The experimental distention of dissected bile duct for the restoration of its continuity in dogs using a device of own construction

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Abstract

Purpose: The segmental resection of constricted bile duct and end-to-end biliary anastomosis could be an attractive alternative in the treatment of benign biliary tract stricture. The aim of this study was to restore the anatomical integrity of the hepatic-common bile duct after an artificially produced defect while maintaining the large duodenal papilla, using microsurgical technique.

Material and methods: The experiments were carried out on 25 mongrel dogs. The common bile duct was ligated in all of the animals during laparotomy, as a model of bile duct obstruction in humans. Relaparatomy was performed 3 days after the initial operation. The segment of bile duct, 4 cm in length was resected together with the ligature. The continuous bile flow into the duodenum was assured by a polyvinyl catheter introduced into both ends of dissected bile duct. The proximal end of the hepatic-common bile duct was fixed to a device constructed by us for the distention of the bile duct (DDBD). The anterior part of the device was exteriorized through a separate fistula and fixed to the abdominal wall. The hepatic-common bile duct distention was gradually continued during 18 days, by pulling out the mobile part of the device. After 18 days the device was removed and the distended proximal end of the hepatic-common bile duct was anastomosed end-to-end with its distal end. The sequels of this procedure were observed for up to 6 months.

Results: The hepatic-common bile duct was distended 4 cm within 18 days. The histopathological examination has shown partial damage of the duct framework due to the distention and tension. However the patency of the duct was preserved and the recovery of normal structures were observed after the device was removed and anastomosis fashioned.

Conclusion: This method, developed by us, offers the possibility of restoring the integrity of injured extrahepatic bile ducts, allowing effective treatment of benign biliary strictures.

Key words: bile ducts, biliary strictures, distention, biliary anastomosis.

Introduction

The incidence of benign strictures of the biliary tract has increased over the past decade. A number of factors with a higher risk of injury, including iatrogenic complications after laparoscopic cholecystectomy, have been identified [1]. It is necessary to diagnose and treat even low-grade biliary obstruction because of the severe consequences for the patients, like ascending cholangitis, sepsis, jaundice, hepatic cirrhosis or bile stones formation [2]. The most commonly employed surgical procedure to bypass the stricture is Roux-en-Y choledocho- or hepatico-jejunostomy, but sometimes there is a need for reinterventions for anastomotic stricture [3]. The role of endoscopic treatment by repeat balloon distention or stenting have increased, but morbidity occurrs more frequently in patients treated with endoscopic procedures, than those treated surgically [5,6]. The choice of surgical technique depends on the location and extension of the stricture [7].

This is a big challenge for surgeons: is there a possibility to resect the constricted part of bile duct and to create end-to-end biliary anastomosis for reconstruction of biliary tree? At least for some selected patients, it would be a permanent solution to their problem.

The duct-to-duct anastomosis becomes a valid alternative to standard hepatico-jejunostomy in living donor liver transplantation [8,9]. However, bile leakage occurrs in up to 27% of

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Figure 1. Extrahepatic bile ducts in a dog. A: hepatic ducts. B: common bile duct. C: cystic duct. D: common hepatic duct. The levels of common bile duct ligation and the place of segmental resection are depicted.

