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ASSESSMENT AND MONITORING OF LIVER GRAFT VIABILITY AND INITIAL FUNCTION USING INTERSTITIAL MICRODIALYSIS

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Assessing the viability and monitoring the function of liver graft in the early postoperative period are critical clinical tasks. One possible solution is to determine the changes in concentration of blood glucose, its metabolites and glycerol in the graft using interstitial microdialysis. **Objective:** to study the dynamics of interstitial glucose, lactate, pyruvate and glycerol in the early post-liver transplant period – depending on the initial graft function (IGF) – and to compare with the results of standard laboratory blood tests. **Materials and methods.** Four selected clinical observations of deceased donor liver transplantation are presented. Two of the observations showed normal IGF, one observation – early allograft dysfunction (EAD), complicated by hepatic artery thrombosis (HAT), while one observation demonstrated primary non-function (PNF). Collection of microdialysis samples began after arterial reperfusion of the liver graft and continued continuously for 7 days or until death. Standard blood biochemistry and coagulation tests were performed at least once a day. **Results.** With normal IGF and a smooth postoperative period, interstitial concentrations of glucose, lactate, pyruvate and glycerol remained stable throughout the observation period, ranging from 5 to 20 mmol/L, 1.1 to 7.5 mmol/L, 90 to 380 μmol/L, and 10–100 μmol/L, respectively. EAD was associated with initially higher levels of glucose, lactate, and pyruvate. With HAT development, there was a rapid (within 2–4 hours) five-fold increase in interstitial concentration of lactate with simultaneous decrease in glucose and pyruvate levels to 0.1 mmol/L and 11 μmol/L, respectively. In the case of PNF, there was an initially high concentration of interstitial lactate – 16.4 mmol/L, which increased further to 35.5 mmol/L. Glucose concentration was close to 0. Changes in interstitial glucose, its metabolites and glycerol concentrations chronologically preceded the corresponding changes in peripheral blood composition by 3–5 hours. **Conclusion.** Microdialysis measurement of interstitial glucose, lactate, pyruvate and glycerol concentrations facilitates real-time monitoring of liver graft viability and function. The high sensitivity of the method could help in accelerating diagnosis of vascular complications (HAT in particular), as well as graft dysfunction with other causes. Therefore, the method is feasible in clinical practice.

Keywords: microdialysis, liver transplantation, early allograft dysfunction, hepatic artery thrombosis, primary graft non-function.

INTRODUCTION

Assessing the initial liver graft function is an extremely important clinical task, especially in organ transplantation from an expanded criteria donor. The key points are to determine as early and objectively as possible the degree of ischemia-reperfusion injury and the reversibility of graft dysfunction. There is no doubt that initial graft function depends not only on the donor's parameters, but also on the severity of the recipient's condition, the peculiarities and complexity of the surgical intervention and anaesthetic support.

Conventionally, graft function is assessed by determining a number of laboratory indicators in peripheral blood (aspartate transaminase (AST) and/or alanine aminotransferase (ALT), bilirubin, prothrombin time, prothrombin index, international normalized ratio (INR)), sometimes taking into account such clinical signs as severity of encephalopathy, bile production rate, and need for fresh frozen plasma (FFP) infusion. This requires dynamic follow-up and collection of laboratory samples within postoperative days 2–7 [1]. It should be emphasized that the relatively low sensitivity and specificity of individual signs of graft dysfunction require their combined analysis. Sometimes, multidirectional trends in changes in the set of laboratory indicators and possible inconsistency with the clinical picture lead the need to extend the follow-up period, thereby delaying diagnosis. It must be borne in mind that changes in the peripheral blood composition, reflecting the liver graft function, occur with a certain time delay, and the use of renal replacement therapy, albumin dialysis, FFP and clotting factor concentrate in patients with severe graft dysfunction and coagulopathy may create a false impression of restored liver function.

So far, several methods have been developed and tested in the clinic for direct assessment of liver function, including during liver transplantation. They include

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determination of the maximal liver functional capacity by clearance of C^{13} methacetin (LiMAx test) [2, 3], measurement of liver function and perfusion by indocyanine green clearance (LIMON test) [4, 5], and interstitial microdialysis [6]. The first two methods are based on non-invasive measurement of the concentration of substances that are specifically metabolized (C^{13} methacetin) or secreted (indocyanine green) by the liver.

