

Association of hyperglycemia and markers of hepatic dysfunction with dextrose infusion rates in Korean patients receiving total parenteral nutrition

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Parenteral nutrition is an integral part of medical treatment for patients who are unable to use normal physiological means of nourishment. Metabolic complications associated with total parenteral nutrition (TPN) are numerous and may be potentially fatal. Hyperglycemia and hepatic dysfunction are the most common of these complications.¹⁻³ Hyperglycemia can lead to many serious problems, such as hyperosmolar, nonketotic coma; osmotic diuresis resulting in depletion of potassium, sodium, and phosphate; and a reduction in phagocytosis and microbicidal rates.⁴⁻⁸ The most commonly reported hepatic abnormalities are fatty liver, cholelithiasis, and cholestasis. These hepatic dysfunctions can be detected by elevated serum liver function measurements, such as total bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP).⁹⁻¹⁵

The primary energy source in TPN solutions is carbohydrate, usu-

Abstract: The association of hyperglycemia and markers of hepatic dysfunction with dextrose infusion rates in Korean patients receiving total parenteral nutrition (TPN) was studied.

A retrospective study of 122 patients with normal glucose levels and liver function tests (LFTs) was conducted. Pharmacy and medical records of all patients who received TPN from three university-affiliated teaching hospitals in Korea between January 1998 and December 1999 were reviewed. Each patient was categorized as receiving dextrose at (1) ≤ 5 or > 5 mg/kg/min and (2) ≤ 4 , 4.1-5, 5.1-6, or > 6 mg/kg/min.

Fifty-five patients received dextrose at a rate of > 5 mg/kg/min for 15.1 ± 12.8 days and 67 patients at a rate of ≤ 5 mg/kg/min for 10.1 ± 6.8 days. Two patients in each group did not have follow-up glucose levels. Of the 53 patients in the > 5 mg/kg/min group, 16 exhibited hyperglycemia, compared with 21 of the 65 receiving lower rates of dextrose infusion. Elevated aspar-

tate transaminase was the most common abnormal LFT value in both groups (25% and 29% in the ≤ 5 - and > 5 -mg/kg/min groups, respectively). In the group receiving dextrose at > 5 mg/kg/min, 22.2% had two hepatic enzyme levels elevated concurrently, while 18.5% had two hepatic enzyme levels elevated in the group receiving dextrose at ≤ 5 mg/kg/min. Regression analysis revealed that duration of TPN and dextrose infusion rate were positively correlated with blood glucose levels and that duration of TPN was positively correlated with abnormal LFT values.

A retrospective study of Korean patients revealed no significant difference in the risk of hyperglycemia or hepatic dysfunction between those receiving ≤ 5 and > 5 mg/kg/min dextrose infusion in their TPN.

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ally in the form of dextrose monohydrate. Dextrose in TPN formulations is oxidized at a maximum rate of 4-7 mg/kg/min in humans. The amounts

infused beyond this rate are used by the liver for repletion of glycogen stores and lipid synthesis.^{1,16} Higher dextrose infusion rates may contrib-

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ute to the development of metabolic complications such as hyperglycemia, excess carbon dioxide production, lipogenesis, and abnormal liver function test (LFT) values secondary to fatty liver.^{15,16}

To prevent hyperglycemia and hepatic dysfunction, a TPN dextrose infusion rate of 5 mg/kg/min or less is generally recommended.¹⁷ However, patients who are given a dextrose-based TPN formula, with provision of lipid emulsion only once or twice weekly to prevent essential fatty acid deficiency, often receive a dextrose infusion rate in excess of the recommendation. This is especially true in Korea, because insurance reimburses hospitals only for one or two bottles of lipid emulsion per week for patients receiving TPN. The primary purpose of this study was to determine the frequency of hyperglycemia and evaluate changes in glucose levels, serum liver enzymes, and bilirubin in Korean patients who received TPN dextrose in excess of 5 mg/kg/min.

