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• *BRIEF REPORTS* •

Dextrose in the banked blood products does not seem to affect the blood glucose levels in patients undergoing liver transplantation

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Abstract

AIM: Hyperglycemia commonly seen in liver transplantation (LT) has often been attributed to the dextrose in the storage solution of blood transfusion products. The purpose of the study is to compare the changes of the blood glucose levels in transfused and non-transfused patients during LT.

METHODS: A retrospective study on 60 biliary pediatric patients and 16 adult patients undergoing LT was carried out. Transfused pediatric patients were included in Group I (GI), those not transfused in Group II (GII). Twelve adult patients were not given transfusion and assigned to Group III (GIII); whereas, four adult patients who received massive transfusion were assigned to Group IV (GIV). The blood glucose levels, volume of blood transfused, and the volume of crystalloid infused were recorded, compared and analyzed.

RESULTS: Results showed that the changes in blood glucose levels during LT for both non-transfused and minimally transfused pediatric groups and non-transfused and massively-transfused adult groups were almost the same.

CONCLUSION: We conclude that blood transfusion does not cause significant changes in the blood glucose levels in this study.

Key words: Organ; Liver surgery; Transplantation; Anesthesia; General monitoring; Blood glucose transfusion; Bank blood component; Infusion; 5% dextrose in 1/4 saline.

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INTRODUCTION

Contrary to earlier reports[1], hyperglycemia during liver transplantation (LT) is a common finding[2-4]. Normal blood glucose levels could even be maintained during LT procedure in humans[2] and dogs[5] with blood as the only source of dextrose. The mechanism is attributed to blood transfusion, which contains dextrose as part of the storage solution[2,3]. Blood transfusion in LT was once a common feature in the past, however, with increasing LT experience, the blood loss and subsequent blood and blood product replacement during operations have decreased gradually[6,7]. LT can now be performed without pack blood cell[8] and fresh frozen plasma[9]. In our living donor LT setting, some patients do not receive any banked blood products[10] but hyperglycemia is still noted. Therefore, we hypothesize that hyperglycemia seen in LT might not be related to blood transfusion. In this study, blood glucose levels of pediatric patients with biliary atresia undergoing LT with or without blood transfusion and four massively-transfused adult patients *vs* 14 non-transfused adult patients were compared and analyzed.

MATERIALS AND METHODS

The approval of the Ethics Committee of the Department of Health, Taiwan, was obtained and written informed consent for anesthesia and surgery were also obtained from the adult patients or the parents of the pediatric patients. Sixty biliary pediatric patients who underwent living donor liver transplantation (LDLT) and 16 adult LT patients at Chang Gung Memorial Hospital, Kaohsiung Medical Center from January 1999 to April 2002 were included. The anesthesia records were analyzed retrospectively. The pediatric patients were grouped as transfused (GI) and non-transfused (GII) group. Since the transfusion of GI was minimal, an additional four adults in our cadaveric series, who were massively transfused over 10 L of blood products (GIV) were compared with 12 of our 28 adult LDLT patients (G III) who did not receive blood transfusion. Anesthesia for all patients was maintained with isoflurane in an oxygen-air mixture. Fentanyl was given whenever necessary and atracurium was used as muscle relaxant. Continuous monitoring with ECG, pulse oximetry, arterial blood pressure, central venous pressure, end tidal CO_2, urine output and naso-pharyngeal temperature was performed. At least four intravenous lines were set for

fluids and blood replacements. Crystalloids such as normal saline, half saline, lactated Ringer, dextrose 5% in 1/4 saline were used. Five percent albumin and crystalloids instead of blood products were used to replace blood, ascites and transudate losses to maintain a state of normovolemia. Transfusion threshold was set at hemoglobin of 6-7 g/dL for as long as the patients remained hemodynamically stable. The amount of packed RBC (preserved in CPDA-1) transfused was estimated to reach a Hb of no greater than 8-9 g/dL after transfusion. LDLT without veno-venous bypass was performed as reported previously[11,12]. Continuous intravenous dopamine infusion was given at a rate of 2 μg/(kg·h) throughout the operation. Arterial blood gases and blood sugar were recorded after induction of the anesthesia, every 2 h during liver dissection, at anhepatic phase, 10 min after reperfusion and at the end of the operation. Blood glucose levels, total amount of fluids and blood components (including crystalloids with or without 5% dextrose, 5% albumin, packed red cell and fresh frozen plasma) were recorded. Blood glucose levels were compared between the transfused and non-transfused pediatric patients; likewise, comparison between the non-transfused adult patients and massively-transfused adult patients was made. Measurements between groups were compared using Mann-Whitney *U* test. All the data were given in mean±SD. Statistical calculations were performed using the SPSS advanced statistics module (SPSS Inc, Chicago, IL, USA). $P<0.05$ was regarded as significant.

