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Self-expandable biodegradable biliary stents in porcine model

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ABSTRACT

Background: Treatment or prevention of a benign biliary tree stricture is an unresolved problem. A novel self-expandable biodegradable polydioxanon biliary stent in a porcine model was studied.

Materials and methods: This new stent was used in 23 pigs. Feasibility and safety of surgical stenting, time of biodegradation, and histologic reaction in 2, 8, 13, and 20 wk of a follow-up were studied. All stents were inserted into a common bile duct through a duodenal papilla following small dilatation. After surgical evaluation of abdominal cavities, the pigs were sacrificed to remove common bile ducts with the stents. All bile ducts were assessed by macroscopic and histopathologic examination.

Results: Self-expansion was correct in all cases. Neither bile duct obstruction nor post-surgical complications were observed. Macroscopic evaluation indicated lightening of the stent color in 2 wk, a partial disintegration in 8 wk, and a complete absorption in 13 and 20 wk. Histologic evaluation in general substantiated a mild-to-moderate inflammatory reaction in the lamina propria during the whole follow up and had no clinical consequences. No cholangitis, necrosis, abscess, or excessive fibroplasia was found in a hepatoduodenal ligament.

Conclusions: Our results suggest that polydioxanon biodegradable self-expanding stents seem to be useful for biliary system implantation, offer a good biocompatibility, and completely degrade within 13 wk.

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1. Introduction

A benign stenosis or stricture of a biliary tract is an unresolved problem. In contemporary medicine, there are opportunities to diagnose and treat this complication by dilatation and stenting via endoscope [1–8], transhepatic drainage [9–12], rendezvous techniques [13], or by surgical procedure [14–21]. Only a few authors seem interested in surgical stricture intervention [22,23]. Biliary stenosis incidence, depending on etiology, was observed in 3–12% of patients, and treatment procedure had to be repeated [24–27].

Over the last decade, there were only a few experimental and clinical studies focused on new possibilities for biliary stenosis prevention and treatment. These studies referred to multiple plastic stents, which required repeated replacement due to obstruction. Metallic stents were not generally accepted in benign stenosis because of obstruction potential and the impossibility of removal. Covered metallic stents are referred to as retrievable, but their use is accompanied by placement, migration, and extraction complications [4,28,29]. To avoid these disadvantages, the potential of self-expandable biodegradable stents [30–36] placed after balloon dilatation [37], secured by stitches, [38], and covered with chemotherapeutics [23] have recently been studied during the past few years.

The aim of this study was to investigate the feasibility and safety of surgical stenting, verify mucosal reaction, and mainly determine the length of biodegradation after placement of the novel self-expandable biodegradable polydioxanon (SBP) stent in a porcine model. Current examples of clinical use and future opportunities for surgical and other practices with this new stent are discussed.

2. Methods

2.1. Stent and delivery system

Braided stents were manufactured from commercially available polydioxanon monofilament EP 3 or EP 3.5 fiber (European Pharmacopoeia; n EP = n × 0–1 mm; EP 3 = 0–3 mm = USP 2-0). All stents were handmade according to our requirements (Ella DV biliary stent; Ella-CS s.r.o., Hradec Králové, Czech Republic, CZ). A sterile stent was packed separately from the delivery system because of its plastic deformation and was loaded manually into the delivery system just before the implantation (Figs 1 and 2). Stents of 6, 8, and 10 mm in diameter with a 30 mm length and delivering system of 12, 13, and 15 Fr in diameter, respectively, (French catheter scale; Fr = n × $^1/_3$ mm; 12 Fr = 4 mm) were used. A radial expansion force of 8 mm and 10 mm stents is 90% and 133%, respectively, in comparison with a routinely used metallic nitinol stent (Ella-CS s.r.o., HK, CZ). The SBP stent was delivered into the bile duct with the aid of a fine stainless steel wire as a leader.

2.2. Animal care and stent deployment

The complete study was only undertaken after project approval from the Ethics Committee of the Veterinary University in Brno and the Ministry of Health, in accordance with law applicable to experimental animal protection. Twenty three white domestic pigs (age, 3 mo; weight, 30–35 kg, females only—because of their different anatomy during midline laparotomy) were divided into four groups (A = 4, B = 8, C = 4, and D = 7 pigs) used for implantation of intrabiliary stents, and one group of five pigs was an untreated control without any surgery on a common bile duct (K). This number of pigs was chosen with respect to our grant funding limits. Animals were placed into the animal house of the Veterinary Research Institute in Brno, Czech Republic. Implantation was realized at the Department of Surgery of the Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Sciences in Brno, Czech Republic. Pigs were fed at a basic rate with access to water all day.

The pigs were anesthetized with the following protocol: tiletamin 2 mg/kg + zolazepam 2 mg/kg (Zoletil 100, Virbac, United Kingdom) + ketamine 2 mg/kg (Narketan, Vetoquinol, United Kingdom) + xylazine 2 mg/kg (Sedazine, Fort Dodge, USA) intramuscular (i.m.) for introduction following placement of intravenous (i.v.) canula, and administration of propofol (Propofol, Fresenius, Germany) 2 mg/kg i.v., placement

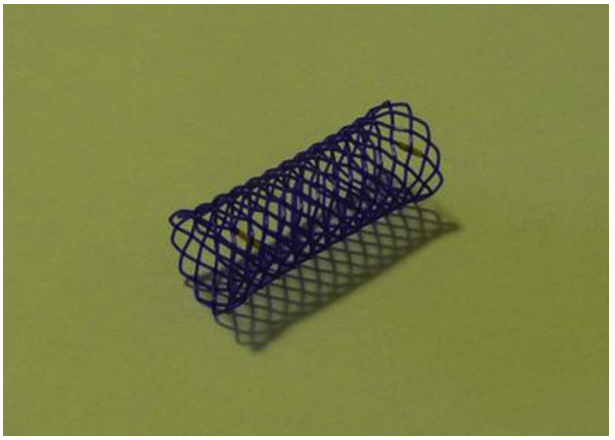

Fig. 1 – Polydioxanon self-expandable stent 10 × 30 mm. (Color version of the figure is available online.)

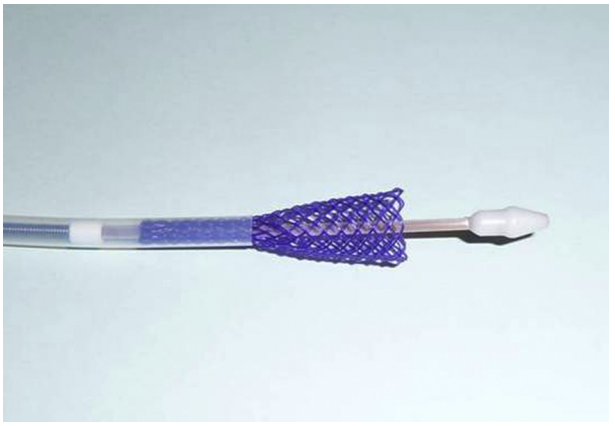

Fig. 2 – Stent loading into the delivery system. (Color version of the figure is available online.)