Methods

Clinical information was collected retrospectively. Pharmacy and medical records of all patients who received TPN from three university-affiliated teaching hospitals (all with more than 1000 beds) in Korea between January 1998 and December 1999 were reviewed. Patients over 18 years of age who received TPN through a central line for more than five days were included in the study. Because it is difficult to determine which body weight (actual versus ideal versus adjusted) should be used when calculating the dextrose infusion rate, obese and significantly underweight patients were excluded (actual body weight of $\geq 120\%$ or $\leq 80\%$ of ideal body weight). Others excluded were patients receiving peripheral or cyclic parenteral nutrition, patients receiving more than 500 kcal/day of oral or enteral nutrition, and patients with hyperglycemia or abnormal LFT values before starting TPN (glucose, >180 mg/dL; AST, >40 IU/L; ALT, >40 IU/L; ALP, >120 IU/L; or total bilirubin, >1.2 mg/dL). Patients with conditions that might predispose them to hyperglycemia (e.g., diabetes mellitus, pancreatotomy, sepsis) or hepatic dysfunction (e.g., alcoholism, hepatitis), patients taking corticosteroids, and patients who had undergone cancer chemotherapy or radiotherapy were also excluded.

Basic information about each study patient (age, sex, height, actual body weight, ideal body weight, body mass index [BMI], diagnosis, and duration of TPN) were recorded, along with drugs received, dextrose infusion rate (from TPN and other intravenous fluids), and lipids and amino acids received. Blood glucose values at baseline (within 72 hours before TPN administration) and on days 2 or 3, 4 or 5, and 6 or 7 were recorded (expressed as days 3, 5, and 7 hereafter). If only one glucose level was measured on either day 2 or 3, that value was recorded. If glucose values were available on both days, higher values were recorded. The same was done for days 5 and 7. Hyperglycemia was defined as a blood glucose level over 180 mg/dL, the value commonly accepted by clinicians in Korea. AST, ALT, ALP, and total bilirubin values at baseline (within 72 hours before TPN administration) and on days 7, 14, 21, and 28 were recorded. Each subject was categorized as receiving dextrose at (1) ≤ 5 or >5 mg/kg/min and (2) ≤ 4 , 4.1–5, 5.1–6, or >6 mg/kg/min.

Descriptive data were expressed in terms of the mean \pm S.D. To determine the differences in laboratory values among patients receiving different dextrose infusion rates, Student's *t* and analysis of variance tests were performed. To determine the differences in the frequency of hyperglycemia and hepatic dysfunction among patients receiving different dextrose infusion rates, chi-square

tests were performed. Pearson's correlation coefficient was used to determine the relationship between each independent variable and the blood glucose concentration or hepatic enzyme levels. To determine their predictive ability for blood glucose levels on days 3, 5, and 7, the following factors were included in the analysis: age, BMI, duration of TPN, dextrose infusion rate, and amount of daily amino acid. The same independent variables were again analyzed for serum liver enzyme and bilirubin values on days 7 and 14. Daily lipid intake were initially excluded from the analysis because it did not differ among subgroups. Also, medication data were excluded from analysis because patients taking medications known to alter glucose or hepatic functions were excluded from the study. The a priori level of significance was 0.05.

Results

The baseline characteristics and nutrients provided to patients are summarized in Tables 1 and 2, respectively. Of the 122 patients included in the study, 55 received dextrose at rates of >5 mg/kg/min (2 without follow-up glucose levels and 10 without follow-up LFTs), and 67 received dextrose at rates of ≤ 5 mg/kg/min (2 without follow-up glucose levels and 2 without follow-up LFTs). The mean \pm S.D. dextrose infusion rates were 6.1 ± 0.7 and 3.6 ± 0.6 mg/kg/min, respectively. These two groups were comparable except for surgical history, cancer diagnosis, amount of amino acid received, and duration of TPN. The group receiving dextrose at rates of ≤ 5 mg/kg/min had a higher percentage of surgical and cancer patients, while the group whose infusion rate was over 5 mg/kg/min received TPN with a larger amount of amino acid for a longer duration. All patients in both groups received a gradual increase in the dextrose content of their TPN formulation in a stepwise manner dur-

