Hyperbaric Oxygen Therapy for Hepatic Artery Thrombosis After Liver Transplantation in Children

George V. Mazariegos, Kevin O'Toole,† Luis A. Mieles,§ Igor Dvorchik,* Manuel Meza,‡ George Briassoulis,* Jose Arzate,* Geraldo Osorio,* John J. Fung,* and Jorge Reyes**

Early hepatic artery thrombosis (HAT) after pediatric orthotopic liver transplantation (OLT) can cause significant morbidity and mortality, leading to liver failure or septic complications requiring urgent retransplantation. Experimental evidence that hyperbaric oxygen (HBO) may ameliorate hepatic ischemic-reperfusion injury led to this study of HBO in pediatric liver transplant recipients who developed HAT. Children undergoing OLT under primary tacrolimus immunosuppression and University of Wisconsin organ preservation between August 1, 1989, and December 31, 1998, who developed HAT were the basis for this study. Patients who developed HAT between March 1, 1994, and December 31, 1998, were treated with HBO therapy until signs of ischemia resolved (absence of fever, normalizing liver injury test results) or for 2 weeks. The pediatric OLTs performed from August 1, 1989, to February 28, 1994, who developed HAT served as a control group. Primary outcome measures were survival, retransplantation rate, time to retransplantation, incidence of hepatic gangrene, and days to collateral formation. Three hundred seventy-five consecutive pediatric patients underwent 416 OLTs between August 1, 1989, and December 31, 1998. Thirty-one patients (7.5%) developed HAT at a mean time of 8.2 days (range, 1 to 52 days) post-OLT. In 17 patients, HBO treatment was begun within 24 hours of HAT or immediately after the revascularization attempt and performed twice daily for 90 minutes at 2.4 atmospheres pressure. Fourteen patients were treated without HBO. None of the HBO-treated patients developed hepatic gangrene. Eight HBO patients (47%) were bridged to retransplantation at a mean time of 157 days (range, 3 to 952 days) after initial OLT and all survived. Mean time to retransplant in the control group was 12.7 days (range, 1 to 64 days). HBO was well tolerated without significant complications. Although there was no significant difference in survival or retransplantation rates, HBO significantly delayed retransplantation, potentially by hastening the development of hepatic artery collaterals.

Hepatic artery thrombosis (HAT) after orthotopic liver transplantation (OLT) can result in hepatic gangrene and liver failure in as many as 1 of 3 patients.[1] This syndrome, a consequence of the lack of oxygen-saturated arterial blood and translocation of gas-forming bacteria, is fatal unless immediate retransplantation is performed.[2] More commonly after HAT, septic complications related to bile leak, biloma, abscess, or cholangitis force urgent or remote retransplantation. In either case, the continuing organ shortage and current lack of effective bioartificial support place patients with HAT at risk for serious morbidity and early post-OLT mortality. Historical experience with hyperbaric oxygen (HBO) therapy for organ preservation in clinical human liver allografts[3] and recent experimental evidence that HBO may ameliorate hepatic ischemic-reperfusion injury[4] led to this study of HBO in pediatric liver transplant recipients who developed HAT.

Materials and Methods

Pediatric patients who received a liver transplant under primary tacrolimus immunosuppression and University of Wisconsin organ preservation between August 1, 1989, and December 31, 1998, who developed HAT

*From the *Department of Surgery, Thomas E. Starzl Transplantation Institute; the †Department of Emergency Medicine, the University of Pittsburgh Medical Center; the ‡Department of Radiology, Children's Hospital of Pittsburgh, Pittsburgh, PA; and §Strong Memorial Hospital, University of Rochester, Rochester, NY.*

Supported in part by research grants from the Veterans Administration and Project Grant no. DK 29961 from the National Institutes of Health, Bethesda, MD.

Address reprint requests to Jorge Reyes, MD, Thomas E. Starzl Transplantation Institute, 3705 Fifth Ave, University of Pittsburgh Medical Center, Children's Hospital of Pittsburgh, Pittsburgh, PA 15213.