Microdialysis is a more versatile technology, as it allows to measure the concentration of almost any substance in the intercellular space of the tissue under study. It is based on passive diffusion of substances through a semipermeable membrane by concentration gradient. To assess the viability and functional state of the liver, like any other tissue of the body, glucose, lactate and pyruvate concentrations are measured and correlated in the intercellular fluid. This allows to determine the nature (anaerobic or aerobic) and the rate of glucose metabolism. Moreover, the analysis can be complemented by studying glycerol (a product of degradation of membrane phospholipids) levels, which reflects the degree of cytolysis.

The aim of this work is to study the characteristics of glucose metabolism in a liver graft in the early post-transplant period, to determine typical patterns of changes in interstitial concentrations of glucose, lactate, pyruvate, and glycerol, and to compare them with results from routine laboratory methods used for diagnosing early liver graft dysfunction or primary non-function.

MATERIALS AND METHODS

Study design

Since August 2017, the Center for Surgery and Transplantology, Burnazyan Federal Medical and Biophysical Center, Moscow has been conducting a non-randomized, single-center, observational study titled "Study of the characteristics of glucose metabolism in a liver graft for early diagnosis of dysfunction". The study is approved by the institution's local ethics committee and the Expert Council of the Russian Science Foundation (project No. 17-75-10010). The work does not provide for changes in patients' selection criteria for transplantation, surgery technique, anesthetic treatment, treatment and follow-up tactics in the postoperative period, as well as choice of drugs and doses. The study includes male and female subjects aged 18 years and above, who underwent a liver transplant surgery and has a microdialysis catheter installed in them during the operation. The study does not include patients operated on for acute liver failure, who underwent multivisceral transplantation and received a liver fragment from a living related donor.

The following events and conditions were established as endpoints: 1) early allograft dysfunction (EAD) according to the criteria by K. Olthoff et al., 2010 [6]; 2) primary graft non-function (PGNF) according to UNOS criteria [7]; 3) graft loss (recipient death or retransplantation); 4) recipient death. The severity of the patient's pre-transplant condition was assessed using the well-known and commonly used scales MELD, MELD-Na, and Child-Pugh. For donors, the donor risk index (DRI) was calculated [8].

The study lasted for 7 days (160–175 hours) after completion of liver transplant operation. During this period, microdialysis samples of the intercellular fluid of the graft were continuously collected. The peripheral blood composition (acid-base state, electrolyte levels, biochemical analysis, coagulogram) was examined at least once a day. The recipients had a 6-month follow-up period after the end of the study.

Receiving, collecting and analyzing intercellular fluid samples

The principle of the method and its use in liver transplantation are detailed in [9–12]. The microdialysis catheter (61 Hepatic Microdialysis Catheter, M Dialysis AB, Sweden) is a 1 mm diameter polyurethane tube with two concentrically located lumens. The outer surface of the 3 cm long terminal part of the catheter is made of a semipermeable membrane (Fig. 1).

During transplantation, before wound suturing, the catheter is placed by puncture in segment IV of the liver, fixed to the falciform ligament, and is brought to the anterior abdominal wall through a counter-opening. A standard isotonic solution (Perfusion Fluid T1, M Dialysis AB, Sweden) is fed through the inner lumen of the catheter using a micropump (106 MD Pump, M Dialysis AB, Sweden) at 0.3 μL/min. When the perfusion fluid reaches the semipermeable membrane, passive transport of substances from the intercellular fluid into the catheter cavity begins by a concentration gradient. The resulting solution is continuously evacuated at the same rate through the second lumen of the catheter and collected in a microtube. Microtubes are changed (i.e. individual samples are obtained) at least once every 3 hours. Glucose, lactate, pyruvate and glycerol concentrations are measured using a set of standard reagents on analyzer ISCUS Clinical Microdialysis Analyzer (M Dialysis AB, Sweden) within 24 hours from the time the sample is received.

Clinical cases

Four clinical cases were selected to demonstrate and discuss the first results of the study, depending on the initial graft function:

Case No. 1 (normal initial graft function)

A 51-year-old male recipient diagnosed with cirrhosis resulting from hepatitis C, Child-Pugh B. Was waitlisted for liver transplant for 4 months. Preoperative MELD-Na score was 13.

