Is There Any Difference in Anesthetic Management of Biliary Atresia and Glycogen Storage Disease Patients Undergoing Liver Transplantation?

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Background. The purpose of the study was to compare the intraoperative blood glucose changes and the dosage of glucose infused between biliary atresia and glycogen storage disease (GSD) patients undergoing living donor liver transplantation (LDLT).

Patients and methods. The anesthesia records of biliary atresia and GSD patients undergoing LDLT were reviewed retrospectively. The levels of intraoperative blood glucose before operation, after induction of anesthesia, in the dissection, anhepatic, 10 min after reperfusion, and at the end of operation, as well as the dosage glucose infused, were compared between groups. The Mann–Whitney U test was used for statistical analysis; \( P < 0.05 \) was regarded as significant.

Results. Seventy-two biliary atresia patients were grouped into group I (GI) and 8 GSD patients into group II (GII). The blood glucose levels of both groups increased after operation and remained hyperglycemic, around 100–300 mg/dl, until the end of the operation. The mean glucose amounts infused were 2.7 ± 1.9 and 2.5 ± 1.15 mg/kg/min for GI and GII, respectively.

Conclusion. No significant difference was found in the anesthetic management between groups. The only difference was that the GSD patients required continuous glucose supply the night before the operation, while biliary atresia patients did not. © 2005 Elsevier Inc. All rights reserved.

Key Words: patients; biliary atresia; glucose storage diseases; surgery; liver transplantation; monitoring; blood glucose level; infusion; glucose contained crystalloid.

INTRODUCTION

The glycogen storage diseases (GSD) are a heterogenous group of inherited disorders caused by abnormalities of the enzymes that regulate glycogen synthesis and degradation. As a result of these abnormalities, inadequate glycogen breakdown occurs, resulting in hypoglycemia during periods of fasting or stress and in excessive storage of glycogen, predominantly in the liver. Hepatomegaly, hypoglycemia, hyperlipidemia, and growth retardation are the main manifestations in children, while liver cirrhosis and/or hepatocellular carcinoma may occur later [1, 2]. Advances in treatment have greatly improved metabolic control and hence the quality of life and survival. Patients with poor metabolic control, multiple liver adenomas, or progressive liver failure are candidates for liver transplantation [2].

The glucose requirements of the GSD patients is mostly dependent on exogenous administration. Failure to supply exogenous glucose on time will place patients in danger of hypoglycemic convulsion, but the dosage of supplemental exogenous glucose to maintain sufficient blood glucose levels during surgery, especially a long and stressful surgical procedure such as liver transplantation, is not clear. Whether there should be any difference in glucose administration in comparison to that with other end stage liver disease patients undergoing the same operation to maintain...
sufficient blood glucose levels is also not known. The purpose of the current study was to compare the blood glucose changes and the glucose administered retrospectively between GSD patients and biliary atresia patients undergoing liver donor liver transplantation.

METHODS AND PATIENTS

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 parents of the pediatric patients. Seventy-two biliary pediatric patients and 8 GSD patients from our 130 living donor liver transplantation (LDLT) series were included. Only patients with biliary atresia were included in the current study, because most of our pediatric patients undergoing LDLT were biliary atresia patients who had undergone the Kasai operation, representing children of the same age group and in a similar physiological state with the same disease entity. The anesthesia records were analyzed retrospectively. The biliary patients were group I (GI) and GSD pediatric patients group II (GII). Children with GSD received intravenous 5% dextrose in 0.225% saline with an infusion rate of 4 ml/kg/h through the night before operation, while biliary patients came into the operation room without an intravenous line. Anesthesia for all patients was maintained with isoflurane in an oxygen–air mixture. Fentanyl was given whenever necessary and atracurium was used as a muscle relaxant. Continuous monitoring of ECG, pulse oximetry, arterial blood pressure, central venous pressure, end tidal CO₂, urine output, and nasopharyngeal temperature was performed. At least four intravenous lines were set for fluids and blood replacements. Crystalloids such as normal saline, half saline, lactated Ringer, and 5% dextrose in 0.225% saline were used. The latter was given in one of the four lines with a infusion rate of approximately 3 ml/kg/h throughout the operation; 5% dextrose in water was also used for infusion drips of dopamine (2 μg/kg/min) after induction of anesthesia until the end of the operation and prostaglandin E1 after reperfusion with a drip of 0.01 μg/kg/h. The cumulative dosage of glucose infused was expressed in mg/kg/min.