Table 1.
Baseline Characteristics of Patients

Variable	Dextrose Infusion Rate (mg/kg/min)	
	≤5 (n = 67)	>5 (n = 55)
Mean ± S.D. age (yr)	55.8 ± 13.8	56.9 ± 15.4
% Male	66	67
% Postoperative	84	47 ^a
% With cancer	87	47 ^a
Mean ± S.D. BMI (kg/m ²) ^b	22.1 ± 2.4	20.7 ± 2.1
Mean ± S.D. blood glucose concentration (mg/dL)	121.4 ± 23.1	124.6 ± 28.1
Mean ± S.D. serum protein concentration (g/dL)	5.6 ± 0.8	5.8 ± 0.9
Mean ± S.D. serum albumin concentration (g/dL)	3.4 ± 0.5	3.1 ± 0.6
Mean ± S.D. serum AST (IU/L)	21.7 ± 7.0	22.4 ± 7.6
Mean ± S.D. serum ALT (IU/L)	14.6 ± 6.8	16.7 ± 8.2
Mean ± S.D. serum ALP (IU/L)	68.0 ± 19.2	75.0 ± 21.6
Mean ± S.D. serum total bilirubin (mg/dL)	0.6 ± 0.3	0.6 ± 0.2

^a*p* < 0.05.
^bBMI = body mass index, AST = aspartate transaminase, ALT = alanine transaminase, ALP = alkaline phosphatase.

Table 2.
Comparison of TPN between Infusion-Rate Groups^a

Variable	Dextrose Infusion Rate (mg/kg/min)	
	≤5 (n = 67)	>5 (n = 55)
Mean ± S. D. dextrose infusion rate (mg/kg/min)	3.6 ± 0.6	6.1 ± 0.7 ^b
Mean ± S.D. daily amino acids (g/kg/day)	0.9 ± 0.2	1.4 ± 0.2 ^b
% patients receiving lipids	48	51
Mean ± S.D. duration of TPN (days)	10.1 ± 6.8	15.1 ± 12.8 ^b

^aTPN = total parenteral nutrition.
^b*p* < 0.05.

ing the first 48 hours (i.e., <250 g/day during first 24–48 hours).

Of the patients with follow-up glucose levels, 16 (30%) of the 53 patients who received dextrose at >5 mg/kg/min exhibited hyperglycemia, and 21 (32%) of the 65 patients who received dextrose at ≤5 mg/kg/min exhibited hyperglycemia; the difference was not significant. Differences among groups in the frequency of hyperglycemia were not significant when patients were divided into four infusion-rate groups (≤4, 4.1–5, 5.1–6, and >6 mg/kg/min). There were 14 patients in the ≤5-mg/kg/min and 10 patients in the >5-mg/kg/min groups who had hyperglycemia on day 3; 9 and 10 patients on day 5; and 1 and 8 patients on day 7, respectively. Eight

patients (14%) exhibited hyperglycemia for two days or longer in the >5-mg/kg/min group, as did 3 patients (4%) in the ≤5-mg/kg/min group.

Elevated AST values were the most common abnormal LFT values in both groups (25% in the ≤5-mg/kg/min group and 29% in the >5-mg/kg/min group). Of 45 patients receiving dextrose infusion of >5 mg/kg/min, 10 had two elevated hepatic enzyme levels, and 2 had three elevated hepatic enzyme levels. In the ≤5-mg/kg/min group, 12 of 65 patients had two elevated hepatic enzyme levels, and 5 of 64 had three elevated hepatic enzyme values. However, the differences in the frequency of abnormal LFT values were not significant between the two

groups. When the four infusion-rate groups were compared, the differences in the frequency of elevated AST, ALT, and total bilirubin values were significant. However, higher infusion rates were not necessarily associated with higher frequency. The 4.1–5- and >6-mg/kg/min groups generally had a higher frequency of elevated AST, ALT, and total bilirubin than the ≤4- and 5.1–6-mg/kg/min groups (Table 3).

