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A Study on Liver-Injury of SD Rats with Autologous Orthotopic Liver Transplantation by Bile Duct Angiography using Meglumine Diatrizoate and Omnipaque

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ABSTRACT

Objective: To investigate the liver-injury of the SD rats in autologus orthotopic liver transplatation using Meglumine Diatrizoate and Omnipaque. **Methods**: The portal veins of 60 healthy SD rats were perfused to set up orthotopic liver autotransplatation models. Then the external drainages of rats' bile duct were built up by bile duct cannula. The ALT and AST in blood serum were detected 24h and 48h after the operation respectively using the recommended dose of Meglumine Dia- trizoate, Omnipaque and normal saline. The blank trial group and simlpe operation group were the control group.**Results**: The ALT in the SD rats with orthotopic liver autotransplatation are higher than that in the blank trial group there is no significant difference between the blank trial group with the normal saline and simple operation group. Although there is significant difference between the blank trial group with the Meglumine Diatrizoate and the Omnipaque group. The bile duct angiography were performed after 24h and 48h. The AST in the SD rats with orthotopic liver autotransplatation are higher than that in the blank trial group;there is no significant difference between the blank trial group and simple operation group. But there is significant difference between the blank trial group with the Meglumine Diatrizoate and the Omnipaque group; there is significant difference after 24h between the blank trial group and the normal saline group; however there is no significant difference after 48h between the blank trial group and the normal saline group.**Conclusion**: Meglumine Diatrizoate and Omnipaque can damage the liver of SD rats in autologous orthotopic liver transplantation during bile duct angiography. The damage from Meglumine Diatrizoate is much more than Omnipaque.

Key Words: Liver-injury, Orthotopic liver autotransplatation Model, Meglumine Diatrizoate, Omnipaque.

INTRODUCTION

Biliary imaging diagnosis is the gold standard in biliary diseases because it can found biliary disorders, indicate the damage level, and can guide the interventional therapy. However, there is no report about the side effects of contrast medium produce to patients with liver transplantation. Angiography or contrast CT is performed prior to surgical intervention to assess tumour resectability, for a preoperative visualisation of vascular anatomy, as well as in non-diagnostic findings in ultrasound and simple computerised tomography. Diagnostic and therapeutic interventional techniques in the liver (fine needle puncture, perfusion, embolisation) and the bile ducts (PTC, ERCP, PTCD, endoprosthesis, stents) are performed selectively in patients with pre and post liver transplant in close co-operation with surgeons, radiologists and gastroenterologists.

MATERIALS AND METHODS

Experimental materials

Ordinary syringe,0-4 degrees Celsius ringer

solution Contains heparin sodium (50 U/mL),dexamethasone (10 mg), and adenosine triphosphate (ATP 100 mg),8-0 and 9-0 without damage Prolene suture vessels,a set of surgical microscopic devices,microcomputer infusion pump,Water chloric aldehyde 10%,Meglumine Diatrizoate 76%,15.2g/20ml, produced by Shanghai XuDong hoop pharmaceutical Co.,LTD and Omnipaque 300mgI/ml , produced by General electric Co., Shanghai Co., LTD.

Experimental methods

Experimental animals and grouping

Sixty healthy SD pure male rats from the medical animal laboratory center of Xi'an Jiaotong University were taken, each weight 200-250 g. All the rats divided into five groups randomly: blank trial group, simple operation group(S group),normal saline group, Meglumine Diatrizoate group and Omnipaque group(O group).

Animal models

Experimental rats were fed by free food and general feeding . They were 6 h Preoperatively fasting. 10% hydration chlorine aldehyde given to anesthetized rats and then performed abdominal midline incision, exposed sword hilt and sternal elevation. Using self-made pull hook, then open abdominal wall and counterclockwise liver, and free the inferior vena cava by dissecting the liver. Expose the first liver completly, and cut open the duodenum ligament of the liver , then free portal (PV) from the junction of mesenteric vein and spleen vein. Using microvascular clip closes the liver duodenal ligament of the junction of superior mesenteric vein and splenic vein , then block (PV) and hepatic artery, and put needle into (PV) inject heparin saline (30U/ml) 5ml and fixed the needle. Puting microvascular clamps on SHVC and IHVC, attention on microvascular clamps less as far as possible. In IHVC slightly above clip intramural venous blood perfusion 1mm to cut open for fluid flow. The PV puncture site microcomputer intravenous infusion pump 5ml/min with the slow continuous infusion (20ml liquid), and ice solution on liver surface for lowing temperature, then the whole liver became yellow and liver perfusion over. Pulling the needle,then using 9-0 Prolene line to repair PV puncture point, and using 8-0 Prolene line to repair IHVC outflow. After the completion of the examination, loosing microvascular clamps respectively while making liver restore temperature with warm saline.

