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INSITU LIVER AUTOTRANSPLANTATION IN DOGS WITHOUT VENOVENOUS BYPASS, NOVEL TECHNIQUE FOR TRAINING ON LIVER TRANSPLANTATION

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ABSTRACT

Introduction : Living-related liver transplantation is gaining increasing acceptance in Egypt and is the only available liver transplantation technique as cadaveric grafts are not approved by law. However it needs high surgical skills regarding hepatic surgery, micro vascular anastomosis & training on small biliary anastomosis.

Aim : Provide surgical team responsible for living-related liver transplantation with frequent training on a model very similar to that in human. The aim is to acquire the required surgical skills.

Methodology : This technique was done in 9 adult mongrel dogs of both

sexes weighing between 8.5-15 kg, in experimental animal house in Urology nephrology center. General anesthesia is used in all dogs with intubation. Through midline incision and insertion of ring retractor. dissection of hepatic artery, portal vein, common bile duct and hepatic veins is done with preservation of IVC and isolated dissection of LHV and RHV. Division of HA, PV, CBD is then carried out followed by clamping RHV & LHV and anterior venotomy of LHV. Infusion of PV with cold ringer's solution at 4 C° with drainage from LHV venotomy. Reanastomosis of HA, PV, CBD & closure of venotomy is done at the end with revascularization of the graft. Wedge liver biopsy was taken before portal clamping, at 30 min ischemia, after

portal reperfusion and after arterial reperfusion. Postoperative fluids and antibiotics are given. Follow up for survival up to 6 months is done with scarification of living dogs for assessment.

Results : All dogs survived the operation and up to 24 hours. One dog survived up to 6 months and scarified to assess success of technique. Biliary leak occurred in one dog and discovered after 2 weeks. Average survival in other dogs is 2 weeks. Minimal focal necrosis of the liver was noted after 30 min ischemia. Reperfusion changes are minimal mainly neutrophil infiltration and mild vacular degeneration.

Conclusion : Liver transplantation in dogs is an excellent model for training surgical team responsible for liver transplantation as the number of cases is not enough to reach the high level of surgical experience required. It will be also valuable as research tool, to study ischemia and reperfusion injury.

INTRODUCTION

Living-related liver transplantation has been the focus of much attention as the available option for end stage

liver disease in Egypt. Increasing organ demand and excellent recipient survival reported by several leading groups (Millis et al., 2000 & Inomata et al., 1999) has urged adoption of this outstanding modality. However, safe and successful segmental living donor liver transplantation can only be achieved by very experienced surgeons. Surgical techniques for transplantation of kidney were developed in dogs. Subsequent techniques were developed for transplantation of liver, hearts and lung.

The canine model could be an effective surgical model for technical training of surgeons and even more useful for basic transplantation research (Cherqui et al., 1990 & Kasia et al., 1997).

Experiments with the animal models were first reported in the mid 1955. In 1955, Welch performed the first heterotopic liver transplantation in dogs (Welch 1955). The first known efforts at experimental Orthotopic liver transplantation were made by Cannon in 1956 at the University of California at Los Angeles (Cannon 1956).

Several techniques of canine partial liver transplantation are based on

that of Cherqui et al which uses 40% of canine liver volume including left lateral & medial segments (Cherqui et al., 1990). Ku-Yong Chung et al described a technique of partial living donor liver transplantation using 70% of liver (Ku-Yong Chung et al., 2002). Also, Segmental auxiliary liver transplantation was designed as a technique by Lygidakis et al., 1987.

Pig models for training liver transplantation were used. However they are expensive and clamping of the venous splanchnic system during orthotopic liver transplantation is responsible for high morbidity and mortality rates. Therefore the use of venovenous bypass is essential (Oike et al., 2001).

MATERIAL AND METHODS

This study was conducted in Urology nephrology center experimental animal house on 9 adult mongrel dogs of both sexes weighing between 8.5-15 kg. All dogs were acclimatized in animal center for one week before operation and were fasted before. Dogs are catheterized with shaving the abdomen before surgery.

