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Original article

Mesh fixation with sutures versus fibrin sealant in hernioplasty with reabsorbable prosthesis (polyglycolic acid and trimethylene carbonate). Experimental study in animals

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ABSTRACT

Introduction: Current studies have shown the validity of the atraumatic fixation with fibrin glue (Tissucol®) compared to conventional sutures in polypropylene mesh fixation. We propose to study the behaviour of absorbable mesh.

Material and methods: We used 20 Wistar white rats. Two hernia defects were made in the abdominal wall, which were repaired using absorbable PGA-TMC preperitoneal mesh. The right side of the mesh was fixed with Tissucol® and left side with conventional suture attached to the muscle fascia. One group of 10 rats were sacrificed at day 14 (series A) and the other 10 rats at 28 days (series B). We used 2 tests to assess the contingency of the abdominal wall; pressure test: pneumoperitoneum more than 40 mm Hg maintained for 1 min, traction test: dynamometry of the affected area more than 300 mg per cm^2 of traction. Abdominal wall was analysed to determine the integration of the new generation mesh.

Results: The fixation of the mesh after the pressure and traction tests showed no statistically significant changes in either group. The integration of the mesh and vessel neoformation was higher in the cases of fixation with fibrin glue.

Conclusions: Biological fixation with fibrin glue is similar to the conventional. Absorbable mesh was suitably integrated and vascular neoformation and integration of the mesh was also found to be better than conventional sutures when fibrin sealant was applied.

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Fijación con sutura frente a sellante de fibrina en hernioplastia con prótesis reabsorbible (ácido poliglicólico y carbonato trimetileno). Estudio experimental en animales

Palabras clave:
Cirugía
Hernia
Malla reabsorbible
Estudio experimental
Sellante de fibrina

RESUMEN

Introducción: Dado que estudios actuales han mostrado la validez de la fijación atraumática con cola de fibrina (Tissucol®) frente a las suturas convencionales con malla de polipropileno, en este trabajo se quiere estudiar el comportamiento en las mallas reabsorbibles.
Material y métodos: Se utilizaron 20 ratas blancas Wistar. Se realizaron 2 defectos herniarios en la pared abdominal, que se repararon de forma preperitoneal con malla reabsorbible de ácido poliglicólico y carbonato trimetileno, en el lado de la derecha la malla se fijó con Tissucol® y en el lado de la izquierda se fijó con sutura convencional fijada a la fascia muscular. Se sacrificaron 10 ratas a los 14 días (serie A) y el resto a los 28 días (serie B). Se emplearon para comprobar la contingencia de la pared abdominal 2 test; el test de presión: neumoperitoneo mayor de 40 mmHg mantenido durante 1 min, y el test de tracción: dinamometría de la zona afectada mayor de 300 g de tracción por cm^2. Se analizó la pared abdominal para determinar la integración de la malla de nueva generación.
Resultados: La fijación de la malla tras los test de presión y de tracción no evidenció alteraciones estadísticamente significativas en los 2 grupos. La integración de la malla fue mayor en los casos de fijación con cola de fibrina, donde se observó un aumento del número de neovasos.
Conclusiones: La fijación con colas biológicas de fibrina equiparó a la convencional. La malla reabsorbible se integró adecuadamente y se comprobó que tanto la neoformación vascular como la propia integración de la malla es más notable al aplicar el sellante de fibrina que con la sutura convencional.

Introduction

Prosthetic hernia repair is one of the most common procedures in general surgery. Progress in surgical techniques, postoperative care, and biomaterials have a great impact on the final result of surgery and patient satisfaction.