1074-3022/99/0505-0012$3.00/0

documented by ultrasonography are the basis for this report. Patients who developed HAT between August 1, 1989, and February 28, 1994, were treated with intravenous antibiotics and appropriate drainage of hepatic abscesses or bile duct strictures and relisted for retransplantation. Between March 1, 1994, and December 31, 1998, children who developed HAT were also treated with HBO therapy until signs of ischemia resolved (absence of fever, normalizing liver injury test results, recanalization of hepatic artery collaterals on ultrasound) or for 2 weeks. Retransplantation was performed for consequent biliary complications, such as bile leak or unmanageable bile duct strictures. In both groups, hepatic artery revascularization (HAR) was attempted if the diagnosis of HAT was made within 24 hours of OLT or within 24 hours of a previously normal ultrasound result.

Primary outcome parameters were survival, retransplantation rate, time to retransplantation after HAT, incidence of hepatic gangrene defined as the presence of confluent hepatocyte necrosis affecting the hepatic parenchyma, and days to collateral formation documented by Doppler ultrasonography.

HBO Treatment

HBO treatment was started within 24 hours of the diagnosis or immediately after the revascularization attempt. HBO treatments were performed twice daily for 90 minutes at 2.4 absolute atmospheres (ATA). Middle-ear barotrauma was prevented with pseudoephedrine premedication and autoinflation. In infants unable to autoinflate, tympanotomy tubes were placed before HBO treatment.

Statistical Analysis

Overall patient and graft survival were assessed by the Kaplan-Meier method, with Breslow's test used for comparison between treated and nontreated groups. To compare time to retransplantation and time to collateral development between treated and nontreated groups, the Mann-Whitney test was used. Fisher's exact test was used to compare the proportion of patients who underwent retransplantation. SPSS statistical software was used (SPSS Inc, Chicago, IL); $P \leq .05$ was considered significant.

Results

Three hundred seventy-five consecutive pediatric patients underwent 416 OLTs between August 1, 1989, and December 31, 1998. Thirty-one patients (7.5%) developed HAT at a mean time of 8.2 days (range, 1 to 52 days) post-OLT, documented by Doppler real time ultrasonography in all cases and confirmed operatively or with hepatic arteriography in 22 cases. Fourteen patients who underwent OLT between August 1, 1989, and February 28, 1994, who developed HAT and were not treated with HBO serve as a historical control group. Seventeen patients who underwent OLT between March 1, 1994, and December 31, 1998, who developed HAT were treated with HBO therapy. The mean number of treatments was 15.6 (range, 3 to 30 treatments). The demographics, timing, and degree of liver injury in the patients with HAT are listed in Table 1. Alanine aminotransferase (ALT) levels at the time of diagnosis, peak ALT levels during the first 10 days after HAT, and time from OLT to HAT were not different between the control and treatment groups.

Table 1. Demographics, Timing, and Degree of Liver Injury in Patients With HAT

	Control	HBO	*P*
No. of patients	14	17	
Sex (M/F)	9/5	6/11	
	Biliary atresia (9)	Biliary atresia (10)	
	Fulminant hepatic failure (1)	Allagile's syndrome (3)	
	Glycogen storage disease (1)	Tyrosinemia (1)	
	Cystic fibrosis (1)	$Alpha_1$-antitrypsin deficiency (1)	
	Oxolosis (1)	Cystic fibrosis (1)	
	Histiocytosis (1)	Neonatal hepatitis (1)	
Age at transplant (mo)	42.6 (4.6-178.2)*	33.2 (0.9-125.2)*	NS
ALT (IU/L), day 1 HAT	573 ± 806.9	523 ± 1216	NS (.95)
ALT (IU/L) peak, days 1-10	886 ± 1322.7	700 ± 1224	NS
Time HAT after OLT (d)	5.25	9.56	NS (.25)

Abbreviations: ALT, alanine aminotransferase; NS, not statistically significant.
*Range.

Clinical Presentation of HAT

HAT developed during the first week post-OLT in 18 patients, during the second week in 9 patients, during the third week in 3 patients, and in 1 patient at 49 days. Patients presented with elevation in liver function test results (n = 11), fever (n = 6), abdominal complaints (n = 1), bile leak (n = 2), and bacteremia (n = 5) or HAT was discovered on routine screening ultrasound (n = 6).

