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Hypomagnesemia during pediatric orthotopic liver transplantation

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Abstract: We evaluated the incidence and severity of serum magnesium (Mg) abnormality along with other electrolyte and acid-base disturbances before and during the course of orthotopic liver transplantation (OLT) in pediatric patients. Serum Mg, Na, K, ionized Ca, pH, and blood gas measurements were performed before and hourly during the course of OLT. Hypomagnesemia was frequently observed in children undergoing OLT. Of a total of 30 recipients, 27 (90%) had hypomagnesemia before surgery; the mean serum Mg value at this time was 0.77 ± 0.15 mmol/L. In most of the recipients, the serum Mg value showed a gradual decrease during the course of OLT until magnesium sulfate supplements were administered. On the other hand, the serum Na, K, and ionized Ca levels and acid-base balance were normal before the beginning of surgery. However, hypernatremia, hypokalemia, a decrease in ionized Ca, and metabolic acidosis were commonly observed during the course of OLT. We conclude that electrolyte abnormalities, including hypomagnesemia and metabolic acidosis, commonly develop in children during the course of OLT. The frequent assessment of electrolytes, pH and blood gases is essential for the correction of these abnormalities during the course of OLT.

Key words: Hypomagnesemia, Liver transplantation, Pediatric orthotopic liver transplantation

Introduction

The prevalence of disturbances in sodium (Na), potassium (K), ionized calcium (Ca^{++}) homeostasis and metabolic acidosis in children during the course of orthotopic liver transplantation (OLT) is well documented [1]. However, little is known about the prevalence of serum magnesium (Mg) abnormality.

Low serum Mg level has been reported to be frequent in pediatric patients who are suffering from hepatobiliary disease [2]. This condition may lead to hypertension, tetany, seizures, and respiratory muscle weakness [3,4]. In addition, recent studies have suggested that hypomagnesemia is associated with an increased mortality rate [5,6]. The purpose of this study was to evaluate the incidence and severity of serum Mg abnormality along with other electrolyte and acid-base disturbances during OLT in pediatric patients.

Materials and methods

Twenty-seven pediatric patients who received OLT at the Royal Children's Hospital in Brisbane between May 1, 1990 and March 31, 1992 were enrolled in this study. The mean age of the 14 girls and 13 boys was 40 ± 43 months, and their mean weight was 12.9 ± 7.5 kg. The underlying diseases consisted of extrahepatic biliary atresia in 23 patients, α_1-antitrypsin deficiency in 2 patients, Crigler-Najjar syndrome in 1, and histiocytosis X in 1. Three of the children underwent a second OLT following failure of the first graft during the study period. In 24 recipients, the donated livers were portions of adult livers of appropriate size obtained by the Brisbane technique [7]. The remaining six recipients received whole liver transplants.

The induction and maintenance of anesthesia were performed with isoflurane and fentanyl. The radial artery was cannulated to obtain blood samples for the measurement of serum Mg, Na, K, Ca^{++}, pH, and blood gases. These measurements were performed an average of 12 times (range, 6–17 times) before and during the course of OLT. In each patient, the first blood sample was obtained just before surgery, and sampling was repeated hourly thereafter during the course of OLT. The concentration of serum Mg was measured by atomic absorption spectrophotometry; the normal range encountered in our laboratory is 0.9–1.2 mmol/L. The concentrations of serum Na, K, and Ca^{++} were mea-

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sured with a Synchron-CX7 (Beckman, Brea, Calif.) arterial blood gas and pH were measured with an ABL-520 (Radiometer, Copenhagen, Denmark). During the course of OLT, severe hypomagnesemia, hypokalemia, hypocalcemia and metabolic acidosis were corrected using 49.3% magnesium sulfate, 7.5% potassium chloride, 2% calcium chloride, and 8.4% sodium bicarbonate, respectively. To minimize citrate intoxication, all of the banked red blood cells were washed in an Electromedics AT1000 autologous transfusion device (Electromedics, Eaglewood, Colo.) and suspended in normal saline with almost no citrate residue before they were administered.

All values are expressed as mean ± SD. Statistical analysis were performed using analysis of variance with repeated measures followed by application of Bonferroni's modification of the paired *t*-test. A *P* value of less than 0.05 was considered to be significant.

Results

Table 1 shows the mean values of serum Mg, Na, K, and Ca^{++} at five time points before and during the course of OLT. Of the total of 30 recipients, 27 (90%) showed hypomagnesemia just before surgery, at which time the mean serum Mg value was 0.77 ± 0.15 mmol/L. Figure 1 shows the initial serum Mg value in each patient before surgery and the lowest value before the first magnesium sulfate supplement was administered. Of the 24 recipients who received intravenous magnesium sulfate supplement, 7 received it twice during the course of surgery. Fifteen patients received the supplement during the preanhepatic phase, 5 during the anhepatic phase, and 11 during the postanhepatic phase. An average of 3.5 mmols of Mg (ranging from 1 to 20 mmols) was administered during the course of OLT in these recipients. Of these 24 patients, 4 received intravenous magnesium sulfate supplement soon after the first measurement was obtained. In 6 recipients who showed mild hypomagnesemia during the course of surgery, magnesium sulfate was not administered. In most recipients, the serum Mg value showed a gradual decrease during the course of OLT until magnesium sulfate supplement was administered.

