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Algal supplementation of vegetarian eating patterns improves plasma and serum docosahexaenoic acid concentrations and omega-3 indices: a systematic literature review

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Abstract

Vegetarians are likely to have lower intakes of preformed docosahexaenoic acid (DHA) than omnivorous populations who consume fish and animal products. As such, vegetarian populations have omega-3 indices up to 60% lower than those who consume marine products. Algae, the primary producer of DHA in the marine food chain, offer an alternative source of DHA for those who do not consume marine or animal products. This systematic review aims to examine the evidence for the relationship between supplementation with algal forms of DHA and increased DHA concentrations in vegetarian populations. The SCOPUS, Science Direct and Web of Science scientific databases were searched to identify relevant studies assessing the effect of algal DHA consumption by vegetarian (including vegan) populations. Four randomized controlled trials and two prospective cohort studies met the inclusion criteria. All included studies reported algal sources of DHA significantly improve DHA concentrations (including plasma, serum, platelet, and red blood cell fractions) as well as omega-3 indices in vegetarian populations. An evident time or dose response was not apparent given the small number of studies to date. Future studies should address long chain n-3 polyunsaturated fatty acid deficiencies in vegetarian populations using algal DHA and explore the potential physiological and health improvements in these individuals.

Keywords

supplementation, vegetarian, eating, algal, patterns, review, improves, plasma, serum, docosahexaenoic, acid, concentrations, omega-3, indices:, systematic, literature

Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

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Algal supplementation of vegetarian eating patterns improves plasma and serum docosahexaenoic acid concentrations and omega-3 indices: a systematic literature review

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Key words: Docosahexaenoic acid; Omega-3; Vegetarian; Supplementation; Algal

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Abbreviations

ALA; alpha-linolenic acid

DHA 22:6n-3; docosahexaenoic acid

EPA 22:5n-3; eicosapentaenoic acid

LA; linoleic acid

LCn-3FA; long chain omega-3 fatty acids

PL; phospholipid

RBC; red blood cells

RBC-PC; RBC-phosphatidylcholine

RBC-PE; RBC-phosphatidylethanolamine

Abstract

Vegetarians are likely to have lower intakes of preformed docosahexaenoic acid (DHA) than omnivorous populations who consume fish and animal products. As such, vegetarian populations have omega-3 indices up to 60% lower than those who consume marine products. Algae, the primary producer of DHA in the marine food chain, offer an alternative source of DHA for those who do not consume marine or animal products. This systematic review aims to examine the evidence for the relationship between supplementation with algal forms of DHA and increased DHA concentrations in vegetarian populations. The SCOPUS, Science Direct and Web of Science scientific databases were searched to identify relevant studies assessing the effect of algal DHA consumption by vegetarian (including vegan) populations. Four randomized controlled trials and two prospective cohort studies met the inclusion criteria. All included studies reported algal sources of DHA significantly improve DHA concentrations (including plasma, serum, platelet, and red blood cell fractions) as well as omega-3 indices in vegetarian populations. An evident time or dose response was not apparent given the small number of studies to date. Future studies should address long chain n-3 polyunsaturated fatty acid deficiencies in vegetarian populations using algal DHA and explore the potential physiological and health improvements in these individuals.

Introduction

Vegetarian eating patterns are increasing in popularity as the associated health benefits become evident [1-3]. Protection against chronic disease has been observed in those following a vegetarian eating pattern including coronary heart disease, hypertension, diabetes mellitus, obesity and some cancers [1, 2, 4]. Eating patterns of this nature are typically higher in fruits and vegetables leading to increased oligo- and polysaccharides, fiber, and phytochemicals while being lower in saturated fat and cholesterol compared to omnivorous eating patterns [5, 6]. Approaches to vegetarian eating range from the complete exclusion of animal products through to their inclusion at varying levels; eggs or dairy may be consumed [7] referred to as ovo- and lacto- forms of vegetarian eating, respectively. Individuals adhering to a vegan eating pattern exclude all products of an animal origin.