Bile duct angiography

In the process of animal model establishment, separating the common bile duct and inserting epidural anesthesia line in position of common bile duct into duodenal upstream about 0.5 cm,and the embedding line fixed in large part subcutaneous scaffolds while the proximal line is fixed. After 24 hours of the establishment of the animal model ,using external orifice connecting with venous infusion pump and microcomputer with 10ml/min speed to syringe injection of contrast and saline (In accordance with the recommended dose (76% of 1ml) amine generic Portuguese champions, but parker/kg of 1.2 mL/kg configured).

Collecting specimen

After 24 hours of bile duct angiography, taking the rats' tail venous blood 1-2 ml to get centrifugal serum under normal temperature 1 500 ml/min 5 min and to keep at low temperature.In 48 hours after Bile duct angiography , anesthetized the second rats laparotomy, taking the rats' inferior vena cava blood 1-2 ml to get centrifugal serum under normal temperature 1 500 ml/min 5 min and to keep at low temperature. Cliping the tissue from the left lobe of liver around 0.4 cm x 0.5 cm x 1.0 cm to fixed in 40 g/L polyphosphate formaldehyde solution, then paraffin , and getting 5μm thick slices for sending histopathologic examination.

Serologic test

Alanine amino shift enzyme (ALT) and aspartate amino shift enzyme (AST) were tested by automatic biochemistry analyzer in Xi 'an jiaotong university medical school first hospital biochemical room.

Statistical analyses

Values were expressed as mean ± standard deviation. Single factor analysis of variance of SPSS16.0 statistical analysis software was used. The statistical significance level was set at 0.05.

RESULTS

After 24 hours and 48 hours of bile duct angiography ALT activity test

The ALT in the SD rats with orthotopic liver autotransplatation are higher than that in the blank trial group (Table 1); there is no significant difference between the blank trial group with the normal saline and simple operation group. There is significant difference difference between the blank trial group with the Meglumine Diatrizoate and the Omnipaque group.

Table 1; Please Captions here.

Group	24h		48h	
	ALT	AST	ALT	AST
K	27.20± 4.87▲	60.60± 21.93▲	24.80± 9.52▲	60.20± 37.79▲
D	87.40± 11.67◇	164.20± 13.70◇	78.20± 6.06◇	147.40± 15.37◇
S	122.20± 31.62*	324.40± 36.08*	100.80± 15.43*	142.20± 10.43*
F	328.80± 167.15☆	956.80± 214.70☆	481.60± 203.96☆	1209.80± 307.15☆
O	145.60± 17.94△	484.60± 66.97△	165.60± 22.83△	692.80± 157.79△

After 24 hours of bile duct angiography ALT activity test shows that: **and ◇compare with▲ p<0.05 *and compare with ◇p＞0.05 and*compare with△ p<0.01； * compare with△p＞0.05.*

After 24 hours of bile duct angiography AST activity test shows that: *◇compare with▲p＞0.05； ☆、*and△compare with▲p<0.01； *compare with◇p<0.05； ◇、*and compare with☆p<0.01； * compare with△p<0.05.*

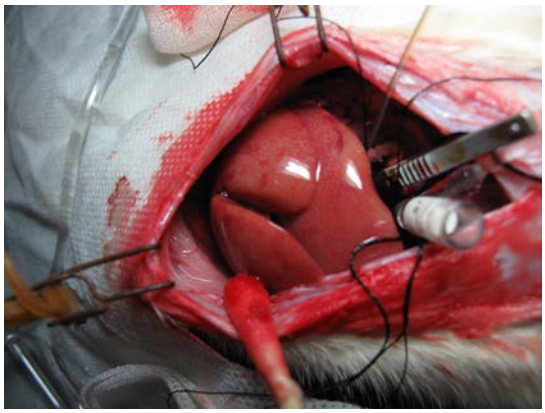
After 48 hours of bile duct angiography ALT activity test shows that: **and ◇compare with▲ p＞0.05； △ compare with▲ p<0.05 ☆ compare with▲ p<0.01； * and △compare with◇p＞0.05； ◇、* and compare with☆p<0.01； * compare with△p＞0.05.*

