

Liver Health and HBO

Effects of hyperbaric oxygen treatment on liver functions, oxidative status and histology in septic rats.

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OBJECTIVE: The liver is thought to be responsible for multiple organ failure during sepsis. Increase in tissue oxygen consumption is a major component of the septic response. Hyperbaric oxygen (HBO) therapy provides more oxygenation in the whole body. This study examined the effect of HBO alone or in combination with cefepime (CEF) on the liver in septic rats. **DESIGN AND INTERVENTIONS:** We divided 90 male rats into six groups; control, HBO, sepsis (SEP), SEP+HBO, SEP+CEF, and SEP+CEF+HBO. Sepsis was induced with an intraperitoneal injection of *Escherichia coli* (2.1×10^9 cfu). A total of six HBO sessions were performed at 2 atm absolute for 90 min at 6-h intervals. CEF was administered intraperitoneally at a dose of 50 mg/kg twice daily. Animals were killed 48 h after sepsis induction. Their liver and blood were removed for biochemical and histopathological analysis. **MEASUREMENTS AND RESULTS:** Liver thiobarbituric acid reactive substances as well as serum alanine transaminase, aspartate transaminase and alkaline phosphatase levels increased while the activity of the antioxidant enzymes superoxide dismutase and catalase decreased significantly in septic rats. These parameters returned to nearly control levels in the SEP+CEF+HBO group. Histological observations supported these findings: Hepatocellular degeneration was observed and intensive polymorphonuclear cell infiltration appeared in all fields of septic animal livers. HBO alone could not sufficiently reverse these histopathological changes, but most liver sections presented normal histology when it was combined with CEF. **CONCLUSIONS:** HBO may be a useful adjuvant therapy modality to improve the efficacy of sepsis treatment.

The effects of hyperbaric oxygen treatment on oxidant and antioxidants levels during liver regeneration in rats.

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The effects of hyperbaric oxygen (HBO) therapy on oxidant/antioxidant metabolism are controversial and its effects on hepatic regeneration are not known. In this study, we investigated a possible beneficial effect of HBO therapy on oxidant and antioxidants levels during liver regeneration. To conduct this study, seventy percent hepatectomy was performed on forty-eight Sprague-Dawley rats and the rats were divided into two equal groups: HBO-treated group and untreated group (non-HBO group). We determined the levels of malondialdehyde (MDA), an oxidative stress marker, and the levels of antioxidant enzymes/reagents, including glutathione (GSH), superoxide dismutase (SOD) activity, copper (Cu) and zinc (Zn), in the remnant liver samples. We also measured mitotic index (MI) and proliferating cell nuclear antigen (PCNA) levels to assess the degree of liver regeneration. HBO treatment significantly decreased MDA levels, whereas it increased SOD activity, GSH and Zn levels. In contrast, Cu levels were lower in the HBO-treated livers than the levels in the untreated remnant livers. The effect of HBO treatment may be mediated by the suppression of certain enzymes that are responsible for lipid peroxidation. In addition, HBO treatment may induce the production of antioxidant enzymes/reagents by remnant liver tissues. The HBO-treated rats maintained their body weights but the

untreated rats lost body weights. HBO treatment also increased MI and PCNA levels, indicating HBO treatment enhances liver regeneration. These results indicate that HBO treatment has beneficial effects on liver regeneration by decreasing MDA and by increasing antioxidant activities. We therefore suggest that HBO therapy may be useful after liver resection.

Hyperbaric oxygenation in the combined therapy of infectious diseases

Ivanov KS, Liashenko IuI, Kucheriavtsev AA, Finogeev IuP, Zhdanov VP, Khodzhaev GA.

Klin Med (Mosk). 1992 Jan;70(1):90-2.

Hypoxia plays an important role in pathogenesis of infectious diseases. Therefore, its correction is an essential factor in pathogenetic antibacterial treatment. Hyperbaric oxygenation (HBO) as a leading method in current antihypoxic therapy was studied in combined medication for typhoid, diphtheria, meningococcal infection, viral hepatitis. HBO sessions were given to 331 patients, 363 controls did not receive HBO. Utilization of HBO provided much better saturation of blood with oxygen, eliminated metabolic disorders, warranted favorable course and outcomes of the diseases.