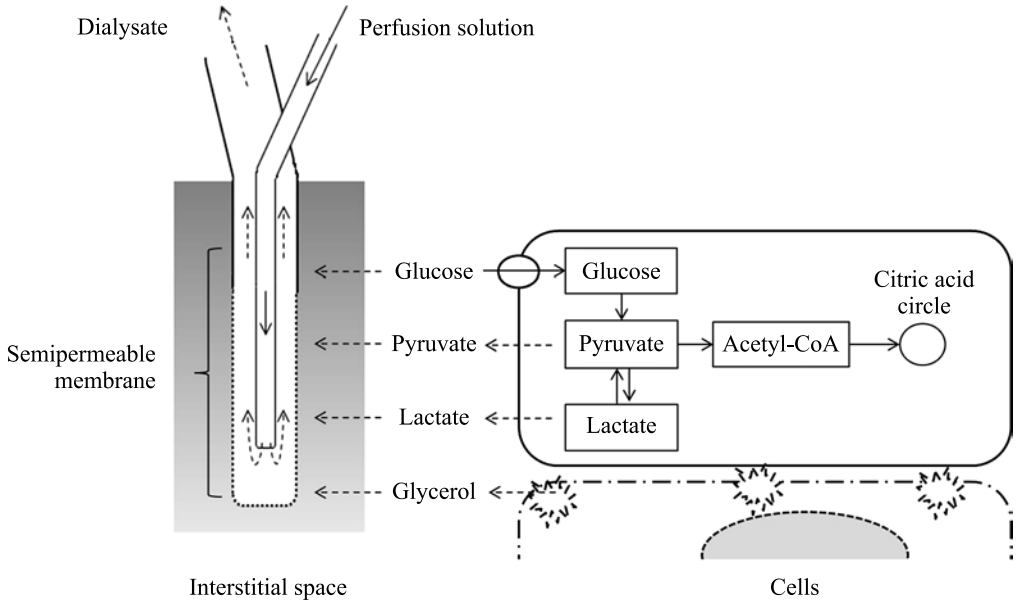

Fig. 1. Microdialysis catheter – the circuit and device operation principle

A 39-year-old male donor, 1.24 DRI. Brain death resulted from traumatic brain injury (TBI). Length of ICU stay under mechanical ventilation was 2 days before multi-organ procurement was performed. Laboratory findings: AST 26 IU/L, ALT 17 IU/L, total bilirubin 6 µmol/L, creatinine 100 µmol/L, and Na 145 mmol/L. Stable hemodynamics (blood pressure (BP) 120/70 mm Hg) against the background of noradrenaline (norepinephrine) infusion at 700 ng/kg/min.

Visual quality assessment of liver graft: normal color, rounded edge of the right lobe, sharp edge of the left lobe, no parenchymal edema, normal consistency, satisfactory perfusion quality, steatosis ≤30% (retrospectively via histological examination – 0%).

Cold ischemia time was 8.5 hours. Transplant surgery lasted for 7 hours. The anhepatic phase lasted for 80 minutes. Warm ischemia time was 48 minutes. IVC clamping time was 50 minutes. Intraoperative plasma transfusion volumes: red blood cells 900 mL, FFP 3,100 mL, blood reinfusion 543 mL.

Trachea was extubated within the first 24 hours. Laboratory MELD score at 24 hours following transplantation was 13. Maximum AST/ALT level at day 7 was 215 IU/L, total bilirubin at day 7 was 22 µmol/L, INR at day 7 was 1.1. Patient was discharged from the hospital on postoperative day 14.

Case No. 2 (normal initial graft function)

A 64-year-old female recipient diagnosed with hepatocellular carcinoma (the size and number of nodes meet the UCSF criteria [13]) against the background of cirrhosis resulting from hepatitis C, Child-Pugh C. She had a history of myocardial infarction, whose duration is uncertain and acute ischemic stroke in the basin of left middle cerebral artery in August 2016. Was waitlisted for liver transplant for 10 months. Preoperative MELD-Na score was 13.

A 25-year-old male donor, 1.27 DRI. Brain death resulted from TBI. Length of ICU stay under mechanical ventilation was 1 day before multi-organ procurement was performed. Laboratory findings: AST 46 IU/L, ALT 40 IU/L, total bilirubin 11 µmol/L, creatinine 85 µmol/L, Na 148 mmol/L. Stable hemodynamics (BP 120/80 mmHg) without vasopressors and inotropes.