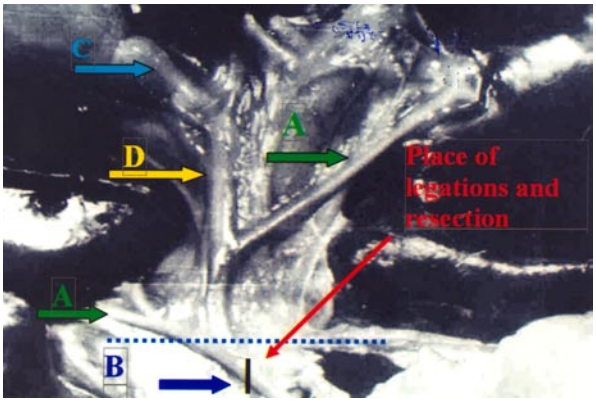
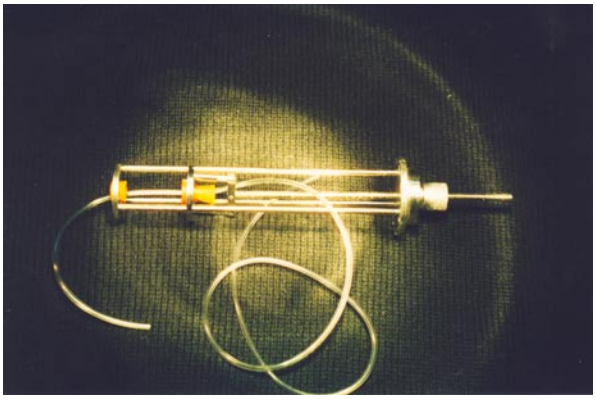


Figure 2. The device for the distention of the bile duct (the description in the text).



liver transplant patients after biliary reconstruction, even when longitudinal stress is absent [10]. In order to optimize end-to--end ductal anastomosis, different approaches to interpose the resected part of the bile duct and to preserve a tight junction of both ends of the reconstructed bile duct have been used in experimental studies. Autologous vein graft in rats aided by a plastic stent, using microsurgical technique have been successfully used to repair segmental common bile defect [11]. In another study, bilio-biliary anastomosis was performed in dogs, using Gore-Tex vascular graft prior to resection of the stenotic area with consecutive release of cholestasis [12]. In both of these studies, the observation period was 12 weeks and 3 months respectively; the later effects are not known.

Our original idea was to assess the possibility to repair a bile duct stricture, by resection of the involved area, and adaptation of the dissected duct to end-to-end biliary anastomosis by gradual distention of the hepatico-choledochal part of the biliary tree.

Therefore the purpose of our study was to restore bile duct integrity, after an artificially produced defect, corresponding to the removed stricture of this duct, by the distention of the dissected bile duct, using temporarily implanted device of our own construction in dogs.

Material and methods

The experiments were carried out on 25 mongrel dogs of both sexes, 12-23 kg of body weight. The animals were housed in standard laboratory conditions under 12 hr day-and-night cycles, with a pelleted laboratory diet and water ad libitum. Care was provided according to current guidelines for the use of laboratory animals and experiments were performed according to the Helsinki Declaration.

The choice of experimental animals

The dog's liver is comprised of 6 lobes. Extra hepatic bile ducts are represented by hepatic ducts, cystic duct, common hepatic duct and common bile duct (*Fig. 1*). The gall bladder is pyriform, well developed and located on the liver middle lobe. The length of the gall bladder varies from 3.5 cm to 7.0 cm. The width varies from 2.5 to 4.5 cm. The length of the cystic duct varies from 1.5 to 3.5 cm. Six hepatic ducts come out of the liver lobes. Four of them are connected between each other and the cystic duct to form the common hepatic duct. However, it is necessary to note that two hepatic ducts are connected with the common hepatic duct below the cystic duct to create the common bile duct. Therefore, the part of the bile tree from the outlet of the cystic duct to the outlet of the common bile duct into the duodenum is called hepatico-common bile duct (ductus hepaticocholedochus). The length of the common bile duct can reach up to 6 cm and the diameter varies from 1.5 to 2.5 mm. Despite these differences, the common bile duct in dogs could be a satisfactory model of the common bile duct in humans to create biliary end-to-end anastomosis, after segmental resection of the stricture.

Construction of the device for the distention of the bile duct (DDBD)

Our DDBD consisted of a metal part, 12 cm in length and 2 cm in width, presented in *Fig. 2*, and a polyvinyl catheter 15 cm in length and 2 mm in width on the inside, passing through two small dacron rings (orange), for the fixation of the resected proximal end of the common bile duct between the two rings. The second, distal ring was connected with a metal axis, passing through a bigger metal ring with 4 small holes for the fixation of it to the anterior wall of the abdomen by sutures, after exteriorization of it by the fistula, made in the abdominal wall by separate incision (*Fig. 3*). After positioning the device, the external end of the axis could be gradually pulled out about 4 cm. The procedure of extension could be regulated according to the scale located on the axis.

