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Behavior of a new long-chain cyanoacrylate tissue adhesive used for mesh fixation in hernia repair

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ABSTRACT

Background: Synthetic tissue adhesives (TA) are sometimes used in hernia repair surgery. This study compares the use of a new, noncommercial, long-chain cyanoacrylate (n-octyl) TA and Ifabond for mesh fixation.

Materials and methods: In two implant models in the rabbit, expanded polytetrafluoroethylene meshes were fixed to the parietal peritoneum using a TA or tacks (intraperitoneal model), or polypropylene meshes used to repair partial abdominal wall defects were fixed with a TA or sutures (extraperitoneal model). Animals were euthanized 14 or 90 d postsurgery and implant specimens were processed for microscopy (labeling of macrophages and apoptotic cells), peritoneal fluid and biomechanical strength testing.

Interleukin 6 (IL-6) and tumor necrosis factor α (TNF-α) were determinated in peritoneal fluid.

Results: Mesothelial cell deposition on the intraperitoneal implants fixed using the new TA and Ifabond was adequate and similar IL-6 and TNF-α levels were detected in these implants. Intraperitoneal meshes fixed with tacks showed IL-6 overexpression. Three months after surgery, macrophage and apoptotic cell rates were higher for the intraperitoneal implants fixed with Ifabond *versus* the new TA or tacks. In the extraperitoneal model, reduced macrophage and cell damage responses were observed in the meshes fixed with sutures *versus* both TA. Tensile strengths were greater for the tacks *versus* TA in the intraperitoneal implants and similar for the sutures and TA in the extraperitoneal implants (90 d).

Conclusions: Both TA showed a good cell response in both models. Their use in an intraperitoneal location resulted in reduced tensile strength compared with the tacks. However, strengths were comparable when extraperitoneal implants were fixed with these adhesives or sutures.

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Introduction

One of the numerous surgical applications of a tissue adhesive (TA) is its use to fix a prosthetic mesh for hernia repair. So far, the preferred TA for this purpose has been the biological fibrin glue[1] and synthetic adhesives have been used in smaller measure. Among the synthetic TA, those composed of a cyanoacrylate have been the most popular.[2] However, despite their long history, the routine use of cyanoacrylate glues for internal surgical procedures is still met with certain reticence.

One of the roles of a TA is to replace sutures or other mesh fixation method in an effort to minimize tissue insult.[3] For example, when repairing an inguinal hernia via an open surgical procedure, the trapping of nerves structures is a significant postoperative complication that causes groin pain, which is sometimes disabling, and often requires a second surgery for its resolution.[4-6] This complication could be avoided using a TA, and this has been confirmed in several clinical studies.[7]

Some forms of hernia repair involve the intra-abdominal placement of a prosthetic mesh during laparoscopic surgery. In this type of procedure, the mesh implants are usually fixed using tacks. However, as with sutures, these can give rise to complications including adhesions[8] or parietal nerve trapping,[9] producing patient discomfort or even serious complications such as intestinal fistula.[10] Clinical experience in laparoscopic surgery using biological TA has led to good outcomes when repairing small hernia defects.[11] However, the use of cyanoacrylate glues for this purpose has been scarce and practically limited to preperitoneal repair procedures.[12-14]

Modifications to the chemical structure of cyanoacrylates have given rise to new synthetic TA. Exothermic reactions and formaldehyde release when in contact with tissues are well-known effects of synthetic TA.[15] These effects can be minimized by chain lengthening such that longer chained cyanoacrylates are better tolerated.[16] Other properties such as viscosity (determining a greater or lesser fluidity of the TA) or polymerization time are further factors that affect their behavior[17] and are susceptible to modification. This constant development of synthetic TAs determines a need for preclinical studies to examine tissue responses such as wound repair, foreign body reaction, and biotolerance.

The objective of this experimental study was to compare the *in vivo* behavior in models of open and laparoscopic hernia repair of the more conventional fixation devices sutures and tacks with the behavior of two TAs: one currently used in clinical practice Ifabond (n-hexyl) and a longer-chain cyanoacrylate TA (n-octyl), which has never been used for this purpose.

All four fixation devices were used to fix expanded polytetrafluorethylene (ePTFE) or polypropylene (PP) meshes at the intraperitoneal or extraperitoneal interfaces, respectively. Then, in both models, the devices were compared in terms of their biocompatibility (host tissue incorporation and inflammatory response), degradation (microscopy observation), and the biomechanical strength of the repair zone conferred by the devices.

Materials and methods

Experimental animals

Seventy-eight male New Zealand White rabbits of mean weight 3000-3200 g were used. The animals were housed, fed, and handled during the entire study period according to the recommendations detailed in the Guide for the Care and Use of Laboratory Animals of the National and European Institutes of Health (Spanish law 32/2007, Spanish Royal Decree 53/2013, European Directive 2010/63/UE, and European Convention of the Council of Europe ETS123).

The study was performed at the Animal Research Center of the University of Alcalá. The study protocol received approval from the Committee on the Ethics of Animal Experiments of the University of Alcalá (registered code: ES280050001165).

Prosthetic materials

Surgipro (PP): a high-density PP mesh (Covidien, Mansfield, MA).

Preclude (ePTFE): an ePTFE mesh (W.L. Gore & Associates, Inc, DE).

Fixation devices

Tacks: titanium spiral tacks (Protack, Covidien).

Sutures: 4/0 PP (Surgipro II, Covidien).

TAs: Ifabond an n-hexyl cyanoacrylate (IFA medical, Bobigny, France) and n-octyl cyanoacrylate (an experimental TA).

Surgical technique

Surgery was performed under aseptic conditions. The procedures used for anesthesia, and analgesia have been described elsewhere.[18]

Intraperitoneal implants

For these implants, we used 54 animals. In 36 animals, a midline laparotomy some 4.5-5 cm long was made, starting 3 cm from the xiphoid process. A 3 × 3-cm patch of ePTFE mesh was then placed on the parietal peritoneum on the right side of the peritoneal cavity 1 cm from the midline. In a random manner, these meshes were fixed by placing a drop (50 μL) of either Ifabond or n-octyl cyanoacrylate (n-octyl) at each mesh corner or using tacks at each of the corners (Fig. 1A and B). At pre-established time points (14 or 90 d postimplant), six animals per group (Ifabond, n-octyl, or tacks) were euthanized with a lethal dose of 20% sodium pentobarbital (Dolethal, Vetoquinol SA, Lure, France). Specimens retrieved from these animals were used for morphologic and immunohistochemical studies.

In the remaining 18 animals, four ePTFE meshes were implanted—two on the right side and two on the left side of the cavity. These animals were used for the biomechanical study and distributed as follows: tacks ($n = 6$), Ifabond ($n = 6$), and n-octyl ($n = 6$). Three of them were euthanized at 14 d and