Development of swine model for the evaluation of novel compounds in the prevention of postoperative adhesions

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Statement of Purpose: Adhesions following surgery represent a significant problem often resulting in pain, disability, and additional surgeries[1-3]. Compounds are available for the prevention of postoperative adhesions, but effectiveness is difficult to assess; current models of adhesion comparison are limited to qualitative methods with much potential bias[4]. Without an objective quantitative method for assessing adhesions, comparisons of adhesion barriers' efficacy cannot be made; creation of a quantitative model suitable for testing adhesions depends on several principles. A technique must first be devised that reliably creates significant adhesions neither too strong to be prevented, nor too weak to be insignificant; significant adhesions are usually defined qualitatively as dense, thick, and vascular[2]. The adhesions created must be physically appropriate for a quantitative analysis. And the adhesions should have clear validity for surgical methods under consideration; replicating adhesions following open or closed surgery. The method described here was created to meet the above criteria. For this model, swine were used because of similar organ size, healing mechanism, and weights to humans.

Methods: The primary focus of this research was the creation of an adhesion complex that was suitable to quantitative testing using the Material Testing System (MTS^{TM} System Corp, Eden Prairie, MN) machine platform. Following a midline infraumbilical laparotomy, bowel packing and retraction, and adequate exposure of the uterine horns and adjacent pelvic sidewall, a salpingostomy is made using electrocautery 1cm caudal the uterus-fallopian tube junction. A 7cm 8fr. latex urinary catheter, reinforced with a coaxial internal semi-rigid 5fr. polypropylene catheter, is inserted until it lies entirely within the lumen of the uterus. A 10cm segment of 6.35mm ID latex rubber drain tubing is secured to the dorsal aspect of the broad ligament medial the uterine horn; this is placed to prevent sidewall-broad ligament adhesion avoiding interference with the sidewall-uterus adhesion. The uterus and latex rubber drain are attached to the sidewall of the pelvis. The peritoneum lateral to the attached uterus is coagulated along the full length of the catheter insert at a setting of 6/10 (17W output) using a shielded electrocautery tip; cauterized area corresponds to the uterine horn lie and is limited to the peritoneum only. This injury is mirrored on the cannulated uterus to desiccate the superficial layer, and repeated on the contralateral side. Upon completion of the injury, antibiotic rinse is administered, excess fluid is removed via suction, packing and retractors are removed and abdomen is closed.

Following a 2-week survival, a midline laparotomy is again performed; the surgeon visual assesses the pelvic uterine horn adhesion. Euthanasia is achieved and the entire complex of cannulated uterine horn, sutures, adherent pelvic sidewall and muscle is removed en bloc. The sample is marked cranial and caudally for reference; muscle, broad ligament, and latex rubber drain are cautiously dissected away. The remaining uterine horn and pelvic sidewall is cut at 1.5cm and 4.5cm from the cranial suture. The catheters are replaced by a 0.64cm OD by 8cm stainless steel rod. The length of uterus being tested is measured and recorded. Rubber O-rings, 0.95cm OD and 1.28cm OD, are placed to prevent lateral movement and stabilize the specimen during testing. The peritoneal sidewall is tightly secured within a jig clamp and the complex is loaded on the MTS machine platform. The hydraulically controlled ram moves the stainless steel rod a total of 40mm at 1.6mm/sec; force and displacement measurements are recorded during the pull. Histological assessment adjacent to the testing site is completed.

Results: The MTS measures force by displacement which can be quantitatively analyzed and interpreted, while the histology provided a comprehensive description, including vascularity, density, collagen content, and organization of the adhesion being quantified. Blocking on the swine, the cranial and caudal histology scores were shown to have a positive correlation ($p < 0.002$, $r2 = 0.46$) and were not significantly different from one another. Furthermore, the visual score showed no correlative relationship with either histological score or with any MTS force parameters. This model is unique and advantageous in its ability to quantitatively assess the strength of the adhesion complex, minimizing the potential for bias.

Conclusions: The significant advantage of this method is that the adhesions are created in a manner appropriate for quantitative assessment using the MTS system. The ultimate utility of this technique lies not with the testing of adhesions themselves, but in testing and comparing of adhesion prevention techniques. A study is currently under way designed to demonstrate that this technique can quantify and compare treated and untreated adhesions, eventually resulting in a quantitative method for assessing the performance of potential adhesion barriers.

References:

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