Whilst many beneficial characteristics have been attributed to vegetarian eating patterns, vegetarian populations generally have lower plasma concentrations of docosahexaenoic acid (DHA; 22:6n-3; percentage of total fatty acids)[8] and lower omega-3 indices compared to those who eat fish [9]. The index is calculated using the sum of eicosapentaenoic acid (EPA; 22:5n-3) and DHA in erythrocyte membranes expressed as a percentage of total fatty acids [10].

DHA is one of the two most prevalent polyunsaturated fatty acids in brain and retinal phospholipids (along with arachidonic acid), and plays a key role in normal neurotransmission [11] and visual function [12] and can be incorporated into cardiac [13] and skeletal muscle [14, 15]. DHA is a long-chain omega-3 polyunsaturated fatty acid with a range of proposed health benefits including assisted foetal development [16], improved cardiovascular function [16, 17], reduced incidence of dementia [18], and improved cognitive functioning [11, 16].

Vegetarian eating patterns are typically higher in alpha-linolenic acid (ALA), a precursor to DHA, compared to omnivorous eating patterns, however conversion of ALA to DHA is limited within the human body [9, 19]. Several studies have reported varying conversion rates of ALA to DHA in humans, from no detectable conversion, to nine percent conversion [20-22]. Nonetheless, long-term vegetarian populations may have an increased capacity for synthesizing long chain omega-3 fatty acids (LCn-3FA) particularly DHA due to evolutionary pressures for improved ALA metabolism [23, 24].

The richest dietary sources of DHA are fatty fish and seafood, however, fish are not the originators of DHA. Fish, like humans, do not readily synthesize DHA but feed on zooplankton which feeds on algae, the primary producer of the omega-3 DHA in the marine food chain [25]. Algae and algal supplements are rich in DHA, with some supplements containing no EPA at all [26]. Human consumption of algal DHA rather than fish or seafood forms of DHA may provide adequate intakes of DHA for those who do not eat fish or seafood, although a consensus on the effect of algal supplementation on circulating DHA concentrations and incorporation into membranes has not been established.

With the proposed health benefits and the limited research exploring the bioavailability of algal DHA compared to fish and fish oil, an important question arises: Does supplementation with algal forms of DHA in vegetarian populations improve their DHA concentrations? This review aims to address this question in relation to reported DHA fractions and/or omega-3 indices as markers of membrane incorporation.

Methods

Study protocol

A systematic review of the literature was conducted using the SCOPUS, Science Direct and Web of Science scientific databases (all years to February 2016). The review was registered with PROSPERO, the international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO, registration number CRD42015020724). The search strategy used the following keyword and Boolean combinations; "delta-6 desaturase enzyme" OR "Docosahexaenoic Acid" OR DHA OR "Omega 3" OR "Eicosapentaenoic acid" OR EPA OR "Linolenic acid" OR LA OR "Alpha-linoleic acid" OR ALA OR "Essential fatty acid" OR "α-Linolenic acid" OR "Omega 3 index” AND vegetarian* OR *vegetarian OR vegan* OR "plant-based" AND Human AND supplemen* in the article, keywords or abstract.

Study selection

Included publications met the following requirements: the studies (i) assessed the effect of consumption of algal sources of DHA in vegetarian (vegan, ovo-lacto-, ovo-, lacto-) populations aged 18 years or over, (ii) reported DHA fractions including plasma, serum, platelet, fat, RBC concentrations and/or omega-3 indices. Studies where vegetarian populations were included alongside omnivorous groups were included. Publications that met the following exclusion criteria were omitted: (i) not published in the English language, (ii) conference papers, short surveys, letters, notes, editorials, articles in press, book series, erratum and conference proceedings, (iii) intervention studies focused on fatty acids other than DHA (such as ALA, EPA), (iv) populations following a pesco-vegetarian, flexitarian (plant-based eating patterns consuming fish or meat) or semi-vegetarian eating pattern. Duplicate publications were removed using EndNote (version X7, 2013 Thomson Reuters; Philadelphia, Pennsylvania). Where results from the same study were reported in multiple publications, the first published study was included to avoid duplication of results.