Patients' mean ± S.D. blood glucose concentrations on days 3, 5, and 7 are listed in Table 4. The differences in blood glucose levels among different dextrose infusion rates were significant only on day 7. Although the glucose level in the >5-mg/kg/min group was higher than that in the ≤5-mg/kg/min group, the mean glucose values were still less than 180 mg/dL. Also, none of the patients in either group received insulin during TPN.

The liver function values (AST, ALT, ALP, and total bilirubin) on days 7 and 14 are listed in Table 5. The differences in these values among different dextrose infusion rates were only significant for ALP on day 7, when two groups (≤5 and >5 mg/kg min) were compared, and for AST and ALT on day 14 and ALP on days 7 and 14, when four groups were compared (*p* < 0.05). The >6-mg/kg/min group had higher AST, ALT, and ALP values on day 14. There were only seven patients (five in the >5-mg/kg/min group and two in the ≤5-mg/kg/min group) whose liver function was tested on days 21 and 28, respectively. Three patients in the >5-mg/kg/min group had elevated AST and ALT levels on day 21 (two patients) or 28 (one patient). Of the patients in the ≤5-mg/kg/min group, none had elevated liver enzyme values. All seven patients with LFT values on days 21 and 28 received TPN for more than one month.

Regression analysis revealed that the duration of TPN and dextrose infusion rate were positively correlated

Table 3.
Fraction (%) of Patients with Hyperglycemia or Abnormal LFT Values^a

Abnormality	Dextrose Infusion Rate (mg/kg/min)					
	≤5	>5	≤4	4.1-5	5.1-6	>6
Hyperglycemia	21/65 (32)	16/53 (30)	16/51 (31)	5/14 (36)	6/27 (22)	10/26 (38)
Elevated AST	16/64 (25)	13/45 (29)	8/49 (16)	8/15 (53)	3/22 (14)	10/23 (43) ^b
Elevated ALT	14/65 (22)	12/45 (27)	6/50 (12)	8/15 (53)	4/22 (18)	8/23 (35) ^b
Elevated ALP	5/55 (9)	8/33 (24)	3/43 (7)	2/12 (17)	4/18 (22)	4/15 (27)
Hyperbilirubinemia	7/56 (13)	3/41 (7)	2/41 (5)	5/15 (33)	0/20 (0)	3/21 (14) ^b
2 LFT values elevated	12/65 (19)	10/45 (22)	6/50 (12)	6/15 (40)	2/22 (9)	8/23 (35) ^b
3 LFT values elevated	5/64 (8)	2/45 (4)	2/50 (4)	3/14 (21)	0/22 (0)	2/23 (9)

^aTPN = total parenteral nutrition, AST = aspartate transaminase, ALT = alanine transaminase, ALP = alkaline phosphatase, LFT = liver function test.

^b*p* < 0.05 when four groups (≤4, 4.1-5, 5.1-6, and >6) were compared.

Table 4.
Mean ± S.D. Serum Glucose Values (mg/dL)

Time	Dextrose Infusion Rate (mg/kg/min)					
	≤5	>5	≤4	4.1-5	5.1-6	>6
Baseline	121.4 ± 23.1	124.6 ± 28.1	123.7 ± 21.6	113.1 ± 27.0	122.7 ± 26.9	126.6 ± 29.6
Day 3	146.9 ± 34.4	143.0 ± 37.3	147.6 ± 35.5	144.6 ± 31.5	146.1 ± 39.7	140.0 ± 35.5
Day 5	138.3 ± 28.6	150.3 ± 51.9	138.8 ± 26.2	136.8 ± 36.5	149.9 ± 58.9	150.7 ± 46.0
Day 7	123.1 ± 19.6	150.2 ± 45.2 ^a	126.6 ± 18.8	121.0 ± 23.8	149.1 ± 34.9	151.8 ± 55.5 ^b

^a*p* < 0.05 when two groups (≤5 and >5) were compared.

^b*p* < 0.05 when four groups (≤4, 4.1-5, 5.1-6, and >6) were compared.