Impact on Patient Survival

Tables 2 and 3 list outcome after HAT in the control and HBO-treated groups, respectively. Sixteen of 17 HBO-treated patients (94%) are alive with a current follow-up of 31.2 months compared with 9 of 14 control patients (64%) with a current follow-up of 99.5 months. Mean survival time is 5.5 years in the control group and 4.8 years in the treated group ($P < .07$). Control patients had a 5-year survival rate of 59% compared with 94% at 5 years in the HBO group. Patient survival is shown in Fig. 1.

One patient in the HBO group who was critically ill before OLT died postoperatively. This 9-month-old boy with end-stage liver and intestinal failure underwent only an isolated liver transplantation because of his pre-OLT severity of illness, ventilatory requirements, and intermittent vasopressor requirement. He developed HAT on the first postoperative day and was treated with HBO until he recanalized his hepatic artery on the eighth day after HAT. His liver function stabilized at that point but deteriorated after a septic episode from an intestinal perforation, which made weaning from total parenteral nutrition impossible. All 8 patients who underwent retransplantation are alive and well.

There were five deaths in the control group; two deaths occurred after retransplantation. Patient no. 11 died of acute hepatic gangrene 24 hours post-OLT. Two other patients who died before retransplantation had evidence of hepatocellular necrosis (patient no. 5) or biliary sepsis with cholangitis

Table 2. Outcome After HAT in Control Group

Patient No.	Re-Tx	Current Status	Cause of Death
1	Yes	Alive	
2	Yes	Alive	
3	Yes	Alive	
4	No	Alive	
5	No	Died	Sepsis and multiple system organ failure
6	No	Alive	
7	No	Alive	
8	No	Died	Respiratory distress syndrome secondary to cholangitis
9	Yes	Alive	
10	Yes	Died	Sepsis, peritonitis
11	No	Died 24 hours post-OLT	Acute hepatic gangrene
12	Yes	Alive	
13	Yes	Alive	
14	Yes	Died	Refractory rejection, fungal peritonitis

Abbreviation: Re-Tx, retransplantation.

Table 3. Outcome After HAT in HBO Group

Patient No.	Re-Tx	Current Status	Cause of Death
15	No	Alive	
16	Yes	Alive	
17	Yes	Alive	
18	No	Alive	
19	No	Alive	
20	Yes	Alive	
21	Yes	Alive	
22	Yes	Alive	
23	No	Alive	
24	Yes	Alive	
25	Yes	Alive	
26	No	Alive	
27	No	Alive, mild biliary strictures noted on MRCP, no biliary obstruction	
28	No	Died	Sepsis and multiple system organ failure
29	Yes	Alive	
30	No	Alive	
31	No	Alive, temporary percutaneous biliary catheter placed to dilate central biliary stricture	

Abbreviations: Re-Tx, retransplantation; MRCP, magnetic resonance cholangiography.

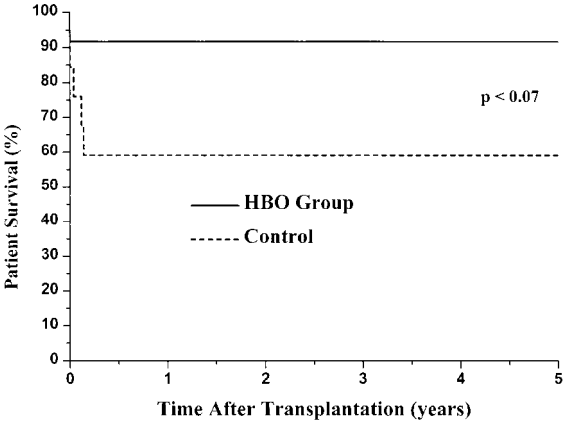

Figure 1. Patient survival.

(patient no. 8). The two patients who died after retransplantation had fungal hepatic parenchymal abscesses in the explanted liver and had undergone retransplantation in an urgent fashion.

