Unintentional Weight Loss in Long Term Care Residents with Alzheimer's Disease and Weight Response with the Use of Docosahexaenoic Acid (DHA)/ Eicosapentaenoic Acid (EPA) and Bioflavonoids: A Case Series

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INTRODUCTION

Cachexia/dehydration may be the immediate cause of death in the end stage of dementia in as many as 35% of nursing home residents.[8] Cachexia is associated with suppressed appetite, food intake and body weight while proinflammatory cytokines are increased.[9] Proinflammatory cytokines directly result in feeding suppression and lower intake of nutrients and cachexia is nearly always accompanied by anorexia. IL-1 beta and tumor necrosis factor alpha (TNFa) act on the glucose-sensitive neurons in the satiety and hunger sites in the hypothalamus.[10]

An association between high levels of circulating TNFa and unexplained weight loss in AD has been shown. [13] Serum TNFa has been shown to be lower in mild-moderate Alzheimer's disease (AD) compared to severe AD.[12] The levels of TNFa, IL-1beta, IL 6, and IL10 were elevated in the serum of patients with dementia.[14, 15, 18] A minority of studies have shown no significant differences between AD subjects and controls in the mean serum levels of TNFa and other cytokines.[17] Brain synthesis of cytokines has been shown in peripheral models of cancer, peripheral inflammation, and during peripheral cytokine administration11 and strikingly increased CSF levels of TNFa have been demonstrated in AD.[16]

METHODS

Two residents in one facility, cared for by the investigator, in a moderate stage of dementia with 10% or greater weight loss over the previous six months despite the usual interventions at the facility (the addition of fortified foods, 2 Cal Supplement® bid, offering snack tid, and 1 on 1 assistance with meals in a small dining room setting) were chosen. A TSH, CBC, complete metabolic profile, urinalysis, physical examination, medication review and Cornell Scale for Depression in Dementia (CSDD) were performed during the 6 month period. Both residents were on an acetylcholinesterse inhibitor (ACHE) and had a 10 day washout prior to intervention.

After informed consent was obtained from the family of each resident, 570 mg DHA and 870 mg EPA plus 225 mg of bioflavonoid per day were administered. A proprietary formulation of bioflavonoids, OPC-3® was used. OPC-3 consists of an isotonic formulation of well studied flavonoids derived from extracts of bilberries, citrus fruit, French maritime pine bark (Pycnogenol), red wine (resveratrol), and grape seeds. The usual interventions were continued. Weights were followed over the 6 month period following the intervention.

RESULTS

Resident 1*: 92 y.o, diagnoses: Alzheimer's disease, depression, hypothyroidism, hypertension, diabetes II, hyperlipidemia. Medications: donepezil 10 mg, memantine 10 mg bid, levothyroxine, citalopram 10 mg., KCl, multivitamin. MMSE 14, 50-80% meals consumed, weight loss 1% over 1 month and11% over 6 months immediately prior to intervention.

Resident 2*: 94 y.o., diagnoses: Alzheimer's disease, COPD, Oseteoarthritis. Medications: donepezil 10 mg, memantine 10 mg bid, vitamin D 800 IU, multivitamin, Ca carbonate 1000mg. Failed trial of mirtazapine 15 mg daily for weight loss. Hospice care during the last 3 months of weight loss prior to intervention and throughout the intervention period. MMSE 13, 0-50% meals consumed, weight loss 3.7% over 1 month and 10% over 6 months immediately prior to intervention.

Post intervention total percent weight change (Fig. 1): I, 3 and 6 months respectively for Resident 1 were +0.9%, +5.1%, +6.9% and for Resident 2 were 0%, +1%, -1%. Both residents showed an improvement in appetite and general increase in percent of meals eaten. At request of Resident 2's family the intervention was stopped at 6 months but restarted 1 month later due to a 6% weight loss. Subsequent total weight gain was 3% at 1 month and 5.1% at 2 months. Weight change in pounds (Fig. 2-Resident 1, Fig.3-Resident 2)

*Laboratory work, CSDD, physical examination unremarkable and no change in appetite with the 10 day ACHE washout in both residents (ACHE restarted after washout).