ANAESTHESIA :

Anesthesia was induced by Xyla-

zine (2 MG/KG, I.M injection) and after intubation maintained by thiopental 15MG/KG I.V. Dogs were ventilated mechanically by positive pressure ventilation. Atropine sulphate subcutaneous 0.03 mg/kg and .I.V fluids in the form of warm lactated ringer's solution 10 ML/KG/Hour was used. Analgesia is maintained by Ketofan 1 MG/KG every 2 hours. Prophylactic cephalosporin antibiotic is given to all dogs (Rocephin).

Incision :

Midline incision from xiphoid process. We use a ring self-retractor.

Procedures :

Mobilization and dissection of the liver from its ligaments was done starting from right and left triangular ligaments. Dissection of the CBD with preservation of adventitia & blood supply and put on a vessel loop, then dissection of the hepatic artery with removal of adventitia & put on vessel loop, dissection of the portal vein with removal of all the lymphatic & fibro fatty tissue & put on tape (Picture 1).

Dissection of hepatic veins from IVC with isolation of left & middle hepatic vein and the right hepatic vein: each on vessel loop (Picture 2).

Division of CBD at its middle between bull dogs, followed by division of hepatic artery between bull dogs with irrigation by heparinized saline and removal of all excess adventitia. Magnifying loop 4.5 is used. Division of portal vein at its middle after control by debakey clamp with insertion of small Nelaton tube number 12 in the proximal end. This is attached to the irrigating cold ringer solution. Clamping of the left and right hepatic veins with vascular clamp is then done with Incision of anterior wall of the left hepatic vein & middle hepatic vein for effluent of irrigation fluid (Picture 3).

Irrigation through the portal vein by cold ringer's solution at 4 C° 500-1000 is started until the effluent fluid is clear, then the catheter is removed.

Porto-portal anastomosis end-to-end using 6/0 prolene, Posterior layer continuous & anterior layer interrupted sutures is done first, followed by Closure of the venotomy in left & middle hepatic vein using 6/0 prolene continuous suture. Reperfusion of the liver through the portal vein is then established

Hepatic artery end-to-end anastomosis using 7/0 prolene on 8 mm

needle interrupted suture in first cases and 8/0 prolene on last cases. Irrigation of the artery with saline heparin is used with flushing. Duct-to-duct anastomosis \pm stent 7fr inside using interrupted 6/0 PDS is lastly done (Picture 4).

Closure of the abdomen after homeostasis without drain using vicryle and nylon loop. Post operative care is conducted in animal house with intra-operative & post operative antibiotics (cephalosporins) and fluids.

RESULTS

All dogs subjected to the procedure were alive up 24 hours. One dog survived 6 months and sacrificed later to assess patency of anastomosis (Picture 5).

Other dogs survive between 10 to 21 days. Mean duration of procedure 3.5 hours, cold ischemia 25 minutes, hot ischemia 5 minutes, mean period of PV anastomosis 10 minutes, HA 30 minutes, CBD 30 minutes & HV closure 5 minutes.

PATHOLOGICAL EXAMINATION OF LIVER BIOPSY IN 4 DOGS IS SHOWN IN TABLE 1.

Short time cold ischemia (30 M),

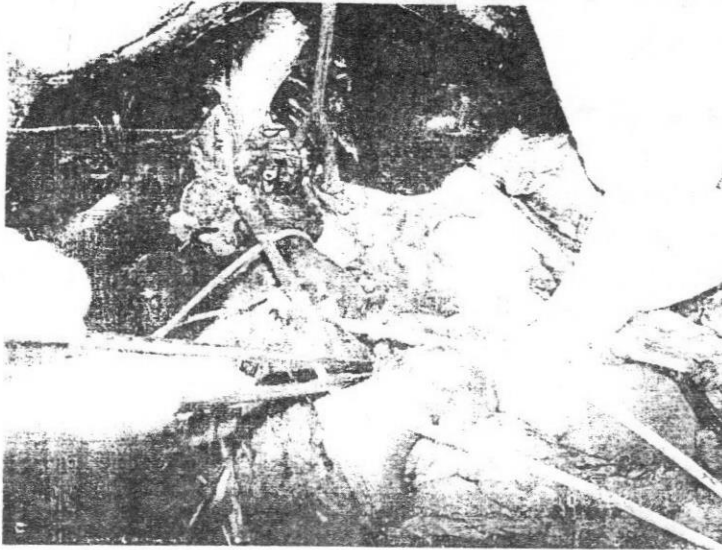
has no significant pathological changes on liver biopsy. The changes are minimal, in the form of rare lytic necrosis.

