

# THRIVE-1: A Multi-center, Cross-sectional, Observational Study to Assess the Prevalence of Choline Deficiency in Patients Dependent on Parenteral Support

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## BACKGROUND

- Choline is a quaternary amine that is an essential dietary nutrient in humans<sup>1,2</sup>
- Choline is essential for patients with intestinal failure (IF) who are dependent on Parenteral Support (PS), given that deficiency can lead to hepatic injury, neuropsychological impairment, muscle damage, and thrombotic abnormalities<sup>3-6</sup>
- Current PS formulations lack choline, affecting an estimated 40,000 long-term PS patients who are or may become deficient<sup>7</sup>
- Currently, there are no approved intravenous (IV) choline products for PS patients globally

## PURPOSE

- The purpose of this study was to assess the prevalence of choline deficiency and liver injury in adolescents ( $\geq 12$  years of age) and adult patients ( $\geq 18$  years of age) with IF who are dependent on PS

## METHODS

- THRIVE-1 was a multi-center, cross-sectional observational study
- Data collection occurred during a single clinic visit
- PS dependence was defined as at least 4 days/week on PS for 10 to 24 weeks (capped at 25%) and 24 weeks or longer

## RESULTS

- 78 enrolled patients, 75 completed, and 3 withdrew the study

### Demographics (Table 1)

- 55.1% male, 92.3% White, and 96.2% Not Hispanic or Latino

### Parenteral Support (PS) (Table 2)

- Mean duration: ~9 years
- Mean PS frequency: 6.6 days/week (SD: 0.95)
- Most patients received mixed or plant-based lipids

### Choline Deficiency and Liver Injury (Table 3)

- Mean plasma free choline concentration: 7.5 nmol/mL (SD: 3.9)
- Choline deficiency was present in 78.2% (61/78) of patients
- The prevalence of choline deficiency was also evaluated by age group, PS duration, lipid type and underlying condition
- Among the choline-deficient participants, 63% (38/60) had liver injury

**TABLE 1. Overview of Demographics, Baseline Characteristics**

Characteristics	Enrolled Set (N = 78)
<b>Age (years)</b>	
Mean (SD)	51.9 (16.6)
<b>Age group, n (%)</b>	
12-<18	2 (2.6)
18-65	61 (78.2)
>65	15 (19.2)
<b>Sex, n (%)</b>	
Male	43 (55.1)
Female	35 (44.9)
<b>Race, n (%)</b>	
Asian	2 (2.6)
Black or African American	3 (3.8)
White	72 (92.3)
Other	1 (1.3)
<b>Ethnicity, n (%)</b>	
Hispanic	3 (3.8)
Non-Hispanic	75 (96.2)
<b>Height (cm)</b>	
Mean (SD)	167.6 (10.2)
<b>Weight (kg)</b>	
Mean (SD)	64.7 (13.5)
<b>BMI (kg/m<sup>2</sup>)</b>	
Mean (SD)	23.0 (3.8)

## REFERENCES

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**TABLE 2. Overview of Parenteral Support History**

Characteristics	Enrolled Set (N = 78)
<b>Total Infusion Volume (mL) of PS/day or night</b>	
Mean (SD)	2614.9 (1151.8)
<b>Infusion Duration (minutes/day)</b>	
Mean (SD)	708.5 (124.1) or ~12 hours
<b>Number of Weeks from Start of PS to Screening – All Patients</b>	
Mean (SD)	482.3 (484.3) or ~9 years
<b>PS Frequency (days per week)</b>	
Mean (SD)	6.6 (0.9)
<b>Amino Acids (grams per day per week)</b>	
Mean (SD)	60.7 (33.5)
<b>Amino Acids (grams per kg day per week)</b>	
Mean (SD)	1.0 (0.5)
<b>Dextrose (kcal per day per week)</b>	
Mean (SD)	997.5 (595.3)
<b>Dextrose (kcal per kg day per week)</b>	
Mean (SD)	16.4 (11.4)
<b>Lipid Frequency (days per week)</b>	
Mean (SD)	3.0 (2.4)
<b>Lipid Type, n (%)</b>	
No Lipids	8 (10.3)
Fish Oil Based	1 (1.3)
Plant Based	38 (48.7)
Mixed Oil	31 (39.7)
<b>Lipids (grams per day per week)</b>	
Mean (SD)	18.7 (18.2)
<b>Lipids (grams per kg day per week)</b>	
Mean (SD)	0.3 (0.3)
<b>Vitamin B12 added each night?, n (%)</b>	
Yes	78 (100.0)
<b>Folic Acid added each night?, n (%)</b>	
Yes	78 (100.0)