Screening of titles and abstracts was initially applied to exclude irrelevant papers, followed by retrieval of full-text publications. Reference lists of all included publications were also examined for relevant studies. Data extraction included information related to: the publication year, study design/quality, total sample size, population type, intervention and results. National Health and Medical Research Council levels of evidence [27] were applied to the included studies. Study quality was assessed using the quality criteria checklist of the Evidence Analysis Library (http://www.andeal.org/) of the Academy of Nutrition and Dietetics (2012) [28].

Results

The literature search identified 695 publications (Figure 1). After duplicates were removed, 626 publications were excluded by title and abstract, while a further five were excluded following full text assessment. Seven publications (describing six studies) met the inclusion criteria, which included two prospective cohort studies and five intervention studies (Fig 1) [(29-35)]. Two publications used the same data from one study and therefore the second publication (by date) was excluded [(33)] resulting in a total of six publications included in the review. All studies received positive scores after the quality criteria checklist of the Evidence Analysis Library study was applied [(28)] (data not shown).

The doses of DHA provided via algal supplements ranged from 172 mg/day to 2.14 g/day in the included studies (Table 1). Five studies [(30-32, 34, 35)] investigated the effects of DHA supplementation on vegetarians with one study including vegans, exclusively [(29)]. The study durations ranged from two weeks to four months with sample sizes ranging from twenty to 108 participants.

DHA outcome measurements varied among studies and included serum total phospholipid (PL) DHA[(34) (31) (30)], platelet total PL DHA[(31) (30)], RBC total lipid DHA, RBC-phosphatidylethanolamine (RBC-PE) DHA, RBC-phosphatidylcholine (RBC-PC) DHA, plasma-PL DHA[(32)], low-density lipoprotein (LDL) DHA concentrations [(35)] and omega-3 indices [(29, 32)]. All included studies reported increases in serum, plasma, platelet and RBC DHA fractions and/or omega-3 indices following algal DHA supplementation. Increases in omega-3 indices were reported to range from 55% - 82% [(29, 32)] within groups supplemented with algal DHA. Similarly, DHA serum total phospholipids and platelet phospholipids were also elevated after algal supplementation, with increases ranging from 238% – 246% [(30, 31)], and 209 – 225% [(30, 31)] in total and platelet phospholipids respectively. The sole study exploring DHA plasma as a percentage of total fatty acids reported a 59% increase from baseline [(34)]. Geppert et al [(32)] reported increases within groups in RBC total lipids (80% increase), RBC PE wt% (86% increase), RBC PC (174% increase) and plasma PL (164% increase) ($p<0.001$).

[Insert Figure 1 Here]

[Insert Table 1 Here]

Discussion

The results of this review suggest that consumption of algal sources of DHA in vegetarian populations considerably increased levels of circulating DHA, including those measured in plasma, serum, platelet and RBC DHA fractions as well as omega-3 indices. This review highlights algal supplementation as a viable method of addressing the low DHA levels often seen in vegetarians and vegans [8, 9] however, given the varying doses, supplement periods and tissues, a clear dose response to recommend a threshold for effective increases in omega-3 status was not apparent. Providing DHA in the diet is clearly associated with positive health outcomes, including cardiovascular disease. As such, optimizing the tissue concentrations of DHA in vegetarian populations by using algal oil will be an important avenue of further research in nutrition translation and practice, and may also be relevant for omnivorous populations.

