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CORRESPONDENCE

Letter to the editor: Eicosapentaenoic acid containing nutritional supplements for the treatment of cancer cachexia

In the excellent article: ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology,[1] it is difficult to see why only a C grade was given to eicosapentaenoic acid containing oral nutritional supplement (EPA/ONS) in view of the definitions of the various grades.[2] Certainly EPA/ONS has had at least one RCT as reviewed[1] and should therefore be graded A (1b) rather than C, particularly if some of the studies are discounted because they do not reach the threshold where therapeutic efficacy might be detected.

The primary action of EPA is to increase lean body mass through attenuation of the increased activity and expression of the ubiquitin-proteasome pathway,[3] the primary pathway thought to be responsible for skeletal muscle atrophy in cancer cachexia.[4] This is supported by clinical data showing that EPA/ONS caused a significant increase in lean body mass, with no change in either fat mass or percentage total body water.[5] This increase in lean body mass is translated into an increased physical activity level, which may reflect an improved quality of life,[6] as was seen in patients receiving EPA/ONS and gaining body weight.[7] This is in contrast with progestins such as megestrol acetate (MA) where patients who gained weight showed an increase in adipose tissue and body fluid, but with no change in lean body mass.[8] Unlike EPA/ONS, quality of life does not improve in patients receiving MA, whilst the performance status tends to worsen.[9] As might be expected, it takes longer to reverse the muscle atrophy of cachectic patients than it does to increase fat and water, and thus body weight gain with EPA/ONS is not evident for a minimum of 3 weeks and becomes progressively larger as time progresses.[5] In addition, pilot studies showed that patients need to consume at least 2 g/day of EPA in order to have a therapeutic effect.[5,10] Compliance has been a problem in RCT of EPA/ONS with intakes as low as 1.5 g EPA/day,[7] although compliance seems much better in patients receiving fish oil capsules.[11]

Thus studies with EPA of a shorter duration than 3 weeks,[12] where compliance was not monitored[12,13] and where dose levels less than 2 g/day are administered[12] might be expected to produce contradictory results. Although EPA/ONS has been shown to be equivalent to MA as an appetite stimulant,[13] it should be remembered that the primary effect is to improve lean body mass and the end-point of any study should reflect this. There is an urgent need for more RCT with EPA in order to assess its therapeutic efficacy. Future studies should concentrate on including additional novel agents within EPA/ONS, but all studies need measurements of plasma EPA before definitive conclusions can be drawn.

References

1. Arends J, Bodoky G, Bozzetti F, et al. ESPEN Guidelines on enteral nutrition: non-surgical oncology. *Clin Nutr* 2006;**25**: 245–59.
2. Schűtz T, Herbst B, Koller M. Methodology for the development of the ESPEN guidelines on enteral nutrition. *Clin Nutr* 2006;**26**:203–9.
3. Whitehouse AS, Smith HJ, Drake JL, Tisdale MJ. Mechanism of attenuation of skeletal muscle protein catabolism in cancer cachexia by eicosapentaenoic acid. *Cancer Res* 2001;**61**: 3604–9.
4. Khal J, Hine AV, Fearon KCH, Dejong CHC, Tisdale MJ. Increased expression of proteasome subunits in skeletal muscle of cancer patients with weight loss. *Int J Biochem Cell Biol* 2005;**37**:2196–206.
5. Barber MD, Ross JA, Voss AC, Tisdale MJ, Fearon KCH. The effect of an oral nutritional supplement enriched with fish oil on weight-loss in patients with pancreatic cancer. *Br J Cancer* 1999;**81**:80–6.
6. Moses AWG, Slater C, Preston T, Barber MD, Fearon KCH. Reduced total energy expenditure and physical activity in cachectic patients with pancreatic cancer can be modulated by an energy and protein dense oral supplement enriched with n-3 fatty acids. *Br J Cancer* 2004;**90**:996–1002.
7. Fearon KCH, von Meyenfeldt MF, Moses AGW, et al. Effect of a protein and energy dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial. *Gut* 2003;**52**: 1479–86.
8. Loprinzi CL, Schaid DJ, Dose AM, Burnham NL, Jensen MD. Body-composition changes in pateints who gain weight while receiving megestrol acetate. *J Clin Oncol* 1993;**11**:152–4.
9. DeConno F, Zecca ME, Balzarini A, Venturino P, Groff L, Caraceni A. Megestrol acetate for anorexia in patients with far-advanced cancer: A double-blind controlled clinical trial. *Eur J Cancer* 1998;**34**:1705–9.
10. Wigmore SJ, Ross JA, Falconer JS, et al. The effect of polyunsaturated fatty acids on the progress of cachexia in patients with pancreatic cancer. *Nutrition* 1996;**12**(Suppl.): S27–30.

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11. Burns CP, Halabi S, Clamon G, et al. Phase II study of high dose fish oil capsules for patients with cancer-related cachexia. *Cancer* 2004;**101**:370–8.
12. Bruera E, Strasser F, Palmer JL, et al. Effect of fish oil on appetite and other symptoms in patients with advanced cancer and anorexia/cachexia: a double-blind, placebo-controlled study. *J Clin Oncol* 2003;**21**:129–34.
13. Jatoi A, Rowland K, Loprinzi CL, et al. An eicosapentaenoic acid supplement versus megestrol acetate versus both for patients with cancer-associated wasting: A North Central Cancer Treatment Group and National Cancer Institute of Canada collaborative effort. *J Clin Oncol* 2004;**22**:2469–76.

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