Fig. 1 Percent Weight Change Pre/Post Intervention (DHA/EPA + Bioflavonoids)

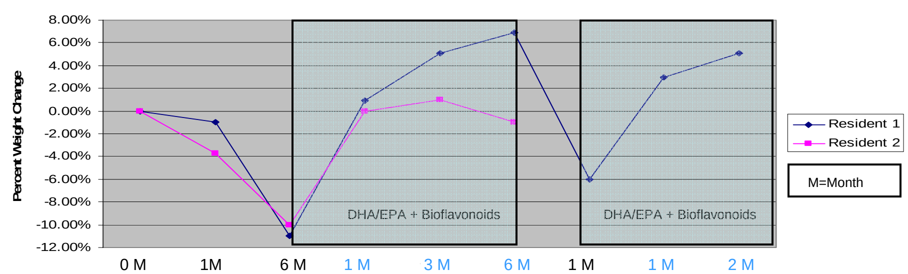


Fig.2 Weight Change Pre/Post Intervention (DHA/EPA + Bioflavonoids)

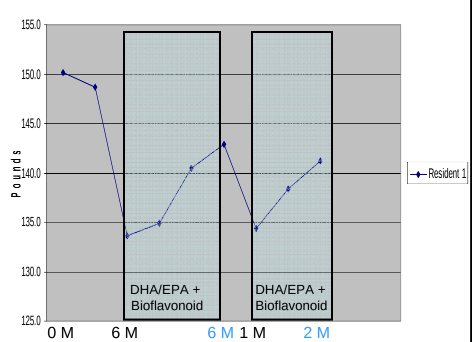
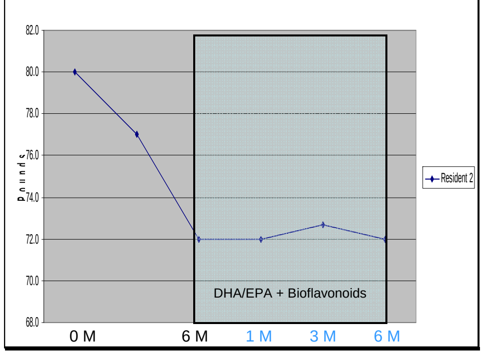


Fig. 3 Weight Change Pre/Post Intervention (DHA/EPA + Bioflavonoids)



DISCUSSION/CONCLUSION

The importance of ingesting foods and supplements high in antioxidants is becoming more valued as oxidative stress from reactive oxygen species is being uncovered as a common pathologic mechanism to inflammatory states by the induction of proinflammatory cytokines.[4]

In recent years, the constituents in fruits and vegetables predominantly responsible for their health benefits have been identified as bioflavonoids which are anti-inflammatory. Reductions of plasma oxidative stress status by 10.1% and plasma C-reactive protein by 52.1% have been demonstrated with OPC-3 use.[5] Adequate dietary intake of omega-3 polyunsaturated fatty acids increases tissue concentrations of EPA and DHA that reduce proinflammatory cytokine production[1,2] and downregulate inflammation.[3, 19, 20]

Although this was an uncontrolled intervention, resident 1 showed clinically meaningful weight gain through the entire 6 month observation period and resident 2 showed stabilization of weight loss within 30 days of the intervention with continued weight maintenance throughout the 6 month observation period. Resident 1 also showed weight loss when the intervention was discontinued and clinically meaningful weight gain when restarted.

CONCLUSION

Given the evidence in the literature supporting a mechanism for these nutritional interventions with our observed improvement in weight and appetite, further study in a controlled setting is warranted.

