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Hydrolysed protein enteral nutrition is not superior to polymeric whole protein feeding with regard to gastrointestinal feeding tolerance and feeding adequacy

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See related research by Jakob et al., https://ccforum.biomedcentral.com/articles/10.1186/s13054-017-1730-1

We would like to comment on the SPIRIT trial by Jakob and co-workers comparing the effects of hydrolysed protein enteral nutrition (EN; Peptamen AF®) and isocaloric control polymeric whole protein feed (Isosource® Energy) on gastrointestinal feeding tolerance, including diarrhoea and feeding adequacy [1]. No differences in diarrhoea-free days and number of diarrhoea events were observed.

In a recent meta-analysis [2] only 121 patients from four studies were included, 63 in peptide-based groups and 58 patients in control arms. Combining these data with the SPIRIT trial results (N = 211 patients), no benefits with respect to diarrhea incidence during intensive care unit (ICU) stay and feeding adequacy are observed in favour of peptide-based EN (Table 1).

We disagree with the last part of the authors' conclusion: "While the data of this pilot study do not indicate that modification of the protein and fat content can attenuate the incidence of diarrhea, it does show that a product like Peptamen® AF can effectively deliver a high daily protein amount without overfeeding the ICU patients." Both feeds are isocaloric but Peptamen® AF delivers 25%, and Isosource® Energy 16% of energy by proteins. Per calorie administered, the protein dose is higher (25/16 × 100% = 56.3%) in the Peptamen® AF group.

When gastrointestinal tolerance is similar, using the same caloric targets means protein intake in the Peptamen® AF should at least be 56% higher.

Protein intake was higher but the difference was lower than expected (1.13/0.80 = 41%). Furthermore, the accumulated caloric deficit difference was significantly larger in the Peptamen® AF group ($P < 0.014$). Thus, higher protein intake in the Peptamen® AF group is mainly due to differences in product composition and not due to better gastrointestinal tolerance.

The authors relate differences in caloric intake to more stoppages in the Peptamen® AF group; however, this post-hoc observation must be qualified considering that interruptions of EN are also related to gastrointestinal tolerance and the inability to deliver EN to achieve prescribed targets is part of the definition of feeding intolerance [3]. The claim by the authors can only be substantiated when an isocaloric and isonitrogenous control feed is used and protein delivery is better in the peptide-based feeding arm. The SPIRIT trial does not answer this.

In the absence of any benefits on EN tolerance or diarrhoea, and considering higher costs of hydrolysed protein feeds, we feel supported by recent guidelines recommending use of a polymeric formula when initiating EN in critically ill patients [4].

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Table 1 Randomized controlled trials addressing diarrhoea frequency in critically ill patients associated with enteral feeds

Diarrhoea		Peptide-based EN			Polymeric whole protein EN		
Study	Year	Events (n)	Percentage	Total (n)	Events (n)	Percentage	Total (n)
Brinson (as in [2])	1988	1	14.3	7	3	60.0	5
Meredith (as in [2])	1990	0	0.0	9	4	44.4	9
Mowatt-Larssen (as in [2])	1992	6	28.6	21	6	30.0	20
Heimburger (as in [2])	1997	10	38.5	26	4	16.7	24
Jakob et al. [1]	2017	29	63.0	46	31	70.5	44
Total		46	42.2	109	48	47.1	102

Abbreviations
EN: Enteral nutrition; ICU: Intensive care unit

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Not applicable.

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Not applicable.

Competing interests
Arthur R.H. van Zanten reported that he has received honoraria for advisory board meetings, lectures, and travel expenses from Abbott, Baxter, BBraun, Danone-Nutricia, Fresenius Kabi, Nestle-Novartis and Lyric. Inclusion fees for patients in nutrition trials were paid to the local ICU research foundation. Gunnar Elke received lecture fees and travel support from Abbott, Baxter, BBraun and Fresenius Kabi. He was the European study coordinator for the Reducing Deaths Due to Oxidative Stress (REDOXS) trial and a member of the REDOXS post-trial advisory board meeting (Fresenius Kabi) and Gastro-Intestinal tolerance advisory board meeting (Nutricia).

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