Therapeutic effect of hyperbaric oxygenation in various manifestations of acute renal-hepatic insufficiency

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The studies of the clinical pattern, chest X-ray films, central hemodynamic parameters, hepatic blood flow and respiratory functions in patients with acute renal-hepatic failure due to various exo- and endotoxemias have shown that hyperbaric oxygenation decreases the degree of first to second stage pulmonary hyperhydration and hepatic encephalopathy. Parallel correction of the cardiac output, recovery of the decreased hepatic blood flow and normalization of respiratory function have been observed.

Hepatic tissue respiration in pathology of the biliary system and the effect of hyperbaric oxygenation on the course of hepatic insufficiency

Belokurov IuN, Murav'eva LA, Rybachkov VV.

Under study was the effect of hyperbaric oxygenation in 46 patients on the course of bile tract diseases, complicated with hepatic insufficiency. Hyperbaric oxygenation was found to render a positive effect on the course of hepatic insufficiency.

The use of hyperbaric oxygenation in treating viral hepatitis B and the reaction of the blood leukocytes.

Gabrilovich DI, Musarov AL, ZmyzgoVA AV, Shalygina NB.

A total of 75 patients with virus hepatitis B of medium gravity were examined for the effect of HBO on the clinical course of the disease and blood leukocyte reaction. This reaction was tested on the basis of a complex of rosette-forming and cytochemical tests. HBO was found to produce a favourable effect if used at the early stages of the treatment (the first week of hospitalization). The effect consisted in significant reduction of the rate of exacerbations and residual phenomena. HBO provoked a decrease in the content of T and B lymphocytes by the 10th session of the treatment. A close relationship was revealed between HBO efficacy and the initial level of functional metabolic activity of leukocytes. The use of HBO was always accompanied by the rise of that activity during the treatment. The use of HBO at later times of the treatment (weeks 4-5) did not produce any well-defined clinical effect. Thus, HBO

(8-10 sessions, pressure 1.5 absolute atmosphere, exposure 45 min) may be indicated as a prophylactic measure in respect of an unfavorable disease course with regard to the patients' selection on the basis of a complex of cytochemical tests.

Effect of hyperbaric oxygenation on the disease course and blood coagulation function in patients with acute viral hepatitis.

Kuznetsova EN, Musarov AL, Zmyzgova AV, Lomazova KD.

The paper is concerned with an analysis of clinico-biochemical indices and 14 parameters of the plasmatic and platelet links of hemostasis in 29 patients with acute virus hepatitis of a varying degree of severity treated by hyperbaric oxygenation and in 40 controls. HBO made a modulating effect on most indices of hemocoagulation and fibrinolysis bringing them nearer to a certain standard which was optimum for a certain stage and degree of AVH. Probable mechanisms of the HBO effect on various indices of homeostasis in AVH and clinico-pathogenetic importance of the state of hemocoagulation against a background of HBO-therapy were discussed.

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Clinical pathological study of treatment of chronic hepatitis with hyperbaric oxygenation.

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OBJECTIVE: To detect the feasibility and theoretic basis for treatment with hyperbaric oxygenation (HBO) in chronic hepatitis and to compare the changes in hepatic function, immunity, pathologic morphology, ultrastructure and HBV in hepatic tissues before and after treatment. **METHODS:** Sixty cases of chronic hepatitis were randomly selected and divided into two groups: the experiment ($n = 30$) and control groups ($n = 30$). Patients in the experimental group were treated with HBO for 6 courses. Patients in the control group were treated for 60 days with the usual drugs used in the clinic. The function and bloodstream graph of liver were examined and liver biopsies were made before and after treatments. Routine paraffin sections were stained with HE and observed under the light microscope. Ultra thin slides from paraformaldehyde and glutaraldehyde fixed liver tissue were stained with lead citrate and observed with the transmission electric microscope. HBsAg and HBcAg in liver of the experimental group were detected with ABC immunohistochemistry method before and after treatment. **RESULTS:** For the experimental group, ALT, SB, gamma-GT, AKP, IgG, and IgM in blood and the degeneration and necrosis of hepatocytes were remarkably decreased ($P < 0.05$), the mean contractive wave of bloodstream in liver and the bloodstream in right ramus of janitrix were remarkably increased ($P < 0.05$), and the swelling of mitochondria, increase of lysosomes, generation of Kupffer cells, infiltration of lymphocytes in portal area and capillary generation were all remarkably alleviated ($P < 0.05$) after treatment with HBO. There were significant differences between the experimental and control groups after treatment with different methods ($P < 0.05$). For patients in the experimental group, the fibrosis and fat-storing cells in the liver were not reduced ($P > 0.05$), and the expression of HBsAg and HBcAg in liver was not weakened ($P < 0.05$) after treatment. **CONCLUSIONS:** Treatment with HBO for chronic hepatitis was effective and recommendable, but it could not reverse liver fibrosis.

