Supplementary Materials

Exploring a tolerable and effective dosage of omega-3 fatty acids as a supplement in enterally fed patients with severe pneumonia: A pilot study

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Supplementary Table 1. The rationale and calculation process of the second interventional dosage

Study	Author	Intervention dosages		
		EPA (g/d)	DHA (g/d)	EPA + DHA (g/d)
1	Gadek et al[1]. 1999	6.9	2.9	9.8
2	Grau-Carmona et al[2]. 2011	5.4	2.3	7.7
3	Kagan et al[3]. 2015	5.5	2.3	7.8
4	Rice et al[4]. 2011 (Trial stopped early due to worse outcome)	6.8	3.4	10.2
5	Pontes-Arruda et al[5]. 2006	4.9	2.2	7.1
6	Pontes-Arruda et al[6]. 2011	4.6	2	6.6
7	Singer et al[7]. 2006	5.4	2.5	7.9
8	Stapleton et al[8]. 2011	9.8	6.8	16.6
9	Van Zanten et al[9]. 2014	N/A	N/A	4.5
Average intervention dosage				8.6889 g/d
Average intervention dosage excluding study 4				8.5 g/d

Referece:

1. Gadek JE, DeMichele SJ, Karlstad MD, et al. Effect of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in patients with acute respiratory distress syndrome. Enteral Nutrition in ARDS Study Group. Crit Care Med 1999;27:1409-20. doi: 10.1097/00003246-199908000-00001 [published Online First: 1999/09/02]

2. Grau-Carmona T, Moran-Garcia V, Garcia-de-Lorenzo A, et al. Effect of an enteral diet enriched with eicosapentaenoic acid, gamma-linolenic acid and anti-oxidants on the outcome of mechanically ventilated, critically ill, septic patients. Clin Nutr 2011;30:578-84. doi: 10.1016/j.clnu.2011.03.004

3. Kagan I, Cohen J, Stein M, et al. Preemptive enteral nutrition enriched with eicosapentaenoic acid, gamma-linolenic acid and antioxidants in severe multiple trauma: a prospective, randomized, double-blind study. Intensive Care Med 2015;41:460-9. doi: 10.1007/s00134-015-3646-z

4. Rice TW, Wheeler AP, Thompson BT, et al. Enteral omega-3 fatty acid, gamma-linolenic acid, and antioxidant supplementation in acute lung injury. JAMA 2011;306:1574-81. doi: 10.1001/jama.2011.1435

5. Pontes-Arruda A, Aragao AM, Albuquerque JD. Effects of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in mechanically ventilated patients with severe sepsis and septic shock. Crit Care Med 2006;34:2325-33. doi: 10.1097/01.CCM.0000234033.65657.B6

6. Pontes-Arruda A, Martins LF, de Lima SM, et al. Enteral nutrition with eicosapentaenoic acid, gamma-linolenic acid and antioxidants in the early treatment of sepsis: results from a multicenter, prospective, randomized, double-blinded, controlled study: the INTERSEPT study. Crit Care 2011;15(3):R144. doi: 10.1186/cc10267 [published Online First: 2011/06/11]

7. Singer P, Theilla M, Fisher H, et al. Benefit of an enteral diet enriched with eicosapentaenoic acid and gamma-linolenic acid in ventilated patients with acute lung injury. Crit Care Med 2006;34(4):1033-8. doi: 10.1097/01.CCM.0000206111.23629.0A [published Online First: 2006/02/18]

8. Stapleton RD, Martin TR, Weiss NS, et al. A phase II randomized placebo-controlled trial of omega-3 fatty acids for the treatment of acute lung injury. Crit Care Med 2011;39(7):1655-62. doi: 10.1097/CCM.0b013e318218669d [published Online First: 2011/03/23]

9. van Zanten AR, Sztark F, Kaisers UX, et al. High-protein enteral nutrition enriched with immune-modulating nutrients vs standard high-protein enteral nutrition and nosocomial infections in the ICU: a randomized clinical trial. JAMA 2014;312(5):514-24. doi: 10.1001/jama.2014.7698 [published Online First: 2014/08/07]

