ANOMALOUS METAPLASTIC OSSIFICATION OF ANIONIC COLLAGEN COATED PolyPROPYLENE MESH AFTER IMPLANTATION IN THE ABDOMINAL WALL.


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RESUMEN

Polymeric mesh are recently the most recommended materials for the reconstruction of the abdominal wall, with special emphasis for polypropylene mesh. This work describes the preparation, characterization and the biocompatibility studies on polypropylene mesh coated with anionic collagen or in the form of a double layer with poly (vinyl chloride), as a biomaterials for the reconstruction of the abdominal wall. Materials were characterized by electron scanning microscopy, differential scanning calorimetry and by microscopic study of their implantation in the abdominal wall of sheep for periods from 01 to 18 weeks. The results showed that the double layer of polypropylene:poly (vinyl chloride) was the most biocompatible and less susceptible in relation to intestine adhesion, suggesting its potential use as a permanent biomaterial for abdominal wall reconstruction. For the same reasons poly (vinyl chloride) by itself, particularly due to the lack of intestine adhesion after 9 weeks, may constitute in
an efficient and low cost biomaterial for short term abdominal wall repair. In the case of anionic collagen coated polypropylene, the biological response was associated with an anomalous metaplastic ossification surrounding the polypropylene making the material improper for the purpose intended in this work. Although we do not have a plausible explanation for this anomalous tissue response, due to the well known good behavior of collagen implants, we think that this may be associated to the significant higher dielectric properties of anionic collagen in comparison to native collagen biomaterials. In vivo this property is closely related to bone tissue growth and remodeling.

Key words: polypropylene | poly (vinyl chloride) | anionic collagen | abdominal wall | reconstruction metaplastic ossification

Palabras clave: polipropileno | poli (cloruro de vinilo) | colágeno aniónico | pared abdominal | reconstrucción | osificación metaplásica
INTRODUCCIÓN

Marlex®, Prolene® and Trelex® are polypropylene (PLP) mesh

Being the most widely used materials for hernia repair and abdominal wall reconstruction

Repair mechanism:
- Just as mechanical reinforcement (sublay technique) or
- The induction of a scar tissue around the polymeric mesh
Cause for failures:

- Inappropriate surgical techniques
- Mechanical changes in the mechanical properties of the implant during or after implantation
- The persistence of a active and constant inflammatory process leading to irregular scar tissue formation of low intensity

Low integration of the implant at the interface of the regeneration tissue

Consequences:

- Minor
  - Seromes (30-50%)
  - Indisposition (10-20%)
  - Restriction of the mobility of the abdominal wall (25%)
- Major
  - Bowel adhesion at the surface of the implant

In spite of the problems mentioned above, polypropylene mesh are still the most efficient artificial materials for abdominal wall reconstruction

The ideal implant: It should incorporate to the native tissue during tissue remodeling by means of a milder inflammatory response

Solutions:

The use of biodegradable biomaterials that include:

- PLP: peritoneum sandwiches
- Poliésteres: polyglycolic acid
- Polyester mesh : fluoroapassivated gelatins
- Crosslinked bovine pericardium
Purpose of this work:

The development and the characterization (physicochemical and tissue response) of polypropylene mesh modified by coating with anionic collagen (AC) and intended for short and long term abdominal wall repair

What is expected is a material with the appropriate mechanical properties of PLP associated with less intense bowel adhesion due to the high biocompatibility demonstrated for anionic collagen and more favorable inflammatory responses.

Experimental:

Collagen preparation: AC was prepared and characterized as described in Goissis, G. et al. “Biocompatibility studies of anionic collagen membranes with different degree of glutaraldehyde cross-linking”. Biomaterials., v.20, p.27-34, 1999. No glutaraldehyde was used for collagen crosslinking.

Polypropylene: was commercially available and of medical uses in the repair of abdominal wall.

Anionic collagen coating: coating of the PLP mesh was preformed with 1% (w/w) AC gels by immersion under vacuum.