Although the serum Na value was not abnormal just before surgery, it increased gradually in all recipients during the course of OLT, even though sodium chloride was not administered. The mean value of serum Na before the end of anesthesia was significantly increased compared with that just before surgery.

Although the serum K value was normal just before surgery, 28 of the 30 recipients showed hypokalemia during the course of OLT. An average of 17 mEq of K (ranging from 6 to 78 mEq) was administered during the course of OLT in these recipients.

The serum Ca^{++} value did not show any abnormality just before surgery. However, 29 of the 30 recipients showed a decrease in Ca^{++} during the course of OLT. An average of 400 mg of Ca (ranging from 160 to 1420 mg) was administered during the course of OLT in these recipients. The mean value of Ca^{++} before the end

Table 1. Mean values of Mg, Na, K and Ca^{++} at five time points before and during the course of orthotopic liver transplantation

	A	B	C	D	E	ANOVA
Mg (mM/L)	0.77 ± 0.15	0.87 ± 0.23	0.86 ± 0.20	0.90 ± 0.31	0.83 ± 0.17	NS
Na (mEq/L)	137 ± 5	143 ± 5*	144 ± 5*	146 ± 4*	149 ± 5*	$P < 0.05$
K (mEq/L)	3.7 ± 0.7	3.9 ± 0.5	3.9 ± 0.6	3.7 ± 0.6	4.2 ± 0.6	NS
Ca^{++} (mM/L)	1.10 ± 0.16	1.21 ± 0.21	1.08 ± 0.24	1.23 ± 0.32	1.51 ± 0.30*	$P < 0.05$

All values are mean ± SD.
A, just before surgery; B, before the anhepatic phase; C, after the start of the anhepatic phase; D, after reperfusion of the transplanted liver; E, before the end of anesthesia; ANOVA, analysis of variance of difference from value at time A; NS, not significant;
* significantly different from value at time A (Bonferroni's modification).

Table 2. Mean values of arterial pH, Pao_2/Fio_2, $Paco_2$, and base excess at five time points before and during the course of orthotopic liver transplantation

	A	B	C	D	E	ANOVA
pH	7.39 ± 0.08	7.36 ± 0.07	7.36 ± 0.07	7.28 ± 0.10*	7.43 ± 0.06	$P < 0.05$
Po_2/Fio_2	438 ± 87	483 ± 94	489 ± 77	460 ± 75	432 ± 95	NS
Pco_2	38 ± 7	37 ± 4	35 ± 5	41 ± 5	38 ± 6	NS
BE	−1.5 ± 4.5	−4.0 ± 4.3*	−4.8 ± 3.9*	−7.1 ± 5.5*	1.4 ± 3.7	$P < 0.05$

All values are mean ± SD.
A, before the beginning of surgery; B, before the anhepatic phase; C, after the start of the anhepatic phase; D, after reperfusion of the transplanted liver; E, before the end of anesthesia; BE, base excess; ANOVA, analysis of variance; NS, not significant.
* significantly different from value at time A (Bonferroni's modification).

