Postreperfusion hyperkalemia in liver transplantation using donation after cardiac death grafts with pathological changes

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BACKGROUND: With the increasing use of donation after cardiac death (DCD), especially of the graft liver with steatosis or other pathological changes, the frequency of postreperfusion hyperkalemia in liver transplantation has increased significantly. The present study aimed to determine the factors associated with developing postreperfusion hyperkalemia in liver transplantation from DCD.

METHODS: One hundred thirty-one consecutive adult patients who underwent orthotopic liver transplantation from DCD were retrospectively studied. Based on serum potassium within 5 minutes after reperfusion, recipients were divided into two groups: hyperkalemia and normokalemia. According to preoperative biopsy results, the DCD graft livers were classified into five categories. Univariate analysis was performed using Chi-square test to identify variables that were significantly different between two groups. Multivariate logistic regression was used to confirm the risk factors of developing hyperkalemia and postreperfusion syndrome. Correlation analysis was used to identify the relationship between the serum concentration of potassium within 5 minutes after reperfusion and the difference in mean arterial pressure values before and within 5 minutes after reperfusion.

RESULTS: Twenty-two of 131 liver recipients had hyperkalemia episodes within 5 minutes after reperfusion. The rate of hyperkalemia was significantly higher in recipients of macrosteatotic DCD graft liver (78.6%, $P<0.001$) than that in recipients of non-macrosteatotic DCD graft liver. The odds ratio of developing postreperfusion hyperkalemia in recipients of macrosteatotic DCD graft liver was 51.3 ($P<0.001$). Macrosteatosis in the DCD graft liver was an independent risk factor of developing hyperkalemia within 5 minutes after reperfusion. The highest rate of postreperfusion syndrome also occurred in the recipients with macrosteatotic DCD graft liver (71.4%, $P<0.001$). A strong relationship existed between the serum potassium within 5 minutes after reperfusion and the difference in mean arterial pressure values before and within 5 minutes after reperfusion in macrosteatotic DCD graft liver recipients.

CONCLUSION: Macrosteatosis in the DCD graft liver was an independent risk factor of developing hyperkalemia and postreperfusion syndrome in the recipients.

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KEY WORDS: liver transplantation; hyperkalemia; reperfusion injury; macrosteatosis

Introduction

Severe hyperkalemia is a serious complication during orthotopic liver transplantation (OLT). Xia et al[1] showed that it can occur in both prereperfusion and postreperfusion period during OLT operation. Hyperkalemia episodes were also found to be more frequent in early postreperfusion, a short period within 5 minutes after reperfusion of the graft liver, than at other phases during OLT.[1, 2]

In general, the causes of hyperkalemia during the early postreperfusion period are considered to be: i) extracellular shift in H^+ exchange because of severe metabolic acidosis in the anhepatic phase, ii) exogenous potassium with the transfusion of red blood cell (RBC), and iii) the preservative fluid University of Wisconsin (UW) solution, which contains a high potassium concentration, flow into systemic circulation during reperfusion of the graft liver.[3-5] To prevent potassium flow into system circulation, cold lactated Ringer's solution with al-

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bumin has been routinely used to flush out UW solution, and blood (300-500 mL) was selectively vented via the vena cava before graft reperfusion. Units of intravenous insulin is routinely administered together with the RBC transfusion to transport extracellular potassium into cells and alkalizing agents were administered to counteract the severe metabolic acidosis during the operation period. However, despite these measures, the incidence of hyperkalemia episodes in the early postreperfusion period of OLT did not decrease significantly when using liver grafts from donation after cardiac death (DCD). Several studies[1, 6] have demonstrated that adopting DCD graft liver in OLT was an independent risk factor for postreperfusion hyperkalemia. Warm ischemia time was relatively longer in DCD graft liver than cadaver or brain death grafts, which may result in hypoxic damage to hepatocytes of DCD graft liver. After reperfusion, hepatocyte membrance suffered further damage because of oxygen free radicals which led to potassium release from hepatocytes.[7-10] Previous studies[11, 12] have also revealed that steatotic DCD graft livers were more sensitive to the ischemia/reperfusion injury.

The present study was to identify the pathological characteristics in DCD graft liver associated with postreperfusion hyperkalemia in adult recipients. We hypothesized that preexisting pathological changes in the DCD graft livers are associated with high incidence of postreperfusion hyperkalemia in the liver recipients.

Methods

Preoperative and intraoperative data retrieval

The study population consisted of adult patients who underwent OLT from DCD in our hospital between March 1, 2011 and March 31, 2014. All recipients provided informed consent and the study was approved by the hospital ethics review committee. Recipient variables including age, gender, weight, model for end-stage liver disease (MELD) score, blood urea nitrogen, blood creatinine, baseline serum concentration of potassium and etiology of liver diseases were recorded and stored in our OLT database. Intraoperative variables including the units of transfused RBCs before reperfusion, anhepatic time, mean arterial pressure (MAP) and blood gas including pH, serum lactate level and base excess, were recorded and stored in our OLT database. Baseline serum potassium concentration was defined as the first intraoperative laboratory value or the value measured immediately before operation. MAP was measured directly via a catheter inserted into the radial artery. The difference in MAP values before and within 5 minutes after reperfusion was calculated and a 30% decrease in MAP during this period was considered postreperfusion syndrome (PRS). In addition to the routine check every hour, MAP, blood gas and serum potassium concentration were measured within 5 minutes after DCD graft liver reperfusion. Hyperkalemia was defined as serum potassium concentration >5.5 mmol/L.

The donor data

The donor variables including liver biopsy before operation, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB), intensive care unit (ICU) days, vasopressor administration, cold ischemia time (CIT) and warm ischemia time (WIT) were recorded in our OLT donor database. DCD donors were generally younger than 55 years with body mass index (BMI) lower than 30 kg/m^2, and serum aminotransferase levels at procurement were less than twice of the normal values. The CIT of DCD grafts was less than 12 hours. Artificial life supports of all DCD donors had a planned withdrawal in the operating room or ICU. An independent physician from the donor hospital was assigned to declare death. Following a 5-minute mandatory waiting period after asystole, procurement began. Livers were stored at 4 ℃ for transport after flushed with 4-6 L of cold UW solution via both the abdominal aorta and inferior mesenteric vein. In our study, graft procurement WIT started when the life support was withdrawn and ended when cold perfusion started. Biopsy of the DCD graft liver was routinely completed before OLT operation.

Recipient grouping

Recipients were divided into two groups according to serum potassium level within 5 minutes after reperfusion. Hyperkalemia group consisted of recipients with a serum potassium level >5.5 mmol/L; Normokalemia group with a serum potassium level ≤5.5 mmol/L. According to the results of routine biopsy before operation, the pathological characteristics of DCD graft livers were classified as 1) macrosteatosis, with ≥20% of hepatocytes demonstrating macrosteatosis; 2) microsteatosis, with ≥20% of hepatocytes demonstrating microsteatosis; 3) piecemeal necrosis of hepatocytes; 4) diffused swelling of hepatocytes; and 5) normal DCD liver with no significant pathologic changes. According the pathological classification of the adopted DCD graft liver, the recipients were also divided correspondingly into the following groups: 1) macrosteatosis group, 2) microsteatosis group, 3) piecemeal necrosis group, 4) diffused swelling group and 5) normal DCD liver group.

Statistical analysis

Data were expressed as mean±SD and median values