Why are fish oil supplements apparently failing to reproduce fish consumption epidemiology in RCT for cardiovascular disease?

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Abstract
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A DOSE-RESPONSE TRIAL OF LACTOFERRIN INTERVENTION ON GENE EXPRESSION PROFILE IN POSTNATAL PIGLETS

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Background/Aims: The aim of this study was to investigate the dose-response effect of lactoferrin (Lf) intervention on gene expression in the hippocampus of postnatal piglets during neurodevelopment.

Methods: Fifty-one 3-day-old piglets were randomly allocated into a high (H) Lf dose group (n = 18), a low (L) Lf dose group (n = 17) and a control (C) group (n = 16). Piglets were fed sow milk replacer supplemented with Lf at 285 mg/kg/d (H), 155 mg/kg/d (L) and 16 mg/kg/day (C). Piglets were euthanized at 38 days of age. RNA transcript profiling in the hippocampus was carried out using RNA isolated from 10 piglets/group on Porcine Affymetrix A TaqMan® Gene expression assay based on qPCR was used to validate the microarray findings. The results were analyzed using the Partek Genomics Suite 6.5 software and Ingenuity System.

Results: Low-dose Lf activated neurotrophin signalling pathways and modulated expression of genes associated with neurodevelopment, learning & memory, including BDNF, FGFR, IRS1 and CAMK1. Functional analysis showed network signalling impacted brain development, neuron structure and long-term potentiation. In contrast, piglets on the high dose of Lf showed no effect on neurotrophin signalling but an increase in gene expression and signalling pathways leading to cell death/apoptosis and decreased neurogenesis.

Conclusions: Low-dose Lf supplementation up-regulated neurotrophin signalling pathways associated with neurodevelopment and cognition, a finding in contrast to piglets on a high dose of Lf. The molecular mechanism(s) underlying this paradoxical finding remains under study.

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CONCURRENT SESSION 2: LIPIDS. POSTPRANDIAL TRIGLYCERIDES RESPONSE TO KRILL OIL SUPPLEMENTATION IN HEALTHY WOMEN

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Background: Krill oil (KO) has been suggested to have higher bioavailability of EPA and DHA compared with fish oil. There are limited reports on the postprandial effects of KO. This study investigates the impacts of supplementation with KO and fish oil (FO) on plasma lipid profiles in the postprandial state.

Methods: This is a randomised cross-over study. Test meals consisting fresh mashed-potato and 15 g of olive oil (OO) and 5 g of with three oil supplements (KO, FO or OO) were randomly provided on each study day with seven days wash-out period between. Blood samples were collected at the baseline and post consumption of test meal/supplement on hourly basis for 5 hours. Postprandial changes were assessed using SPSS. SPANOVA for repeated measure was performed to assess the changes between the treatments. One-way ANOVA and multiple comparisons using Tukey HSD post-hoc analysis were also performed to assess the changes in the parameters over time within the treatment group. P < 0.05 was considered statistically different.

Results: There were no significant changes in the postprandial TAG levels in either chylomicron or plasma between the three oil treatments (p = 0.783). However within the treatment groups, changes in TAG with time after oil consumption were significantly different (p < 0.0001) and the magnitude of changes varies in each treatment.

Conclusions: There were no significant difference in the absorption of TAG in chylomicron or plasma between FO and KO. Since KO contains n-3 fatty acids in phospholipids, n-3 profile in postprandial plasma phospholipid should be examined.

Funding source(s): College of Health and Biomedicine, Victoria University, Melbourne, Australia.

WHY ARE FISH OIL SUPPLEMENTS APPARENTLY FAILING TO REPRODUCE FISH CONSUMPTION EPIDEMIOLOGY IN RCT FOR CARDIOVASCULAR DISEASE?

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Background/Aims: Regular fish consumption is associated with low cardiovascular disease risk. However, randomised control trials (RCT) of fish oil supplements produce variable results, recently interpreted to no longer support beneficial effects of long chain n-3 polysaturated fatty acids (LCn-3PUFA) EPA and DHA in treating or preventing cardiovascular disease.

Methods: This review considers issues key to understanding the contradiction.

Results: 1) Most RCT report no exclusion criteria for fish eaters and fewer analyse n-3 PUFA status. Even in RCT with exclusions overlap of tissue n-3 PUFA status remain between control and treated groups. 2) Cardiac effects (sudden death, heart failure) derive from myocardial membrane incorporation of DHA. The LCn-3PUFA intake in cohort studies derives from seafood, providing more DHA than EPA, whereas most RCT use supplements rich in EPA, low in DHA. 3) Nutritional and therapeutic effects of LCn-3PUFA derive from direct and indirect mechanisms. Effects on heart rate, heart failure and sudden death occur at lower intakes than influence classical coronary artery disease risk factors such as hypertriglyceridaemia. RCT designs combining cardiac and arterial disease populations and composite endpoints propose a common substrate and assume common mechanisms of action.

Conclusions: Many fish oil RCT included in systematic reviews are methodologically unsound, failing to consider background diet and multiple mechanisms of LCn-3PUFA or clinical disease Mechanisms of action must be better understood and RCT design and analysis improved to resolve apparent contradictory effects of LCn-3 PUFA supplements and eating fish.

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DAILY VS. WEEKLY ADMINISTRATION OF FISH OIL: BIOAVAILABILITY AND EFFICIENCY OF DIETARY LONG CHAIN OMEGA-3 FATTY ACIDS

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Background/Aims: The recommendations on the intake of long chain omega-3 polysaturated fatty acids (n-3 LC-PUFA) vary from eating oily fish (‘once to twice/week’) to consuming specified daily amounts of EPA and DHA (‘250–500 mg/day’). It is not known if there is a difference in the uptake/bioavailability between these two feeding strategies. In this study, the bioavailability of a daily dose of n-3 LC-PUFA (Constant treatment) versus a large weekly dose of n-3 LC-PUFA (Spike treatment) was assessed.

Methods: Six-week old male Sprague-Dawley rats were fed either a Constant, a Spike or Control treatment (no oil supplements) with seven days wash-out period between. Blood samples were collected at the baseline and post consumption of test meal/supplement on hourly basis for 5 hours. Postprandial changes were assessed using SPSS. SPANOVA for repeated measure was performed to assess the changes between the treatments. One-way ANOVA and multiple comparisons using Tukey HSD post-hoc analysis were also performed to assess the changes in the parameters over time within the treatment group. P < 0.05 was considered statistically different.

Results: There were no significant changes in the postprandial TAG levels in either chylomicron or plasma between the three oil treatments (p = 0.783). However within the treatment groups, changes in TAG with time after oil consumption were significantly different (p < 0.0001) and the magnitude of changes varies in each treatment.

Conclusions: There were no significant difference in the absorption of TAG in chylomicron or plasma between FO and KO. Since KO contains n-3 fatty acids in phospholipids, n-3 profile in postprandial plasma phospholipid should be examined.

Funding source(s): College of Health and Biomedicine, Victoria University, Melbourne, Australia.