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Sutures *versus* new cyanoacrylates in prosthetic abdominal wall repair: a preclinical long-term study

Gemma Pascual, PhD,[a] *Marta Rodríguez, PhD,*[b] *Claudia Mesa-Ciller, PhD,*[b] *Bárbara Pérez-Köhler, PhD,*[b] *Mar Fernández-Gutiérrez, PhD,*[c] *Julio San Román, PhD, MD,*[c] *and Juan M. Bellón, PhD, MD*[b,*]

[a] *Department of Medicine and Medical Specialities, Faculty of Medicine and Health Sciences, University of Alcalá, Networking Biomedical Research Centre on Bioengineering—Biomaterials and Nanomedicine (CIBER-BBN), Alcalá de Henares, Madrid, Spain*

[b] *Department of Surgery, Medical and Social Sciences, Faculty of Medicine and Health Sciences, University of Alcalá, Networking Biomedical Research Centre on Bioengineering—Biomaterials and Nanomedicine (CIBER-BBN), Alcalá de Henares, Madrid, Spain*

[c] *Polymer Biomaterials Group, Polymer Science and Technology Institute-Consejo Superior de Investigaciones Científicas (ICTP-CSIC), Networking Biomedical Research Centre on Bioengineering—Biomaterials and Nanomedicine (CIBER-BBN), Madrid, Spain*

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ABSTRACT

Background: As an alternative to sutures, meshes used for hernia repair can be fixed using cyanoacrylate-based adhesives. Attempts to improve these adhesives include alkyl-chain lengthening to reduce their toxicity. This preclinical study compares the long-term behavior of cyanoacrylates of different chain lengths already used in hernia repair and new ones for this application.

Materials and methods: Partial abdominal wall defects were repaired using a Surgipro mesh in 18 New Zealand White rabbits, and groups were established according to the mesh fixation method: sutures (control), Glubran 2 (n-butyl), Ifabond (n-hexyl), and the new adhesives SafetySeal (n-butyl), and Evobond (n-octyl). Six months after surgery, recovered implants were examined to assess adhesive degradation, host tissue reaction, and biomechanical strength.

Results: All the cyanoacrylate groups showed good host tissue incorporation in the meshes. Macrophage responses to Glubran and Ifabond were quantitatively greater compared with sutures. Cell damage caused by the adhesives was similar, and only Glubran induced significantly more damage than sutures. Significantly lower collagen 1/3 messenger RNA expression was induced by Ifabond than the remaining fixation materials. No differences were observed in collagen expression except slightly reduced collagen I deposition in Glubran/Ifabond and collagen III deposition in the suture group. Mechanical strengths failed to vary between the suture and cyanoacrylate groups.

Conclusions: All cyanoacrylates showed good long-term behavior and tolerance irrespective of their long or intermediate chain length. Cyanoacrylate residues persisted at 6 mo,

* *Corresponding author*. Department of Surgery, Medical and Social Sciences, Faculty of Medicine and Health Sciences, University of Alcalá, Ctra. Madrid-Barcelona, Km 33,600, Alcalá de Henares, 28871 Madrid, Spain. Tel.: +34 91 8854540; fax: +34 91 8854885.
E-mail address: juanm.bellon@uah.es (J.M. Bellón).
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indicating their incomplete degradation. Biomechanical strengths were similar both for the adhesives and sutures.

Introduction

Meshes used for hernia repair can be fixed in the patient using a tissue adhesive (TA) as an alternative to the placement of sutures.[1-3] Complications attributed to the routine use of sutures for mesh fixation (both absorbable and nonabsorbable) include nerve entrapment, by its deep introduction into the surrounding tissue, resulting in chronic pain.[4,5] Thus, clinicians have turned their attention to the use of a more superficial method to fix a prosthetic material because this could improve postoperative patient comfort by avoiding the pain that sometimes follows a hernioplasty associated with the suture stitches themselves.[6,7]