However, it might be able to delay or prevent the liver from fibrosis, so it might be more effective at the early and middle stages of chronic hepatitis. HBO could not inhibit the HB virus. So we consider that treatment with HBO should be simultaneous with anti HBV therapy.

Some pathogenetic aspects of developing liver failure and preventing it in patients with liver cirrhosis after portosystemic shunting

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Patients with cirrhosis of the liver were found to have a considerable suppression of the system of biotransformation of the liver before operation which correlated with the data of the direct indices of monooxygenase system of hepatocytes--cytochrome P-450 and activity of N-demethylase of amidopyrine. Operative interventions on such patients independent of the type of portosystemic shunting result in considerably decreased content of metabolites of amidopyrine--4AAP and N-ac-4-APP in urine as compared with the preoperative level ($p < 0.05$). Hyperbaric oxygenation is the optimal stimulator of activity of the liver biotransformation system. Better indicators characterizing the increased metabolic activity of the liver were noted in patients with selective portosystemic anastomoses and hyperbaric oxygenation in the postoperative period.

Hyperbaric oxygen prevents bacterial translocation in rats with obstructive jaundice.

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This study was designed to demonstrate bacterial translocation following bile duct ligation and investigate preventive effects of hyperbaric oxygen on obstructive jaundice-related bacterial translocation in an animal model. Hyperbaric oxygen treatment significantly reduced the endogenous colony counts in distal ileum of normal rats both in the short (two days) and long (seven days) term. Endogenous bacteria in distal ileum significantly increased in bile duct ligated rats in the short and long term, and presence of bacterial translocation was proven by bacterial growth in mesenteric lymph nodes, liver, spleen, and blood. Short- and long-term hyperbaric oxygen treatments significantly reduced the intestinal colony counts and prevented the bacterial translocation almost completely in rats with bile duct ligation. It is concluded that obstructive jaundice causes bacterial overgrowth and translocation, and hyperbaric oxygen treatment can prevent both bacterial overgrowth and translocation effectively.

Hyperbaric oxygen therapy in parenchymal liver disease.

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Use and efficacy of hyperbaric oxygen therapy (HOT) in liver disease has not been established. A prospective control study of HOT in liver diseases was undertaken. Sixty cases were selected for this study (30 with HOT and 30 with conventional therapy only). Almost equal number of Hepatitis B virus surface antigen (HbsAg) positive cases were included in both groups. All patients were male. Only cases with serum bilirubin over 10 mg/dl were included in this study. It was found that study cases recovered faster, gained appetite and had an earlier sense of well-being. There was faster disappearance of pruritus, earlier achievement of normal liver function, HbsAg negativity and overall shorter duration of hospital stay and convalescence. Short term adverse effects were unremarkable.