The experimental procedure

The abdominal cavity was opened under sterile conditions under ethyl-ether ventilated general anesthesia. The common bile duct was ligated in all of the dogs, 2.5 cm above its outflow into the duodenum and the wall of the abdomen was sutured. The relaparotomy was performed 3 days after the initial operation. The segment of ligated common bile duct, 4 cm in length was resected, together with the ligature, close to the duodenum. The shorter end of the polyvinyl catheter of DDBD was introduced into the ductus hepaticocholedochus for the bile drainage. The other, longer end of the catheter was

inserted into the distal part of the common bile duct and fixed with ligature, to assure free bile flow into the alimentary tract. The remaining, proximal part of the common bile duct, cannulated with a catheter was fixed between the rings of the device, with its wall inside them, using medical glue (MK-7) (Russia). The device was positioned in the cover with latex and fixed to the anterior abdominal wall after exteriorization of its metal ring. The proximal part of the common bile duct was gradually distended between the rings (about 2 mm daily) during 18 days. The polyvinyl catheter and DDBD were removed 18 days after the initial surgery during another relaparotomy and the distended proximal part of the hepatic-common bile duct was anastomosed end-to-end with the distal end of the common bile duct. Microsurgery technique was used for end-to-end biliary anastomosis. The microsurgical procedures were performed under a microscope (Zeiss, Germany) using 7/0 sutures (Ethicon). The resected ends of the duct were positioned closely to each other and the posterior wall was sewn up first by separate sutures. The sutures were made as closely as possible in order to avoid any leakage of bile.

All of the animals were observed under the standard vivarium conditions and sacrificed in general surgical anesthesia at different interval after the first operation. In 8 dogs, the experiment has been finished on the 3, 5, 10 and 18 days after the second operation (2 dogs in each point of time). The dynamic changes after distention were evaluated by histology, after 20, 30, 50, 80, 120, 150 days (2 dogs in each interval) and after 180 days (3 dogs) following the second operation.

Roentgen graphic examinations

The completeness of common bile duct ligation and the patency of biliary anastomosis were controlled by Roentgen graphic examination, using i.v. contrast medium (60% solution of Triombrastum, Russia).

Biochemical assays

The presence of cholestasis was evaluated by routine laboratory estimation of the bilirubin level and AST activity in the venous blood plasma.

Histopathological examination

At autopsy, the specimens of distended and anastomosed bile ducts, and the livers were taken for histopathological examinations, which included the staining with haematoxyline and eosine (H&E) and according to van Gieson. The preparates were evaluated at x60 and x90 original magnification.

Statistical analysis. The results are descriptive, therefore the statistical analysis is not applicable.

Results

Postoperative Complications and Mortality

None of the animals suffered postoperative complications, nor died within the first 15 days after surgery. One dog died after 26 days because of bile peritonitis and another one 62 days after the surgery because of mechanical jaundice. The cause of bile peritonitis was the necrosis of common bile duct wall after biliary anastomosis. The cholestasis in other dog evolved because of technical problems in microsurgery. They caused the obliteration of common bile duct lumen in its anastomosed part.

Figure 3. External part of the device for the distention, fixed to the anterior wall of the dog abdomen after fashioning of fistula.

Figure 4. Dilatation of the ductus hepaticocholedochus in the dog, after its ligation (roentgenogram).

Roentgen graphic findings

Roentgenograms of ligated – duct animals have shown a complete obstruction of common bile duct (*Fig. 4*). After positioning of the DDBD, the bile freely flowed into the duodenum (*Fig. 5*). Consecutively, after fashioning of biliary anastomosis, all survived animals showed no signs of its stenosis. The contrast medium also flowed freely into the duodenum in each case. Dilatation of the bile ducts proximal to the anastomosis was not observed in any animal (*Fig. 6*).

