## Enteral protein supplementation in critically ill children: a randomized controlled pilot study

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**Aims and Objectives**: Protein supplementation may be associated with improved clinical outcomes in critically ill children. The aim of this study was to assess the safety and tolerance of protein supplementation, and its impact on clinical outcomes in critically ill children on enteral nutrition (EN).

**Methods**: Three-arm, controlled trial in critically ill children. Children on mechanic ventilation and on EN therapy were randomized to one of 2 interventional groups; polymeric and oligomeric protein supplementation, or control group receiving standard EN. In the interventional groups, protein supplement was administered by syringe before the EN therapy, to reach the protein goal within 4 days. Demographic characteristics and clinical outcomes were recorded. EN interruptions, stool frequency and abdominal distension were evaluated as signs of intolerance. Blood urea and creatinine values were recorded.

**Results**: Among 363 patients admitted, 70 were eligible, and 34 were randomized. At baseline there were no differences between the groups (Table 1). The number of enteral nutrition interruption and  $\geq$ 3 defecations/day were similar between the groups. Abdominal distension was present in 30% of the control, 12.5% of the polymeric and 0% of the oligomeric group. There were no increases in serum urea and creatinine values in all 3 groups. There were no differences in clinical outcomes between the 3 groups (Table 2).

**Conclusion**: Enteral protein supplementation with oligomeric or polymeric modules is safe and well tolerated in critically ill children. Multicenter study with larger sample size is necessary to examine the impact of protein supplementation on clinical outcomes.

Trial registration: Brazilian Registry of Clinical Trials nº RBR-3h4x97

**Keywords:** Pediatric intensive care units. Enteral nutrition. Protein. Randomized controlled trial. Morbidity. Length of stay.

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Variable	Total	Polymeric	Oligomeric	Control	p-value	
	N=34	n=11	n=12	n=11		
Sex (male) n (%)	20 (65.82)	4 (36.36)	8 (66.67)	8 (72.73)	0.2531	
Age (months)	4.29 (2.01;	4.98 (2.08; 20.33)	3.25 (1.88; 9.85)	7.06 (1.48; 12.94)	0.855 <sup>2</sup>	
	13.46)					
PIM 2 (%)	3.6 (1.9; 13.4)	3.7 (1.7; 13.4)	2.7 (1.8; 25.1)	4.1 (1.9; 12.5)	0.986 <sup>2</sup>	
Diagnostic n (%)						
Medical	30 (88.24)	9 (81.82)	11 (91.67)	10 (90.91)	0.8281	
Surgical	4 (11.76)	2 (18.18)	1 (8.33)	1 (9.09)		
Nutritional status						
z-BMI	-0.57 (-1.74; 1.03)	-0.55 (-1.78; 1.80)	-0.64 (-1.42; 0.42)	-0.17 (-1.82; 1.81)	0.857 <sup>2</sup>	

 $\begin{tabular}{ll} \textbf{Table 1}-Baseline \ characteristics \ of \ the \ population \ on \ mechanical \ ventilation \ and \ enteral \ nutrition \end{tabular}$ 

<sup>1</sup>Fischer <sup>2</sup>Kruskal-Wallis; PIM 2: Pediatric Index of Mortality; z-BMI: z-score of body mass index for age; MUAC: mid-upper arm circumference

Table 2 –	Tolerance,	safety	and	clinical	outcomes	in	included	patients
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Variables	Polymeric	Oligomeric	Control	p-value	
	n=8	n=11	n=10	-	
After 5 days of admission					
Adverse effects					
EN interruption n (%)	7 (87.5)	6 (54.5)	7 (70.0)	0.3231	
Abdominal distension n (%)	1 (12.5)	0 (0.0)	3 (30.0)	-	
$\geq$ 3 defecations/day n (%)	1 (12.5)	1 (9.1)	1 (10.0)	$1.000^{1}$	
Constipation <sup>3</sup> n (%)	0 (0.0)	2 (18.2)	1 (10.0)	0.759	
Laboratory parameters					
Urea					
Baseline	24 (12; 51)	26.5 (13.5; 37)	26 (18; 36)	0.852 <sup>2</sup>	
After intervention	13 (12; 35)	19.5 (9.5; 35.5)	24.5 (16; 46)	0.414 <sup>2</sup>	
p-value <sup>3</sup>	0.593	0.465	0.753		
Creatinine					
Baseline	0.3 (0.3; 0.4)	0.4 (0.2; 0.4)	0.3 (0.2; 0.6)	0.935 <sup>2</sup>	
After intervention	0.3 (0.3; 0.4)	0.3 (0.3; 0.4)	0.3 (0.2; 0.4)	0.953 <sup>2</sup>	
p-value <sup>3</sup>	1.000	1.000	0.719		
Clinical outcomes					
At discharge					
Nosocomial infection n (%)	3 (42.9)	2 (18.2)	4 (40.0)	0.4651	
Duration of MV (days)	5.5 (4.0; 15.0)	9.0 (4.0; 11.0)	9.5 (5.0; 13.0)	0.819 <sup>2</sup>	
Hospital LOS (days)	18.0 (10.5; 33.0)	26.0 (16.0; 31.0)	29.5 (13.5; 40.0)	0.747 <sup>2</sup>	
PICU LOS (days)	11.0 (6.0; 18.5)	12.0 (8.0; 26.0)	11.5 (8.0; 20.0)	0.772 <sup>2</sup>	
PICS n (%)	1 (27.6)	0 (0.0)	1 (10.0)	-	

<sup>1</sup>Fischer; <sup>2</sup>Kruskal-Wallis. <sup>3</sup> 0 defecation within 5 days; EN: enteral nutrition; MV: mechanical ventilation; LOS: length of stay; PICS: Persistent Inflammation, Immunosuppression and Catabolism Syndrome; PICU: Pediatric Intensive Care Unit