- Post- portal reperfusion biopsy shows minimal focal necrosis, minimal to mild vacular degeneration and occasional neutrophils in parenchyma.
- Post- arterial reperfusion biopsy

shows similar; however, more evident changes like the post-portal one. There is more neutrophils infiltrate and more evident vacular degeneration. Vacular degeneration shows zonal pattern, mainly sparing periportal area. On the other hand no zonal predilection to neutrophil infiltrates.

Table (1) Pathology results

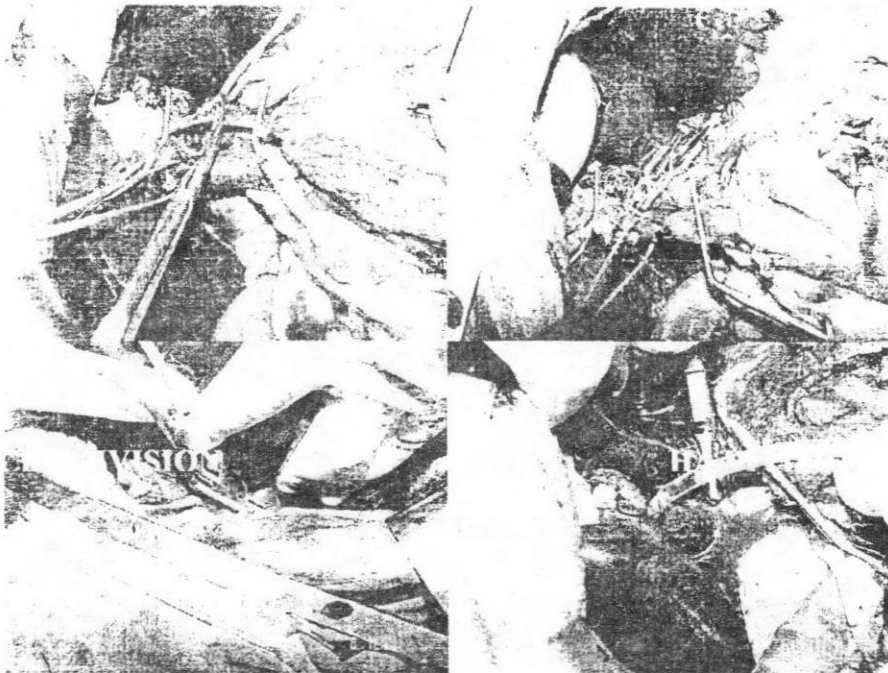
	30 Minutes ischemia	portal reperfusion	Arterial reperfusion
Dog 1	Mild focal necrosis	Mild focal necrosis	Mild focal necrosis
Dog 2	Mild focal necrosis	1- Mild focal necrosis 2- Portal & sinusoidal congestion	Neutrophil infiltrates. Vacular degeneration zone 3&2
Dog 3	Focal neutrophil infiltrate	Portal congestion	1- Focal neutrophilic aggregate 2- Lytic necrosis mainly zone 3
Dog 4	1- Mild focal necrosis 2- Neutrophil infiltrate	Vacular degeneration	1- Neutrophil aggregate 2- Vacular degenerate