**TABLE 3. Overview of Choline Deficiency and Liver Injury**

Characteristics	Enrolled Set (N = 78)
<b>Choline Concentration (nmol/mL)</b>	
Mean (SD)	7.5 (3.9)
<b>Number of Patients with Choline Deficiency, n (%)</b>	
All	61/78 (78.2)
<b>By Age Subgroup</b>	
12 years to 18 years	1/2 (50.0)
18 years to 65 years	49/61 (80.3)
>65 years	11/15 (73.3)
<b>By PS Duration</b>	
$\leq 6$ months	2/3 (66.7)
>6 months to $\leq 12$ months	5/6 (83.3)
>12 months to $\leq 24$ months	8/13 (61.5)
>24 months to $\leq 36$ months	4/4 (100.0)
>36 months to $\leq 48$ months	4/4 (100.0)
>48 months to $\leq 60$ months	0/0
>60 months	38/48 (79.2)
<b>By Lipid Type</b>	
Fish Oil	1/1 (100.0)
Plant Based	27/38 (71.1)
Mixed Oil	26/31 (83.9)
<b>By Underlying Condition (IF Classification)</b>	
Short Bowel Syndrome	38/46 (82.6)
Mucosal Diseases	28/36 (77.8)
Chronic Intestinal Dysmotility Disorders	20/26 (76.9)
Mechanical Obstruction	2/6 (33.3)
Intestinal Fistulae	4/5 (80.0)
<b>Number of Patients with Liver Injury, n (%)</b>	
All Patients	46/76 (60.5)
Choline Deficient Patients	38/60 (63.3)

Note: Percentages are based on the number of patients in the Enrolled Set with observed data.

Note: Choline deficiency is defined as  $< 9.5$  nmol/ml. Various studies in PS-dependent patients report choline deficiency as baseline concentrations of plasma free choline ranging from approximately  $5.2 \pm 2.1$  nmol/mL to  $7.15 \pm 2.5$  nmol/mL (Buchman et al., 1993; Buchman et al., 1994; Buchman et al., 2001a; Compher et al., 2002).

Note: IF Classification is based on ESPEN Pathophysiological IF Classification; Patients may fall into more than one category.

Note: Liver injury was defined as any elevated liver tests (1.5xULN; ALP, AST, ALT, GGT, Direct Bilirubin, Total Bilirubin) or Steatosis (MRI-PDFF  $\geq 8\%$ ).

## DISCUSSION

- The THRIVE-1 study highlights a significant prevalence of choline deficiency (~78%) among PS-dependent patients
- A strong association was found between choline deficiency and liver injury, with 63% of deficient patients showing signs of liver damage
- The study population was predominantly White and non-Hispanic, yet the diversity of underlying conditions suggests that choline deficiency is a widespread issue across various etiologies of intestinal failure

## CONCLUSIONS

- The high prevalence of choline deficiency among patients with IF dependent on PS underscores the urgent need for choline supplementation
- This population has a significant unmet need for IV choline that should be addressed
- The observed heterogeneity in liver injury also warrants further investigation
- Choline Chloride for Injection, an investigational phospholipid substrate replacement therapy, is being developed as a source of choline to potentially enhance health outcomes for long-term PS-dependent patients