RESULTS

Thirty-eight patients were included in the transfused group (GI), while twenty-two patients were included in the non-transfused group (GII). Table 1 shows the characteristics of the patients of GI and GII. The age, weight, height of the patients and anesthesia duration were not significantly different between groups. Higher hemoglobin levels were observed in GII. More intraoperative blood loss requiring packed blood cells and fresh frozen plasma transfusion was noted among GI patients. There was no difference between the two pediatric groups with regard to the mean amount of crystalloids with or without 5% dextrose and 5% albumin given. Mean urine output measured in pediatric groups showed no statistical difference. Blood glucose levels in both groups were almost the same with a tendency towards hyperglycemia at 170-270 mg/dL(Figure 1). The changes in blood glucose levels in the four massively-transfused adult patients (with 8 020±6 544 mL red blood cells and 4 085±2 888 mL fresh frozen plasma) were similar to the changes seen in the GIII patients (Figure 2).

Table 1 Patients' characteristics between pediatric groups

	GI (n = 38)	GII (n = 22)	P
Age (yr)	2.18±0.4	3±1.9	0.35
Weight (kg)	10.6±4.9	12.6±4.3	0.46
Height (cm)	82.1±23.6	86.8±15.4	0.43
Anesthesia time (h)	14.2±2.6	12.8±1.4	0.56
Blood loss (mL)	172.1±134	66.1±53.6	0.000
RBC (mL)	171±110	0	0.000
FFP (mL)	101.5±169	0	0.002
5% Albumin (mL)	419±392	489±2 670	0.253
Platelet transfusion	0	0	
Crystalloids without dextrose (mL)	1 246±662	1 154±550	0.613
Crystalloid with 5% dextrose (mL)	499±279	367±209	0.096
Urine (mL/(kg·h))	3.0±1.4	3.3±1.1	0.137
Preoperative Hb (mg%)	8.2±1.8	10.7±1.1	0.000
Postoperative Hb (mg%)	7.6±1.1	7.7±2.0	0.638

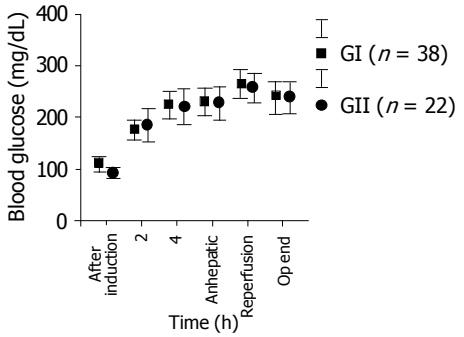

Figure 1 No significant changes of blood glucose level between groups during LT in biliary atresia patients with and without blood transfusion.

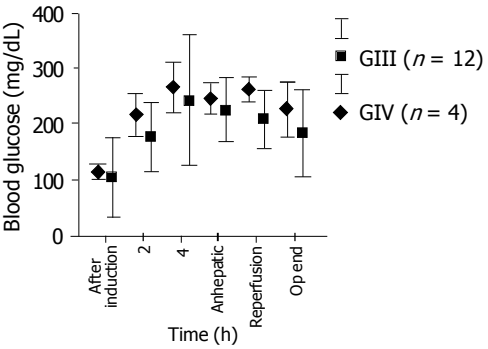

Figure 2 No significant changes of blood glucose level between groups during LT in adult patients with and without blood transfusion.

DISCUSSION

The liver plays an important role in carbohydrate metabolism and glucose homeostasis. Impaired gluconeogenesis and glucogenolysis, glucose intolerance or insulin resistance may occur in patients with end stage liver disease, predisposing these patients to fasting hypoglycemia or postprandial hyperglycemia[13-17]. In view of the complexity of glucose regulation and disease-specific anesthetic management[18], our study primarily focuses on pediatric biliary atresia patients, who have had Kasai operation. This specific group of patients represents children of the same age group in a similar physiological state with the same disease entity. Figure 1 shows that the blood glucose increased significantly 2 h after induction of anesthesia from 108±46 to 174±60 and 92±22 to 185±73 mg/dL for GI and GII, respectively. Likewise, Figure 2 shows the similar changes of the blood glucose for GIII and GIV patients. The levels of the blood glucose for all groups remained lightly hyperglycemic until the end of the operation regardless of transfusion.