Biochemical parameters

The postoperative estimations have shown the evidence of cholestasis within the first 18 days after the first surgery. Maximal level of bilirubin reached 18.8 μmol/L (normal 0.9--10.6 μmol/L) and maximal activity of AST achieved 80.5 U/L (normal 8.9-48.5 U/L). The cause was probably the polyvinyl catheter inserted into the ductus hepaticocholedochus. The parameters of cholestasis were normalized after removing of the catheter and fashioning of biliary anastomosis. All esti-

Figure 5. The roentgenogram of the device for the distention of bile duct in working position with the proximal end of ductus hepaticocholedochus fixed to the device.

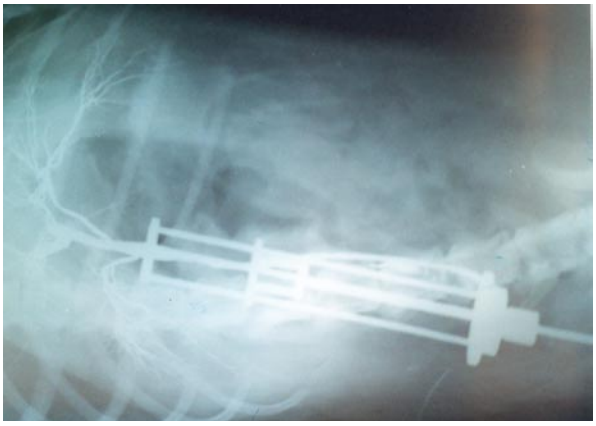
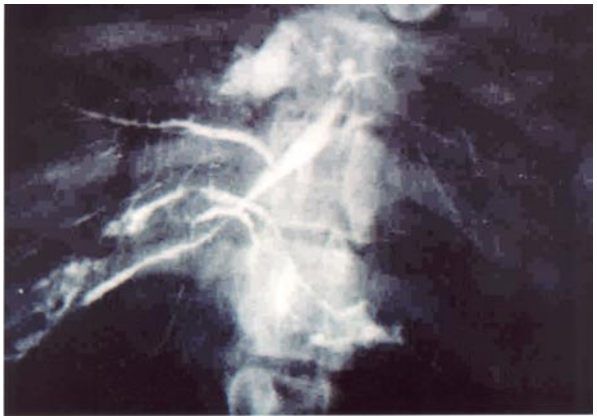


Figure 6. The roentgenogram of the dog biliary tree after fashioning of biliary end-to-end anastomosis. Free bile flow into the duodenum is evident.



mated biochemical parameters have been normalized within a month and remained within normal range throughout the whole period of the observation.

Macroscopic findings

At the autopsy, the presence of connective tissue capsule around the distention device was observed. The color of common bile duct anastomosis was normal. No signs of hyperemia or ischemia of proximal end of ductus hepaticocholedochus, nor changes of its diameter were observed. The bile flowed freely into the duodenum via the catheter. In the dogs after the device removing and biliary anastomosis fashioning, at the autopsy 20, 30, 50, 80, 120 days later, the reconstructed ductus hepaticocholedochus was not increased in diameter and the bile free passage into the alimentary tract was observed.

Histopathological changes

Histological examinations, performed consecutively during the ductus hepaticocholedochus distention have shown sclerotisation of mucosal layer. The muscular fibers following axis of ductus hepaticocholedochus have been evidently affected by the distention and tension. The loosening and swelling of muscular fibers were observed 3 days after the second operation. The local accumulation of young fibroblasts was noted beginning 5 days after the second operation. Analogical picture was seen in the dense connective tissue of biliary anastomosis. Newly formed fibers were distributed regularly. They were more densely packed and straightened. The wall of biliary anastomosis was thickened due to accumulation of newly formed tissue within 18 days. The results of histological examination indicate on partial destroying of the ductus hepaticocholedochus connective tissue, due to the distention and tension. The recovering of common hepatic duct and common bile duct mucosa was observed after removing of the device and bilio-biliary anastomosis creation. The area of anastomosis was revealed as not distinctly delineated. The liver biopsy performed at the same time has shown normal parenchyma in all animals, without signs of cholangitis, cholestasis, or biliary cirrhosis.