Visual quality assessment of liver graft: normal color, sharp edge, no parenchymal edema, normal consistency, excellent perfusion quality, no steatosis (retrospectively via histological examination – 0%).

Cold ischemia time was 11 hours. Transplant surgery lasted for 7.5 hours. The anhepatic phase lasted for 40 minutes. Warm ischemia time was 30 minutes, IVC clamping time was 40 minutes. Intraoperative plasma transfusion volumes: red blood cells 570 mL, FFP 2300 mL, blood reinfusion 0 mL.

Trachea was extubated within the first 24 hours. Laboratory MELD score at 24 hours following transplantation was 10. Maximum AST/ALT level at day 7 was 544 IU/L, total bilirubin at day 7 was 10 µmol/L, INR at day 7 was 1.1. Patient was discharged from the hospital on postoperative day 20.

Case No. 3 (early allograft dysfunction, hepatic artery thrombosis)

A 45-year-old male recipient diagnosed with cirrhosis resulting from primary sclerosing cholangitis, Child-Pugh class B. Was waitlisted for liver transplant for 8 months. Preoperative MELD-Na score was 16.

A 42-year-old male donor, 1.41 DRI. Brain death resulted from TBI. Length of ICU stay under mechanical ventilation was 2 days before multi-organ procurement was performed. Laboratory findings: AST 40 IU/L, ALT 35 IU/L, total bilirubin 8 μmol/L, creatinine 70 μmol/L, Na 154 mmol/L. Stable hemodynamics (BP 120/80 mmHg) against the background of noradrenaline (norepinephrine) infusion at 200 ng/kg/min.

Visual quality assessment of liver graft: normal color, sharp edge, no parenchymal edema, normal consistency, excellent perfusion quality, steatosis ≤30% (retrospectively via histological examination – 0%).

Cold ischemia time was 9 hours. Transplant surgery lasted for 6.5 hours. The anhepatic phase lasted for 50 minutes. Warm ischemia time was 40 minutes, IVC clamping time was 45 minutes. Intraoperative plasma transfusion volumes: red blood cells 620 mL, FFP 2140 mL, platelet concentrate – 1 dose, blood reinfusion 942 mL.

Trachea was extubated within the first 24 hours. Laboratory MELD score at 24 hours following transplantation was 20 баллов, AST – 5254 IU/L, INR – 1.58. On postoperative day 2, AST increased to 6461 IU/L, INR went up to 1.99. Control ultrasound examination could not locate the hepatic artery, hepatic artery thrombosis is suspected. CT scan with intravenous contrast confirmed hepatic artery thrombosis. Emergency angiography was performed; attempts at thrombus extraction from the right hepatic artery and the anastomotic area, brown thrombotic masses were obtained, which, however, did not restore antegrade blood flow. Balloon angioplasty restored blood flow in the proximal sections of the left and right hepatic arteries without filling the distal bed. The patient was placed on the waiting list for urgent liver transplantation. Due to intensified encephalopathy and respiratory failure, repeated tracheal intubation was performed, mechanical ventilation was resumed. Due to absence of a suitable donor organ, despite ongoing intensive therapy, the patient died on postoperative day 5.

Case No. 4 (primary graft non-function)

A 41-year-old male recipient diagnosed with cirrhosis resulting from secondary biliary cirrhosis, Child-Pugh class B. Was waitlisted for liver transplant for 2 months. Preoperative MELD-Na score was 17.

A 61-year-old male donor, 1.41 DRI. Brain death resulted from acute stroke. Length of ICU stay under mechanical ventilation was 2 days. Laboratory findings: AST 68 IU/L, ALT 73 IU/L, total bilirubin 10 μmol/L, creatinine 74 μmol/L, Na 137 mmol/L. Stable hemodynamics (BP 130/90 mmHg) against the background of noradrenaline (norepinephrine) infusion at 700 ng/kg/min.

Visual quality assessment of liver graft: normal color, sharp edge, no parenchymal edema, normal consistency, excellent perfusion quality, steatosis ≤30% (retrospectively via histological examination – 0%).

