Ω-3 INSIGHT
MINAMI NUTRITION NEWSLETTER

MINAMI NUTRITION
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"HPEPA-01" - Placebo controlled, randomised, double-blind, multicenter study of PLUSEPA® (a PUFA, Polyunsaturated Fatty Acids, supplement) as treatment for ADHD (combined type) with co-morbidity in Swedish children ages 7-12.

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RESEARCH QUESTIONS

1. Does an unselected group of children with ADHD seeking medical help benefit from EPA treatment?
2. Is this the case only for children with coexisting problems (oppositional behaviour = rebellious and disobedient to aggressive, less hyperactivity/impulsivity, more neuromotor problems/dyspraxia)?
3. If some children respond to EPA treatment, does their fatty acid status have any characteristic pattern?

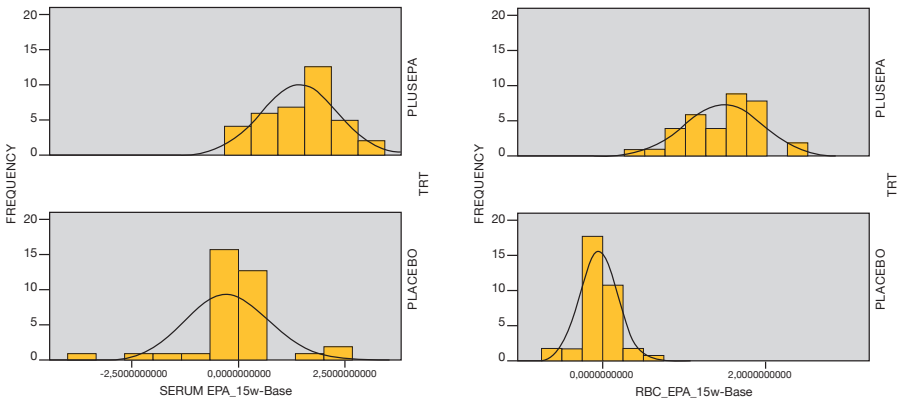
MATERIALS AND METHODS

The study comprised 82 children, 66 boys (mean age 9.8 yr) and 16 girls (10.2 yr) with ADHD (DSM-IV) admitted for pharmacological treatment. The experiment group received 0.5 g EPA omega-3 fatty acid/day for 15 weeks, placebo was rape seed oil. Efficacy evaluation was done with Conners Teacher Rating Scales (CTRS, 28 items). Hyperactivity/impulsivity was evaluated with a computerised test (Qb-test). Fatty acids were analysed in serum and red blood cell membranes.

COMORBIDITY

45% of the children were rated on CTRS as showing oppositional behaviour, 48% had neuromotor problems (Developmental Coordination Disorder) and 51% had objective hyperactivity.

RESULTS



Treatment	N	Mean	Std. Deviation	p(t-test, 2-sided)	P (M-W) 2-sided	Effect size
PLACEBO	20	3,30	9,58	0,015	0,021	0,56
PLUSEPA	23	12,65	13,73			

EPA increased considerably in both serum and red blood cell membranes (RBC). There was no treatment effect in the unselected group of children (n=82) with ADHD. However, children with coexisting oppositional behaviour (n=43) improved significantly. Children with little hyperactivity/impulsivity (n=33) also improved significantly (p=0.046).

CONFOUNDERS

Age, gender, socio-economic factors, fish consumption or treatment were not correlated to outcome site.

FATTY ACID ANALYSIS

When further looking at improvement on CTRS in the group of children with significant oppositional behaviour problems, it was found that the children in the PLUSEPA group had a two-peak appearance. With a cut-off for "Responders" at 16 points improvement (one standard deviation on CTRS baseline score) half of the children in the PLUSEPA group were above this cut-off, compared to 2 out of 20 in the Placebo group.

Children who responded to EPA treatment had significantly lower EPA levels (p=0.002), higher quotients AA/EPA (p=0.001) and AA/DHA (p=0.049), in serum at baseline, and higher AA (p=0.013), lower EPA levels (p=0.068), higher quotients AA/EPA (p=0.010) and AA/DHA (p=0.036), in Red blood cell membranes at baseline. In a word, the omega-6/omega-3 quotient was higher in both serum (p=0.116) and Red blood cell membranes (p=0.028).

CONCLUSION

About 20% of an unselected group of children with ADHD seeking medical help improved considerably after 15 weeks treatment with 0.5 g EPA/day. This subgroup was characterized by a higher level of problems at school, especially more oppositional behaviour, and less hyperactivity/ impulsivity. Children that responded to EPA treatment had significantly lower omega-3 levels and a higher quotient omega-6/omega-3 in serum and RBC.

Thus we found improvement in subgroups with special characteristics, but not in the whole, unselected group of children with ADHD seeking medical help. That is in line with the notion that EPA supplementation only could be beneficial for children who have some form of omega-3 deficiency at baseline.