After 48 hours of bile duct angiography AST activity test shows that: **and ◇compare with▲ p<0.05； *compare with◇p＞0.05； ◇、 * and compare with ☆p<0.01； * compare with △p<0.01.*

After 24 hours and 48 hours of bile duct angiography AST activity test

The AST in the SD rats with orthotopic liver autotransplatation are higher than that in the blank trial group (Table 1); there is no significant difference between the biank trial group and simple operation group. There is significant difference between the biank trial group with the Meglumine Diatrizoate and the Omnipaque group; there is significant difference after 24h between the blank trial group and the normal saline group; there is no significant difference after 48h between the blank trial group and the normal saline group.

Before the perfusion



After the perfusion

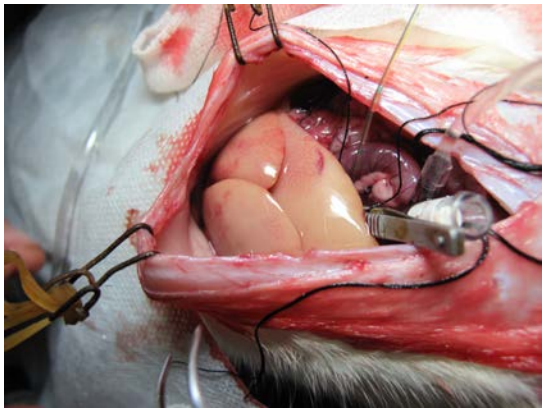


Fig. 1: Liver was red before the perfusion, while it turned to yellow after perfusion.

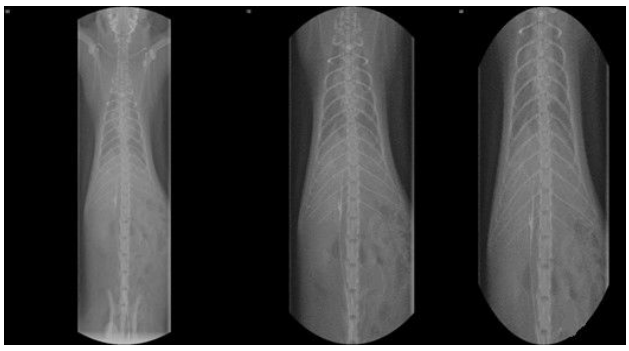


Fig. 2: Bile Duct Angiography

DISCUSSION

Liver transplantation in China has effected the advanced international level, after reviewing a large amount of data of clinical patients; we found that the postoperative biliary complications are an important factor to the survival of the graft[1]. In the 1990s, postoperative minor and major biliary complications are 30% ~50% and 20% ~30%[2], respectively, which are the main factors threatening the graft survival[3]. With the improvement of the organ preservation technology and surgical technique liver transplantation incidence of mortality and biliary complications were reduced, by 8% ~ 25% and 1% ~ 5% respectively, which accounts for postoperative death in 15% ~ 34%[4,5].

Biliary complications have been reported to occur at a relatively constant rate of approximately 10–15% of all deceased donor full size OLTs. There is a wide range of potential biliary complications which can occur after OLT. In ordinary disease patients contrast tests, contrast agents couse specific physical-chemical reaction,with serious side effects which have been reported in many studies[6]. Ordinary biliary diseases animal model test also confirmed that iodine in contrast damage the liver cell[7]. We should not ignore the damage of the contrast to graft liver. The rat model of orthotopic liver transplantation autologous in this experiment features simple operation[8], the survival rate is high, reported in the literature model about 95%[9], avoid immune rejection rate[8], but still need careful surgical operation skill[10].

The method to analysis the liver damage caused by contrast is feasible by testing the ALT, AST activity after 24, 48 hours of bile duct angiography and the result is reliable: the higher level of aminotransferase and the higher level of degree of damage[11]. This experiment was clear picture of graft injury itself. We should take to minimize the number of imaging, the use of nonionic media, as well as complete recovery after liver transplantation in imaging measures to reduce the damage. Whether the damage of liver transplantation in liver cell metabolism contrast and the specific mechanism caused need further study.

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