When interpreting the results of this systematic literature review, it is important to note that while all included studies were assessed as being of positive quality, certain studies exhibited stronger methodology. Von Shacky et al [36] demonstrated that for cardiovascular protection to be observed as a health benefit of omega-3 fatty acids, evidence of tissue incorporation is required and study design is imperative. For example, Sarter et al [29] and Geppert et al [32] used a duration of four and two months, respectively, reporting both baseline and post-supplementation omega-3 indices, which provided a more rigorous depiction of algal supplementation in vegetarian populations. Conversely, four of the included studies [30, 31, 34, 35] reported the effects of short-term supplementation (two to six weeks) on serum total phospholipid DHA, platelet phospholipid DHA or LDL-DHA concentrations. The results may have been indicative of circulating concentrations and it is unclear if these elevated DHA concentrations would have been incorporated into heart, skeletal muscle and brain tissue for health benefits to be observed.

One included prospective cohort study [31] compared total phospholipid DHA in platelets between omnivorous and vegetarian populations after both groups were supplemented with algal oil. Similar increases in total phospholipid DHA were observed in both groups suggesting that algal oil supplementation has relevance for both omnivorous and vegetarian populations. Only one included study [34] explored the bioequivalence between fish oil and algal oil in a three-arm randomized controlled trial with no significant differences observed between groups. There appears to be a paucity of literature evaluating the efficacy between fish and algal forms of DHA, however from the limited human studies, it appears algal sourced DHA may have comparable bioavailability to fish sourced DHA [37, 38]. Comparing algal DHA to fish DHA supplements is an area which warrants further investigation.

Recently, concern has been expressed for omega-3 fatty acid controlled trials exploring cardiac outcomes [39, 40]. Much of the criticism surrounds the disparity in study design when comparing standard pharmacological controlled trials to fish oil trials. In drug trials, the intervention is given to those in the experimental group, but not to those in the control group. In fish oil trials, both experimental and control groups are exposed to DHA due to background dietary intakes and baseline levels [39]. Nonetheless, as this review explored DHA supplementation in *vegetarian populations* this flaw is somewhat negated as the control groups would theoretically be consuming none, or very small amounts of DHA and EPA. Furthermore, from a systems physiology perspective, there is no doubt that consumption of long chain omega-3 can provide support for optimizing heart function [17], however the translation of these benefits to a vegetarian population is currently unknown. A meta-analysis by Huang et al [41] showed vegetarians already have a 29% reduced risk of death from ischemic heart disease compared to omnivores, but there is a lack of research exploring if vegetarians would acquire even further protection with an increased omega-3 indices.

Algae and algal supplements tend to have a higher DHA to EPA ratio, with many supplements containing no EPA [26]. Thus, this review focused on the effect of algal supplements on DHA levels, however the increased levels of DHA observed in the studies in this review may also have additional benefits on other fatty acids. Supplementation with DHA may result in improved EPA concentrations via retro-conversion from DHA to EPA. For instance, Conquer and Holub [30] used an EPA-free preparation of DHA which was supplemented daily by an omnivorous group and vegetarian group. DHA concentrations (serum and platelet PL) significantly increased in both groups, as did EPA via retro-conversion of DHA to EPA. The increase in serum PL EPA concentration was 9.4% overall with no significant difference between omnivores and vegetarians. EPA has been linked to favorable health characteristics, such as cardiovascular protection [42] and reduced inflammation [43]. Given that EPA concentrations (plasma PL) have also been reported to be significantly lower in vegetarian populations when compared to groups who consume moderate to large amounts of meat [44], supplementation with algal DHA may provide an alternate method of increasing EPA levels for those who do not consume fish.

While this review has provided insight into the effect of algal DHA supplementation in vegetarians, there are some limitations. Large double-blinded randomized controlled trials measuring baseline and post-supplementation omega-3 indices with algal forms of DHA would be beneficial to substantiate these results. Publication bias may also have influenced the results of this review. Regardless of the limitations, the findings were consistent across studies with all six included studies reporting increases in various plasma and serum fractions and/or erythrocyte LDL-DHA concentrations and/or omega-3 indices across a range of doses and intervention durations.