So far, the use of prostheses in hernia surgery is the reference method, and the material most commonly used is non-absorbable mesh fixed with sutures usually non-absorbable as well.[1]

Advances in surgical materials have brought along new hydrophilic mesh almost 100% absorbable. This new mesh could be used to surgically repair the abdominal wall reducing incidence of long-term complications, occasionally caused by non-absorbable prostheses as a consequence of a chronic inflammatory process often associated with pain and long-term discomfort. These materials would be indicated for inguinal hernia surgery as a substitute for polypropylene plug or the use of absorbable mesh in contaminated fields.[2,3]

Recent studies have shown that biologic glues can be very useful for atraumatic fixation, which is more physiologic and less aggressive to the tissue involved.[4] The combination of absorbable materials and fibrin glue could play an important role in the future. Because there are no current data available, this experimental study was carried out by associating materials to check their application in everyday surgery. Experimental animals were used in the operating room.

Material and methods

Material

- Experimental animals:
  Twenty Wistar white rats were used. Their weight was 200 to 350 g and their sex was negligible. We used 20 animals for both sample groups.
- Suture:
  - Polypropylene (Prolene® 2.0) for mesh fixation.
  - Plaited silk (2.0) to suture skin.
- Ketamine: intraperitoneal application as general anaesthesia.
- Fibrin glue: Tissucol Duo® (2 mL) (Baxter, Hyland Inmuno), 1 mL to fix each mesh.
- Prosthesis: microporous absorbable PGA (*polyglycolic acid*)-TMC (*trimethylene carbonate*) mesh: 67% PGA and 33% TMC, W. L. Gore & Associates, Inc.;[2,3] dimensions: 2.5×2 cm by 0.10 cm thick.
  Forty PGA-TMC implants were used to repair abdominal hernia (1.5×1.5 cm).

Technique

A) Anaesthesia: after animal preparation intraperitoneal ketamine was applied at 20 mg/kg.
B) Surgery: two hernia defects were made in each experimental animal after removing fascia and anterior

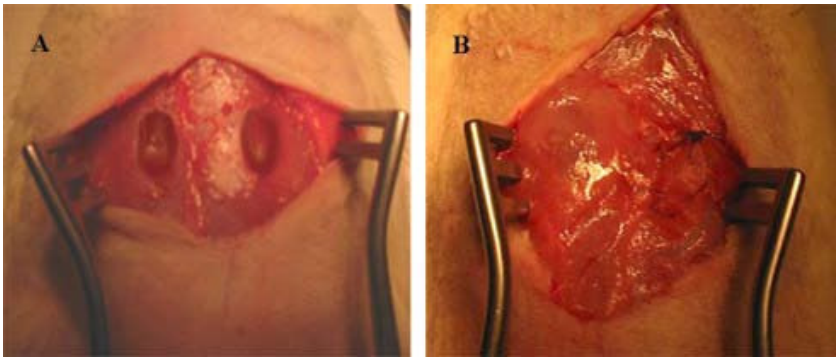

Figure 1 – Macroscopic image of the method used in experimental study. A. Creation of hernia defects. B. Hernioplasties. Left: absorbable prosthesis fixed with fibrin sealant. Right: absorbable prosthesis fixed with conventional non-absorbable suture.

rectum muscle (reaching peritoneal plane without opening it) of approximately 1.5×1.5 cm. The hernia was made by cutting fascia and muscle down to the peritoneum. Retromuscular placement was carried out of a square 2.5×2 cm (5 cm^2) PGA-TMC mesh attached to the aponeurotic fascia with continuing suture using non-absorbable material in right hemiabdomen; same procedure was used for left hemiabdomen but attaching the mesh with Tissucol Duo® directly applied (no *spray*), first with irrigation of retromuscular plane (0.5 mL); once mesh was placed Tissucol® (0.5 mL) was spread on top and over the edges to fasten mesh to aponeurotic fascia. Skin was sutured with loose stitches of plaited silk (Figure 1).

Subsequently, each animal was kept in its individualised cage and 10 rats were sacrificed at postoperative day 14 (series A) to assess mesh macroscopically; pressure and traction tests were performed to test repair effectiveness and explantation of abdominal prosthesis was made to study it by pathologic anatomy. Ten rats were sacrificed at day 28 (series B) to perform the same tests mentioned above and explantation of prosthesis for microscopic analysis.