This is the first clinical trial of its kind that has been conducted with constant evaluation by the Swedish Medical Board

(while average food supplement studies are not subject to such inspection)

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PlusEPA® secures its position as antidepressant: "Comparison of therapeutic effects of omega-3 fatty acid eicosapentaenoic acid and fluoxetine, separately and in combination, in major depressive disorder."

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RESEARCH QUESTIONS

1. Do major depressive patients benefit from EPA monotherapy?
2. If patients with major depression respond to EPA treatment, how does this antidepressant effect compares to that of an antidepressant such as fluoxetine?
3. Does EPA treatment in addition to treatment with an antidepressant (fluoxetine) have an added value compared to a single treatment with the antidepressant?

MATERIALS AND METHODS

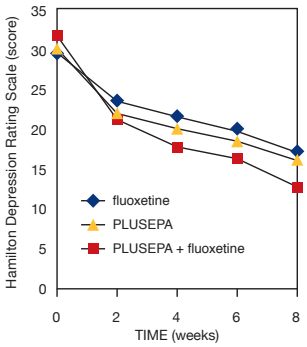
Sixty patients (20-59 years of age) participated in this 8 week balanced randomised, double-blind study. They were diagnosed with moderately severe major depression making the inclusion of a placebo-only group unethical.

The researchers compared the therapeutic effect of EPA (1 g/day) with that of the antidepressant fluoxetine (20 mg/day) en their combination (EPA + fluoxetine). Forty-eight participants were eligible for response analysis (16 in each study group).

A positive response was defined as a ≥ 50% decrease in the Hamilton Depression Rating Scale (HDRS, 17 items). The response was compared across the three study groups at week 8 by using the ANCOVA analysis of covariance for HDRS.

RESULTS

- ✓ EPA was equally as effective as fluoxetine in controlling depressive symptoms.
- ✓ The EPA+fluoxetine combination was significantly better than either fluoxetine or EPA alone (p = 0,005 and p = 0,009, respectively). Treatment was effective from he fourth week onward.
- ✓ Response rates were 50%, 56% and 81% in the fluoxetine, EPA and EPA+fluoxetine groups, respectively



CONFOUNDERS

Depressive symptom scores were adjusted for baseline scores, age of onset of the first depressive episode and number of previous depressive episodes.

ADVERSE EVENTS

The Fisher's exact test showed significant differences among groups in frequency of anxiety and loss of appetite (p=0.009 and p=0.002 respectively). Anxiety was reported by nine patients in the fluoxetine group, one patient in the EPA group and three patients in the combined group. It was limited to the first weeks for all subjects who reported it. Decreased appetite was only reported by six patients in the fluoxetine group.

CONCLUSION

According to what the physician considers most relevant for each individual patient EPA (PLUSEPA®) can be used either as a single intervention or as an adjunct to the usual antidepressants. Because EPA is a dietary supplement PLUSEPA® may be more acceptable to patients than antidepressants.

When explaining why PLUSEPA® provides unprecedented bioavailability and benefit, it is necessary to realize what it is comprised of and how this compares to the typical omega-3 supplements that most consumers are used to purchasing…

PLUSEPA® from Minami Nutrition is an exceptional omega 3 supplement for mental health that physicians around the world are identifying with as a "first" for the following reasons:

- Highest concentrated omega-3 supplement currently available on the market.
- 90% EPA with NO DHA, nor superfluous unsaturated or saturated fatty acids.
- Unprecedented level of purity that can be proven at www.neutrogenics.com.

The reality of these product traits is simple:

- Specific dosing and readily identifiable benefit.
- EPA can be metabolized and function in the brain without potential interference from other fatty acids (e.g., GLA, arachidonic acid and DHA).
- Reduced risk of exposing patients to unnecessary and undesirable impurities (e.g., methyl mercury)
- The pure EPA is allowed to fully metabolize and underpin the greatest health outcome possible through omega-3 therapy.

This benefit is starting to be realized through science:

Two recent clinical trials are showing PLUSEPA®'s efficacy in the treatment of depression (compared with fluoxetine) as well as for ADHD in children age 7-12 with oppositional behavior and/or attention problems. There are further trials under way which highlight the role of a high EPA supplement in the treatment of neurodegenerative conditions (e.g., Parkinson, Huntington, and Alzheimer diseases) as well as cardio-protection.

Minami Nutrition makes PLUSEPA® by the use of a patented extraction process:

- The production plant applies 'Good Manufacturing Practice' (GMP) guidelines and is EMAS certified (a European standard for environmental management).
- The extraction process results in Environmentally Friendly Purification Certification – your assurance of the "gold standard" omega-3 supplement with the smallest environmental footprint.

The absence of flavourings and the gastro-resistant capsule makes PlusEPA suitable for individuals who are allergic to flavours and/or have a sensitive stomach.

Scientifically proven

✓ No fishy aftertaste thanks to the gastroresistent softgels

✓ 90% pure EPA per softgel (no DHA, no other fatty acids)

✓ 1 softgel per day (500 mg EPA)

✓ Environmentally Purified natural Product (EFP® logo)

✓ 2 softgels per day (1000 mg EPA)

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