REFERENCES

1. Dinarello CA. Interleukin 1 and interleukin 18 as mediators of inflammation and the aging process. Am J Clin Nutr 2006;83(2): 447S–455S.
2. Endres S. Messengers and mediators: interactions among lipids, eicosanoids, and cytokines. Am J Clin Nutr 1993;57(5 supplement): 798S–800S.
3. Ziboh VA. Nutritional modulation of inflammation by polyunsaturated fatty acids/eicosanoids. In: Gershwin ME, German BJ, Keen CL, eds. Nutrition and immunology: Principles and practice. Totowa, N.J.: Humana; 2000:157–67.
4. Gaté L, Paul J, Ba GN, Tew KD, Tapiero H. Oxidative stress induced in pathologies: the role of antioxidants. *Biomed Pharmacother.* 1999;53:169-180.
5. Cesarone, M, Di Renzo A, Errichi S, Schönlau F, Wilmer J, Blumenfeld J. Improvement in Circulation and in Cardiovascular Risk Factors With a Proprietary Isotonic Bioflavonoid Formula OPC-3® Angiology 2008 59: 408-414.
6. Opie LH, Lecour S. The red wine hypothesis: from concepts to protective signaling molecules. *Eur Heart J.* 2007;28:1683-1693.
7. Zern TL, Wood RJ, Greene C, et al. Grape polyphenols exert a cardioprotective effect in pre- and postmenopausal women by lowering plasma lipids and reducing oxidative stress. *J Nutr.* 2005;135:1911-1917.
8. Koopmans RT, van der Sterren KJ, van der Steen JT. The 'natural' endpoint of dementia: death from cachexia or dehydration following palliative care? Int J Geriatr Psychiatry. 2007 Apr;22(4):350-5.
9. Thomas DR. Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia. Clin Nutr. 2007 Aug;26(4):389-99.
10. Espat NJ, Moldawer LL, Copeland III EM. Cytokine-mediated alterations in host metabolism prevent nutritional repletion in cachectic cancer patients. J Surg Oncol 1995;58:77–82.
11. Plata-Salamán CR. Central nervous system mechanisms contributing to the cachexia-anorexia syndrome. Nutrition. 2000 Oct;16(10):1009-12.
12. Paganelli R, Di Iorio A, Patricelli L, Ripani F, Sparvieri E, Faricelli R, Iarlori C, Porreca E, Di Gioacchino M, Abate G. Proinflammatory cytokines in sera of elderly patients with dementia: levels in vascular injury are higher than those of mild-moderate Alzheimer's disease patients. Exp Gerontol. 2002 Jan-Mar;37(2-3):257-63.
13. Mahieux F, Couderc R, Fénelon G, Maachi M. Relationships between weight loss and circulating cytokines in patients with Alzheimer's disease. Psychol Neuropsychiatr Vieil. 2006 Dec;4(4):281-6.
14. Angelopoulos P, Agouridaki H, Vaiopoulos H, Siskou E, Doutsou K, Costa V, Baloyiannis SI. Cytokines in Alzheimer's disease and vascular dementia. Int J Neurosci. 2008 Dec;118(12):1659-72.
15. Zuliani G, Ranzini M, Guerra G, Rossi L, Munari MR, Zurlo A, Volpato S, Atti AR, Blè A, Fellin R. Plasma cytokines profile in older subjects with late onset Alzheimer's disease or vascular dementia. J Psychiatr Res. 2007 Oct;41(8):686-93. Epub 2006 Apr 4.
16. Tarkowski E, Liljeroth AM, Minthon L, Tarkowski A, Wallin A, Blennow K. Cerebral pattern of pro- and anti-inflammatory cytokines in dementias. Brain Res Bull. 2003 Aug 15;61(3):255-60.
17. Lanzrein AS, Johnston CM, Perry VH, Jobst KA, King EM, Smith AD. Longitudinal study of inflammatory factors in serum, cerebrospinal fluid, and brain tissue in Alzheimer disease: interleukin-1beta, interleukin-6, interleukin-1 receptor antagonist, tumor necrosis factor-alpha, the soluble tumor necrosis factor receptors I and II, and alpha1-antichymotrypsin. Alzheimer Dis Assoc Disord. 1998 Sep;12(3):215-27.
18. Fillit H, Ding WH, Buee L, Kalman J, Altstiel L, Lawlor B, Wolf-Klein G Elevated circulating tumor necrosis factor levels in Alzheimer's disease. Neurosci Lett. 1991 Aug 19;129(2):318-20.
19. LeBlanc CJ, Horohov DW, Bauer JE, Hosgood G, Mauldin GE. Effects of dietary supplementation with fish oil on in vivo production of inflammatory mediators in clinically normal dogs. Am J Vet Res. 2008 Apr;69(4):486-93.
20. Trebble T, Arden NK, Stroud MA, Wootton SA, Burdge GC, Miles EA, Ballinger AB, Thompson RL, Calder PC. Inhibition of tumour necrosis factor-alpha and interleukin 6 production by mononuclear cells following dietary fish-oil supplementation in healthy men and response to antioxidant co-supplementation. Br J Nutr. 2003 Aug;90(2):405-12.