Video Article

Creation of Reversible Cholestatic Rat Model

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URL: <http://www.jove.com/details.php?id=2692>

DOI: 10.3791/2692

Citation: Subhas G., Bhullar J., Mittal V.K., Jacobs M.J. (2011). Creation of Reversible Cholestatic Rat Model. JoVE. 51. <http://www.jove.com/details.php?id=2692>, doi: 10.3791/2692

Abstract

Cholestasis is a clinical condition commonly encountered by both surgeons and gastroenterologists. Cholestasis can cause various physiological changes and affect the nutritional status and surgical outcomes. Study of the pathophysiological changes occurring in the liver and other organs is of importance. Various studies have been done in cholestatic rat models.

We used a reversible cholestatic rat model in our recent study looking at the role of methylprednisolone in the ischemia reperfusion injury. Various techniques for creation of a reversible cholestatic model have been described. Creation of a reversible cholestatic rat model can be challenging in view of the smaller size and unique hepatopancreatobiliary anatomy in rats. This video article demonstrates the creation of a reversible cholestatic model.

This model can be used in various studies, such as looking at the changes in nutritional, physiological, pathological, histological and immunological changes in the gastrointestinal tract. This model can also be used to see the effects of cholestasis and various therapeutic interventions on major hepatic surgeries.

Protocol

1. Rat biliary anatomy

The average bile duct diameter and length was 1 mm and 29 mm, respectively. The average distance between the pylorus and the duodenal papilla was 28 mm. There are two main pancreatic ducts which open into the bile duct - the anterior duct opens on the left side and the posterior duct opens on the right side. In addition to these major ducts, a number of minor ducts that drain all three portions of pancreas open directly to the bile duct.⁶

2. Technique

All animal experiments were performed in agreement with the National Institutes of Health guidelines for ethical research and were approved by the institution's Research Committee and Animal Care Committee. Male Sprague-Dawley rats aged 8 weeks were used for this demonstration. The rats were obtained from Charles River Laboratories in Wilmington, MA and all were over 300 grams. Rats had access to standard laboratory diet and were housed together in standard laboratory conditions.

Rats were initially anesthetized with isoflurane and kept under anesthesia during surgery with isoflurane through a mask. A midline incision of 2 cm was made starting from the xiphisternum. Once the fascia was opened, the liver lobes were retracted cranially with a Sen's retractor, and the duodenum was retracted caudally using Q-tips. The bile duct was identified as a tubular structure entering the duodenum. The bile duct was placed under tension and partially cut open. A sterile 5 cm long polyethylene tube with an inner diameter of 0.6 mm and an outer diameter of 0.9 mm was used. One end of this tube was heat sealed and the other end was gently beveled. The beveled end was then passed into the bile duct. This was secured in place using 8-0 Nylon sutures both proximal and distal to the opening in the bile duct. The remaining tube along with the sealed end was placed in the peritoneal cavity. The operative site was irrigated with normal saline. The abdomen was then closed in 2 layers, with 4-0 Polyglactin suture. The linea alba was closed with continuous sutures and the interrupted dermal sutures were placed. Skin glue was then applied on skin. The rats were allowed to recover under standard laboratory conditions with daily body weight monitoring to ensure proper hydration.

For the cholestasis reversal operation, the rats were anaesthetized using isoflurane as described previously. The abdomen was opened over the previous incision site. The tube was identified and taken out from the peritoneal cavity. Omental adhesions around the tube are freed using blunt and sharp dissection. A site in the duodenum was then identified for comfortable positioning of the duodenostomy tube. A purse string suture, 2-3 mm in diameter, was then placed using 8-0 Nylon. The duodenum was then opened inside this purse string suture. The sealed end of the tube was then cut to appropriate length. Free flow of bile was ensured. This end of the tube was then placed into the duodenum and the purse string suture was tightened. The abdomen was irrigated and closed in layers.

In a previous study, wherein choledochoduodenostomy was performed using a different technique, the rats were survived for 12 weeks and the rats were healthy during that period. Also this study confirmed the reversal of biochemical and histological changes after choledochoduodenostomy in rats subjected to obstruction of the bile duct for a period of 2 weeks.⁷

Discussion

Cholestasis leads to a myriad of changes in the gastrointestinal system. Studies have been done looking the changes in the immune system and nutritional status.¹⁻³ Cholestasis can affect outcomes of hepatic surgeries. Studies have been performed to improve the outcomes of hepatic

surgeries in the presence of cholestasis.⁴⁻⁵ With improvements in medicine and research, further studies will be done on cholestasis. Hence it is necessary to have a good cholestatic model. The rat is preferred as an experimental animal because it is readily available, easily handled, inexpensive and a sturdy model for studying the hepatopancreatobiliary system.⁶ Through this video article we demonstrate the creation of a reversible cholestatic model which can be used in future studies.

Disclosures

No conflicts of interest declared.

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