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The Association between a Four-Oil Lipid Emulsion and Parenteral Nutrition Associated Liver Disease-Related Laboratory Values in Adult Patients Receiving Home Parenteral Nutrition.

Background: Home parenteral nutrition (HPN) is recommended for patients who are unable to meet their nutrition needs through an oral or enteral route. HPN includes lipid injectable emulsions (ILE) as a macronutrient component. Traditional ILE include those composed of soybean oil, a source of essential fatty acids that prevents essential fatty acid deficiency (EFAD). The pro-inflammatory nature of soybean oil is a potential factor in parenteral nutrition associated liver disease (PNALD) development.[1] An ILE containing four types of oils (soybean oil, medium-chain triglycerides [coconut oil], olive and fish oil) is now approved for use as a calorie and fatty acid source.[2] Studies in HPN patients have shown mixed results with regard to changes in liver function tests and fatty acid profiles while receiving a four-oil ILE.[3-5]

Purpose statement/objective: The purpose of this study was to evaluate the association between a four-oil lipid emulsion and PNALD-related laboratory values in adult HPN patients with baseline abnormal liver function tests.

Methods: Twelve branches of a large home infusion pharmacy in nine states were selected as study sites. Eligible subjects included adult HPN patients with baseline abnormal alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) or total bilirubin (T bili) and receiving a four-oil ILE (Smoflipid®). One of these values was required to be at least 1.5 times the high normal limit. Seventy-seven adult patients were enrolled in the study. Sixty-two (80.5%) of these patients were receiving a soybean oil-based ILE prior to starting a four-oil ILE. Data were retrospectively collected at the following time points: Baseline, 1 Month, 2 Months, 3 Months, 6 Months and 12 Months. Laboratory sampling coincided with the patients' routine lab monitoring and included ALP, ALT, AST, T bili, triglycerides (TG) and triene: tetraene ratio. Reports of physical manifestations of EFAD were also collected. Primary outcome measures were changes between time points in ALP, ALT, AST, and T bili. Secondary outcome measures included changes in TG and EFAD manifestation between time points.

Results: Baseline characteristics are listed in Table 1. Kruskal-Wallis tests and post hoc Mann-Whitney U tests were used to detect changes in ALT, AST, ALP, T bili and TG levels between time points. Overall, ALT, AST, ALP, T bili and TG decreased from Baseline to Month 12 time points with several statistically significant decreases (see Table 2). A statistically significant decrease in ALT and AST was first detected between Baseline and Month 1 time points, and a statistically significant decrease in ALP was first detected between Baseline and Month 2 time points. ALT, AST and ALP all showed statistically significant decreases between Baseline and Month 12 time points. There were two reports of physical manifestations of EFAD (dry, flaky skin) at the Baseline (n=1) and Month 1 time point (n=1) in the same patient. Of note, this patient had been receiving a soybean oil-based ILE prior to changing to a four-oil ILE. No triene:tetraene ratio results were reported for any subject at any time point.

Conclusions: Use of a four-oil ILE is associated with a clinically and statistically significant decrease in ALT, AST and ALP adult HPN patients with baseline abnormal liver function tests. Clinical significance is supported by the return from abnormal AST and ALT values at Baseline to a normal reference range at

the Month 1 and Month 2 time points, respectively. There were also statistically significant decreases in ALP and clinical significance supported by a decrease toward normal values. Overall, the use of a four-oil ILE may provide benefit over traditional ILE in adult HPN patients with PNALD-related laboratory values.

Table 1. Baseline clinical and demographic characteristics (N=77)

	Mean ± SD	Range
Age (yr)	54.2 ± 13.3	21-77
Weight (kg)	58.0 ± 15.0	34.0-127.8
BMI (kg/m^2)	20.6 ± 5.0	12.1-48.3
	n	%
Female	45	58.4
Male	32	41.6

Key: SD, standard deviation; yr, year; kg, kilograms; BMI, body mass index; kg/m^2, kilograms per meters, squared

Table 2. Comparison of ALT, AST, ALP, T bili and TG levels between Baseline, 1 Month, 2 Month, 3 Month, 6 Month and 12 Month time points while receiving four-oil lipid emulsion

	Laboratory Values[a]									
	ALT		AST		ALP		T bili		TG	
Normal reference range	10-35		6-40		33-130		0.2-1.2		0-150	
Time point[b]										
Baseline	81.0 (104)	12-401	70.0 (70)	19-549	317.5 (321)	48-1674	0.8 (1.6)	0.2-26.6	97.0 (87)	33-264
1 Month	52.0 (50)	11-313	38.0 (33)	16-169	262.5 (237)	43-1175	0.6 (1.1)	0.1-13.7	103.0 (69)	38-338
2 Month	34.0 (62)	6-345	39.0 (42)	15-200	230.0 (213)	61-1710	0.5 (0.7)	0.2-12.9	99.0 (63)	37-239
3 Month	41.0 (56)	9-194	31.5 (37)	14-332	218.0 (182)	57-1054	0.6 (0.5)	0.1-14.4	104.0 (81)	36-283
6 Month	25.0 (27)	11-94	29.0 (30)	10-469	186.0 (198)	56-1781	0.5 (0.5)	0.1-7.7	106.0 (74)	54-369
12 Month	36.0 (32)	11-69	30.5 (25)	18-63	151.5 (116)	59-353	0.5 (0.6)	0.2-3.9	89.5 (104)	81-246
Significance between time points (*p* value)[c]	<0.001[c]		<0.001[d]		0.003[e]		0.233		0.884	

Key: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; T bili, total bilirubin; TG, triglycerides

[a]Values reported as median (interquartile range) and range
[b]Baseline: ALT, n=75 ; AST, n=76 ; ALP, n=76 ; T bili, n=74 ; TG, n=32
1 Month: ALT, n=68 ; AST, n=66 ; ALP, n=68 ; T bili, n=67 ; TG, n=36
2 Month: ALT, n=51 ; AST, n=50 ; ALP, n=51 ; T bili, n=50 ; TG, n=28
3 Month: ALT, n=46 ; AST, n=46 ; ALP, n=45 ; T bili, n=44 ; TG, n=25
6 Month: ALT, n=27 ; AST, n=27 ; ALP, n=27 ; T bili, n=26 ; TG, n=19
12 Month: ALT, n=12 ; AST, n=12 ; ALP, n=12 ; T bili, n=12 ; TG, n=6
[c]ALT: $p \leq 0.05$: Baseline to 1 Month, 2 Month, 3 Month, 6 Month & 12 Month; 1 Month to 6 Month & 12 Month; 2 Month and 3 Month to 6 Month
[d]AST: $p \leq 0.05$: Baseline to 1 Month, 2 Month, 3 Month, 6 Month & 12 Month
[e]ALP: $p \leq 0.05$: Baseline to 2 Month, 3 Month, 6 Month & 12 Month; 1 Month to 12 Month

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