Effectiveness of the combined use of lactic acid film and polypropylene mesh in the formation of intraperitoneal adhesions - an experimental model in rats

Efetividade do uso combinado de filme de ácido lático e tela de polipropileno na formação de aderências intraperitoneal – um modelo experimental em ratos

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A B S T R A C T

Objective: To evaluate the efficacy of a lactic acid biomaterial (SurgiWrap®) as a protector of the polypropylene mesh (Marlex®) regarding the formation of intraperitoneal adhesions in rats. **Methods:** Forty Wistar rats formed the following groups: Group 0 (Sham) - only laparotomy; Group I - polypropylene mesh; Group II - polypropylene mesh protected by a film of lactic acid. These animals were submitted to laparotomy and placement (or not) of the meshes at closing. After 21 days they were sacrificed for analysis of the adhesion type (0-3), percentage of affected area and strength needed to rupture. **Results:** Group 0 showed no intraperitoneal adhesions. Regarding classification, type 3 adhesions had the highest prevalence in both groups 1 and 2. As for the strength to break adhesions, Group 1 had an average of 1.58 N and Group 2, 1.23 N. The mesh was surrounded by adhesions in more than 50% of their surface area in 87% of Group 1 subjects and in 84% of Group 2 individuals. Through different statistical methods we found that there was no significant difference between groups for both variables. **Conclusion:** The combined use of polypropylene mesh and lactic acid bioprotector showed similar results in relation to intraperitoneal adhesion formation when compared to the sole use of the same mesh.

Key words: Wistar rats. Hernia. Ventral hernia. Peritoneum.

INTRODUCTION

The use of synthetic meshes to correct defects in the abdominal wall has significantly changed the treatment of hernias. By allowing tension-free repair, the use of prostheses has reduced recurrence rates from over 50% to less than 24%[1,2].

The polypropylene mesh is commonly used in the correction of abdominal wall hernias. It has good tensile strength and causes pronounced and persistent inflammatory reaction. The combination of these features and its macroporous structure allows the prosthesis to be enclosed by fibrous scar tissue, resulting in a more consistent repair[1,3,4].

But the same characteristics that give this material its capacity to incorporate also induce the formation of adhesions[2]. These are common consequences of the healing process after surgery, but may lead to serious complications such as fistula and intestinal obstruction[1,5].

The prevention of adhesion formation is a constant search of the surgeon dedicated to working with abdominal wall hernias[6]. Coating of the mesh with protective materials has been suggested for this purpose. This material should have few adverse reactions and complications, including lack of foreign body reaction or inflammation, be simple to use and to handle and be absorbed spontaneously[7,8]. Numerous substances, permanent or biodegradable, have been interposed, forming an anti-adherent barrier between the viscera and mesh/peritoneum.

SurgiWrap® (Mast Biosurgery AG Corporate) is a bioabsorbable anti-adhesive barrier film that is used to minimize the growth of scar tissue and prevent adhesion formation in surrounding tissues. This material can be used individually or together with suture materials. The implant

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protects and maintains the stability of tissues during the healing process and is subsequently absorbed by the body[9,10].

METHODS

This study was conducted at the Institute of Basic Health Sciences, Federal University of Rio Grande do Sul, in accordance with the rules established for experimental research in laboratory animals by the University. Ethical consent was provided by the Ethics and Research Committee.

This is an experimental study with albino rats of the Wistar species that were handled according to standardized protocols for research. Animals received rodent food and water *ad libitum*. They were kept in captivity with the appropriate population density of five animals per cage. A sample of 40 animals weighing approximately 200g were randomly used in the setting of the following groups: Group 0 (n = 5) underwent laparotomy with primary closure of the abdominal wall, called "Sham Operation", Group 1 (n = 15) with intraperitoneal fixation of a polypropylene mesh (Marlex®) 2X2cm, Group 2 (n = 20) with intraperitoneal fixation of a polypropylene mesh (Marlex®) associated with a protective film of lactic acid SurgiWrap® 2.5X3cm (Figure 1).

Surgical Procedure

All animals were anesthetized by intramuscular injection of xylazine (0.1 ml of 2% solution diluted in 0.2 ml 0.9% saline) at a dose of 5 mg/kg and ketamine (0.35 ml of solution 50mg/ml) at a dose of 50mg/kg.

After anesthesia was reached we performed abdominal epilation and antisepsis of the operative field with an alcoholic solution of 2% chlorhexidine. Animals were operated according to the standard technique, minding the particularities of the group they belonged to.