Five percent albumin and crystalloids not containing dextrose instead of blood products were primarily used to replace blood, ascites, and transudate losses to maintain a state of normovolemia [3]. The transfusion threshold was set at hemoglobin of 6–7 g/dl for as long as the patients remained hemodynamically stable. The volume of packed RBC (preserved in CPDA-1) transfused was estimated to reach a Hb of no greater than 8–9 g/dl after transfusion [4]. LDLT without venovenous bypass was performed as reported previously [5]. Measurements of arterial blood gases and blood sugar were performed after induction of anesthesia, then at approximately 2- to 3-h intervals during dissection, at anhepatic, 10 min after reperfusion, and at the end of the operation. Infusion of glucose was increased if the blood glucose level was lower than 70 mg/dl and decreased when it was over 300 mg/dl; treatment with insulin was considered when the blood glucose was over 500 mg/dl [6]. Blood glucose levels and the total amount of fluids and blood components (including crystalloids with or without 5% dextrose, 5% albumin, packed red cells, and fresh frozen plasma) were recorded. The data between groups were compared and analyzed by using the Mann–Whitney U test. All of the data are given as means ± SD. Statistical calculations were performed using the SPSS advanced statistics module (SPSS Inc., Chicago, IL). A P value <0.05 was regarded as significant.

RESULTS

Table 1 shows the characteristics of the patients of both groups. Only age and weight were found to be significantly different between groups. The other parameters, such as the anesthesia time, blood loss and its replacement, including packed blood red cells, fresh frozen plasma, 5% albumin, and crystalloids, as well as the urine output and the preoperative and postoperative hemoglobin and hematocrit, were not significantly different. The preoperative and postoperative pH as well as the amount of sodium bicarbonate used to buffer the metabolic acidosis during the procedure were nonsignificant between groups. Fig. 1 shows the changes in blood glucose levels during the procedures in both groups. The levels increased significantly after the operation and remained hyperglycemic until the end of the operation. The levels of glucose administration were 2.7 ± 1.9 and 2.5 ± 1.15 mg/kg/min for the GI and GII groups, respectively. No patient required insulin treatment for hyperglycemia.

DISCUSSION

The liver has the function of storing glucose in glycogen, as well as releasing it as glucose into the bloodstream. The rate of storage or release of glucose by the liver is proportional to the degree of hypoglycemia or hyperglycemia, and thus the blood glucose concentration determines whether the liver is a glucose-producing or glucose-using organ [7]. Glycogenolysis is a glucose releasing process from the glycogen that requires a cascade of enzymatic reactions. Once the reaction is activated, hepatic glycogen phosphorylase, a rate-limiting enzyme in glycogenolysis, removes glucose from the outer branches of glycogen, as well as releasing it as glucose into the bloodstream. Glycogenolysis is a glucose releasing process from the glycogen that requires a cascade of enzymatic reactions. Once the reaction is activated, hepatic glycogen phosphorylase, a rate-limiting enzyme in glycogenolysis, removes glucose from the outer branches of glycogen, as well as releasing it as glucose into the bloodstream.
to occur in animals having high blood glucose [11]. Others have concerns about the danger of unrecognized hypoglycemia with potential risk of the development of permanent brain damage due to neuroglycopenia and have suggested that glucose of 4 to 6 mg/kg/min should be administered to keep the blood glucose normal [12].