Table 5.
Mean ± S.D. Changes in Liver Function Test Values

Test ^a	TPN Dextrose Infusion Rate (mg/kg/min)					
	≤5	>5	≤4	4.1-5	5.1-6	>6
AST (IU/L)						
Baseline	21.7 ± 7.0	22.4 ± 7.6	21.9 ± 7.0	17.9 ± 5.7	21.7 ± 7.8	23.0 ± 7.5
Day 7	29.8 ± 14.2	30.9 ± 16.3	27.7 ± 13.7	36.7 ± 14.2	28.9 ± 10.8	32.8 ± 20.6
Day 14	29.0 ± 15.9	34.1 ± 27.3	23.7 ± 7.5	34.4 ± 20.3	22.1 ± 9.1	46.0 ± 34.1 ^c
ALT (IU/L)						
Baseline	14.6 ± 6.8	16.7 ± 8.2	15.2 ± 7.1	12.4 ± 5.3	15.5 ± 7.1	17.9 ± 9.1
Day 7	24.4 ± 19.8	26.1 ± 19.6	22.8 ± 19.9	29.7 ± 18.9	25.9 ± 18.3	26.2 ± 21.3
Day 14	31.2 ± 25.1	38.5 ± 43.6	21.6 ± 10.0	40.7 ± 31.9	20.3 ± 13.1	56.8 ± 55.4 ^c
ALP (mg/dL)						
Baseline	68.0 ± 19.2	75.0 ± 21.6	66.3 ± 19.2	75.7 ± 18.1	77.7 ± 22.7	71.7 ± 20.3
Day 7	67.5 ± 24.1	112.0 ± 74.9 ^b	64.1 ± 21.3	79.0 ± 29.9	95.2 ± 37.3	131.1 ± 100.4 ^c
Day 14	82.0 ± 29.1	122.7 ± 107.7	79.3 ± 35.9	85.1 ± 19.4	85.3 ± 29.5	181.6 ± 157.5 ^c
Total bilirubin (mg/dL)						
Baseline	0.6 ± 0.3	0.6 ± 0.2	0.7 ± 0.2	0.5 ± 0.3	0.6 ± 0.3	0.6 ± 0.2
Day 7	0.5 ± 0.2	0.6 ± 0.5	0.5 ± 0.2	0.6 ± 0.3	0.4 ± 0.2	0.7 ± 0.7
Day 14	0.6 ± 0.3	0.7 ± 0.7	0.6 ± 0.2	0.7 ± 0.4	0.6 ± 0.2	0.8 ± 0.8

^aAST = aspartate transaminase, ALT = alanine transaminase, ALP = alkaline phosphatase.

^b*p* < 0.05 when two groups (≤5 and >5) were compared.

^c*p* < 0.05 when four groups (≤4, 4.1-5, 5.1-6, >6) were compared.

with blood glucose level, while only the duration of TPN was positively correlated with LFT values. Table 6 lists the simple correlation coefficients for each independent variable tested with blood glucose concentration, AST, ALT, ALP, and total bilirubin values.

Discussion

The literature about nutrition support advises that TPN dextrose infusion rates should be limited to 5 mg/kg/min.^{1,16,17} Overly aggressive infusion of hypertonic dextrose can lead to hyperosmolar, nonketotic coma and alterations in immune responses.^{4,6-8} It can also contribute to

the development of persistent hepatic dysfunction in patients without previous liver disease.¹⁻³

Provision of dextrose at rates of >4 mg/kg/min may be associated with hyperglycemia even in nondiabetic patients because insulin resistance is universal in stressed, hospitalized patients in whom insulin

Table 6.
Correlation Coefficients for Association between Independent Variables and Laboratory Test Values

Test and Time	Independent Variable ^a				
	Age	BMI	TPN Duration	Infusion Rate	AA
Glucose					
Day 3	-0.064	0.108	0.015	-0.061	-0.053
Day 5	0.080	0.161	0.029	0.122	0.165
Day 7	0.030	0.095	0.342 ^b	0.316 ^b	0.290 ^b
AST					
Day 7	0.166	-0.034	0.049	0.134	0.156
Day 14	0.068	-0.158	0.332 ^b	0.215	0.217
ALT					
Day 7	0.063	0.068	0.197 ^b	0.093	0.090
Day 14	-0.043	-0.086	0.393 ^b	0.233	0.205
ALP					
Day 7	-0.136	-0.076	0.433 ^b	0.442 ^b	0.385 ^b
Day 14	-0.088	-0.054	0.317 ^b	0.340 ^b	0.324 ^b
Total bilirubin					
Day 7	0.211 ^b	-0.053	0.299 ^b	0.149	0.124
Day 14	0.275	-0.098	0.286	0.066	0.062