Impact on Retransplantation

Eight patients in each group (57% in the control group and 47% in the HBO group; $P = .72$, Fisher's exact test) required retransplantation. The mean time to retransplantation was 12.7 days (range, 1 to 64 days) in the control group compared with 157 days (range, 3 to 952 days) in the treatment group ($P = .04$, Mann-Whitney test). The findings in the explanted liver allografts are listed in Table 4. The explant pathological examination in the control patients who underwent retransplantation showed a significant amount of confluent hepatocellular necrosis, hepatic abscesses, necrotizing cholangitis, and large-zone necrosis or submassive infarcts compared with the HBO-treated patients who required retransplantation.

Of note, there were no retransplantations performed for hepatic gangrene in the HBO-treated group. The HBO-treated group presented with evidence of bile duct complications, such as central biloma with or without bile leak, with only 1 of the

Table 4. Pathological Characteristics of Explanted Allografts

Patient No.	Pathological Findings of Explanted Livers		
Control group			
1	1) Segmental necrosis	2) Submassive infracts	
2	1) Bile duct necrosis	2) Hepatocyte necrosis	
3	1) Organizing subcapsular infarcts	2) Yeast in porta hepatitis	
9	1) Large-zone hemorrhagic/ischemic necrosis	2) Bile duct sloughing	
10	1) Acute cholangitis	2) Hepatic abscess (fungal, gram-negative organism)	
12	1) Patchy cholangitis		
13	1) Focal hemorrhagic necrosis with neutrophils		
14	1) Severe ischemia	2) Necrotizing cholangitis	3) Hepatic *Candida* abscess
HBO group			
16	1) Hilar necrosis		
17	1) Hilar biloma		
20	1) Extensive infracts with necrosis	2) Thrombosis of portal vein and hepatic artery	
21	1) Patchy recent infarctions	2) Bile duct necrosis	
22	1) Diffuse biliary strictures		
24	1) Cholestasis, mild		
25	1) Bile leaks with fungal elements		
29	1) Biloma	2) Hilar necrosis with yeast colonization	

8 patients who underwent retransplantation (patient no. 20) presenting evidence of extensive infarcts, hepatocyte necrosis, or liver failure. This patient had both portal vein thrombosis and HAT.

Retransplantation survival was 8 of 8 patients (100%) in the HBO-treated group, whereas 2 of 8 patients died in the control group (75% survival rate). The two control patients (no. 10 and 14) who died after retransplantation both had fungal hepatic abscesses in the failed allograft, one with necrotizing changes in the intrahepatic biliary tree. Peritonitis developed postoperatively in both patients and contributed to their deaths.

Impact on Liver Ischemia

Peak ALT values from days 4 to 10 did not significantly differ among control or treated patients. Hepatic artery collaterals detected by ultrasonography appear to develop earlier in the treatment than control group at 14.7 ± 1.6 days (mean ± SE; range, 6 to 27 days) versus 30 ± 9.5 days (range, 12 to 64 days) in the treated group, although the difference was not statistically significant ($P = .14$).

Impact of HAR

Urgent revascularization of liver allografts after early HAT in adults effectively restores arterial inflow but does not eliminate infectious complications or the possibility of retransplantation.[5,6] In children, the role of HAR is less well defined.[7] It has been our practice to attempt HAR in pediatric patients after OLT if the diagnosis is made within the first 24 hours post-OLT or within 24 hours of a previously normal ultrasound result. The operation consists of Fogarty catheter embolectomy of the donor hepatic artery after the intraoperative infusion of local intra-arterial urokinase and systemic anticoagulation with heparin. The hepatic artery anastomosis is then redone with or without the placement of an infrarenal aortic graft conduit, depending on the adequacy of arterial inflow and quality of the recipient hepatic artery.

Four of 14 patients (29%) in the control group underwent HAR, with 3 of 4 patients (75%) achieving immediate postoperative arterial patency. Nonetheless, 2 of these 3 patients subsequently required retransplantation for hepatic necrosis and bile leak. One of the 3 patients avoided retransplantation and is currently well. The patient in whom HAR failed underwent successful retransplantation.