C) Sealant application technique: fibrin sealant (Tissucol Duo®) was applied, 1 mL per each hernia repair. First over implantation area (0.5 mL retromuscular) and afterward over mesh and where edges are attached to fascia (0.5 mL).

C) Hernioplasty biophysical study:

Two tests were used to assess contingency of abdominal wall, similar to what has been described in the literature by AP Petter-Puchner[5]:

- Pressure test: pneumoperitoneum more than 40 mm Hg maintained for 1 min.
- Traction test: dynamometry of the affected area more than 300 mg per cm^2 of traction (Figure 2).

E) Anatomopatological study of implants:

Each sample was included in paraffin for microtome sectioning and afterward for haematoxylin-eosin stain. Histologic quality of new abdominal wall and remaining mesh materials were analysed. Both samples were carefully analysed (a section of each specimen magnified to 10 [10×]) with special attention to:

- Neoformed blood vessels;
- Thickness reached by neoformed wall, and
- Inflammatory cell infiltration in centre and lateral repaired areas.

To check for neovascularisation in the operated area, immunohistochemistry techniques for endothelial cells with antigen CD34 were performed. The endothelial marker antigen CD34 is a single chain transmembrane glycoprotein of MW 110 kD expressed in haematopoietic stem cells and, mainly, in the vascular endothelium.

F) Statistical analysis of samples:

Statistical analysis was performed using SPSS 14.0. The sample analysis was performed using nonparametric Wilcoxon test. Statistical significance considered was $P<.05$.

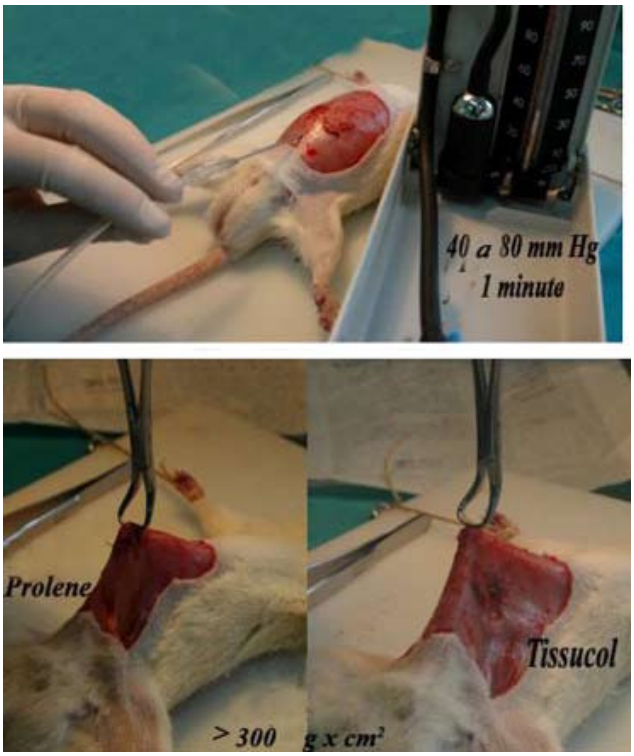

Figure 2 – Traction and pressure test in each animal.

Results

Macroscopic results

- *Series A:*

After 2 weeks 10 animals were sacrificed (series A). PGA-TMC mesh was removed and compared against mesh sutured with polypropylene and mesh fixed with Tissucol®. In the totality of the series (series A, n =10) great macroscopic homogeneity was found in neoformation in the abdominal wall; no infection in any mesh, abscess, skin suture dehiscence or skin abrasion were found.

- *Series B:*

After 4 weeks the other remaining 10 rats were sacrificed (series B) and the same methodology was applied to validate experimental study. All the animals showed good integration and absorption in either mesh. After hernioplasty no relapses, weakness, infection or any other change worthy of mention occurred in any animal of series B (series B, n=10).