Cold ischemia time was 11 hours. Transplant surgery lasted for 11 hours. The anhepatic phase lasted for 50 minutes. Warm ischemia time was 45 minutes, IVC clamping time was 50 minutes. Intraoperative plasma transfusion volumes: red blood cells 930 mL, FFP 1790 mL, blood reinfusion 2,139 mL.

Intraoperatively, after blood flow was started, hypotension developed, which required increasing the doses of vasopressors and inotropes, lactic acidosis (pH 7.19, lactate 18 mmol/L), massive coagulopathic diffuse bleeding. Hemostasis for 4 hours. After the end of surgery and the patient transferred to the ICU, multiple organ failure progressed, the patient died on postoperative day 1.

RESULTS

In all the cases, even with severe coagulopathy, insertion and removal of microdialysis catheters were not accompanied by bleeding from the liver parenchyma and other complications. The installed catheter and the micropump attached to the anterior abdominal wall did not interfere with activation of patients, did not cause them discomfort (cases 1 and 2), and did not create inconveniences during diagnostic tests and postoperative wound care.

Fig. 2, a, b, c show the data on the dynamics of interstitial levels of glucose and its metabolites (lactate and pyruvate), as well as standard laboratory tests used to evaluate graft function – level of aminotransferases, total bilirubin and INR (Fig. 2, d, e, f).

With an uneventful postoperative period and good initial graft function (cases 1 and 2), moderate hyperglycemia (10–15 mmol/L) and successive decrease in lactate levels to 1.5 mmol/L were observed in the peripheral blood of recipients within the first 24–48 hours, and less in the next 24 hours. For seven days, measured glucose and lactate concentrations in the intracellular fluid of the liver were higher than in the peripheral blood, ranging from 5 to 20 mmol/L (average 9.3) and from 1.1 to 7.5 (average 2.4), respectively. Interstitial pyruvate levels ranged from 90 to 380 μmol/L (175 μmol/L average).

In case 3, early graft dysfunction was diagnosed 24 hours after the end of operation based on increase in AST level to 5254 IU/L. At the same time, within the first 24 hours, there was reductions in the initially high levels of glucose (21.3 mmol/L), lactate (14.7 mmol/L) and pyruvate (582 μmol/L) to the values recorded in the cases in the absence of graft dysfunction. The exact time hepatic artery thrombosis developed is difficult to establish because diagnosis was made based on ultrasound and CT scan results, performed 37 and 38 hours after surgery. Decrease in interstitial levels of glucose and pyruvate with simultaneous increase in lactate was noted from the 30th hour, while at the time of angiography (43 hours)

and re-intubation (48 hours) they were 2.2 mmol/L, 41 μmol/L, 23.6 mmol/L and 0.1 mmol/L, 11 μmol/L, 28.3 mmol/L, respectively. A day later (72 hours after transplantation), there was transient increase in interstitial glucose levels (from 0.0 to 6.2 mmol/L) and decrease in lactate levels (from 27.2 to 19.9 mmol/L). We have no reliable explanation for this phenomenon. However, this chronologically coincided with the commencement of noradrenaline (norepinephrine) infusion. Later on, until the onset of death (96 hours), interstitial levels of glucose and pyruvate were close to 0, lactate – to 30 mmol/L.

In case 4, after graft reperfusion, hypotension unresponsive to high-dose vasopressor, severe uncorrected metabolic disorders, severe coagulopathy, massive diffuse bleeding, and acute renal injury developed and increased. The first microdialysis test was obtained 6.5 hours after the start of blood flow through the hepatic artery, and the next 3 were collected with an interval of 2 hours. The test results showed no aerobic glucose metabolism.

It should be emphasized that interstitial levels of glucose, lactate and pyruvate are not physiological constants and may vary interrelatedly within relatively wide ranges. To interpret the observed changes, it is customary to operate not with absolute values of indicators, but to calculate coefficients reflecting the lactate-to-pyruvate (L/P) ratio and the lactate-to-glucose (L/G) ratio. An increase in these coefficients reflects the insufficiency of aerobic glycolysis due to mitochondrial ischemia or dysfunction with normal oxygen delivery. Thus, with normal graft function, L/P and L/G ratios ranged from 10 to 20 and from 0.1 to 0.9, respectively. With hepatic artery thrombosis, a 10-fold increase in L/P ratio and an increase in L/G ratio by 500 times were noted. In the case of PGNF, these coefficients, already at the first measurement, exceeded the norm by more than 10 times and demonstrated further rapid growth (Fig. 3).