A median laparotomy incision of 3 to 4 cm was performed in all animals, with displacement of the subcutaneous space and opening the peritoneal cavity in the midline. In Group 0, abdominal wall closure was immediately performed by suture with 3-0 Prolene®. In Groups 1 and 2, the surgical procedure was followed, respectively, with the fixation of a 2x2cm Marlex® mesh or a 2x2cm Marlex® mesh associated with a protective 2.5 x 2.5cm SurgiWrap® film. The implant fixation was initiated by anchoring transfixing points with Prolene® 4-0 to the abdominal wall, initially at the top and bottom of one side and then at the other side, equidistant to the former. After securing the implant with four repair points, the synthesis of the abdominal wall and skin was performed with 3-0 Prolene® (Figure 2).

After surgery all animals were hydrated with 5 ml subcutaneous injection of 0.9% saline and underwent rehabilitation period in a separate and warm environment. When awake, they were put back in their cages.

Analysis and data collection

After 21 days, all animals were sacrificed for analysis. We performed abdominal epilation and a second U-shaped incision comprising the whole abdominal wall. This was repaired in two points and lifted while the percentage of mesh involved in the adhesion process and the type of involved viscera were evaluated. After that the adhesion strength was graded on a scale of 0 to 3, where 0 - absence of adhesions; 1 - thin and easily dividable adhesions; 2 - adhesions requiring blunt dissection for division; 3 - firm adhesions, whose division could only be done with application of significant strength, determining partial or total injury of the involved viscus.

In another step, a repair was put in the viscera involved in the adhesion process and a 5N millimetered

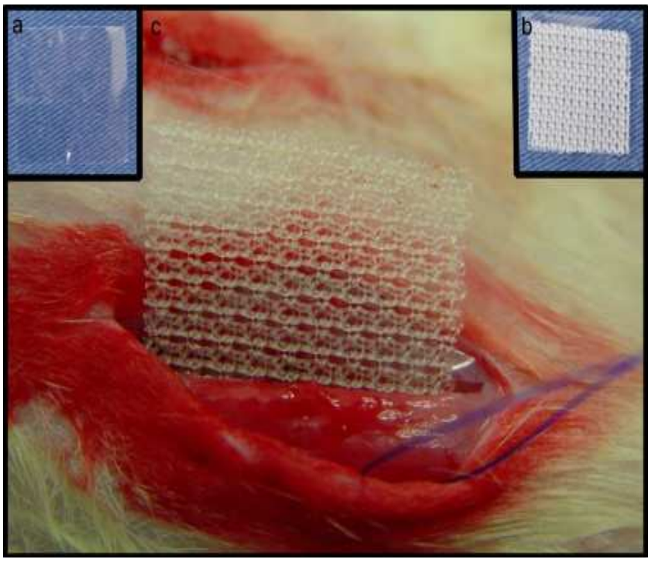

Figure 1- *a) SurgiWrap®; b) Marlex® mesh over SurgiWrap® c) Fixation of Marlex® mesh protected with intraperitoneal SurgiWrap®.*

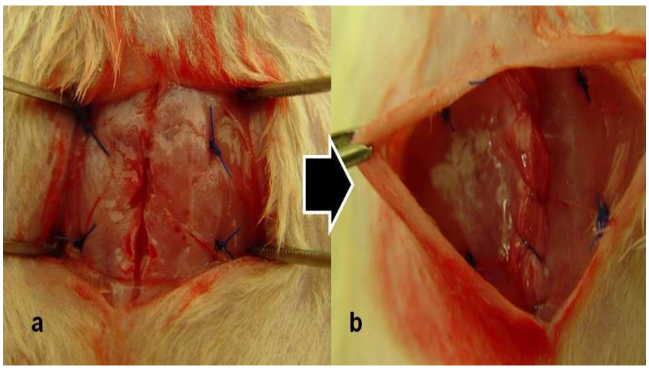

Figure 2 - *a) Intraperitoneal fixation of the mesh with four anchor points, b) closing of the abdominal wall after fixing the mesh to the intraperitoneal space*

dynamometer was used to measure the force required to rupture the adhesion. The sacrificed animals were discarded according to the protocol of the institution.

As for the analysis of data we used the Kruskal-Wallis test for variables with defined outcomes; we performed the chi-square test for analysis of nominal variables; and for analysis of continuous variables the ANOVA test was used. We defined as statistically significant those samples that, when compared, showed $p<0.01$ for measuring of the differences magnitude. The statistical software used was SPSS (Statistical Package for Social Science) version 12.0.