Table 1 – Measurement in centimetres of neoformed abdominal wall thickness

Identification number of each animal	Series B, cm	Series A, cm
1	0.5	0.5
2	0.5	0.6
3	0.6	0.4
4	0.7	0.4
5	0.7	0.6
6	0.8	0.4
7	0.8	0.5
8	0.8	0.5
9	0.9	0.5
10	0.9	0.7

Pressure and traction tests

In series A only one of the animals showed a slight weakness on the wall where hernioplasty was performed, which cannot be considered relapse, as there was neither eventration nor solution of continuity on the abdominal wall, but when pressure test went over 40 mm Hg maintained for 1 min a small swelling could be observed; traction test was normal. Repairs results passed both tests in the rest of the animals and there were no significant differences between hernioplasties and fixations.

Both repairs in each of the animals of series B passed both pressure and traction tests successfully. There were no statistically significant differences between fixation with Tissucol® compared to polypropylene suture in either absorbable PGA-TMC mesh.

Microscopic results

In series B (4 weeks) the neoformed abdominal wall was thicker than in series A (2 weeks), $P<.03$ (Table 1 and Figure 3).

In the microscopic study with haematoxylin-eosin stain, neoformation in the abdominal wall with mesh remains (PGA remains) was larger in series A and with a wall thicker than the wall in series B. No differences were found either in cellularity at explantation based on whether they were fixed with Tissucol® or sutured with polypropylene, nor in quantity of macrophages, mast cells, and other components, with the exception of areas closer to polypropylene sutures, where a larger infiltration of macrophages was observed (Figure 4).

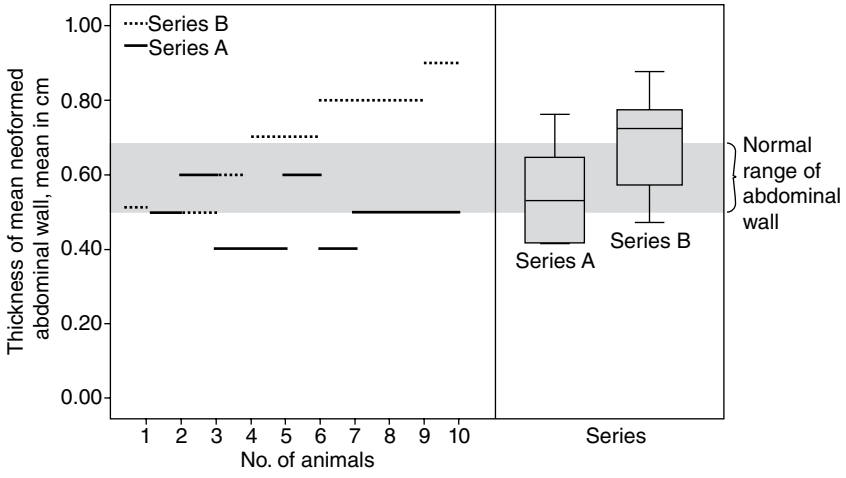

Figure 3 – Chart comparing thickness of neoformed abdominal wall between series (A and B) with values according to animal sectioned (left of chart) and by box plot (right of chart). Mean and extreme values between the series are compared, clearly showing more thickness in series B than in A, and even at higher limits of normal thickness of the abdominal wall of a rat not yet sectioned.