Material characterization

Anionic collagen: polyacrylamide-SDS gel electrophoresis, infrared spectroscopy and differential scanning calorimetry.

Polypropylene: Scanning electron microscopy and differential scanning calorimetry.

Implants

Materials were sterilized with ethylene oxide and implant (PLP and PLC:AC) were performed on male sheep with re-operations at 1, 9 e 18 weeks from implantation. Evaluation of the implants were done in relation to bowel adhesion and tissue response, on microscopic examination (Hematoxylin and Eosin, Von Kossa and Gomori`s Trichrome stain).
Material Characterization:

**Anionic collagen**: as expected anionic collagen was of the type I with an a1/ a2 of 1.95 and a molecular mass ~100000 D; Infrared spectroscopy 1235/1450 cm⁻¹ = 1,07 and a thermal stability of 53.2±0.7 °C suggesting the preservation of collagen triple helix structure.

**Polypropylene**: melt temperature = 171.7 ±0.8°C.

**Polypropylene**: anionic collagen composite:

**Thermal analysis**: thermal transitions at 50.8±0.3 °C (AC) and 173,1±0.4 °C (PLP) in accord with the values determined for PLP and anionic collagen alone

**Scanning electron microscopy**: Those for PLP, and PLP:AC composites are shown respectively by Figure 1a, 1b and Figure 1c

Biological evaluation:

Clinical

- Non infection or displacement of suture
- Serome >> only one animal with one PLP implant (9 weeks)
- **Bowel adhesion** (Jenkinson's classification):
  a. PLP: minimal after 1 and 9 weeks (level 1); moderate to intense after 18 weeks (level 2).
  b. PLP:AC: no adhesion after 1 and 9 weeks (level 0). Minimal after 18 weeks (level 1).

Biological evaluation:

Microscopic pathology of the explants

Microscopic evaluation of polypropylene and polyprolpylene: anionic collagen implant on the abdominal wall of sheep are shown at Table 1 and Figure 2ab, Figure 2cd and Figure 2e. Figures and Table.
Polypropylene implant:

- Near-implant fibrosis: Moderate (3+/5) independent from implantation time;
- Near-implant inflammation: Moderate (2+/5) after 9 weeks; intense (4+/5) after 18 weeks.
- Type of inflammatory reaction: Foreign body-type giant cell reaction, with the predominance of histiocytes and multinucleated giant cells (Figure 2a).

Polypropylene: anionic collagen implant:

- Near-implant fibrosis: On a comparative basis, it was more intense in comparison to PLP (4+/5).
- Near-implant inflammation: Opposite to that observed with PLP: Week 1 > 3+/5; weeks 9 and 18 < 1+/5. Qualitatively the tissular reaction was similar to that observed for PLP, except that a metaplastic ossification or primary ossification was detected around the implant (Figure 1b through 1e).

Spicules of primitive fiberbone (2+/5) > (5+/5) was detected after 01, 09 and 18 weeks in the form of a belt surrounding the implant, with the characteristics of new bone formation (Figure 2ab, Figure 2cd, Figure 2e).
Although PLP coated with anionic collagen was characterized by lower bowel adhesion and improved tissue response in comparison to PLP alone, the formation of new bone tissue around the implant does not recommend its use for the repair of the abdominal wall defects. Nevertheless, this response is an indication for osteoinductive properties of the anionic collagen coating, important for biomaterials for in bone reconstruction.

This response may be related to the improved dielectric properties determined for anionic collagen, particularly when associated with polarized poly(vinylidene fluoride)/trifluorethylene composites (Plepis, A.M.G.; Goissis, G.; Das-Gupta D.K. Dielectric and pyroelectric characterization of anionic and native collagen. Pol. Eng. Sci., 36, 2932 (1996); Goissis, G, Piccirilli, L., Plepis, AMG, Das-Gupta, DK. Preparation and characterization of anionic collagen P(VDF-TrFE) composites. Polymer Engineering Science, 39, 474-482 (1999). (PVDF), due to their ability of these materials to respond with electrical currents upon thermal or mechanical stimulus.

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