The volume of blood transfused in GI was statistically significant but the amount of the dextrose contained in the 272 mL of transfused blood products may be clinically

irrelevant when compared to GII. We find that the volume of blood transfused is not related to blood glucose level in the four massively-transfused adult patients given over 10 L blood components during LT (Table 2). The fresh blood stored in CPDA-1 contained dextrose of 432 mg/dL. This decreases to 282 mg/dL after 35 storage[19]. Blood that is massively lost also contain dextrose. Blood glucose levels will not change despite exogenous dextrose loading if the amount of blood loss is greater than the volume transfused. This may explain why over 10 L of blood products given to GIV patients did not cause significant increase in blood glucose compared to GIII patients. Although Hb in blood product is usually higher than anemic patients requiring blood transfusion, the above mechanism may also explain why there is little increase in Hb level in patients receiving blood transfusion during massive bleeding in which losses are greater than that replaced. The preoperative and postoperative Hb showed that none of our patients was over-transfused (Table 1). It indicates that hyperglycemia encountered during LT in all groups is not related to blood transfusion per se. This observation is shared by other authors[2]. Hyperglycemia is probably caused by stress during LT surgery and from two of methyl-prednisolone given during the operation. Both noxious stimuli and methyl-prednisolone are known to increase blood glucose levels[20,21]. Furthermore, extrahepatic gluconiogenesis[22] and sudden release of glucose from the grafted liver in the reperfusion phase may also cause hyperglycemia[5]. Recent discoveries reveal that extrahepatic gluconiogenesis during anhepatic phase, most notably by the kidneys, contributes to endogenous glucose production in humans[22]. This endogenous glucose production is sufficient to maintain normal blood glucose levels in the anhepatic phase of orthotopic LT. Corollary, reperfusion is usually associated with a sudden increase of blood glucose as a result of massive glucose release from the graft liver as seen in very high glucose levels in hepatic venous blood compared to arterial blood[5].

Table 2 Patients' characteristics between adult groups

	GIII (n = 12)	GIV (n = 4)	P
Age (yr)	43±9.6	57±11.1	0.70
Weight (kg)	66±9.2	59.7±11.5	0.316
Height (cm)	168±7.7	167±4.9	1.0
Anesthesia time (h)	14. ±0.95	18.5±1.4	0.88
Blood loss (mL)	532±364	15 345±182 029	0.001
RBC (mL)	0	8 020±6 544	0.001
FFP (mL)	0	4 085±2 887	0.001
5% Albumin (mL)	1 337±505	2 966±550	0.253
Platelet transfusion (units)	0	24±24	0.003
Crystalloids (mL)	6 851±1 524	17 468±12 171	0.009

Hypo- as well as severe hyperglycemia should be avoided during surgery especially in LT. Our results showed that blood glucose levels of 170-270 mg/dL could be maintained with minimal administration of 499±279 or 367±209 mL 5% dextrose solution or 2.7 and 2 mg/(kg·min) for transfused and non-transfused pediatric patients, respectively. The doses are only one-third to half of the recommended doses (4-6 mg/(kg·min)) in routine non-liver transplant pediatric surgery. We conclude that no significant changes occur in the blood glucose levels among minimally-transfused and non-transfused, as well as in non-transfused and massively-transfused, patients undergoing LT.