Special attention should be paid to the issue of glucose-to-lactate ratio, determined simultaneously in the intercellular fluid of the graft and in the peripheral blood (Fig. 4). With normal graft function (cases 1 and 2 – green markers), these values were close to each other in most measurements, but sometimes differed by 5–7 mmol/L (glucose) and 2–5 mmol/L (lactate), which obviously cannot be neglected. In EAD complicated by hepatic artery thrombosis (case 3 – blue markers), after cessation of adequate arterial blood flow to the graft against the background of a relatively normal blood glucose level (4.5–15.0 mmol/L), its interstitial level was close to 0, while the interstitial lactate level, on the contrary, was 5–6 times higher than that measured in blood. For PGNF (case 4 – red markers), significant differences were also observed in glucose and lactate levels measured in the graft tissue and in the blood.

Glycerol, being a product of degradation of membrane phospholipids, is considered a marker of cytolysis. Its

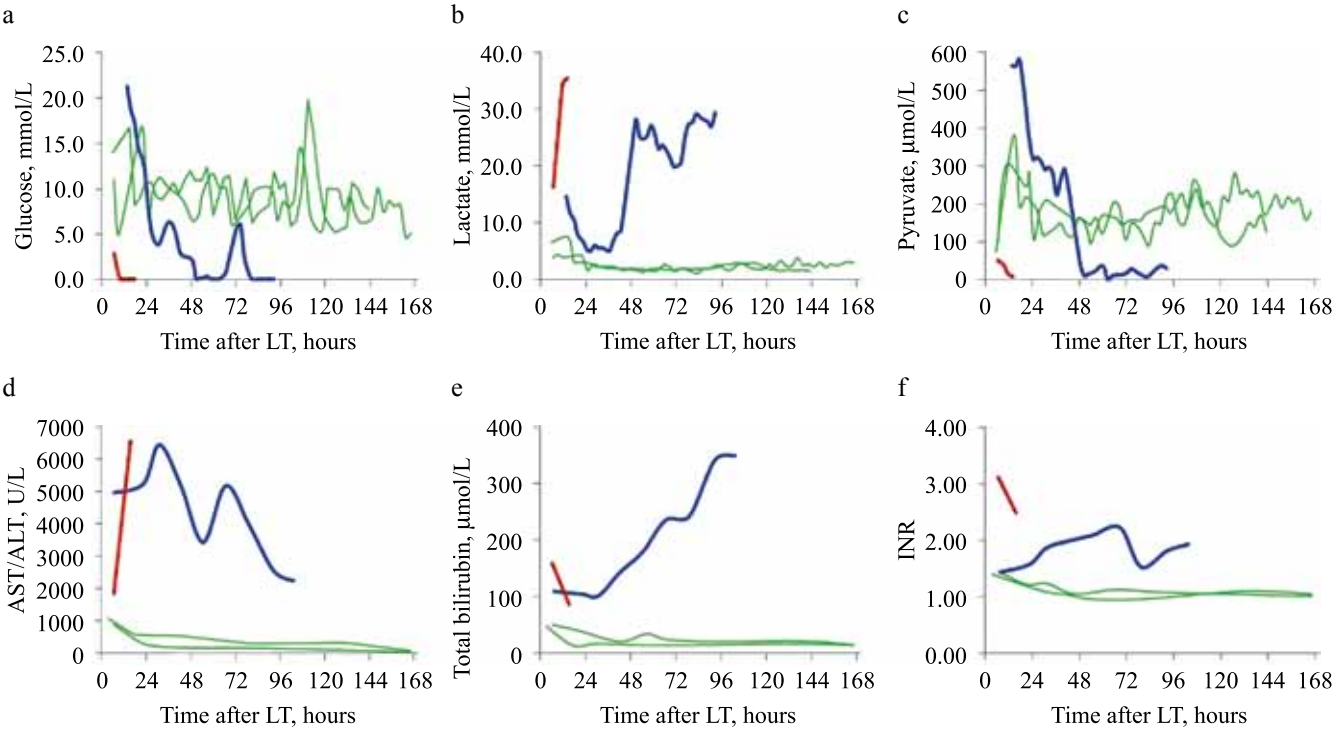

Fig. 2. First post-transplant week dynamics of interstitial graft glucose metabolism parameters (a, b, c) and standard peripheral blood liver function tests (d, e, f). Green lines – normal initial graft function (Cases 1, 2); blue lines – early graft dysfunction complicated with hepatic artery thrombosis on postoperative day 2 (Case 3); red lines – primary non-function graft (Case 4). AST/ALT – maximum of aspartate- or alanine-aminotransferases; INR – international normalized ratio; LT – liver transplantation