Increase in absolute atmospheric pressure in hyperbaric chamber in cirrhosis with ascites: lack of natriuretic response and increase of atrial natriuretic peptide

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In normal subjects increasing atmospheres of absolute pressure (ATA) on the cardiopulmonary system, in a hyperbaric chamber, results in a marked diuresis and an increase of circulating concentration of atrial natriuretic peptide (ANP). The present investigation was designed to determine the effect of ATA in a group of 5 sodium-retaining cirrhotic patients on hydro-saline balance, renin-angiotensin-aldosterone system and ANP. After seven days on a 10 mEq sodium intake, each patient was studied on both a control and experimental (4-hour stay at 2-ATA in hyperbaric chamber) day. On each day, measurement of the following were obtained: plasma ANP, plasma renin activity (PRA) and aldosterone, electrolytes, creatinine clearance, volume and sodium and potassium urinary excretion. The increasing ATA lacked to induce both diuresis, natriuresis and increase in ANP plasma concentration. In these patients baseline, pre-hyperbaric, mean levels of PRA, aldosterone and ANP were 15.5 +/- 11.5 ng/ml/h, 808.4 +/- 360 pg/ml, 86 +/- 10.1 pg/ml, respectively, and were significantly elevated compared with normal range for control subjects without sodium restriction. In conclusion, increasing pressure at 2-ATA, in a hyperbaric chamber is unable to elicit both diuresis and natriuresis as well as modification on ANP and renin-angiotensin-aldosterone system in sodium-retaining cirrhotic patients.

The effect of hyperbaric oxygenation on liver energy metabolism in white rats with acute sodium nitrate poisoning

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The experimental study carried out on white rats, which was introduced of sodium nitrate at a dose of 9,6 g/kg of their mass. It is followed by the development of considerable disturbances of energy metabolism in liver. It has been shown the depression and the uncoupling of oxidation and phosphorylation, decrease of energy quotient in hepatic tissues. The results obtained permit supposing the significant role of nitric oxide (NO) in liver as a factor resulting in decrease of energy potential. The research has stated that the use of hyperbaric oxygenation (HBO) prevents difficult disturbances of energy metabolism in liver of white rats. The results permit supposing that the effect HBO is connected with the decrease of the speed of reduction of nitrate-ions to more toxic products of their biotransformation.

Role of hyperbaric oxygenation in the mechanism of ammonium detoxication in resection of the liver in the presence of chronic hepatitis

Savilov PN, Leonov AN, Iakovlev VN.

Anesteziol Reanimatol. 1994 Nov-Dec;(6):31-4.

Hyperbaric oxygenation (HBO) used in 170 white rats with chronic CCL4-hepatitis after resection of the liver was conducive to repair of the reversible (glutamine synthesis) and irreversible (urea synthesis) routes of ammonium binding in hepatocytes which are disordered in chronic hepatitis. Hyperbaric oxygen regulates the effect of resection of the liver on the glutamine- and urea-synthesizing function of the hepatocytes in chronic hepatitis. Therapeutic effect of HBO persists for 4 days of the posthypoxic period under conditions of posthyperoxic hypoxia.

Protective action of L-carnitine and coenzyme Q10 against hepatic triglyceride infiltration induced by hyperbaric oxygen and ethanol.

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Drugs Exp Clin Res. 1993;19(2):65-8.

This investigation was conducted to ascertain whether administration of L-carnitine and coenzyme Q10 could protect from the experimentally-induced hepatic lipid infiltration and glutathione content decrease in rats exposed to hyperbaric oxygen and prolonged alcohol administration. The results indicate that administration of L-carnitine and coenzyme Q10 in association reduces damage induced by chronic alcohol poisoning and hyperbaric oxygen. This protective action is more marked when L-carnitine and coenzyme Q10 are administered together. The combined complementary biochemical activity of these two compounds is discussed.

Effect of hyperbaric oxygenation on the disease course and blood coagulation function in patients with acute viral hepatitis

Kuznetsova EN, Musarov AL, Zmyzgova AV, Lomazova KD.

Ter Arkh. 1987;59(7):21-5.

The paper is concerned with an analysis of clinico-biochemical indices and 14 parameters of the plasmatic and platelet links of hemostasis in 29 patients with acute virus hepatitis of a varying degree of severity treated by hyperbaric oxygenation and in 40 controls. HBO made a modulating effect on most indices of hemocoagulation and fibrinolysis bringing them nearer to a certain standard which was optimum for a certain stage and degree of AVH. Probable mechanisms of the HBO effect on various indices of homeostasis in AVH and clinico-pathogenetic importance of the state of hemocoagulation against a background of HBO-therapy were discussed.