Supplementary Table 2. Clinical outcomes of control group and intervention groups (APACHE II scores 0-14, 15-24, ≥25)

	Total (n=26)	Control (n=9)	3.50g dose (n=9)	8.75g dose (n=28)	χ^2/F	*p* values
APACHE II scores 0-14					1.05	0.592
LOS (days)	35.5 (24.5, 47.5)	47 (26, 64)	28 (24, 42)	35.5 (27, 66)	2.0	0.368
ICU LOS (days)	15.5 (10.75, 20.75)	23 (16, 41)	11 (10, 15.5)	14.5 (10, 19)	5.556	0.062
Hospital expenses (Chinese Yuan)	152085 (85046.75, 246140.75)	237983 (151307, 378434)	150419 (82885, 134855)	196168 (62638, 275750)	8.722	0.053
Daily hospital expenses (Chinese Yuan)	4756.386 (2845.01, 6114.56)	4878.0465 (4468.8930, 5911.3115)	3568.2917 (2541.1638, 6025.5269)	2946.5263 (2319.9259, 6414.5758)	2.0	0.368
Days of mechanical ventilation	9 (6, 16)	19 (7.5, 32.5)	8(5.5, 11)	9 (5, 12)	3.751	0.153
APACHE II scores 15-24						
LOS (days)	31.5 (27, 49.5)	37 (27, 53)	35 (28.5, 56)	30 (17, 44)	0.977	0.641
ICU LOS (days)	20 (12.25, 32)	15 (9,40)	21 (12.5, 34)	16 (13, 29)	1.660	0.436
Hospital expenses (Chinese Yuan)	198919.50 (137959.5, 302545.75)	178430 (153383, 345121)	224096 (114468, 287269)	162252 (112824, 302564)	0.443	0.801
Daily hospital expenses (Chinese Yuan)	5650.182 (3561.02, 8032.80)	5687.43 (2935.6, 8049.48)	5306.86 (3342.33, 6063.40)	6327.72 (4937.78, 10085.47)	1.834	0.400
Days of mechanical ventilation	14.5 (9, 23.75)	14 (11, 31)	14 (8, 20)	16 (7, 24)	1.418	0.492
APACHE II scores ≥25						
LOS (days)	29.5 (20.75, 47.5)	32(20.5, 42.5)	22 (18.5, 58.5)	29 (21.0, 214)	0.900	0.638
ICU LOS (days)	22.5 (17.7, 32.0)	22.5 (17.75, 34)	22 (18.5, 51.5)	24 (16.5, 168.5)	0..19	0.991
Hospital expenses (Chinese Yuan)	207415 (135907.75, 333313.0)	280536 (134015.25, 367981.0)	139800 (121981.0, 349236.5)	216870 (182469.5, 1239622.5)	1.769	0.413
Daily hospital expenses (Chinese Yuan)	7077.0 (5880.93,9030.04)	7922.51 (6179.61, 9460.09)	6290.79 (5154.78, 7352.05)	8858.34 (4778.67, 9156.40)	1.579	0.454
Days of mechanical ventilation	21.5 (16.75, 32.5)	26 (20.25, 33.5)	22 (17, 54.5)	18 (11.5, 141.5)	0.551	0.759

Supplementary Table 3. Changes of laboratory tests. Measurement of markers of nutrition, immunology and inflammation (APACHE II scores 0-14, 15-24, ≥25)

