinical Evidence, please complete the peer review questionnaire at www.clinicalevidence.com/ceweb/contribute/peerreviewer.jsp