^aBMI = body mass index, TPN = total parenteral nutrition, AA = amount of amino acids per day, AST = aspartate transaminase, ALT = alanine transaminase, ALP = alkaline phosphatase.
^b*p* < 0.05.

production may be inadequate to compensate for high dextrose infusion rates.¹⁸ In a retrospective study conducted by Rosmarin et al.,¹⁹ 48.6% of subjects who received TPN dextrose infusion at rates of >5 mg/kg/min exhibited hyperglycemia, whereas none of the subjects who received ≤4 mg/kg/min of TPN dextrose became hyperglycemic. Of all patients studied, 22.5% exhibited hyperglycemia. In our study, 37 (31%) of 118 patients developed hyperglycemia.

The threshold glucose concentration used to define hyperglycemia varies from study to study. We defined hyperglycemia as blood glucose concentration of >180 mg/dL, the lower end of conventionally accepted values (180–200 mg/dL) by clinicians in Korea.^{20,21} (This value is also the average renal threshold value for glucose, although renal threshold can be different in each individual.) This most likely explains why the rate of hyperglycemia in our study was higher than that found by Rosmarin et al.,¹⁹ who defined hyperglycemia as a blood glucose concentration of >200 mg/dL. However, even with the lower limit, the frequency of hyperglycemia in patients receiving dextrose at rates of >5 mg/kg/min was much lower in our study (30%). Pa-

tients in our study and those in Rosmarin et al.'s¹⁹ were at a fairly low risk for hyperglycemia due to strict inclusion criteria. In a study of critically ill surgical patients, Bjerke and Shabot¹⁸ found that critical hyperglycemia, defined as blood glucose level of >400 mg/dL, occurred in 1.7% of patients receiving TPN compared with 0.7% of patients not receiving TPN. However, when stratified by severity of illness, patients receiving TPN did not have significantly higher glucose levels than those not on TPN.

In our study, higher percentages of surgical and cancer patients in the ≤5-mg/kg/min group may have affected the frequency of hyperglycemia. Patients in the ≤5-mg/kg/min group had a higher frequency of hyperglycemia on day 3 than on day 7; however, our patients were not categorized by stress level or severity of illness, preventing us from properly addressing this issue.

Hyperglycemia is a common metabolic complication associated with TPN, especially when dextrose content of TPN solutions is greater than 250 g/day during the first 24–48 hours of the infusion. The mechanisms responsible for the regulation of plasma glucose concentration dur-

ing a dextrose infusion are fundamental to the entire metabolic response to parenteral nutrition. Two processes can minimize changes in the plasma glucose concentration during initial dextrose infusion: reduction of glucose production and enhanced ability to clear glucose from the bloodstream.¹ During the initial hours of dextrose infusion, the primary operative mechanism is the suppression of glucose production. Although we did not evaluate the frequency of hyperglycemia during the initial 24–48 hours, the dextrose content of TPN for all patients started at less than 250 g/day of dextrose during the first 48 hours of TPN was increased in a stepwise manner.

One might expect to see a rather linear response as the dextrose infusions are increased. However, linear response was not observed with glucose levels as dextrose infusion rates were increased in our study. Although the baseline characteristics of four groups were not listed separately, subgroups did not differ from the two main groups. The two major groups were well matched except for surgery and cancer status, which were expected to be different. In the study by Rosmarin et al.,¹⁹ average glucose levels in each subgroup did

not differ when hyperglycemic and euglycemic patients were separately evaluated, and only the number of subjects with hyperglycemia differed between infusion-rate groups. Thus, the changes in glucose levels could be a reflection of the number of patients with hyperglycemia and not the absolute glucose levels. The glucose values in our study differed between infusion-rate groups only on day 7, and the number of patients with hyperglycemia differed only on day 7. The frequency of hyperglycemia was higher earlier in the ≤ 5 -mg/kg/min group, whereas hyperglycemia persisted throughout the study in those receiving TPN dextrose at a rate of > 5 mg/kg/min. This could be because there were more surgical patients in the ≤ 5 -mg/kg/min group. Also, the frequency of hyperglycemia in groups receiving dextrose at 5.1–6 and > 6 mg/kg/min did not differ.

