USE OF SYNTHETIC SCAFFOLD IN REGENERATIVE SURGERY FOR TREATMENT OF ABDOMINAL WALL HERNIA: EXPERIMENTAL PORCINE MODEL.

Background

Abdominal wall defects are one of the most important problems in surgery [1,2]. We can distingue ventral hernia (due to primary, congenital wall defects) and incisional hernia, affecting up to 20% of patients after laparotomy [3]. Many literature data report a cumulative rate of recurrence after incisional hernia repair of 63% in case of direct suture and 32% for prosthetic repair [4]. Other authors refer that advances in surgical technique reduce recurrences to 10% [5]. Today the use of synthetic meshes becomes the standard treatment to repair large abdominal wall defects, but this procedure can cause various long-term complications such as adhesions formation, graft infection/rejection, fistula as well as hernia recurrence. From this background we understand that in the surgical treatment of abdominal wall defect there are many critical points:

- Surgical technique: literature data demonstrate that direct suture has unsatisfying results with high recurrence rate. The modern surgical procedures, open or laparoscopic, provide mesh placement with different technique: onlay, inlay, sublay and intraperitoneal [6]. The mesh remains as a foreign body in the wall, with high discomfort for the patient, and it sometimes occurs that it can get infected.
- Choise of synthetic mesh: more frequently we can use several types of non-resorbable synthetic meshes made of polypropylene, polyesters and expanded polytetrafluoroethylene (ePTFE). In cases of temporary abdominal closure we need absorbable prosthesis of glycolic acid, polyglycolic acid and carboxycellulose. Particular kinds of implants are biological meshes such as bovine pericardium (Tutomesh®), acellular porcine dermis (Permacol™) and acellular analog of human dermis (AlloDerm®). Biological meshes are most expensive and usually have small size, for these reasons their application is limited to particular clinical conditions like infected abdominal mesh or contaminated operative field. Surgical hernia repairs with absorbable and biological meshes are at high risk of recurrence [7, 8].
- Postoperative changes: many studies suggest that meshes undergo modifications after their implant like shrinkage and adhesions formation with subsequent increased risk of recurrence, cronic pain and postoperative complication [9, 10].

From literature data and clinical experience surgeon knows that “ideal mesh” does not exist until now. An optimal mesh to repair ventral hernia should have several characteristics. The mesh has to be chemically inert and biocompatible in order to avoid abnormal inflammatory reactions or allergic responses. Furthermore, biomechanical properties of the mesh are fundamental to guarantee long-term surgical results. One way to improve the properties of the meshes is to use tissue-engineered materials combined or not with non-resorbable synthetic substance, as polypropylene. Regenerative medicine is an interdisciplinary field of research focused on the repair, replacement and regeneration of cells, tissues or organs to restore damaged functionality. In "tissue engineering" we use a scaffold to support the regeneration of damaged tissue [11]. Scaffolds are biocompatible and completely resorbable, natural or synthetic materials which promote the regeneration of damaged tissue with adhesion and implantation of cells by providing a three-dimensional structure similar to the extracellular matrix that supports the tissue regeneration process without determine adverse reactions by the host organism [12, 13]. Biocompatible and resorbable scaffolds has been used for biliary duct repair and vascular regeneration. The regenerative process has obtained the growth of a new tissue with the same morphological and functional features as the native tissue [14, 15].

Aim

The ambition of this project is to achieve the regeneration directly in vivo by implanting a scaffold, biocompatible and completely resorbable, and allowing it to be colonized by circulating or contiguous stem cells. The mechanical properties of the material and the growth factors released for a naturally moderate inflammatory process should ensure an adequate cellular homing and proper differentiation towards typical cellular phenotypes of the abdominal wall tissue (muscle cells, fibroblasts, endothelial cells).

Material and methods

In this study we propose to use a synthetic planar scaffold to repair abdominal wall defects in an experimental porcine model. The polymeric scaffolds for testing are prepared in the Biocompatible Polymers Laboratory of the Department of Molecular and Biomolecular Sciences and Technologies (STEMBIO) of the University of Palermo. The starting polymer, used to produce the copolymers, is α,β-poly(N-2-hydroxyethyl)-dl-aspartamide (PHEA). PHEA is a biocompatible synthetic polymer which has already been used as a drug carrier [16]. This polymer, combined with PCL (polycaprolactone) and PLA (polylactic acid), constitutes the base of the scaffold. PHEA-PLA+PCL is an elastic material with high mechanical resistance and adequate biocompatibility. Planar or tubular scaffolds are prepared by electrospinning, a procedure that uses a high voltage source to charge a polymeric solution or molten polymer which is then drawn by a collector having the opposite charge, thus producing continuous biomaterial [17]. A preliminary study evaluated biocompatibility and biodegradability of electrospun PHEA-PLA+PCL scaffolds in an experimental murine model with initial cellular colonization which gave rise also to formation of a new tissue. At the following observation the material was partially degraded [18]. The same scaffold was tested in a porcine experimental model for vascular regeneration with optimal biocompatibility [15].

Our research involves the use of at least 6 pigs weighing 40-45 kg each and of 4-6 months years old. During general anesthesia, in all animals we will perform a surgical removal of an area of approximately 3 cm^2 of all layers of abdominal wall, from the skin to the peritoneum, around the umbilical region. We will temporary treat these injuries by suturing only the skin to allow healing of the wound. After 15 days, the acquired abdominal hernia will be repaired with laparoscopic technique in 5 pigs (cases group). In this group, previous disinfection of operating field with povidone iodine 10%, we will establish pneumoperitoneum by using Veress needle in the left upper quadrant and 3 trocars (two 5 mm and one 10 mm) will be placed in the left flank of the abdomen. At the beginning of surgical procedure, we will also perform a laparoscopic exploration in order to identify other unexpected intra-abdominal finds. Hernia repair will be carried out by interposing a 5x5 cm planar scaffold of PHEA-PLA+PCL, fixed to the wall with double circular line of absorbable spiral tacks. In the sixth animal (control group) we will make a direct suture. All surgical procedures will be carried out under adequate general anesthesia (premedication: Zolazepam + Tiletamine 6.3 mg/Kg + Xylazine 2.3 mg/Kg - induction: Propofol 0.5 mg/Kg - Maintenance: Isoflurane + Pancuronium 0.07 mg/Kg), with the animal in a supine position and the four limbs secured to the operating table. After the surgical procedure, all the pigs will receive post-operative antibiotic treatment with oxytetracycline (20 mg/Kg a day for 3 days) and will be monitored clinically and with blood analysis. The animals will be subjected to ultrasound examination at one week after surgery and then a few days before the sacrifice, to evaluate in vivo, the absence of recurrence or the presence of complications. We forecast to sacrifice the first two animals at one month after surgical procedure, while the other three respectively at 3, 6 and 9 months after surgery, except in case of a worsening of clinical conditions requiring a change of the scheduled deadlines. The control pig will be sacrificed at 9 months. In all cases a microscopic histological and immunohistochemical examination of the grafted section will be done to assess the response of the host and the degree of tissue regeneration.

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