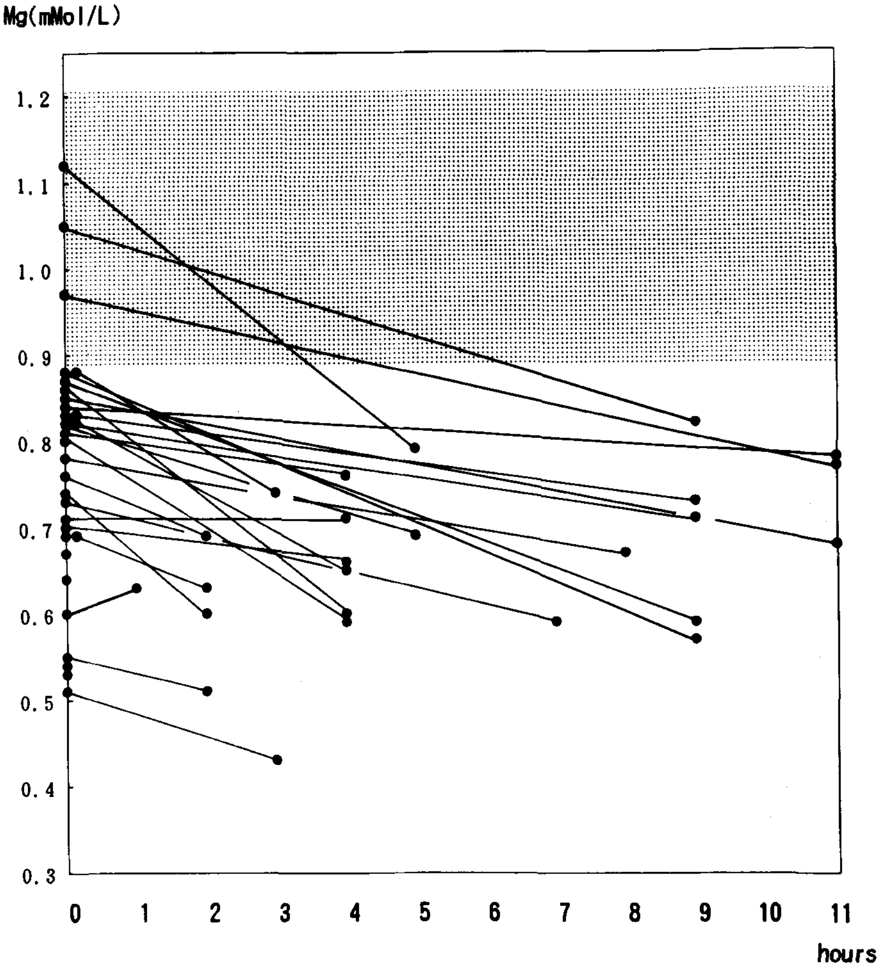

Fig. 1. The initial and lowest serum Mg values during orthotopic liver transplantation (OLT) in each patient before the first Mg supplement was administered. The *shaded area* shows the normal range of serum Mg level encountered in our lab oratory (n = 30)

of anesthesia was significantly increased compared with that before the beginning of surgery.

Table 2 shows mean values of pH, Pao_2/Fio_2 ratio, $Paco_2$ and excess base at the same five time points before and during the course of OLT. The values of pH and blood gases did not show any abnormalities just before surgery. Oxygenation and ventilation were well maintained during the course of OLT. However, metabolic acidosis occurred during the course of OLT in all recipients, especially after reperfusion of the transplanted liver.

Discussion

The electrolyte and acid-base balances are crucial to the maintenance of overall physiologic stability. In the present study, it was demonstrated that hypernatremia, hypokalemia, hypocalcemia, and metabolic acidosis commonly occur during the course of OLT. These findings are consistent with those previously reported [1]. In addition, the present findings indicate that 90% of children undergoing OLT have hypomagnesemia before surgery, and that a further decrease in Mg level frequently occurs during the course of surgery. Although the mechanism of this hypomagnesemia is unclear, some possible causes can be cited.

Firstly, the underlying disease in 85% of the children studied was biliary atresia. Intracellular Mg stores and serum Mg level are known to be significantly reduced in patients with hepatobiliary disease [2], especially in infants with biliary atresia, in whom the intestinal absorption of Mg is significantly impaired [2].

Secondly, massive transfusion may produce hypomagnesemia [8]. In our patients, although all of the banked red blood cells were washed and suspended in normal saline before they were transfused to minimize citrate intoxication, an average of 16 units of fresh frozen plasma and 7 units of platelet-rich plasma was transfused during surgery. The citrate present in these blood products has equal binding affinities for ionized Mg and ionized calcium. During OLT, citrate metabolism may be impaired by intraoperative hypothermia, impaired initial liver function, and the absence of the liver during the anhepatic phase [1,9]. The impaired metabolism of citrate during OLT may produce a progressive decrease in serum Mg.

Thirdly, increased renal excretion of Mg may produce hypomagnesemia [10]. The administration of aminoglycoside antibiotics, furosemide, and cyclosporine can increase renal Mg excretion [11,12]. Aminoglycoside antibiotics were used in all of these patients during OLT, and furosemide was used frequently.

Fourthly, the rapid administration of glucose and insulin produce an intracellular shift of Mg [10]. Hyperglycemia developed after massive transfusion of fresh frozen plasma in these patients, and therapeutic insulin was usually used during OLT.

Severe hypomagnesemia produces increased neuromuscular irritability, and may cause tetany and seizures, although this usually occurs only in patients whose serum Mg level is less than 0.4 mmol/L [4]. Other effects of hypomagnesemia include dysrhythmias, hypertension, and vasospasm [13]. We did not observe any adverse effects of hypomagnesemia during OLT in any patient. This may have been due to the close monitoring and early correction of serum Mg levels in the patients in our study.

In conclusion, we demonstrated that electrolyte abnormalities and metabolic acidosis are commonly seen in children during the course of OLT; 90% of the children undergoing OLT in this study had hypomagnesemia just before surgery, and a further decrease in Mg level was frequently observed during the course of surgery. Hypomagnesemia may be associated with hypertension, dysrhythmias, tetany, and seizures. These adverse effects may be masked by anesthesia during surgery. The frequent assessment of electrolytes, pH and blood gases is essential for the correction of these abnormalities during the course of OLT.

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