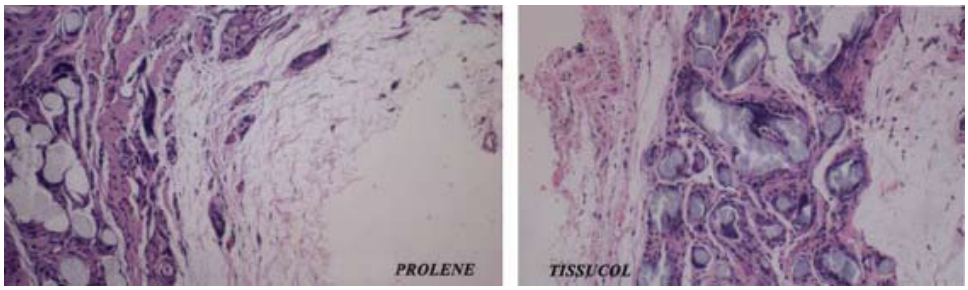

Figure 4 – Microscopic image (haematoxylin-eosin, ×10) of explantation. Left: repair by conventional polypropylene suture (Prolene®). Right: repair by biologic glue (Tissucol®).

Figure 5 – Immunohistochemistry technique by anti-CD34 monoclonal antibody to identify vascular endothelium (magnified to 20 [×20]). Comparison between 2 hernioplasty types in series A in the same animal. Arrows indicate examples of antibody uptake by endothelial cells. 1. Anti-CD34 immunohistochemistry in repair with PGA-TMC mesh fixed with polypropylene (Prolene®) (×20). 2. Anti-CD34 immunohistochemistry in repair with PGA-TMC mesh fixed with fibrin glue (Tissucol®) (×20). A larger vascular neoformation is clearly observed in repair explantation where biologic glue (Tissucol®) was used against conventional repair.

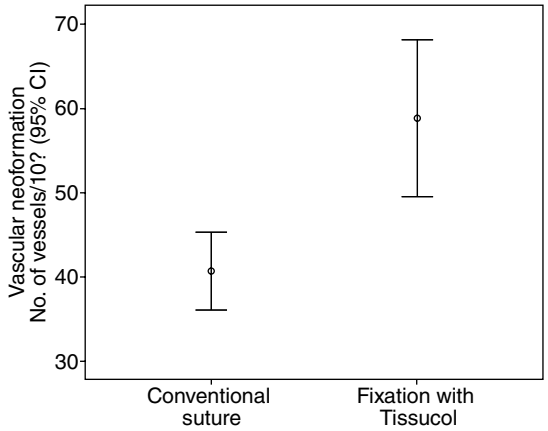

Figure 6 – Box plot, comparison of means and confidence intervals for vascular neoformation (quantity of vessels per field magnified to 10) between repairs with conventional suture and fibrin sealant.

Significant differences were found in distribution of vascular neoformation in relation to fixation with Tissucol® and polypropylene both in series A as in series B, which was studied by immunohistochemistry technique, using as primary antibody Anti-CD34 monoclonal antibody to identify endothelium reactive to anti-CD34 serum. If number of vessels per field 10× was compared between conventional fixation and fibrin glue fixation, statistically significant differences aroused ($P<.000$): number of neoformed blood vessels was larger in hernioplasties fixed with fibrin glue in both series (Figures 5 and 6 and Table 2).

Discussion

Up to the present, prostheses used for reconstruction surgery of the abdominal wall have been non-absorbable, which could be associated with chronic inflammatory processes causing complications in these meshes, such as chronic pain, infection, migration, intestinal obstruction, and fistulisation.[6]

New degradable and absorbable materials may be the solution to these complications that, although infrequent, often become quite serious when they appear. These materials may also be applied to potentially contaminated areas.[7,8] New absorbable prostheses have appeared recently derived from porcine dermis (Surgisis®),[9,10] of allogenic tissue (Alloderm®) or such materials as used in this study: PGA-TMC (Bioabsorbable Plug Gore®).[11] These meshes have

Table 2 – Vascular neoformation (number of vessels per field magnified to 10) in conventional suture and fibrin glue repairs