The GSD patient has abnormal enzymes that regulate glycogen synthesis and degradation, resulting in hypoglycemia during periods of fasting or stress due to inadequate glycogen breakdown [8]. All of the glycogen storage diseases are treated with continuous glucose delivery, by either intermittent administration of uncooked cornstarch or frequent feeding during the day and overnight intragastric feeding [1, 2]. Continuous administration of glucose in GSD patients through intravenous infusion during anesthesia is absolutely required. In a liver transplantation setting, how much intravenous glucose should continuously be given in GSD patients to prevent hypoglycemia on the one hand and severe hyperglycemia on the other is not clear. Likewise, whether there is any dosage difference in comparison to other end stage liver diseases without deficiencies in glycogen breakdown, such as biliary atresia, is also to be defined. Our results show that the blood glucose levels of both groups increased significantly as the operation begin and remained hyperglycemic until the end of the operation (Fig. 1). The glucose doses administered were 2.7 ± 1.9 and 2.5 ± 1.1 mg/kg/min for the GI and GII groups, respectively. The dosages of both groups were obviously much lower than 4–6 mg/kg/min, as recommended [12]. Indeed, hyperglycemia during liver transplantation (LT) is a common finding [13, 14]; such a finding is also valid in GSD patients, as our results have shown (Fig. 1). The mechanism which induces hyperglycemia during LT is not clear. Blood transfusion was once thought to be the cause, because each unit of blood contains 0.5 mg of glucose in storage solution [6] and massive blood transfusion in LT was a common feature in the past. The amounts of blood products used in both groups were minimal (Table 1); it could not be the determinant factor in causing hyperglycemia found in the current study. Despite the fact that the impairment of gluconeogenesis is the main pathogenesis of GSD [1, 2], and in other end stage liver diseases, gluconeogenesis and gluconeogenesis may also be impaired, and glucose intolerance and insulin resistance may be encountered [15, 16]. Our results show that administration of 2.7 ± 1.9 and 2.5 ± 1.1 mg/kg/min in the GI and GII groups, only one third to one half of the recommended doses [12], had resulted in hyperglycemia (Fig. 1), while such doses given to children without cirrhosis were normoglycemic during tympanoplasty [17]. The cause of the difference is not clear; it may probably be due to the fact that LT is a more stressful surgical procedure than tympanoplasty and LT patients received two doses of methylprednisolone intraoperatively. Both noxious stimuli [10] and methylprednisolone [18] may increase blood glucose levels. Even in the absence of hepatic gluconeogenesis, glycogenolysis, and decreased insulin clearance in the anhepatic phase, hyperglycemia was still noted in our results (Fig. 1), instead of profound hypoglycemia, as early proposed [13]. Recent discoveries revealed that extrahepatic gluconeogenesis during anhepatic phases, most notably those of the kidneys, contributed to endogenous glucose production in humans [19] that is sufficient to maintain normal blood glucose in the anhepatic phase of LT [20]. Likewise, reperfusion is usually associated with a sudden increase in blood glucose as a result of the massive release of glucose from the grafted liver, as evidenced by very high glucose levels in hepatic venous blood compared with that of arterial levels, which were relatively low [21, 22].

Why GSD patients had blood glucose levels similar to those of biliary atresia patients in response to minimally exogenous glucose loads under noxious surgical stimuli is not fully understood. The capacity for endogenous glucose production through breakdown of glycogen in GSD is not absolutely disabled. Tsalkian et al. estimated the glucose turnover rates in five children with glycogen storage disease Type I during sequential withdrawal of an infusion of glucose to determine whether their hypoglycemia was the result of decreased glucose production or increased rates of glucose utilization and showed that children with GSD still have glucose production rates that are 40% lower than those of normal children fasted overnight [23].

Hypo- as well as severe hyperglycemia should be avoided during surgery, especially in LT. The current results showed that blood glucose levels around 100–300 mg/dl could be maintained with minimal ad-
ministration of 2.7 ± 1.9 and 2.5 ± 1.1 mg/kg/min for the GI and GII groups, respectively. It indicated that the anesthesia management for biliary atresia and GSD patients undergoing liver transplantation with special focus on glucose monitoring and fluid administration, including the glucose dosage, was principally the same. The only difference was that the GSD patients required a continuous glucose supply the night before the operation, while biliary atresia patients did not.

CONCLUSION

Comparison of the anesthesia management in biliary atresia and GSD patients undergoing liver transplantation with special focus on glucose monitoring and fluid administration, including the glucose dosage, were in practice the same. The blood glucose levels could be maintained around 100–300 mg/dl with minimal administration of 2.7 and 1.9 mg/kg/min for biliary atresia and GSD patients, respectively. The only difference was that the GSD patients required a continuous glucose supply the night before the operation, while biliary atresia patients did not.

REFERENCES