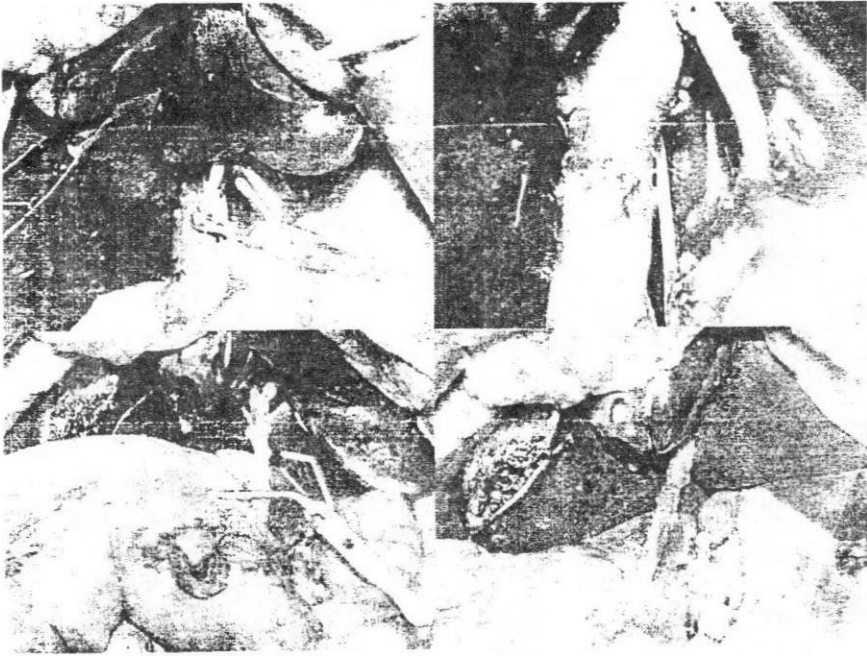
Picture 1. Dissected CBD, P.V., Hepatic artery.



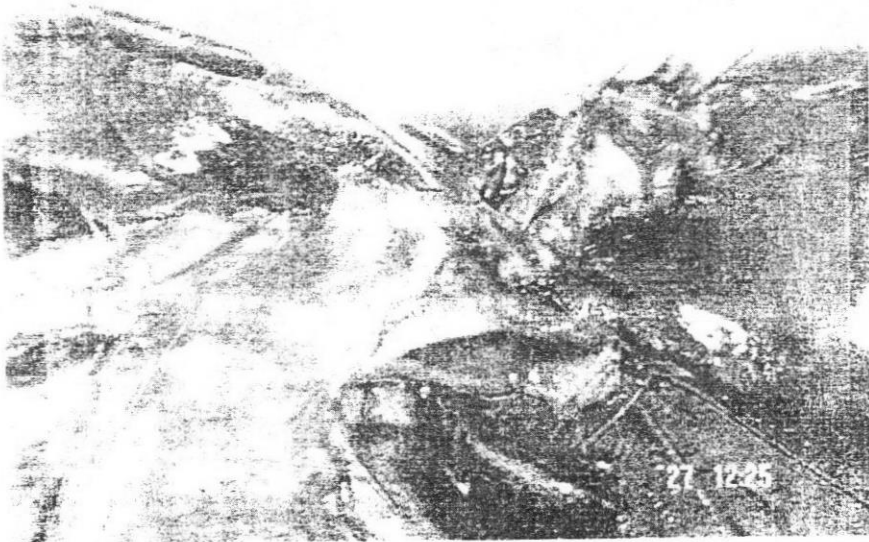
Picture 2. Dissected left & right hepatic vein.