So far, the most popular TAs used for implant fixation have been those of biological origin such as fibrin glues,[8-10] whereas synthetic adhesives such as cyanoacrylates have been employed on a much smaller scale.[11,12] Cyanoacrylates have multiple applications in clinical practice,[13,14] and overall, results have been good. However, there is still some reticence concerning their internal use and this is due to several reasons. The first is related to the low viscosity of cyanoacrylates, making their precise application at a given point difficult. Polymerization time is another important factor such that the rapid polymerization of an adhesive can also determine its placement in a non-desired area of the implant zone. Finally, the biodegradation of an adhesive in the host is a further characteristic to consider because toxicity and the time it remains in the tissue are not known. In an effort to improve the clinical performance of cyanoacrylate TAs and minimize their toxic effects, attempts have been made to modify their structure (by lengthening their chain) or to mix the cyanoacrylate with another product.[15]

Constant developments in the field of synthetic TAs have determined a need for preclinical studies to assess their properties and postimplant behavior. This study was designed to compare the long-term biological and mechanical behavior of several cyanoacrylates, including already marketed products and new materials, when used for abdominal hernia repair. The model used for this purpose was the extraperitoneal fixation of a high-density polypropylene mesh to repair an abdominal wall defect.

Materials and methods

Experimental animals

Eighteen male New Zealand White rabbits (mean weight 3000-3200 g) were used. The animals were housed, fed, and handled during the entire study period according to norms for experimental animals (Spanish law 32/2007, Spanish Royal Decree 53/2013, European Directive 2010/63/UE and European Convention of the Council of Europe ETS123).

The sample size in each group of our study was determined by specialist staff in biomedical statistics that was consulted when we designed the original experiment.

For this study, numbers of animals were calculated, so that results would be scientifically and statistically valid while keeping these numbers to a minimum and also avoiding unnecessary repetitions, attending to the principle of the "three R's" of animal used in the life sciences. This approach is required by law for animal research in the United States and Europe. The study protocol was approved by the Committee on the Ethics of Animal Experiments of the University of Alcalá (registered code: ES280050001165).

Surgical technique

Surgery was performed under aseptic conditions. The procedures used for anesthesia and analgesia have been described elsewhere.[16]

In 12 rabbits, two 5 × 3 cm defects were created on either side of the abdominal linea alba comprising the planes of the internal and external oblique muscles while sparing the transverse muscle and parietal peritoneum. The model used has been detailed in prior work by our group.[17] In the other six animals, a similar partial defect (PD) was created only on the right side. On the free left side, the PD was created at the moment of animal sacrifice for use as a control in the biomechanical resistance study. Hence, this control group was designated PD group. The tissue removed was discarded in all cases.

In a random manner, each defect was repaired using a high-density polypropylene mesh (Surgipro; Covidien, Mansfield, MA) that was slightly larger than the defect. Once the defect was created, the mesh was inserted through the defect to place it over the intact internal transverse muscle, tucking it under the overlying cut edges of the internal oblique muscle. The mesh patch was fixed using six polypropylene 4/0 stitches (Surgipro II; Covidien) or six drops (50 μL per drop) of each TA: Glubran 2, an n-butyl cyanoacrylate (GEM S.r.l., Viareggio, Italy); Ifabond, an n-hexyl cyanoacrylate (IFA medical, Bobigny, France); and two experimental TAs that have never been used in mesh abdominal wall repair, an adhesive (SafetySeal hereafter n-butyl; Noricum S.L., Madrid, Spain) whose major component is an n-butyl that differs from Glubran 2 in its remaining components designed to improve its elasticity, and an n-octyl cyanoacrylate (EVOBOND 060 hereafter n-octyl; Tong Shen Enterprise, Kaohsiung City, Taiwan). The six fixation points for the TAs were the four implant corners and the midpoints of the two longer implant edges. The skin was closed over each implant by placing a running polypropylene 3/0 suture.

According to this design, each of the study groups (PD, suture, Glubran 2, Ifabond, n-butyl, and n-octyl) comprised six implant samples. Implants plus surrounding tissue were collected at 180 d after implantation, and two 1.5 × 7 cm strips