Retrospective Study Evaluating the Prevalence of Liver Disease in Patients Dependent on Parenteral Nutrition

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INTRODUCTION

- Intestinal failure-associated liver disease (IFALD) is a rare and serious disease that occurs in patients dependent on parenteral nutrition (PN)[1,2]
- IFALD is characterized by choline deficiency, hepatic steatosis, cholestasis, and in some patients, rapid progression to end-stage liver disease in the absence of an isolated intestine or intestine/liver transplant[3-5]
- Patients dependent on PN are unable to absorb sufficient choline, an essential component of several metabolic processes, contributing to the development of IFALD[6-8]
- Alkaline phosphatase (ALP) is an established biomarker for cholestasis and a clinically meaningful indicator of IFALD severity and progression

STUDY OBJECTIVE

- The purpose of this study was to determine the prevalence of liver disease in patients receiving long-term home PN (HPN) with a national home infusion company

METHODS

- This study was a non-interventional, retrospective chart review of patients that received long-term HPN
- Multiple data points were captured at designated follow-up intervals during a subject's therapy
- All subjects who had received HPN from Coram® CVS Specialty™ Infusion Services (home infusion company) during the last 3 years for a minimum of 6 months were eligible
- Subject records were pulled from the pharmacy provider's electronic medical record using a specialized query tool and individual chart reviews were undertaken for eligible subjects
- The primary endpoint was the proportion of patients with suspected IFALD
  - Elevated serum ALP concentration >1.5x upper limit of normal (ULN; 147 IU/L)
- The secondary endpoint was the proportion of patients with at least one elevated liver enzyme:
  - Serum direct bilirubin (>1.2 mg/dL)
  - Aspartate aminotransferase (AST; >40 IU/L)
  - Alanine aminotransferase (ALT; 56 IU/L)
  - Gamma-glutamyl transferase (GGT; >48 IU/L)
- Liver enzyme values were summarized from baseline (start of home care) and at Month 6, 12, 24 and 36 as available up to Month 36 to determine whether there was a progressive component to cholestasis
- Data were recorded at each of the designated time-points and presented as observed

REFERENCES

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RESULTS

TABLE 1. DEMOGRAPHIC AND BASELINE CHARACTERISTICS

Characteristics	All Patients (N=468)
Age (years) at Baseline	
N	468
Mean (SD)	44.0 (22.2)
Median	46.0
Min, max	0.3, 98.0
Age Group, n (%)	
<12 years	52 (11.1)
12 years – <65 years	322 (68.8)
≥ 65 years	94 (20.1)
Sex, n (%)	
Male	151 (32.3)
Female	317 (67.7)
Geographic Region, n (%)	
Central	1 (0.2)
Midwest	68 (14.5)
Northeast	80 (17.1)
Southeast	103 (22.0)
Southwest	69 (14.7)
West	147 (31.4)
BMI (kg/m^2) at Baseline	
n	464
Mean (SD)	20.6 (5.9)
Median	19.5
Min, max	7.6, 64.2
History of Liver Disease, n (%)	
Yes	51 (10.9)
No	417 (89.1)

- Overall, 468 subjects were included in this study
- Most subjects (332/468; 68.8%) were 12-65 years of age **(Table 1)**

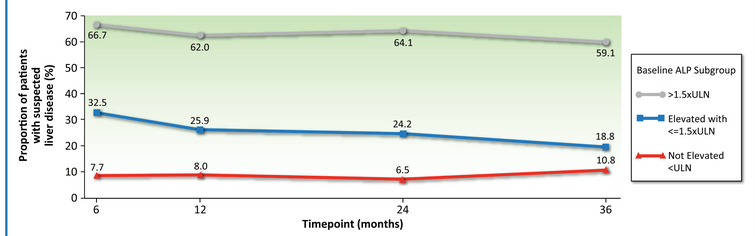
TABLE 2. PROPORTION OF PATIENTS WITH SUSPECTED LIVER DISEASE – OVERALL, BY TIMEPOINT AND BY BASELINE ALP SUBGROUP