Conclusion

This review consolidated existing studies and has reported that supplementing with algal forms of DHA can increase an array of serum and platelet DHA concentrations and omega-3 indices in vegetarians. This finding is relevant given that this population is known to have lower serum and plasma DHA concentrations than omnivorous individuals. Further research is warranted to determine appropriate algal DHA threshold doses / supplement durations to achieve clinically relevant elevations in omega-3 indices. Additionally, research investigating if there are grounds for DHA supplementation in vegetarian populations, which may potentially further optimize their cardiac protection and reduce chronic disease, is indicated.

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Conflicts of Interest - None.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted and that any discrepancies from the study as planned (and registered with) have been explained. The reporting of this work is compliant with PRISMA guidelines.

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Table 1. Summary of included studies using algal DHA supplementation.

Reference	Study design (Level of evidence)	Sample size	Duration of vegetarianism/Population	Age (mean ± SD or range), years	DHA dose /day, mg	Duration, weeks	Study results	DHA outcomes
Sarter et al (2015)[29]	Prospective Cohort (III – 2)	n = 46	- minimum 1 year vegan - omega-3 index < 4%	22 - 85	172	16	- Omega-3 index ↑ 3.1% ± 0.6% to 4.8% ± 0.8 ǂ	Increased
Conquer & Holub (1997)[31]	Prospective Cohort (III – 2)	n = 20	- minimum 6 months vegetarian (ovo, ovo-lacto or lacto)	26.8 ± 1.6	1620	6	- DHA serum total PL ↑ from 2.1 ± 0.2 to 7.1± 0.4 mol% ‡ - DHA Platelet PL ↑ from 1.1± 0.1 to 3.4± 0.2 mol% ‡	Increased
Ryan & Symington (2014)[34]	A pseudorandomised controlled trial (III-1)	n = 12	- duration not reported Δ - vegetarian (ovo, ovo-lacto or lacto) and/or vegan	18 - 65	200	2	- DHA plasma (% of total fatty acids) ↑ 2.76 ± 1.13 to 5.08 ± 0.45 ‡	Increased
Conquer & Holub (1996)[30]	RCT (II)	n = 24	- minimum 6 months vegetarian (ovo, ovo-lacto or lacto)	29.6 ± 1.7	1620 *	6	- DHA serum total PL ↑ from 2.4 ± 0.2 to 8.3 ± 0.2 g/100g ‡ - DHA platelet PL ↑ from 1.2 ± 0.1 to 3.9 ± 0.2 g/100g ‡	Increased

Geppert et al (2005)[32]	RCT (II)	n = 108	- minimum 1 year vegetarian (ovo, ovo-lacto or lacto)	25.9 ± 5.6	940 †	8	- Omega 3 index ↑ from 4.8 to 8.4wt% ǂ ⤈ - DHA RBC total lipids ↑ from 4.4± 0.2 to 7.9 ± 0.2 wt% ǂ ⤈ - DHA RBC PE ↑ from 6.5 ± 0.3 to 12.1 ± 0.3 wt ǂ ⤈ - DHA RBC PC ↑ from 1.38 ± 0.07 to 3.78 ± 0.13 ǂ ⤈ - DHA Plasma PL ↑ from 2.8 ± 0.1 to 7.4 ± 0.2 wt% ǂ ⤈	Increased
Wu et al (2006)[35]	RCT (II)	n = 25	- minimum 1 year vegan and/or lacto-ovo-vegetarian	52.3 ±5.1 (control group) 52.6 ±4.4 (intervention group)	2140 *	6	- LDL-DHA ↑ from 1.35± 0.54 to 3.71 ± 1.03 ⤈	Increased

- Prospective Cohort study, (III-2) - Non-randomised, experimental trial.
- Pseudorandomised controlled Trial (III-1) - Alternate allocation or some other method.
- RCT (Randomized Controlled Trial; II) - A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation.

