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1. *UNICAMP*

COATING WITH S-NITROSOGLUTATHIONE-RELEASING POLY(VINYL ALCOHOL) FILM MODULATED INFLAMMATORY REACTION AND ANGIOGENESIS OF MONOFILAMENT POLYPROPYLENE MESH IMPLANTED IN SUBCUTANEOUS OF FEMALE RATS.

Hypothesis / aims of study

The use of polypropylene mesh to repair urinary incontinence and vaginal prolapse has decreased the recurrence of these conditions. However, it has also been related to specific complications such as vaginal erosions (1). Nitric oxide (NO) can modulate angiogenesis, vasodilation and fibroblastic reaction (2). We studied the effect of a NO donor (S-nitrosoglutathione - GSNO) eluted from a hydrophilic polymeric coating in the inflammatory response of monofilament polypropylene mesh implanted in subcutaneous tissue of rats.

Study design, materials and methods

Twenty adult female Wistar rats were used. Four mesh fragments measuring 10 x 10 mm were implanted in subcutaneous tissue of each rat. Polypropylene fragments were prepared as follows: without coating (control); coated with poly(vinyl alcohol) (PVA); coated with a solution of poly(vinyl alcohol) and poly(vinyl pyrrolidone) (PVA/PVP); coated with PVA containing GSNO in two different concentrations (1 mMol/10mMol) and coated with PVA/PVP containing GSNO at the same concentrations. Ten rats were euthanized at 2 days and the other at 21 days postoperatively. Abdominal wall was excised *en bloc* for microscopic analyses. Inflammatory reaction, edema and angiogenesis were categorized as absent, mild, moderate or severe. Statistical analysis was performed for each of the three variables (inflammatory reaction, edema, and angiogenesis). Fisher's Exact Test was used to compare the coating protocols and ANOVA was used for comparisons between the two times of euthanasia (2 and 21 days). The significance level was 5%. To detail the difference found among the various types of implant, the significance level accepted was divided by the number of tests performed in each protocol. Therefore, the adjusted significance level obtained was 0.05/6=0.0083, because six tests were performed for each variable measured.

Results

No statistical difference was identified among treatments in euthanized rats two days after the implants. However, in rats studied at 21 days, less edema (p=0.0039) and greater angiogenesis (p=0.0031) were observed for meshes coated with PVA/GSNO 1mMol (Figure 1). PVA alone induced a higher angiogenesis (p=0.0027). Furthermore, euthanized rats at 21 days demonstrated a greater inflammatory reaction (p= 0,0115) and less edema (p= 0.0064) than those at two days. In the Table 1 is shown the statistical analysis between coating protocols and controls at 21 days for adjusted significance level.

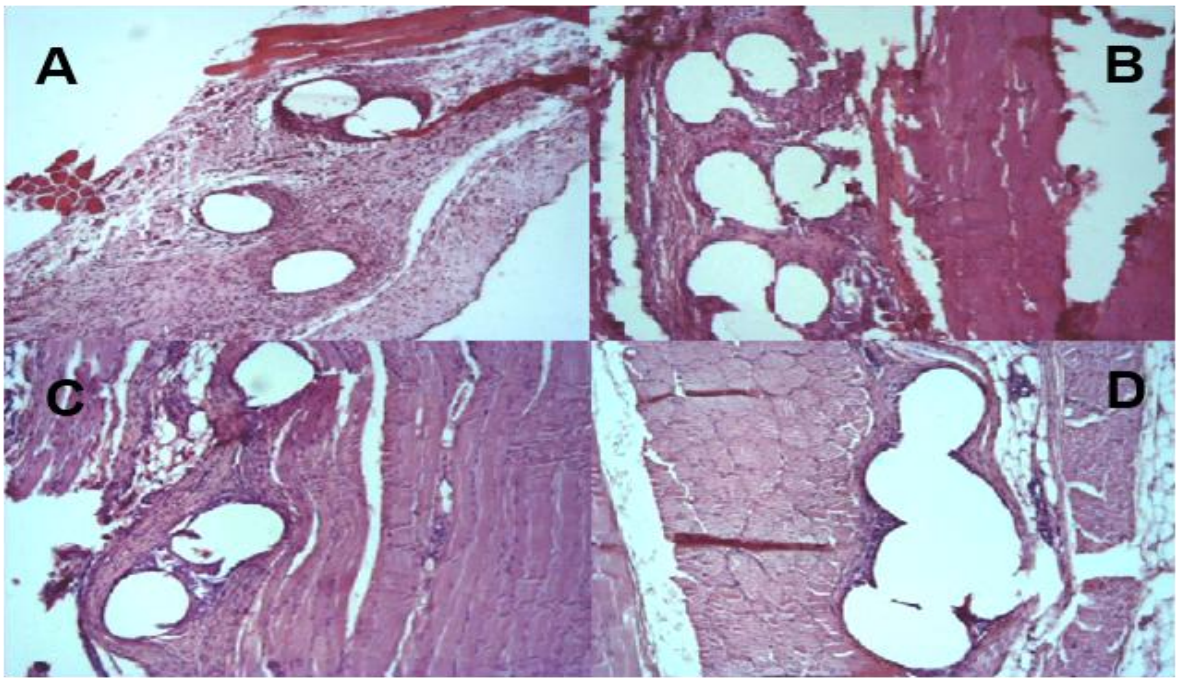

Figure 1: Rats euthanized at 21 days (HE 100x): (A) Control; (B) PVA; (C) PVA+GSNO 1mMol; (D) PVA+GSNO10mMol. Note the different reaction around the mesh (blank space) in B and C samples.

Table 1. Comparison between coating protocols and controls at 21 days*

	Angiogenesis (p-value)	Edema (p-value)	Inflammatory reaction (p-value)
PVA	**0.0027**	0.1532	0.0128
PVP	0.4856	0.0999	0.1762

GSNO1/PVA	**0.0031**	**0.0039**	0.1993
GSNO1/PVP	0.7932	0.8063	0.2291
GSNO10/PVA	0.0613	0.2647	0.1063
GSNO10/PVP	0.7060	0.0660	0.1993

*** Level of significance adjusted to p<0,0086**

Interpretation of results

In a similar study, Hetrick et al, using NO-releasing xerogel-coated silicone implanted in subcutaneous tissue of rats, did not demonstrate differences in inflammatory reaction in NO donors compared to controls less than one week after the procedure (2). In the present study, there was no significant difference between treatments in any of the variables at 2 days. Moreover, in other study, it was demonstrated that the inflammatory reaction would probably represent surgical trauma than induced by the implants (3). In contrast, analysis of rats euthanized at 21 days postoperatively showed that polypropylene mesh coated with GSNO 1 mMol associated with PVA as a vehicle presented less edema of the tissue and greater angiogenesis than the remaining coating protocols. This finding indicated that NO may have a modulating role in the healing process. As a result, a better understanding of its biological effects may promote the development of materials for future clinical use.

Concluding message

Coating with nitric oxide donor substances modulated the integration of polypropylene monofilament meshes implanted in the subcutaneous tissue of adult rats. The main biological effects were observed when using the GSNO solution at a concentration of 1mMol, with PVA as a vehicle. Further studies may result in prostheses with advantages for clinical use.

References

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Comitê de Ética em Expeimentação Animal CEEA / UNICAMP**