Abstract

Background: The main focus of the dissertation is the use of nanofibrous biodegradable materials for the healing support of intestinal anastomoses in colorectal surgery. The altered healing process of intestinal anastomosis leads to several types of local complications. Anastomotic leakage is one of the most feared ones. Severe anastomotic leakage causes peritonitis, sepsis and is a life-threatening condition. Reoperation is necessary in many cases, bringing the need for intensive care, and hospital stays prolongation. Extensive peritoneal adhesions are another source of postoperative complications. These adhesions are a frequent cause of bowel obstruction and abdominal discomfort and are the most common reason for readmission after colorectal procedures. Nanofibrous biodegradable materials showed positive effects on the healing process in various locations. We aimed to develop and perfect a biodegradable patch for both prevention of anastomotic leakage and the formation of extensive peritoneal adhesions. **Methods:** We conducted 3 subsequential experiments on porcine models. In Experiment A, we managed to develop polycaprolactone and polylactic acid-polycaprolactone copolymer nanofibrous patches and applied them on anastomoses on the small porcine intestine. The animals were observed for 3 weeks. Clinical, biochemical, and macroscopic signs of anastomotic leakage or intestinal obstruction were monitored, the quality of the scar tissue was assessed histologically, and a newly developed scoring system was employed to evaluate the presence of adhesions (Perianastomotic Adhesions Amount Score). In Experiment B, newly developed double-layered polyvinyl-alcohol/polycaprolactone patches were tested on a model of defective anastomosis on the small porcine intestine under similar conditions to Experiment A. Newly invented Intestinal Wall Integrity Score was used to determine the quality of the intestinal wall at the site of anastomosis. In Experiment C, a perfected ultrafine polycaprolactone highly porous patch was used in a model of defective anastomosis on the porcine colon under similar conditions. Experimental groups had nanofibrous patches applied over the anastomosis while Control groups had the anastomoses uncovered in each experiment. **Results:** Experiment A showed no adverse effects of the two materials. However, no positive effects on the healing process or risk of anastomotic leakage development were observed. The application of both versions of double-layered materials in Experiment B resulted in inferior healing according to the histology results. The application of the perfected polycaprolactone patch in Experiment C showed no adverse effects on both clinical status and histological results of the experimental animals. Higher amounts of collagen were found at the site of anastomosis in the Experimental group which indirectly suggests higher mechanical strength. The material is also unique for its very low specific weight and high porosity. **Conclusion:** Five versions of nanofibrous biodegradable patches were developed and tested on three different models of porcine intestinal anastomoses. The histological results of the application of the ultrafine polycaprolactone patch from Experiment C seem promising. However, no direct evidence regarding the impact of these materials on the risk of anastomotic leakage was obtained. A perfected version of the polycaprolactone patch with additional antimicrobial activity was already developed and is currently being tested in vitro. Further preclinical testing will be necessary before possible introduction into clinical colorectal surgery.

Key words: Anastomotic leakage, Colorectal surgery, Nanofibrous materials, Polycaprolactone, Animal experiment