Thirty-two percent of the patients (6 of 19 patients) underwent HAR in the HBO-treated group. Only 1 of these patients achieved arterial patency post-HAR. This patient also avoided retransplantation. Two patients in whom HAR failed also avoided retransplantation. HAR appears to have a limited role in the treatment of HAT in children when diagnosed early. However, it did not appear to be a confounding variable between the control or HBO-treated groups.

HBO Treatment-Related Complications

In most cases, HBO therapy was well tolerated. Seventeen patients received a mean of 15.6 treatments (range, 3 to 30 treatments). HBO was continued in 14 of 17 patients until protocol criteria were met. HBO was interrupted in 3 patients for hemodynamic instability precluding transport to the HBO chamber (patient no. 16), pneumonia and respiratory insufficiency (patient no. 19), and availability of a transplant organ (patient no. 20) in a child with both arterial and portal venous thrombosis. There were no serious adverse events or morbidity associated with HBO in this patient population. Since the completion of our study, 1 new patient developed seizures during HBO therapy, which resolved spontaneously and did not recur. This patient was also being treated with imipenem and had mild renal insufficiency, both of which may have reduced his seizure threshold.

Intubated patients have been successfully treated with a modified ventilator suitable for use in a hyperbaric chamber. Intubated patients from the intensive care unit are transported to the HBO chamber by a critical care physician and nurse. When possible, patients were extubated before continuing therapy in the hyperbaric chamber. In patient no. 31, HBO was temporarily suspended until the patient was extubated because of bradyarrhythmias that could have been related to HBO. The arrythmias resolved spontaneously and were hemodynamically insignificant.

Current Status of Patients With Salvaged Grafts

Three patients (21%; no. 4, 6, and 7) in the control group who salvaged their initial grafts are alive and well with normal liver function and a current

follow-up of 103.8 months. All 8 patients (47%) in the HBO group who salvaged their grafts have normal liver function at a mean follow-up of 29.7 months. Two of these 8 patients (25%) are currently stable, but each had a hospital admission for cholangitis related to significant central biliary strictures in 1 patient (no. 31) and mild bile duct strictures noticed on magnetic resonance cholangiography in 1 patient (no. 27). Patient no. 31 has a temporary indwelling percutaneous biliary catheter for intermittent dilatation. Both have been maintained on oral antibiotic therapy and are post-OLT a mean of 5.4 and 21.9 months, respectively. Their liver function is normal. The other 6 patients (75%) who salvaged their initial grafts have no evidence of bile duct stricture or hepatic abscess and have remained clinically well, with follow-up of 35 months.

Discussion

HAT after pediatric OLT continues to be a devastating complication and has been reported in 5% to 15% of pediatric cases. Its presentation is varied, but retransplantation continues to be needed in up to 60% of the cases.[8] The current organ shortage has placed these patients at risk for serious morbidity and early transplant mortality. HAT is still a devastating complication in children, especially in those who develop hepatic gangrene. Tan et al[9] reported 10 cases of HAT among 59 consecutive transplant recipients. There was a high mortality in this group because many (6 of 10 patients) developed hepatic gangrene. The majority of patients in this group were younger than 3 years of age or less than 15 kg in weight. Early total hepatectomy after HAT complicated by hepatic gangrene may be life saving but is attended by considerable morbidity.[10-12]

Current management of HAT involves appropriate antibiotic coverage, drainage of intrahepatic collections or bile duct strictures, and retransplantation in the face of intractable liver failure or septic complications localized to the liver. There has been growing experimental evidence that HBO may attenuate hepatic reperfusion injury and ameliorate the systemic inflammatory response in sepsis.[13] This evidence, coupled with the clinical need to bridge patients with HAT to transplantation or reduce the need for retransplantation altogether, led to this evaluation of HBO in this pediatric patient population.

In this trial, the control and HBO-treated groups were well matched in terms of initial severity of liver injury and timing of presentation of HAT. Initial baseline immunosuppression and organ donor characteristics are the same. Survival and retransplantation rates are similar in both groups. However, the time to retransplantation was significantly increased in the HBO-treated arm. All patients who required retransplantation in the HBO-treated group survived, whereas there were two deaths in the control group. We hypothesize the improved survival at retransplantation is caused by the reduced incidence of hepatic parenchymal abscesses, necrosis, or liver failure in the HBO group, allowing retransplantation to be performed in a more remote and elective fashion. The presence of fungal hepatic abscesses in both control patients who died after retransplantation contributed to their deaths from septic complications and peritonitis postoperatively.