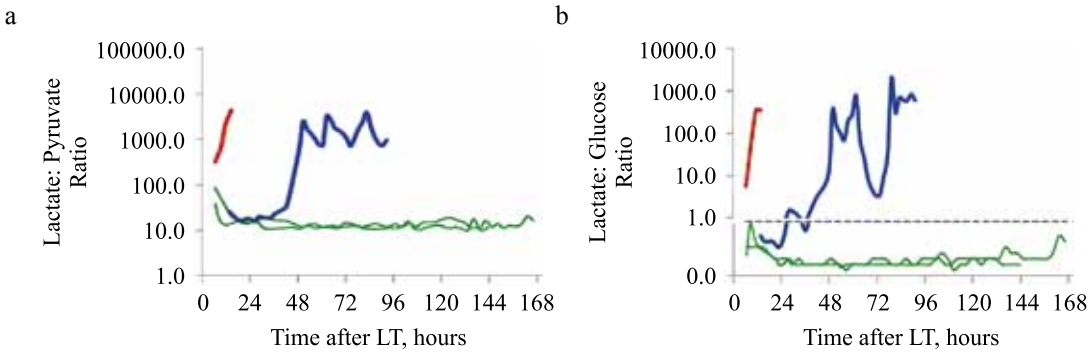

Fig. 3. First post-transplant week dynamics of Lactate : Pyruvate Ratio (a) and Lactate : Glucose Ratio (b). Green lines – normal initial graft function (Cases 1, 2); blue lines – early graft dysfunction complicated with hepatic artery thrombosis on postoperative day 2 (Case 3); red lines – primary non-function graft (Case 4). LT – liver transplantation

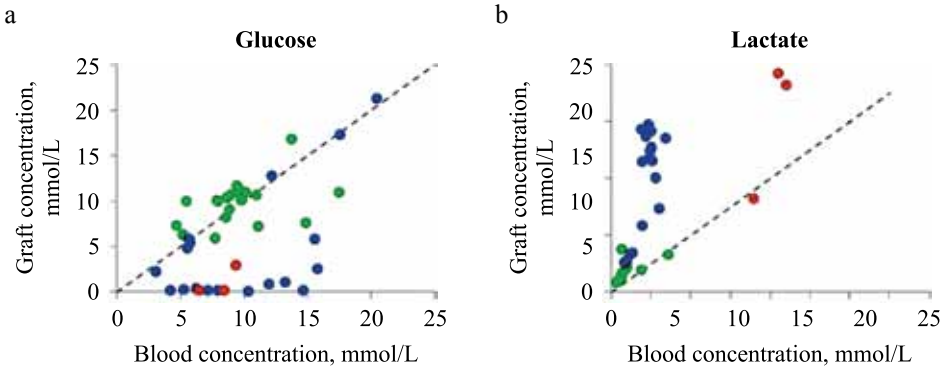

Fig. 4. Glucose (a) and Lactate (b) concentrations in peripheral blood and graft interstitial fluid

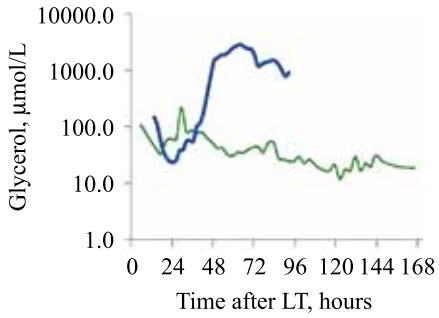

Рис. 5. First post-transplant week dynamics of interstitial graft glycerol concentration. Green line – normal initial graft function (Case 2); Blue line – early graft dysfunction complicated with hepatic artery thrombosis on postoperative day 2 (Case 3)

level measured in the intercellular fluid of a transplanted organ is a quantitative characteristic of this process. Fig. 5 shows the dynamics of glycerol levels in normal graft function (case 2) and in EAD with hepatic artery thrombosis (case 3).

