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Biomechanical and histologic evaluation of two application forms of surgical glue for mesh fixation to the abdominal wall

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ABSTRACT

The use of an adhesive for mesh fixation in hernia repair reduces chronic pain and minimizes tissue damage in the patient. This study was designed to assess the adhesive properties of a medium-chain (n-butyl) cyanoacrylate glue applied as drops or as a spray in a biomechanical and histologic study. Both forms of glue application were compared to the use of simple-loose or continuous-running polypropylene sutures for mesh fixation. Eighteen adult New Zealand White rabbits were used. For mechanical tests in an *ex vivo* and *in vivo* study, patches of polypropylene mesh were fixed to an excised fragment of healthy abdominal tissue or used to repair a partial abdominal wall defect in the rabbit respectively. Depending on the fixation method used, four groups of 12 implants each or 10 implants each respectively for the *ex vivo* and *in vivo* studies were established: Glue-Drops, Glue-Spray, Suture-Simple and Suture-Continuous. Biomechanical resistance in the *ex vivo* implants was tested five minutes after mesh fixation. *In vivo* implants for biomechanical and histologic assessment were collected at 14 days postimplant. In the *ex vivo* study, the continuous suture implants showed the highest failure sample tension, while the implants fixed with glue showed lower failure sample tension values. However, the simple and continuous suture implants returned the highest stretch values. In the *in vivo* implants, failure sample tension values were similar among groups while the implants fixed with a continuous running suture had the higher stretch values, and the glue-fixed implants the lower stretch values. All meshes showed good tissue integration within the host tissue regardless of the fixation method used. Our histologic study revealed the generation of a denser, more mature repair tissue when the cyanoacrylate glue was applied as a spray rather than as drops.

1. Introduction

Biological or synthetic tissue adhesives are an alternative to the more conventional suture stitches used to fix a prosthetic material in hernia repair surgery, especially in open hernioplasty (Paajanen et al., 2011; Shen et al., 2012). The use of sutures for mesh fixation has been a topic of clinical review, as some operated patients experience post-operative pain and this pain has been attributed to the trapping of nerves by the sutures themselves (Campanelli et al., 2008).

The preferred tissue adhesives for mesh fixation are of biological origin such as fibrin glue (Nienhuijs et al., 2007; Kull et al., 2009; Fortelny et al., 2014) while synthetic adhesives such as cyanoacrylates have been used in smaller measure (Kukleta et al., 2012). Several modifications made to the structure and chain length of cyanoacrylates have made them increasingly suitable for clinical use (Quinn, 2005; Artzi et al., 2011), especially for prosthetic mesh fixation in hernia repair. Their quick and easy application to a given area and the scarce tissue trauma induced confers these adhesives several benefits over the use of sutures. Stoikes et al. (2015) compared the fixation properties of fibrin glue and suture fixation of a mesh, noting that sutures were stronger at 24 h. However, after 1 week the mesh fixation strength of the glue exceeded that of the sutures or even the strength of the tissue or mesh alone. Kull et al. (2009) compared the adhesive and strength properties of a cyanoacrylate and fibrin glue used on biologic tissues. These authors reported greater intrinsic tensile strength and resistance bonding among biologic tissues using cyanoacrylate than fibrin, justifying the use of the synthetic adhesive in surgical practice.

Despite these findings, there is still skepticism regarding the use of glue as a fixative for several reasons. For example, the low viscosity of adhesives does not allow for their precise application (Bellón et al.,

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2017). and their too quick polymerization time makes it easy to apply the adhesive in the wrong place. These drawbacks arise especially when the tissue adhesive is applied as drops, which is the most common method used. However, when the glue is applied through a nebulizer or spray, the viscosity effect and polymerization time are less limiting for its application (Druckrey-Fiskaaen et al., 2007; Brand et al., 2013). Few studies have compared these application forms (drops *versus* spray). To the best of our knowledge, only Brand et al. (2013) have examined the impacts of spraying distance and pressure on the final distribution of a fibrin glue used on meshes of varying density and pore size. These authors claimed that the optimal spraying distance was 5–8 cm, and that the prosthetic material (large or small pore size) was a determining factor for adhesive distribution.

The present pre-clinical study was designed to compare several ways of fixing a prosthetic mesh including the use of a medium-chain (n-butyl) cyanoacrylate adhesive widely used in clinical practice applied as drops or as a spray, and the use of running or loose sutures. In an *ex vivo* model, a high-density polypropylene mesh was fixed using the different methods to an excised abdominal wall and then subjected to mechanical tests. This was followed by an *in vivo* study in which we assessed the mechanical behavior and host tissue response to mesh implants fixed using the different methods.

2. Materials and methods

2.1. Experimental animals

The experimental animals for the *ex vivo* mechanical testing were adult, male New Zealand White rabbits (weighing 2.2–2.5 kg), all healthy and free of clinically observable systemic diseases. The animals were housed and maintained under stable conditions of light and temperature following the recommendations of the Guide for the Care and Use of Laboratory Animals of National and European Institutes of Health (Spanish Law 32/2007, Spanish Royal Decree 1201/2005, European Directive 2010/63/UE and European Convention of the Council of Europe ETS123). For the *ex vivo* mechanical tests, eight rabbits were obtained from the Animal Experimentation Facility of the University of Zaragoza. For the *in vivo* study conducted at the animal house of the University of Alcalá we used a further ten rabbits (mean weight 2.5 kg). All procedures were approved by the Ethics Committees for Animal Experiments of the Universities of Zaragoza (project license No. PI 01/11) and Alcalá (Ref. PROEX 161/16).