The mechanism by which HBO may impact on allograft ischemia post-OLT is uncertain. At decreased oxygen tensions, the ability of the host to fight infection and heal wounds is seriously compromised. Bacterial killing by polymorphonuclear leukocytes and macrophages is impaired, and tissue healing is halted by decreased fibroblast proliferation, collagen deposition, and angiogenesis.[14-18]

At 2 ATA, the oxygen content of blood is increased by 25%, whereas plasma and tissue oxygen tension increases tenfold.[19-21] This results in a threefold increase in oxygen diffusion through body fluids, in such a way that more oxygen dissolved in plasma is delivered to ischemic tissues. Thus, HBO is frequently used in situations in which tissue viability and healing is compromised by hypoxia and/or infection. Crush injury, compartmental syndrome, diabetic wounds, irradiated tissue, and skin grafts and flaps with compromised vascular supply are some of the indications for HBO therapy.[22,23]

For HBO to be effective, some degree of blood flow is needed. The presence of a dual blood flow may explain the beneficial effect of HBO in liver allografts with HAT. An intact portal circulation is probably the vehicle through which increased amounts of oxygen, dissolved in tissue fluids, is transported to a liver deprived of arterialized blood flow. This likely explains our finding that the only patient who developed liver failure and large zones of hepatic parenchymal necrosis despite HBO

therapy had both portal vein and arterial thrombosis.

Increasing oxygen delivery may not be the only explanation for the beneficial effects of HBO. Skin grafts and flaps with compromised vascular supply constitute one of the most frequent indications for the use of HBO. Although reducing the initial hypoxic insult will increase graft viability,[24-26] there is also ample evidence that HBO promotes angiogenesis. Manson et al[27] showed capillaries grew distally almost three times further in pedicle flaps or guinea pigs treated with HBO compared with age-matched controls. Other investigators have shown HBO can enhance wound healing and flap survival by accelerating angiogenesis[28] and multiplying the number and size of vessels within the microvasculature.[29]

Of interest in this small series is that Doppler ultrasound confirmed reconstitution of hepatic arterial flow collaterals in patients who received HBO treatments at a mean time of 14 days after the diagnosis of HAT. The control group developed collateral formation at a mean time of 30 days after diagnosis of HAT, which is consistent with that previously reported.[30] This earlier collateralization may be one factor explaining the lower incidence of hepatocyte necrosis and gangrene and also may explain the delay in time to retransplantation experienced in the HBO group.

Middle-ear barotrauma, the most common side effect of HBO therapy, was prevented in our patients by appropriate intervention. Although pulmonary barotrauma during decompression may rarely occur among adult patients with airway obstruction, pulmonary and neurological manifestations of oxygen poisoning are not produced by daily exposures to 2.4 ATA, even in patients with adult respiratory distress syndrome. Extensive clinical experience in major HBO centers indicates ophthalmological, pulmonary, or neurological problems do not usually develop within the 20 to 50 treatments commonly used in clinical practice.[31,32] None of our patients had complications during HBO therapy, except for the possible association with a bradyarrhythmia that spontaneously resolved. Furthermore, the median follow-up of the surviving patients is 23.7 months (range, 5.4 to 111 months), and there have been no long-term complications reported.

Other potential applications of HBO include: (1) liver allograft preservation, (2) reperfusion injury of transplanted livers, and (3) extensive hepatic trauma and/or surgery with nonanatomic resection, in which hypovolemic shock and inflow occlusion may induce ischemic damage to large portions of the liver.

Experience with HBO in organ preservation has been reported since Paquet and Wessel[33] noted the microvasculature of the liver remains intact for double the amount of time when hypothermia is supplemented with HBO. Furthermore, Brettschneider et al[34] achieved successful orthotopic transplantation of dog livers after 24 hours or preservation at 40°C with 3.5 ATA of HBO. Although these studies performed several years ago showed the added value of HBO in enhancing the length of cold storage for liver allografts, to date, no clinical studies have been performed. With better preservation solutions and more readily available and easy-to-operate hyperbaric chambers, the possibility of enhancing cold storage time with HBO therapy might be considered.