Discussion

Our results indicate that the adaptation of ductus hepaticocholedochus in dogs (corresponding to common bile duct in humans) after its partial resection (resembling resection of its stricture) by gradual distention during 18 days, using the device for the bile duct distention (DDBD) of our own construction is suitable procedure to fashion biliary, end-to-end anastomosis by microsurgery technique. The created anastomosis was patent up to 180 days of observation. Only 2 of 25 dogs died during experiments, but the causes of their fatal outcome seems to be avoidable. The remodeling of bile ducts walls, as observed in histological examination, seems to be permanent, assuring the long-lasting effect, however even longer period of observation is necessary to draw final conclusions on the affectivity of this method. The histological feature of the livers was normal, suggesting that the method is safe for the integrity of this organ.

Among many factors determining the choice of optimal surgical method of the benign biliary lesions management, the level and length of the strictures are prominent [7]. The creation of biliary, end-to-end anastomosis is possible very rare in the case of stenosis, when the significant part of the bile duct is intact, easily mobilized without blood flow disturbance. The choledochoduodeno- and choledochojejunostomy are methods of choice in the cases of low strictures. The resection of the stricture and bilio-biliary anastomosis creation are indicated for some middle (circular) strictures. In cases of total or subtotal strictures, most authors prefer to perform the hepaticojejunostomy with a long Roux-en-Y loop [13-16].

The results of biliary-enteric anastomoses are relatively good, however they do not restore the anatomical integrity of bile ducts nor preserve the function of Oddi sphincter. Therefore, more interesting for clinicians are the methods, which give the possibility to remove a stricture, to restore anatomical integrity of extra-hepatic bile ducts and to maintain a function of Oddi sphincter. Different authors tried to solve this problem using different allo- and xeno-transplants or prosthesis made of several synthetic materials for the restoration of bile duct

continuity [11,12]. The results of experimental and clinical application of the above-mentioned grafts were more or less unsatisfactory.

In our previous studies we evaluated the common bile duct reconstruction, after similar segmental resection, by venous auto-graft or by Gore-Tex vascular graft in dogs. We have found, that venous auto-graft might not be suggested for the common bile duct repair because of frequent necrosis of the graft wall, absence of the graft epithelization, the graft wall inflammation and imbibition by bile. As to Gore-Tex vascular prosthesis, the performed investigations have shown that the inflammation developed around the graft on the 2-3 days after the grafting. The pores of Gore-Tex graft were filled by elements of young connective tissue on the 3-4 day after implantation. The formation of the connective tissue capsule around the graft was observed 5-7 days after the operation. At the same time, the graft rejection from newly formed capsule was observed and the space between graft and newly formed capsule was filled by fresh connective tissue. The graft moved spontaneously into the alimentary tract in 20 of 30 animals. In 10 dogs, the graft was retained in the capsule that lead to the obturation of reconstructed common bile duct after 30-40 days. It is noteworthy, that repaired common bile duct has been functioning well during 6 months in the animals, in which the Gore-Tex graft has moved spontaneously into the alimentary tract [17,18].

This encouraging, however not fully satisfactory results of these studies, directed our attention to the possibility of adaptation of common bile duct after resection of its constricted part to end-to-end anastomosis by gradual mechanical distension, using the device for the distention of bile duct (DDBD) of our own construction. Received results have proved, that our method, after further development, could be useful in clinical practice for the restoration of anatomical integrity of bile ducts after the stricture resection in spite of its level and extent.

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