2.2. Prosthetic materials and fixation devices

Two high-density polypropylene meshes were used: *Neomesh Soft*® (DIMA, Aragón, Spain)for the *ex vivo* study and *Surgipro*® (Covidien, Mansfield, USA) for the *in vivo* study.

The fixation materials used were: 4/0 polypropylene (*Surgipro II*®, Covidien, Mansfield, MA, USA) suture thread and N-butyl-cyanoacrylate tissue adhesive (*SafetySeal*®, Noricum, Madrid, Spain).

2.3. Ex vivo study

Eight rabbits were intramuscularly anesthetized with a mixture of medetomidine (0.5 mg/kg, Medeson®; Uranovet, Barcelona, Spain) and ketamine (25 mg/kg, *Imalgene* 1000®; Merial, Barcelona, Spain). The animals were then euthanized with an overdose of intra-venous sodium pentobarbital (150 mg/kg, *Dolethal*®; Vétoquinol, Madrid, Spain) and the complete abdominal wall without skin was surgically excised. In each abdominal wall, two $3x4.5$ cm patches of *Neomesh Soft*® polypropylene mesh were placed at right angles to the midline. The distance of the meshes from the midline was 1.5 cm, beginning 3 cm below the xiphoid process.

Immediately after abdominal wall harvesting, 4 experimental groups for each of the four fixation methods were set up consisting of 12 implants per group and per 2 rabbits: GD (Glue-Drops; n = 12); GS (Glue-Spray; n = 12), SS (Suture-Simple; n = 12) and SC (Suture-Continuous; n = 12). For group GD, six drops (50 µl per drop) of cyanoacrylate glue was used to fix the meshes to the abdominal wall. For GS, this glue was applied (one 300 µl application) using a polypropylene spray diffuser (Sample Spray 2.5; Sunbox Distribution, Barcelona, Spain) at a distance of approximately 10 cm (as recommended by (Stoikes et al., 2015)). In groups SS and SC, the meshes were fixed with 4/O polypropylene suture as six surgeon's knots or by placing an uninterrupted running suture along two of the implant margins, respectively (see Fig. 1).

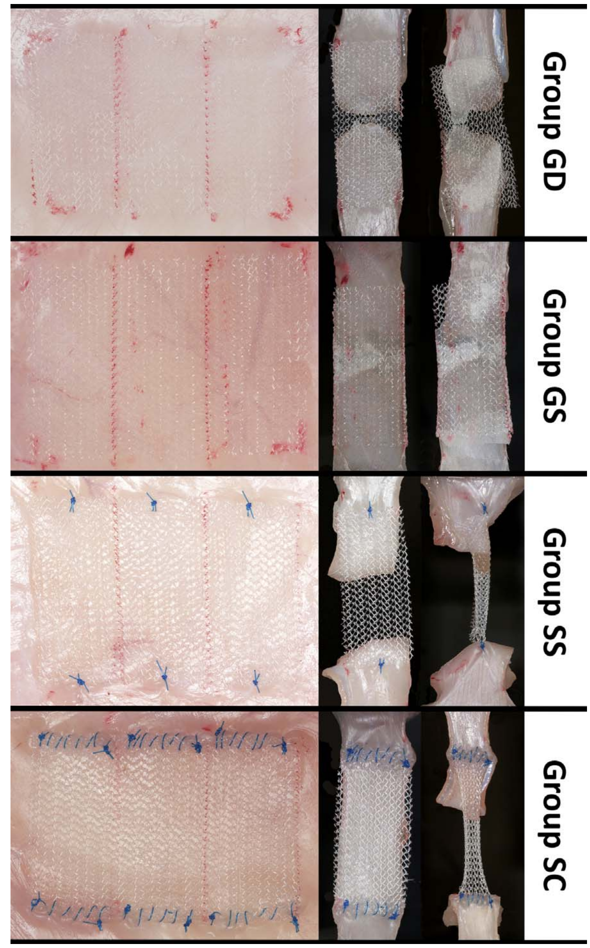

Fig. 1. *Ex vivo* methods used to fix the meshes to the abdominal wall and mechanical resistance test. Group GD (2 glue drops per sample), group GS (1 spray per sample), group SS (2 surgeon's knots per sample) and group SC (2 continuous sutures per sample).

2.3.1. Mechanical tests

Five minutes after fixing the meshes using the four different methods, three mesh/ abdominal tissue strips ($1.5x3$ cm) were obtained from each implant and group. These 5 min were needed for the glue to take hold and dry. All muscle layers of the abdominal wall were incised. Strip length, width and thickness were determined with a digital caliper, making three measurements of each variable on each strip. To minimize tissue degradation, each individual sample was prepared and tested alone within 10 min of harvesting. The strips were clamped vertically between the grips and tests were performed under displacement control in an Instron 5548 Microtester (Illinois Tool Works, Glenview, IL, USA) with a 50 N full-scale load cell. To avoid sample slippage and premature failure, we used 250 N capacity pneumatic grips with serrated surfaces. The displacement rate was 5 mm/min until sample rupture. Strip elongation was expressed as stretch (λ), computed