Destruction of hepatocytes due to graft thrombosis and ischemia led to increase in interstitial levels of glycerol by more than 15 times. At the same time, increase in AST levels (Fig. 1, d, blue curve) was more restrained – from 5,254 to 6,461 IU/L (1.2 times), which makes glycerol more sensitive as a marker of cytolysis. Indicators of interstitial glycerol levels in normal graft function and during an uneventful postoperative period do not seem to exceed 100 μmol/L.

DISCUSSION

Microdialysis is a method for studying the composition of interstitial fluid, widely used both in fundamental research [14] and in clinical (mainly neurosurgical) practice [15]. Despite the availability of experimental and clinical results demonstrating the possibility of using microdialysis in liver [9–12, 16, 17] and kidney [18–20] transplantation, as well as positive assessments made by the authors on the prospects for further research in this direction, it should be admitted that the place for this technology in organ transplantation has not yet been determined. It can be assumed that widespread use of the method is hindered by the limited availability of equipment and consumables, high cost of a single analysis compared to standard laboratory tests, the need to install a catheter into the organ parenchyma (invasive method) and train personnel to work with new equipment, and most importantly, the lack of clearly formulated guidelines for correct interpretation of results, their diagnostic value and association with surgery outcomes. That is why the main goal of the study was to find an answer to

the question about the expediency of studying glucose metabolism indicators in a liver transplant and introducing microdialysis technology into real clinical practice.

Two of the presented cases – early hepatic artery thrombosis and PGNF – are examples of rare (3–8% [21] and 1–9% [1], respectively) but typical post-liver transplant complications. In both cases, results from interstitial determination of glucose metabolism indicators did not contradict the data from standard laboratory and instrumental studies. Moreover, in case 3, taking into account the indicators of interstitial microdialysis, disturbances in blood supply to the graft could be suspected 6–7 hours earlier, which could speed up the diagnostic search and initiation of therapeutic measures. In case 4, when graft non-function became the cause of patient death, the rate of increase and severity of metabolic disorders, coagulopathy and multiple organ failure allowed to establish the PGNF diagnosis even intraoperatively without any additional tests. However, the clinical course of severe and irreversible liver graft dysfunction is not always so lightning-fast, and then, glucose metabolism indicators of the graft may be crucial when choosing retransplantation as the only option to save the patient's life.

In two other cases, the postoperative period was uneventful, the function of both grafts was stable and normal, and the level of interstitial glucose, its metabolites, and glycerol was within relatively narrow limits, starting from the first hours after surgery till the end of the study.

The cases presented demonstrate the clinical significance and expediency of prolonged monitoring of liver graft function in the early postoperative period using interstitial microdialysis. The high sensitivity of the method allows to quickly diagnose graft dysfunction, accelerate implementation of diagnostic measures aimed at clarifying the origin of the dysfunction, and to launch therapeutic actions immediately. The question about the need to include microdialysis in the list of routine diagnostic studies in liver transplantation is still open. Apparently, the optimal strategy is to intraoperatively decide to place a catheter if the operating surgeon has reasonable assumptions that graft dysfunction has developed or that there is increased risk of vascular complications.

We consider the use of microdialysis not only in the postoperative period, but also in the work of the donor service to be a promising area for clinical trials. For hypothermic organ preservation by static storage, blood glucose, lactate and pyruvate levels must be stable and close to zero. This would indicate achievement of the preservation goal – stopping metabolic processes in the graft tissue. Glycerol level and dynamics would allow to objectively assess the severity of ischemic injury. Together with other data, this would allow to reasonably use it for transplantation from expanded criteria donors or to abandon transplantation due to high risk of developing PGNF.

CONCLUSION

Microdialysis allows for continuous monitoring of the viability and functional state of the transplanted liver in the early post-transplant period. The high sensitivity of this method makes it possible to accelerate diagnosis of vascular complications (particularly thrombosis) or graft dysfunction of other origins. Clarification of the boundary values of interstitial levels of glucose, lactate, pyruvate and glycerol in various conditions and complications, as well as application of the method at the preservation stage, should be subjected to future research.

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The authors declare no conflict of interest.

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