RESULTS

There was a 5% mortality (n = 2) due to anesthetic complications.

In Group 0, no animal had abdominal wall adhesions (Figure 3). We observed a partial suture dehiscence in two animals.

As for animals randomized to Group 1, all showed adhesions. Only one animal had wound infection, and the structure most commonly involved in the adhesion process was the great omentum. One case had a firm small intestine adhesion to the polypropylene mesh and the traction resulted in rupture of the bowel segment (Figure 4).

In Group 2, one animal died in anesthesia. All surviving animals had adhesions (Figure 5). No animal had wound complications; however, in two there were loss of the fixation and displacement of the SurgiWrap®. The most common organs involved in adhesions were the great omentum (100%, n = 19), liver (21.05%, n = 4) and small intestine (5.26%, n = 1).

Table 1 shows the findings in Groups 1 and 2 regarding type of adhesion, force required to rupture it and the percentage of animals that had involvement of a mesh area greater than 50%.

The analysis of comparison between groups with regards to the type of adhesion by the Kruskal-Wallis test showed that groups 1 and 2 were statistically similar.

Just as the severity of adhesions, the number of cases in which the percentage of mesh involved in the adhesion process was greater than 50% was similar in Groups 1 and 2 (87% and 84%), as evidenced by the Chi–square test.

Finally, comparison of the tensile strength of adhesion also behaved in a manner similar to that described above, i.e., Groups 1 and 2 did not show a statistically significant difference between them by the ANOVA test (Figure 6).

DISCUSSION

The ideal mesh for abdominal wall hernia must be non-toxic and non-immunogenic and present adequate tensile strength. So the mesh should be effective in maintaining the balance between inversely behaving factors related to the ideal outcome of little adhesive stimulus and maintaining the integrity of the repair[16,17].

The polypropylene mesh has good integration to the wall defect, besides minimal degradation after fixation. However, some barriers are imposed by its deliberate use, such as the formation of adhesions and subsequent intestinal obstruction and fistula[18].

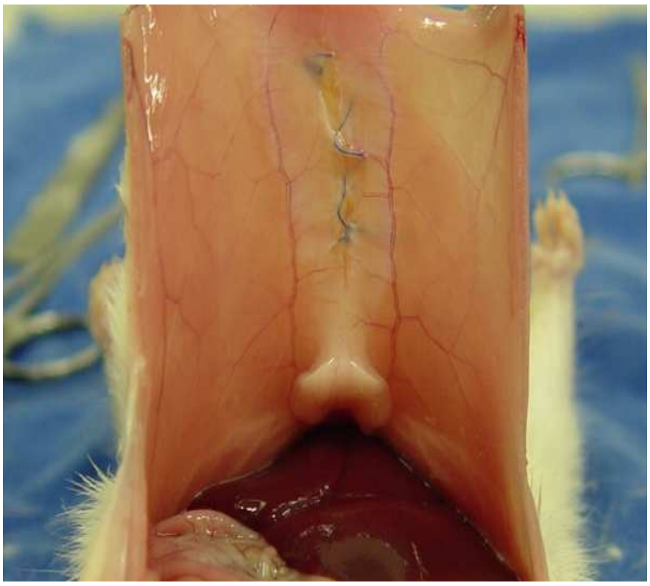

Figure 3 - *Exemplar of Group 0 indicating absence of intraperitoneal adhesion formation.*

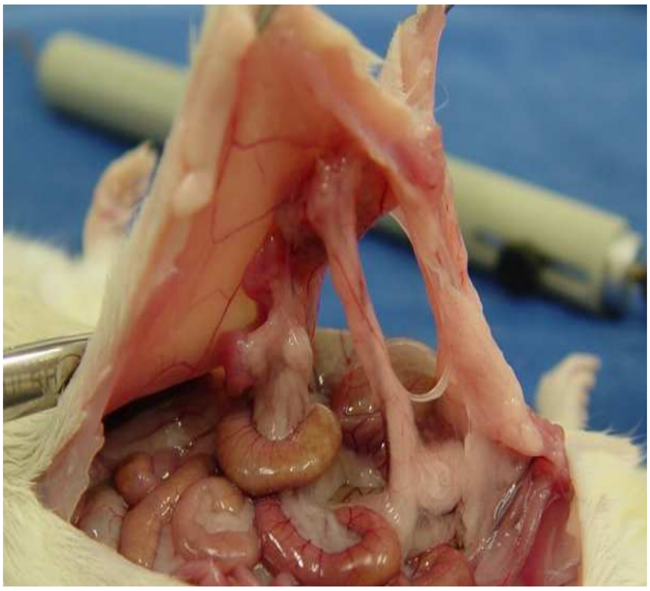

Figure 4 - *Exemplar of Group 1 showing the formation of intraperitoneal adhesions. We can observe the involvement of small bowel in the upper third of the mesh.*