		Baseline ALP Subgroup		
Statistics Timepoint	All Patients (N=468)	Not Elevated <ULN (N=270)	Elevated with ≤1.5x ULN (N=88)	>1.5xULN (N=106)
Patients with suspected liver disease, n1/n2 (%)				
Overall	169/468 (36.1)	29/270 (10.7)	33/88 (37.5)	106/106 (100.0)
Baseline	106/468 (22.6)	0/270 (0.0)	0/88 (0.0)	106/106 (100.0)
Month 6	114/447 (25.5)	20/261 (7.7)	27/83 (32.5)	66/99 (66.7)
Month 12	81/342 (23.7)	16/201 (8.0)	15/58 (25.9)	49/79 (62.0)
Month 24	39/151 (25.8)	5/77 (6.5)	8/33 (24.2)	25/39 (64.1)
Month 36	21/76 (27.6)	4/37 (10.8)	3/16 (18.8)	13/22 (59.1)
≥ Month 6	143/468 (30.6)	29/270 (10.7)	33/88 (37.5)	80/106 (75.5)

Suspected liver disease was defined as ALP serum levels > 1.5x the upper limit of normal (ULN). The ULN of ALP was defined as 147 IU/L. Patients were classified as having suspected liver disease 'Overall' if at least one of their ALP values over the designated time-points including baseline met the defined threshold. Baseline values were defined as those obtained during the start of home care infusion. n1 was the number of patients with suspected liver disease, n2 was the number of patients who have observed data in the specified timepoint. There were 4 patients whose baseline ALP value was 'NR', they were excluded from the baseline ALP subgroup.

- At baseline 106/468 (22.6%) subjects had suspected liver disease. (**Table 2**)
- 143/468 (30.6%) subjects had suspected liver disease at any given time over the course of the study from Month 6 to 36 (**Table 2**)
- The percentage of subjects with suspected liver disease increased over time from baseline up to Month 36

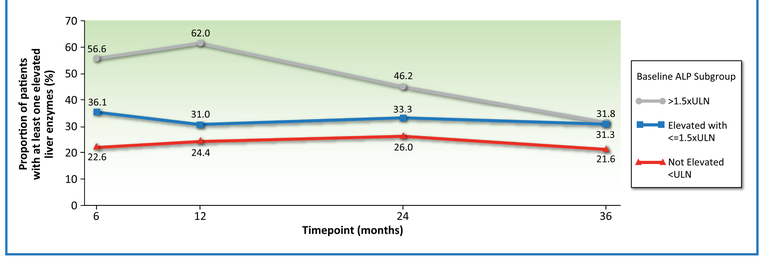
FIGURE 1. PLOT OF PROPORTIONS OF PATIENTS WITH SUSPECTED LIVER DISEASE OVER TIME BY BASELINE ALP SUBGROUP



Suspected liver disease was defined as ALP serum levels > 1.5x the upper limit of normal (ULN). The ULN of ALP was defined as 147 IU/L. Baseline values were defined as those obtained during start of home infusion care. Proportions were calculated using n1/n2 where n1 was the number of patients with suspected liver disease and n2 was the number of patients who have observed data in the specified timepoint within specified subgroup. There were 4 patients whose baseline ALP value was 'NR', they were excluded from the baseline ALP subgroup.

- At any given time during Month 6-36, 80/106 (75.5%) of the subjects with baseline ALP elevations (>1.5x ULN) continued to exhibit elevated ALP (**Table 2**)
- By Month 36, 13/22 (59.1%) of these subjects had elevated ALP (**Figure 1**)

FIGURE 2. PLOT OF PROPORTIONS OF PATIENTS WITH AT LEAST ONE ELEVATED LIVER ENZYME OVER TIME BY BASELINE ALP SUBGROUP



The elevated liver enzymes were defined as bilirubin > 1.2 mg/dl, AST > 40 IU/L, ALT > 56 IU/L, and GGT > 48 IU/L. Baseline values were defined as those obtained during start of home infusion care. Proportions were calculated using n1/n2 where n1 was the number of patients with elevated liver enzyme and n2 was the number of patients who have observed data in the specified timepoint within specified subgroup.

- Overall, 203/468 (43.4%) subjects had at least one elevated liver enzyme (bilirubin, AST, ALT or GGT) over the course of the study (Month 6-36)
  - Similar trends were observed for bilirubin, AST and ALT (**Figure 2**)
  - GGT level data was available only for very few patients therefore no valid comparisons could be made

CONCLUSIONS

- A significant percentage of HPN-dependent patients develop cholestasis
- Serum ALP remained elevated or became increasingly elevated despite medical management in these patients
- Our results support further exploration of investigational therapies such as intravenous choline chloride to treat IFALD

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