Lab measures	Control (n=9)	3.50g dose (n=9)	8.75g dose (n=28)	χ^2/F	*p* values
APACHE II scores 0-14				1.05	0.592
HGB (g/L)	-17 (-21, 12.5)	4 (-9.5, 12.5)	0.5 (-7, 16)	1.005	0.604
Prealbumin (mg/L)	20.4 (-19.5, 107.2)	40 (6.5, 97)	55 (16, 143)	3.111	0.211
IgG (g/L)	0.84 (-0.2, 5.45)	-0.38 (-3.35, 1.3)	1.36 (-0.68, 2.95)	0.722	0.697
IgA (mg/L)	260 (-800, 616)	28 (-160, 221)	190 (-1030, 1970)	0.222	0.895
IgM (mg/L)	53 (-164, 490.5)	-46 (-84, 50.5)	92 (-350, 360)	0.901	0.637
PCT (ng/mL)	-0.02 (-0.386, 0.165)	0.12 (0.08, 0.25)	0.14 (0.09, 0.26)	3.971	0.137
CRP (mg/mL)	-59.7 (-82.8, 12.03)	-9.5 (-64.735, -4.795)	-26 (-125, 8.9)	1.216	0.544
IL-6 (pg/mL)	-84.5 (-155.85, 25.05)	-6.62 (-17.015, 4.595)	0.89 (-32, 8.1)	1.404	0.496
APACHE II scores 15-24					
HGB (g/L)	-5 (-10, 1)	-5 (-13, 10.5)	0 (-20, 8)	0.002	0.999
Prealbumin (mg/L)	44 (-62, 99.9)	-6 (-42, 97)	-24 (-37, 77)	1.418	0.492
IgG (g/L)	0.4 (-1, 4.39)	2.0 (0.845, 3.305)	-0.03 (-3.6, 3.1)	0.443	0.801
IgA (mg/L)	200 (160, 640)	240 (-6.5, 870)	-120 (-500, 430)	3.939	0.139
IgM (mg/L)	35 (-139.0, 118.0)	46 (-103, 118)	-30 (-122, 68)	1.115	0.573
PCT (ng/mL)	-0.18 (-0.26, -0.02)	-0.06 (-0.0215, 0.435)	0.01 (-0.02, 0.11)	2.446	0.294
CRP (mg/mL)	-10.7 (-56.6, -3.5)	-12.8 (-32.5, 24.4)	0.36 (-31.9, 24.8)	1.834	0.400
IL-6 (pg/mL)	-0.81 (-6.4, 40.2)	9 (-50.05, 19.85)	-3.4 (-60, 11.9)	0.209	0.901
APACHE II scores ≥25					
HGB (g/L)	0 (-13.5, 15.25)	6 (-8, 14)	-7 (-18, 6)	0.758	0.685
Prealbumin (mg/L)	-27 (-61.5, 122.8)	-14.9 (-119.5, 217.5)	-16 (-44.5, 18.5)	0.022	0.989
IgG (g/L)	0.94 (-0.0675, 3.328)	1.0 (-7.29, 3.37)	-0.4 (-5.98, 5.09)	0.990	0.609
IgA (mg/L)	102 (-342.5, 102)	0.0 (-415, 729)	-230 (-662, 550)	4.000	0.135
IgM (mg/L)	31.5 (-126.25, 316.5)	350 (168.0, 4195)	-80 (-332.5, 345)	2.500	0.287
PCT (ng/mL)	0.355 (0.0275, 1.375)	0.04 (-0.52, 0.71)	0.00 (-1.08, 0.32)	0.900	0.638
CRP (mg/mL)	25.9 (-19.18, 217.13)	30.0 (-163.95, 127.065)	-1.7 (-52, 21.15)	0.400	0.819
IL-6 (pg/mL)	25.4 (-0.25, 409.75)	75 (-389.28,398.95)	-37.1 (-122.40, 1.03)	3.600	0.165