Serum hepatic enzyme concentrations are poor markers of TPN-associated fatty liver accumulation and liver disease. Hepatic fat accumulation can occur without significant changes in hepatic enzyme levels. Also, TPN-associated liver disease is multifactorial. However, hepatic dysfunction can be manifested by abnormal liver enzyme values, the most common way to identify TPN-associated liver disease in the clinical setting for further workup. Hepatic dysfunction, manifested by abnormal liver enzyme values and intrahepatic cholestasis, is common in children and adults receiving long-term TPN. The prevalence of this complication has been reported to be between 15% and 85%.^{13,14} Clarke et al.¹² reported a gradual but progressive increase in AST, ALP, and bilirubin levels (27%, 32%, and 31%, respectively) in patients with normal pre-TPN LFT values after four weeks of TPN. Patients with cancer and those requiring long-term TPN were more likely to have increased LFT values. Luman and Shaffer¹³ reported that 39% of patients receiving long-

term parenteral nutrition at home had abnormal LFT values, the most common being elevated ALP levels. A shortened small intestine and higher total caloric intake were associated with abnormal LFT values in that study. In another study, Cavicchi et al.¹⁴ found that the rate of liver disease was associated with a high lipid intake and long-term parenteral nutrition.

In our study, 29 (27%) of 109 patients had elevated AST levels and 10 (10%) of 97 had elevated bilirubin values. The frequency of abnormal LFT values did not differ between dextrose infusion rates of ≤ 5 and > 5 mg/kg/min. In addition, most studies defined abnormal LFT values as being at least 1.5–2.0 times the upper limit of normal, whereas we defined abnormal values as any value above the normal limit. Therefore, actual frequency of abnormal LFT values, if defined as 1.5–2.0 times the upper limit of normal, would probably be low compared with other studies. In addition, serious parenteral-nutrition-related hepatobiliary disorders are of concern for patients receiving long-term therapy. However, the mean duration of TPN in our study was shorter than that in most published studies. Although there were more patients with abnormal LFT values on days 21 and 28 in the groups receiving TPN dextrose at a rate of > 5 mg/kg/min, the number of patients with LFT values on day 21 or 28 was too few to evaluate.

The replacement of daily sugar-based calories with fat can minimize the frequency of glucose intolerance and ameliorate the hepatic complications associated with dextrose-based TPN.^{22,23} In Korea, national insurance currently reimburses for only one or two bottles of lipid emulsion per week for patients receiving TPN. Thus, the majority of calories must be administered as dextrose unless the patient is willing to pay for lipid emulsion out of pocket. We evaluated the rate of hyperglycemia and ab-

normal LFT measurements associated with high rates of continuous TPN dextrose infusion. Actual rates were comparable to or lower than those values previously reported. Furthermore, the difference in rates of hyperglycemia and abnormal LFT values was not significant among different infusion rates.

One limitation of our study was the exclusion of patients who were more likely to be sensitive to dextrose loads than was our study population. Future studies are needed to develop more precise TPN dextrose infusion-rate recommendations for obese or significantly underweight patients and those who are otherwise prone to hyperglycemia or hepatic dysfunction. Nevertheless, this study provides the first data on the rate of hyperglycemia and hepatic dysfunction in association with TPN dextrose infusion rates in Korean patients.

Conclusion

A retrospective study of Korean patients revealed no significant difference in the risk of hyperglycemia or hepatic dysfunction between those receiving ≤ 5 and > 5 mg/kg/min of dextrose infusion in their TPN.

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