* Control – Corn Oil, † Control – Olive Oil,

Δ Other study arms described in study – Nil control

ǂ Significant within group ($p<0.001$)

‡ Significant within group ($p<0.05$)

⤈ Significant between control group ($p<0.001$)

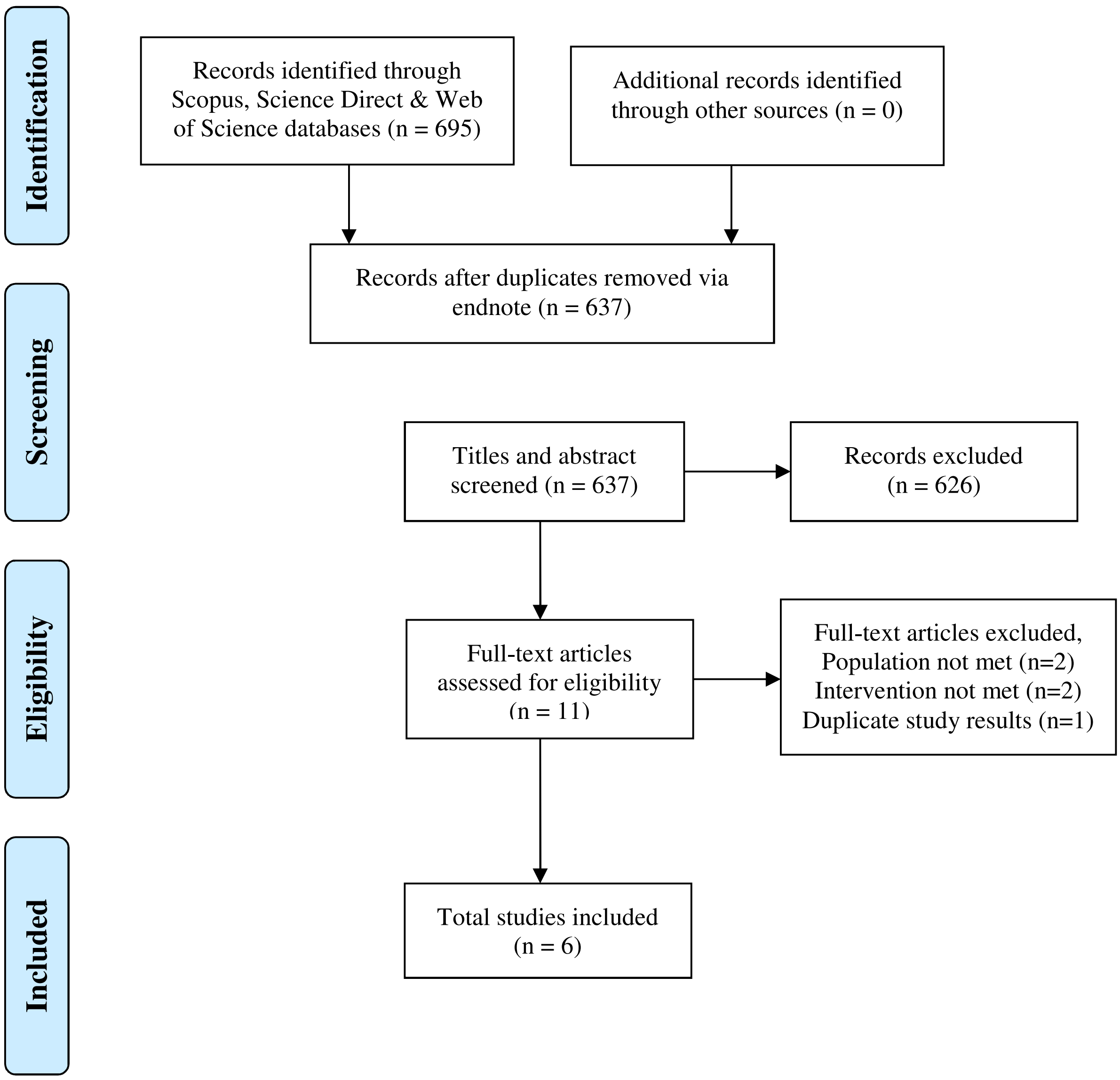

Figure 1. The PRISMA flowchart showing the initial and final number of studies obtained.