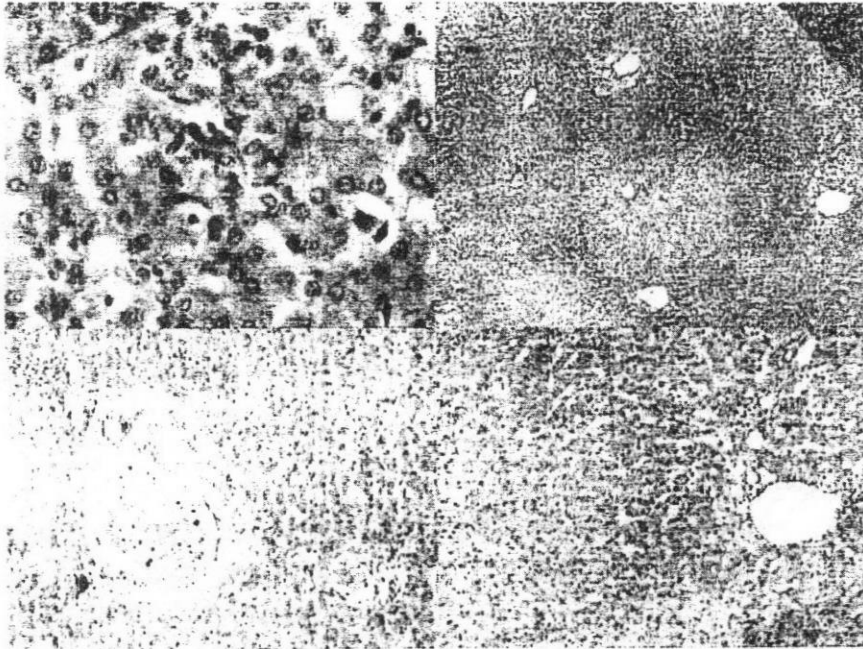
Picture 3. Clamping hepatic artery, P.V. & hepatic veins with perfusion of P.V. by cold ringer.



Picture 4. Anastomosis of HA, P.V., CBD & HV.



Picture 5. Follow up with patent anastomosis.



Picture 6. Pathology: (a) focal necrosis a (b) vacular degeneration
(c) portal congestion (d) neutrophil infiltration

DISCUSSION

Split liver transplantation is an increasingly used technique and because of organ shortage living-related liver transplantation is another technique to overcome this problem & is the only permissible technique in countries like Egypt where cadaveric liver transplantation is not accepted.

Adult living-related liver transplantation is based on grafting right liver lobe with right hepatic artery, right portal vein & right hepatic vein. Biliary reconstruction of right duct or accessory ducts is done. It is efficient and safe if done by experienced surgeon trained on microvascular surgery and using magnifying loops for proper dissection (Boillot O et al., 1999).

It needs special skills in micro vascular anastomosis. This can be gained only with experimental surgery. to be accustomed with the used of magnifying loops. The hepatobiliary surgeon by this way will be able to do the arterial & biliary anastomosis perfectly. Many techniques of experimental surgery in dogs are used, however, to gain experience; there is no need for complete removal of the liver & retransplantation. We did auto

transplantation without venovenous bypass & this modal can be used for research. This model can be an easy one to study ischemia reperfusion injury.

Time zero biopsies frequently have morphological changes not related to preexisting donor disease. They include, hepatocyte ballooning, spotty necrosis/acidophil body formation, neutrophil polymorph aggregates & cholestasis. Similar changes may be seen, generally to lesser degree, in biopsies obtained from donor livers before reperfusion (Kukisop et al., 1990).

Neutrophilic infiltration appear to be largely related to reperfusion injury. Experimental studies. Show that sinusoidal endothelial cells are most susceptible to preservation injury (Hubscher and portmann)

The size of dog and excellent anatomy and low cost with availability makes it superior to other animals like the pig, rabbit and rat. However, it needs equipped animal house and skillful veteran for day follow up and for anesthesia & postoperative care.

This is a start of more extensive

studies on ischemia reperfusion injury in dogs using this model of liver transplantation

sults in dogs HPB Surg.; 2: 189-204.

CONCLUSION

Experimental surgery is the key for advancement of surgical technique & gaining special skills. The dog is good model for training before starting split liver transplantation or living-related liver transplantation. It gives the surgeon the necessary training on micro vascular anastomosis and use of magnifying loops for dissection and anastomosis. Also, Short time cold ischemia (30 M) has no significant pathological changes. Reperfusion changes are mild, mainly neutrophil parenchyma infiltrate and mild vacular degeneration. Changes are more evident after arterial reperfusion.

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