REFERENCES

1 **Aldrete JA,** LeVine DS, Gingrich TF. Experience in anesthesia for liver transplantati. *Anesth Analg* 1969; **48**: 802-814
2 **Atchison SR,** Rettke SR, Fromme GA, Janossy TA, Kunkel SE, Williamson KR, Perkins JD, Rakela J. Plasma glucose concentrations during liver transplantation. *Mayo Clin Proc* 1989; **64**: 241-245
3 **Borland LM,** Roule M, Cook DR. Anesthesia for pediatric orthotopic liver transplantation. *Anesth Analg* 1985; **64**: 117-124
4 **Romero R,** Melde K, Pillen T, Smallwood GA, Heffron T. Persistent hyperglycemia in pediatric liver transplant recipients. *Transplant Proc* 2001; **33**: 3617-3618
5 **DeWolf AM,** Kang YG, Todo S, Kam I, Francavilla AJ, Polimeno L, Lynch S, Starzl TE. Glucose metabolism during liver transplantation in dogs. *Anesth Analg* 1987; **66**: 76-80
6 **Gerlach H,** Slama KJ, Bechstein WO, Lohmann R, Hintz G, Abraham K, Neuhaus P, Falke K. Retrospective statistical analysis of coagulation parameters after 250 liver transplantations. *Semin Thromb Hemost* 1993; **19**: 223-232
7 **Andrews WS,** Wanek E, Fyock B, Gray S, Benser M. Pediatric liver transplantation: a 3-year experience. *J Pediatr Surg* 1989; **24**: 77-82
8 **Cacciarelli TV,** Keeffe EB, Moore DH, Burns W, Chuljian P, Busque S, Concepcion W, So SK, Esquivel CO. Primary liver transplantation without transfusion of red blood cells. *Surgery* 1996; **120**: 698-704; discussion 704-705
9 **Dupont J,** Messiant F, Declerck N, Tavernier B, Jude B, Durinck L, Pruvot FR, Scherpereel P. Liver transplantation without the use of fresh frozen plasma. *Anesth Analg* 1996; **83**: 681-686
10 **Jawan B,** de Villa V, Luk HN, Wang CS, Huang CJ, Chen YS, Wang CC, Cheng YF, Huang TL, Eng HL, Liu PP, Chiu KW, Chen CL. Perioperative normovolemic anemia is safe in pediatric living-donor liver transplantation. *Transplantation* 2004; 77: 1394-1398
11 **Chen YS,** Chen CL, Liu PP, Chiang YC, Wang CC, Shigeru GS, Huang TL, Cheng YF, Eng HL, Cheung HK, Jawan B. Pediatric liver transplantation from living-related donors. *Transplant Proc* 1998; **30**: 3252-3253
12 **Chen CL,** Chen YS, Liu PP, Chiang YC, Cheng YF, Huang TL, Eng HL. Living related donor liver transplantation. *J Gastroenterol Hepatol* 1997; **12**: S342-S345
13 **Merli M,** Leonetti F, Riggio O, Valeriano V, Ribaudo MC, Strati F, Tisone G, Casciani CU, Capocaccia L. Glucose intolerance and insulin resistance in cirrhosis are normalized after liver transplantation. *Hepatology* 1999; **30**: 649-654
14 **Kato M,** Asano H, Miwa Y, Tajika M, Yamato M, Tomita E, Tokuyama K, Muto Y, Moriwaki H. Both insulin sensitivity and glucose sensitivity are impaired in patients with non-diabetic liver cirrhosis. *Hepatol Res* 2000; **17**: 93-101
15 **Collins JR,** Crofford OB. Glucose intolerance and insulin resistance in patients with liver disease. *Arch Intern Med* 1969; **124**: 142-148
16 **Gill RQ,** Sterling RK. Acute liver failure. *J Clin Gastroenterol* 2001; **33**: 191-198
17 **Marco J,** Diego J, Villanueva ML, Diaz-Fierros M, Valverde I, Segovia JM. Elevated plasma glucagon levels in cirrhosis of the liver. *N Engl J Med* 1973; **289**: 1107-1111
18 **Kelly DA**. Pediatric liver transplantation. *Curr Opin Pediatr* 1998; **10**: 493-498
19 **Latham JT,** Bove JR, Weirich FL. Chemical and hematologic changes in stored CPDA-1 blood. *Transfusion* 1982; **22**: 158-159
20 **Glaser F,** Sannwald GA, Buhr HJ, Kuntz C, Mayer H, Klee F, Herfarth C. General stress response to conventional and laparoscopic cholecystectomy. *Ann Surg* 1995; **221**: 372-380
21 **Issekutz B.** Studies on hepatic glucose cycles in normal and methylprednisolone-treated dogs. *Metabolism* 1977; **26**: 157-170
22 **Joseph SE,** Heaton N, Potter D, Pernet A, Umpleby MA, Amiel SA. Renal glucose production compensates for the liver during the anhepatic phase of liver transplantation. *Diabetes* 2000; **49**: 450-456

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