With the current trend of laparoscopic herniorrhaphy, the fear of incidence of complications by intra-abdominal implantation of the prosthesis, promoting direct contact with the viscera, has increased. Indeed, abdominal organs traumatized by the procedure may be exposed to the prosthesis and generate the possible complications that follow adhesions. Thus the use of materials that minimize the formation of adhesions can directly influence the reduction of morbidity in patients undergoing abdominal wall hernia repair[5].

Recently polypropylene meshes with an anti-adherent barrier on its visceral side have been introduced. The purpose of the protective barrier is to keep the visceral surface of the mesh sufficiently separated from the viscera while the healing process occurs in the parietal side of prostheses[1]. Mechanical barriers between damaged tissues and graft have been studied with satisfactory results. Experimental research and clinical trials show that some materials reduce adhesions[19-21].

SurgiWrap® is a film of polylactic acid with widespread use in the fields of neurosurgery and orthopedic surgery, based on its absorptive capacity and low adhesion formation[9,22-24]. In a neurosurgical model, the lactic acid film managed to create a plane of dissection and reduced tissue adhesion to the dura[10]. Though not yet known how the lactic acid film affects coagulation, fibrinolysis and epithelialization are crucial in the formation of adhesions. The effectiveness of the material appears to be achieved by the interposition between surfaces damaged during the critical period of adhesion formation[25]. The unique qualities of SurgiWrap® that make it suitable for abdominal use are derived from its physical characteristics. It is a flexible material that does not bend or dent, is relatively strong and can be fixed with sutures without damaging its structure. In one study the use of a lactic acid film was associated with a reduction of 42.1% in the adhesion rate, as well as to reducing its severity[9]. Various materials have been tested in experimental models to assess their capacity to prevent the adhesion process[6,26].

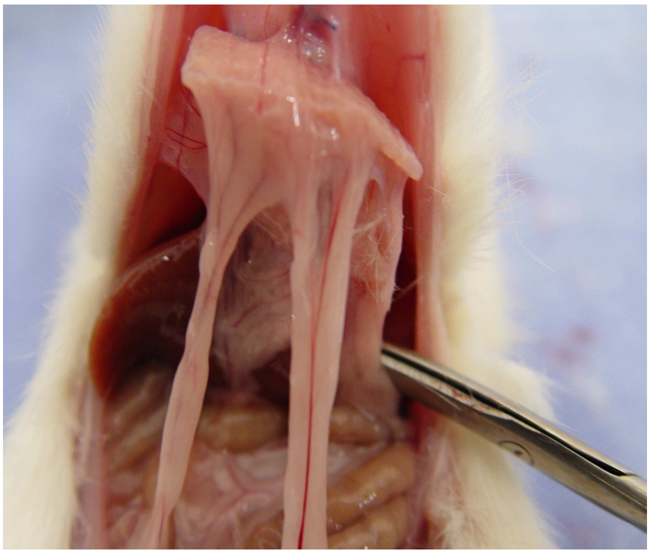

Figure 5 - Analysis of the adhesion process in a subject from Group 2.

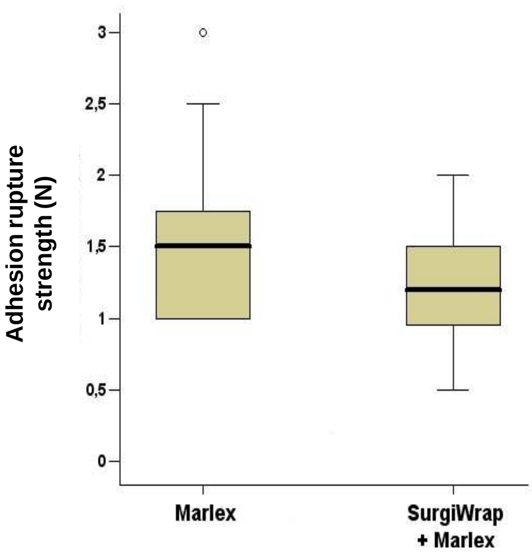

Figure 6 - Comparison of force (N) required to disrupt the adhesions in the groups studied: Marlex *corresponds to Group 1 and* Marlex + SurgiWrap, *to Group 2.*

Table 1- Differences between groups according to the variables concerning to the intraperitoneal adhesion process.