Identification number of each animal	Conventional suture (Prolene®)	Fibrin sealant (Tissucol®)	Series
1	16.00	30.00	Series B
2	51.00	120.00	Series B
3	30.00	55.00	Series B
4	41.00	52.00	Series B
5	38.00	50.00	Series B
6	52.00	56.00	Series B
7	36.00	50.00	Series B
8	42.00	46.00	Series B
9	41.00	80.00	Series B
10	42.00	77.00	Series B
11	39.00	88.00	Series A
12	30.00	52.00	Series A
13	51.00	55.00	Series A
14	49.00	66.00	Series A
15	50.00	60.00	Series A
16	34.00	39.00	Series A
17	54.00	61.00	Series A
18	33.00	44.00	Series A
19	52.00	51.00	Series A
20	32.00	45.00	Series A

been used in various studies and they have shown decrease of postoperative pain, which is associated with smaller inflammatory process, being these materials degradable and absorbable.[12]

In contrast, complications related to mesh fixation have been described. Fixation with conventional suture may involve nerve fibre entrapment causing postoperative pain and discomfort, which has not shown to have improved by using different prosthetic and non-prosthetic techniques (current herniorrhaphies).[13] Although it is not well determined, it is thought that post-hernioplasty neuralgia with the conventional fixation prosthetic materials mentioned above reaches 5% to 12%.

Current studies have shown the effectiveness of fibrin sealant (Tissucol®) in many fields, by forming a non-stick coating which prevents intraperitoneal adhesions[15] or because of atraumatic mesh fixation; compared against suture fixation and metallic clasps in polypropylene mesh and in vivo, this sealant has shown reduction of post-hernioplasty pain, when compared to traumatic fixation systems.[14-19]

These fibrin sealants have shown stabilisation in hernia repair, but only precociously, until they are completely re-absorbed; other sealants using old non diluted formulas (derived from cyanoacrylate) may cause histotoxicity in adjacent tissue. At present, these products have shown to be effective; they are valid for injured tissue repair but they do not act over cellular proliferation, neither fibroblastic nor in collagen production.[17] Fibrin glue used in this study (Tissucol®) contains the following products: fibrinogen, fibronectin, factor xiii, and growth factors: VEGF, TGF-B, EGF, and FGF. Therefore, by incorporating growth factors, a fibroblastic proliferation occurs immediately after placing the mesh, which favours appropriate integration and optimal final results.[18]

There are recent studies of non-absorbable mesh with biologic fixation glues such as Tissucol®, but there are no current data about how these biologic fixation glues interact with the absorbable mesh.[15,20] The authors of the present work have reproduced the experience choosing a methodology and surgical intervention with which it is possible to check parameters such as mesh integration, abdominal wall neoformation, possibility of relapse, and comparison between either 2 absorbable mesh fixation methods.

This study is important in that it aims at reducing current complications in inguinal hernioplasty (chronic pain) by choosing this mesh and atraumatic fixation; besides, it has helped to show that fixation with either material is similar, which means that either fixation approach can be applied depending on the type of hernioplasty to be performed, quality of tissue in patient, or difficulty inherent in surgical intervention.

Regarding the microscopic study, one of the advantages of absorbable materials is that the mesh itself is replaced by tissue; there is also difference in blood vessel neoformation, a notable point in the present study, and neovascularisation is higher using fibrin sealant (with growth factors), identified with immunohistochemistry techniques anti-CD34.[21]

A different event occurred when recounting foreign-body reaction giant cells, very much alike between series and type of mesh fixation at the centre of each implant[22]; great differences only show between recounts at the edges when comparing areas where polypropylene fixation (Prolene®) was performed, as infiltration by inflammatory cells (lymphocytes, macrophages, and mast cells) is higher in areas closer to suture.

From all the above mentioned, it has been shown throughout the duration of the present study that atraumatic fixation with fibrin glue is both effective and adequate, that it favours even more absorbable mesh integration, increases vascular neoformation without interfering in the normal inflammatory process occurring when incorporating material into the organism, thus aiding in biologic fixation and enabling reduction of mechanical fixation.

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