It is conceivable HBO can also limit the ischemic damage of liver allografts with reperfusion injury, reduce the incidence of primary nonfunction, and thereby decrease the need for retransplantation. Using a rat model, Kaelin et al[35] were able to increase the survival of autotransplanted free flaps stored for 24 hours at room temperature by using HBO postoperatively. This beneficial effect was attributed to an increase in superoxide dismutase activity induced by HBO therapy that ameliorated the reperfusion injury.[35] Chen et al[4] recently reported the significant reduction of adherent leucoyctes and improved postsinusuidal flow velocity in a rat model of liver ischemia-reperfusion.

Although this is a small series, HBO can be safely used in children with HAT. This study suggests HBO may diminish the risk for hepatic gangrene and therefore help bridge these patients to a successful retransplantation in a more stable and elective status. Some patients who do not undergo retransplantation may reestablish arterial flow to the liver as early as 1 week after HBO. Furthermore, HBO may reduce the urgent need for retransplantation and allow for a later, more elective, retransplantation, perhaps by hastening collateral development. Given the severity of the complications associated with HAT, it is appropriate to further prospectively study HBO for this indication.

References

1. Tzakis AG, Gordon RD, Shaw BW, Iwatuski S, Starzl TE. Clinical presentation of hepatic artery thrombosis

after liver transplantation in the cyclosporine era. Transplantation 1985;40:667-671.
2. Shaked A, McDiarmid S, Harrison R, Gelebert H, Colonna J, Busuttil R. Hepatic artery thrombosis resulting in gas gangrene of the transplanted liver. Surgery 1992;111: 462-465.
3. Brettschneider L, Daloze PM, Huguet C, Porter KA, Groth CG, Hutchison DE, Starzl TE. The use of combined preservation techniques for extended storage of orthotopic liver homografts. Surg Gynecol Obstet 1968; 126:263-274.
4. Chen MF, Chen HM, Ueng SW, Shyr MH. Hyperbaric oxygen pretreatment attenuates hepatic reperfusion injury. Liver 1998;18:110-116.
5. Pinna AD, Smith CV, Furukawa H, Starzl TE, Fung JJ. Urgent revascularization of liver allografts after early hepatic artery thrombosis. Transplantation 1996;62: 1584-1587.
6. Scheiner PA, Varma CV, Guarrera JV, Cooper J, Garatti M, Emre S, et al. Selective revascularization of hepatic artery thrombosis after liver transplantation improves patient and graft survival. Transplantation 1997;64:1295-1299.
7. Massault PP, Soubrane O, Cardoso J, Dousset B, Pitre J, Devictor D, et al. Graft-saving management of hepatic artery thrombosis in pediatric liver transplantation. Transplant Proc 1997;29:439.
8. Busuttil RW, Seu P, Millis JM, Olthoff KM, Hiatt JR, Milewicz A, et al. Liver transplantation in children. Ann Surg 1991;213:48-57.
9. Tan KC, Yandza T, DeHemptinne B, Clapuyt PH, Claus D, Otte JB. Hepatic artery thrombosis in pediatric liver transplantation. J Pediatr Surg 1988;23:927-930.
10. Drazan K, Shaked A, Olthoff KM, Imagawa D, Jurim O, Kiai K, et al. Etiology and management of symptomatic adult hepatic artery thrombosis after orthotopic liver transplantation (OLT). Am Surg 1996;62:237-240.
11. Husberg BS, Goldstein RM, Klintmalm GB, Gonwa T, Ramsay M, Cofer J, et al. A totally failing liver may be more harmful than no liver at all: Three cases of total hepatic devascularization in preparation for emergency liver transplantation. Transplant Proc 1991;23:1533-1535.
