International Journal of Surgery 20 (2015) 163–169

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Absorbable bioprosthesis for the treatment of bile duct injury in an experimental model

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HIGHLIGHTS

- New absorbable bioprosthesis for the treatment of bile duct injury.
- Demonstration of reepithelization with histological and immunohistochemistry analysis.
- Permeability of the prosthesis in all the experimental models.
- No postoperative complications.
- Modeling of the bioprosthesis to allow different diameters and shapes.

ARTICLE INFO

Article history:
Received 6 May 2015
Accepted 17 June 2015
Available online 9 July 2015

Keywords:
Bioprosthesis
Pig
Bile duct
Bile duct injury
Experimental surgery

ABSTRACT

Introduction: Cholecystectomy is a common surgical procedure in which complications may occur, such as injury to the biliary tract, which are associated with high morbidity. The aim of this study was to demonstrate the efficacy of a polymer-based absorbable bioprosthesis with bone scaffold for the treatment of bile duct injury in an animal model.

Materials and methods: An absorbable bioprosthesis was used to replace the common bile duct in 15 pigs which were divided into 3 groups with different follow-ups at 1, 3 and 6 months. The animals were anesthetized at these time points and laboratory tests, Magnetic Resonance Cholangiopancreatogram [MRCP], Choledochoscopy using Spyglass and Endoscopic retrograde Cholangiopancreatogram [ERCP] were performed. After radiological evaluation was complete, the animals were euthanized and histological and immunohistochemical analyses were performed.

Results: Liver function tests at different time points demonstrated no significant changes. No mortality or postoperative complications were found in any of the experimental models. Imaging studies ([MRCP], [ERCP] and Choledochoscopy with SpyGlass™) showed absence of stenosis or obstruction in all the experimental models.

Discussion: Histological and immunohistochemical staining (CK19 and MUC5+) revealed the presence of biliary epithelium with intramural biliary glands in all the experimental models. There was no stenosis or obstruction in the bile duct.

Conclusions: The bioprosthesis served as scaffolding for tissue regeneration. There was no postoperative complication at 6 months follow-up. This bioprosthesis could be used to replace the bile duct in cancer or bile duct injury. The bioprosthesis may allow different modeling depending on the type of bile duct injury.

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http://dx.doi.org/10.1016/j.ijsu.2015.06.074
1743-9191/

1. Introduction

Background: Cholecystectomy represents one of the most common surgical procedures performed by general surgeons. Complications may arise following this surgical procedure. Iatrogenic bile duct injury, despite its low incidence, has high morbidity and harmful effects on quality of life of patients, with increase in hospital-stay and medical care costs [1]. Iatrogenic bile duct injury is defined as an injury in some part of the extrahepatic bile duct during cholecystectomy or other invasive procedures and it comprises about 95% of all benign bile duct stenosis [2,3]. Roux-en-Y hepaticojejunostomy has been the most commonly performed procedure for biliary reconstruction, especially in cases of ductal transection [4]. Biological tissues have been used for repair of bile duct injuries without satisfactory results, including synthetic materials such as latex, silastic, expanded polytetrafluoroethylene and absorbable polymers which have been utilized as biliary prostheses [5]. The absorbable bioprosthesis functions as an alternative to inserting a T-tube or biliodigestive anastomosis in patients who experienced intraoperative injury of the bile duct, or in patients who develop a postoperative stenosis. This approach provides an innovative treatment of biliary strictures that preserves the function of the papilla of Vater [1]. The importance of this study consists of proposing therapeutic strategies for the management of bile duct injuries, evaluating the usefulness of biomaterials in experimental models, and determining their effectiveness in maintaining patency of the bile duct without stenosis.

Bile duct injuries occur more often during laparoscopic cholecystectomies when compared with open surgery although there is no statistically significant difference between them [6]. Misidentification of the cystic duct and/or the common bile duct is one of the most common causes of injury. Anatomic variations are observed between 10 and 15% of patients and they are difficult to detect during preoperative studies [7,8]. There are many classifications of bile duct injuries, and the final results after repair depends on many factors [9,10]. One of the non-invasive diagnostic studies is magnetic cholangioresonance, which has nearly a 90% sensitivity for diagnosis of biliary conditions when compared with other invasive diagnostic studies such as ERCP [11]. The use of self-expanding metal stents for biliary strictures is associated with disappointing results, and its routine use is not recommended [12]. The aim of this study was to demonstrate the efficacy of an absorbable bioprosthesis with bone collagen scaffold for the treatment of bile duct injury in an animal model.

2. Materials and methods

2.1. Bioprosthesis

The polymer-based (collagen) bioprosthesis with open and interconnected pores were used (Fig. 1). It has a demineralized bone scaffold and was developed in the Biomaterials Institute Laboratory at the National Autonomous University of Mexico (UNAM) in Mexico City. The dimensions of the implants were 3-cm length, 0.32-cm outer diameter, and an inner diameter between 0.24 and 0.25 cm (Fig. 2). The prostheses were coated with ε-caprolactone (Sigma–Aldrich, 704,067) to waterproof and to prevent bile leakage. They were sterilized with hydrogen peroxide plasma. The bioprosthesis was obtained from a cuboid structure which allows different modeling according to the diameter and length of the bile duct.

2.2. Experimental model

Fifteen male Landrace pigs weighing between 30 and 40 kg each were used. The animals were divided into 3 groups with different follow-up times: 1; 3 and 6 months (5 pigs per group). The animals were anesthetized at this time points and MRCP, Choledochoscopy with Spyglass and ERCP were performed. After all the imagings were complete, the animals were euthanized and histological and immunohistochemical studied.

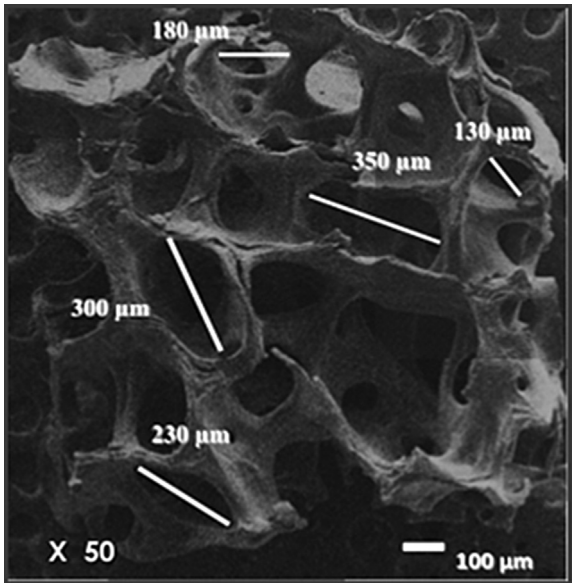

Fig. 1. Electronic microscopy: Bioprosthesis showing its porous structure.

Fig. 2. Absorbable bioprosthesis.

2.3. Ethical considerations

The protocol was approved by the Research Ethics Committees of the National Autonomous University of Mexico. The animals were housed in individual pens, and were handled and anesthetized according to the Official Mexican Norm 062-ZOO-1999 [13].

2.4. Anesthesia protocol

The animals were fasted for 12 h prior to the surgical procedure. Sedation was achieved using Azaperone (40 mg Sural, Lab. Chinoin®, México) 2 mg/kg intramuscular (i.m.) and atropine sulfate (1 mg Atropisa, Pisa livestock Aug, México) 1 mg/10 kg i.m. Subsequently, a short catheter (20-Fr) was placed in the marginal ear vein in order to have an intravenous (i.v.) line and sodium