	Group 1 (n=15)	Group 2 (n=19)
Type of adhesion		
Type 0	0%	0%
Type 1	13,33%	0%
Type 2	33, 33%	42, 1%
Type 3	53,33%	57,90%
Rupture strength		
Average	1,58N	1,23N
SD	0,719N	0,432N.
Mode	1,5N	1,0N
Median	1,5N	1,2N
Area of commitment >50%	87%	84%

The polypropylene mesh proves to be more prone to adhesion formation when compared with expanded polytetrafluoroethylene (PTFE)[13]. Still Martín-Cartes et al. could show that the use of an insulating material (hyaluronidase) may be able to reduce the degree of adhesion even when this mesh is used[27]. Unlike these findings, our study showed the failure of SurgiWrap® as an anti-adherent barrier along with the polypropylene mesh, since all the animals randomized to Group 2 had adhesions. Moreover, the involvement of the greater omentum (100%, n = 19), liver (21.05%, n = 4) and small intestine (5.26%, n = 1) allows to infer that this process has generated a more intense adhesion process. The involvement of more than 50% of the mesh surface in 84% of Group 2 and the finding of 100% adhesion of type 2 and 3 in this sample group showed that the film of lactic acid did not act as expected.

Consequently, the reported findings differ from those found in the literature on the use of this material. However, there is no description within the reviewed literature of studies showing the association of polypropylene film and lactic acid. These results raise the possibility that, although SurgiWrap® works effectively when used alone, it does not when combined with polypropylene mesh.

The search for improvement of surgical techniques and implementation of materials for the surgery of abdominal wall hernias are justified by the character of disease prevalence and importance of its complications. This study was not the first to successfully apply this experimental model for evaluating the adhesion process after intraperitoneal implantation of meshes. The surgical technique and way of assessment and classification of adhesions proved easy to use and allowed for meaningful analysis of the material evaluated[13-15].

It is thus possible to conclude that the use of lactic acid film (SurgiWrap®) as an anti-adherent barrier to the polypropylene mesh, using the mesh/SurgiWrap® combination, showed rates similar to the individual use of the mesh when fixed intraperitoneally in an animal model.

RESUMO

Objetivo: *Avaliar a eficácia do uso de um biomaterial de ácido lático (SurgiWrap®) como protetor de tela de polipropileno (Marlex®) em relação à formação de aderências intraperitoneais em ratos.* ***Métodos***: *Quarenta ratas Wistar formaram os grupos a seguir: Grupo 0 (Sham) – apenas laparotomia; Grupo I – tela de polipropileno; Grupo II – tela de polipropileno protegida por filme de ácido lático. Estes animais foram operados com laparotomia e colocação das telas no fechamento. Após 21 dias foram sacrificados para análise aderencial quanto ao tipo (0 a 3), porcentagem de área acometida e força necessária para rompimento.* ***Resultados:*** *O Grupo 0 não apresentou aderências intraperitoneais. Em relação à classificação foi evidenciado a maior prevalência de aderências tipo 3 em ambos os grupos. Quanto à força para ruptura aderencial o Grupo 1 obteve média de 1,58 N e o Grupo 2 de 1,23 N. A tela foi envolvida por aderências em mais de 50% da área de sua superfície em 87% no Grupo 1 e 84% no Grupo 2. Por diferentes métodos estatísticos constatou-se que não houve diferença significativa entre os grupos nas variáveis estudadas.* ***Conclusão:*** *A utilização do combinado tela de polipropileno e bioprotetor de ácido lático demonstrou índices semelhantes em relação à formação de aderências intraperitoneais quando comparada ao uso individual da mesma tela.*

Descritores: *Ratos Wistar. Hérnia. Hérnia ventral. Peritônio.*

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Received in 23/07/2009
Accepted for publication in 18/09/2009
Conflict of interest: none
Source of funding: none

How to cite this article:

Lontra MB, Bigolin AV, Costa RG, Grossi JV, Scalco P, Roll S, Cavazzola LT. Effectiveness of the combined use of lactic acid film and polypropylene mesh in the formation of intraperitoneal adhesions - an experimental model in rats. Rev Col Bras Cir. [periódico na Internet] 2010; 37(5). Disponível em URL: http://www.scielo.br/rcbc

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