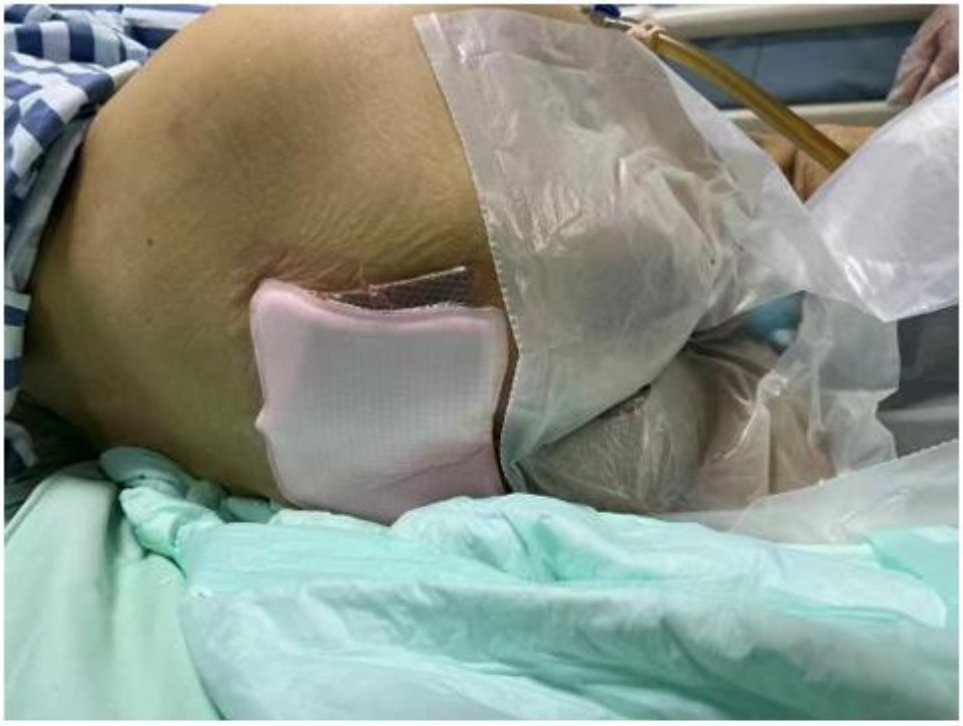
Supplementary Table 4. Clinical outcomes of control group and intervention groups (with fat content adjusted)

	Total (n=84)	Control (n=28)	3.50g dose (n=28)	8.75g dose (n=28)	χ^2/F	*p* values
LOS (days)	32 (24, 47)	36 (26, 50.75)	30.5 (24.75, 43.5)	30 (23, 41)	4.649	0.098
ICU LOS (days)	19.00 (13.0, 28.5)	21.5 (15, 38.75)	20.0 (11.25, 26.50)	16 (13.00, 25.5)	3.503	0.173
Hospital expenses (Chinese Yuan)	189168 (125025.25, 282435.25)	216538.07 (151732.25, 350740.25)	145145 (98901.75, 235383)	198030 (128196, 261606.5)	7.578	0.023
Daily hospital expenses (Chinese Yuan)	5752.95 (4000.9, 7302.67)	5926.18 (4635.76, 7878.29)	5343.29 (3356.05, 6119.26)	6142.89 (3526.79, 8497.7)	5.406	0.067
Days of mechanical ventilation	14 (8.5, 22)	20 (12.5, 32)	13 (7.75, 21.25)	12 (8, 20)	6.665	0.036

Supplementary Table 5. Changes of laboratory tests. Measurement of markers of nutrition, immunology and inflammation. (with fat content adjusted)

Lab measures	Control (n=28)	3.50g dose (n=28)	8.75g dose (n=28)	χ^2/F	*p* values
HGB (g/L)	2.93 ± 14.79	0.64 ± 13.57	2.82 ± 16.88	0.217	0.806
Prealbumin (mg/L)	-15.2 (-87.97, 48.5)	-12 (-89, 15.18)	3 (-75.5, 31.75)	0.112	0.945
IgG (g/L)	-0.82 (-3.79, 0.16)	-1.15 (-2.07, 0.59)	-0.68 (-2.69, 3.19)	1.351	0.509
IgA (mg/L)	-190 (-496.75, 192.5)	-105 (-292.5, 120)	70 (-437.5, 557.5)	1.896	0.388
IgM (mg/L)	-37.5 (-241.5, 139.25)	-28.5 (-203.5, 69.5)	18.5 (-202.5, 104)	1.058	0.598
PCT (ng/mL)	0.02 (-0.14, 0.24)	0.05 (-0.2, 0.13)	0.01 (-0.1, 0.22)	0.061	0.970
CRP (mg/mL)	10.11 (-27.8, 61.94)	12.7 (-2.38, 48.62)	1.16 (-17.85, 33.3)	0.599	0.741
IL-6 (pg/mL)	0.2 (-47.37, 14.81)	2.5 (-22.24, 17.02)	4.8 (-8.12, 42.81)	1.844	0.398

a) A newly attached pouch without stool yet.



b) A ready-to-change pouch with a mixture of stool.

Supplementary Figure 1. An example of the fecal incontinence pouch (view from the patient's back)