12. Ringe B, Lubbe N, Kuse E, Frei U, Pichlmayr R. Management of emergencies before and after liver transplantation by early total hepatectomy. Transplant Proc 1993;25:109.
13. Luongo C, Francesco I, Cuzzocrea S, Filippelli A, Scafuro MA, Mangoni G, et al. Effects of hyperbaric oxygen exposure on zymosan-induced shock model. Crit Care Med 1998;26:1970-1979.
14. Hohn DC. Oxygen and leukocyte microbial killing. In: Davis JC, Hunt TK (eds). Hyperbaric oxygen therapy. Maryland: Undersea Medical Society, 1977:101-110.
15. Hunt TK, Linsey M, Grislis G, Sonne M, Jawetz E. The effect of differing ambient oxygen tensions on wound infection. Ann Surg 1975;181:35-39.
16. Hunt TK, Zederfeldt B, Goldstick TK. Oxygen and healing. Am J Surg 1969;118:521-525.
17. Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. Surg Gynecol Obstet 1972;135:561-567.
18. Niinikoski J: Effect of oxygen supply on wound healing and formation of experimental granulation tissue. Acta Physiol Scand 1969;334:1-72 (suppl).
19. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. N Engl J Med 1996;334:1642-1648.
20. Boerema I, Meijne G, Brummelkamp K, Bouma S, Mensch MH, Kamermans F, et al. Life without blood: A study of the influence of high atmospheric pressure and hypothermia on dilution of the blood. J Cardiovasc Surg 1960;1:133-146.
21. Bassett BE, Bennett BP. Introduction to the physical and physiological basis of hyperbaric therapy. In: Hunt TK, Davis JC (eds). Hyperbaric oxygen therapy. Maryland: Undersea and Hyperbaric Medical Society, 1977:11-24.
22. Grim PS, Gottlieb LJ, Boddic A, Batson E. Hyperbaric oxygen therapy. JAMA 1990;263:2216-2220.
23. Nemiroff PM, Rybak LP. Applications of hyperbaric oxygen for the otolaryngologist head and neck surgeon. Am J Otolaryngol 1988;9:52-57.
24. McFarlane RM, Wermuth RE. The use of hyperbaric oxygen to prevent necrosis in experimental pedicle flaps and composite skin grafts. Plast Reconstr Surg 1966;37: 422-430.
25. Shulman AG, Krohn HL. Influence of hyperbaric oxygen and multiple skin allografts on the healing of skin wounds. Surgery 1967;62:1051-1058.
26. Champion WM, McSherry CK, Goulian D. Effect of hyperbaric oxygen on survival of pedicled skin flaps. J Surg Res 1967;7:583-586.
27. Manson PN, Im MJ, Myers RA, Hoopes HE. Improved capillaries by hyperbaric oxygen in skin flaps. Surg Forum 1980;31:564-566.
28. Meltzer T, Myers B. The effect of hyperbaric oxygen on the bursting strength and rate of vascularization of skin wounds in rats. Am Surg 1986;52:659-662.
29. Nemiroff PM, Lungu AL. The influence of hyperbaric oxygen and irradiation on vascularity in skin flaps: A controlled study. Surg Forum 1987;38:565-567.
30. Wozney P, Zajko AB, Bron KM, Point S, Starzl TE. Vascular complications after liver transplantation: A 5-year experience. AJR Am J Roentgenol 1986;147:657-663.
31. Thom SR. Side effects. A committee report. In: Hunt TK, Davis JC (eds). Hyperbaric oxygen therapy. Maryland: Undersea and Hyperbaric Medical Society, 1992:68-69.
32. Palmquist BM, Philipson B, Barr PO. Nuclear cataract and myopia during hyperbaric oxygen therapy. Br J Ophthalmol 1984;68:113-117.
33. Paquet KJ, Wessel W: Electron microscopic, microangiographic and cytophotometric studies on dog livers after various methods of preservation. Eur Surg Res 1972;4: 18-28.
34. Brettschneider L, Bell PR, Martin AJ, Tarr JB, Taylor PD, Starzl TE. Conservation of the liver. Transplant Proc 1969;1:132-137.
35. Kaelin CM, Im MJ, Myers RA, Manson PH, Hoopes JE. The effects of hyperbaric oxygen on free flaps in rats. Arch Surg 1990;125:607-609.