

Title of the manuscript: **Marine-derived n-3 fatty acids therapy for stroke**

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Marine-derived n-3 fatty acids therapy for stroke

Background

With stroke burden increasing, there remains a need to identify therapeutic options that ameliorate the acute insult. There is substantial evidence for a neuroprotective effect of marine-derived n-3 polyunsaturated fatty acids (PUFAs), associated with better functional outcomes in experimental stroke models.

Objectives

To assess the effects of administration of marine-derived n-3 PUFAs on functional outcomes and dependence in people with stroke.

Our secondary outcomes were vascular-related death, recurrent events, incidence of other type of stroke, adverse events, quality of life, and mood.

Search methods

We searched the Cochrane Stroke Group trials register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL EBSCO, and Web of Science (SCI-EXPANDED, CPCI-S, and BIOSIS Citation Index). We also searched ongoing trial registers and other relevant sources.¹

Selection criteria

We included randomized controlled trials (RCTs) comparing marine-derived n-3 PUFAs to placebo or open control in people with a history of stroke and/or transient ischemic attack.

Data collection and analysis

Two authors independently selected trials for inclusion, extracted data, and assessed risk of bias and quality of the evidence. We conducted random-effects meta-analysis or narrative synthesis, as appropriate.

Results

We included 29 RCTs; nine of them provided outcome data (3339 participants). Only one study included participants with acute stroke (subarachnoid hemorrhage). Doses of marine-derived n-3 PUFAs ranged from 400 to 3300 mg/day. Risk of bias was generally low or unclear, and the quality of the evidence ranged from low to very low. We divided the studies by short (up to three months) and longer (more than three months) follow-up.

Short follow-up

One pilot study reported clinical outcome assessed with Glasgow Outcome Scale Extended (risk ratio (RR) of poor outcome 0.78, 95% confidence interval (CI) 0.36 to 1.68; 40 participants; very low quality evidence). Mood (assessed with GHQ-30, lower score better), was reported by one study and favored control (mean difference (MD) 1.41, 95% CI 0.07 to 2.75; 102 participants; low-quality evidence).

We found no evidence of an effect of the intervention for vascular-related death, recurrent events, incidence of other type of stroke, quality of life, and adverse events (bleeding complications and extracranial hemorrhage).

Longer follow-up

One small trial assessed functional outcome (52 participants; very low quality evidence) with Barthel Index (MD 7.09, 95% CI -5.16 to 19.34; higher score is better) and Rivermead Mobility Index (MD 1.30, 95%CI -1.31 to 3.91; higher score is better).

We found no evidence of an effect of the intervention for vascular-related death, recurrent events, mood and adverse events. Incidence of other type of stroke and quality of life were not reported.

Implications for practice and research

We are very uncertain of the effect of marine-derived n-3 PUFAs therapy on functional outcomes and dependence after stroke as there is insufficient high-quality evidence.

More well-designed RCTs are needed, specifically in acute stroke, to determine the efficacy and safety of the intervention. Future studies might consider starting the intervention as early as possible after the event, as well as using standardized clinically-relevant outcome measures, such as the modified Rankin Scale. Optimal doses remain to be determined; delivery forms and mode of administration also need further consideration.

Disclosures

Dr Thies authored one of the studies included in the review (Thies 2003). However, he was not involved in its assessment at any stage (screening, data extraction and risk of bias assessment) and this study is not contributing any outcome data to the review.

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This paper is based on a Cochrane Review published in The Cochrane Library 2019, Issue 6 (see www.thecochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, The Cochrane Library should be consulted for the most recent version of the review.

References

1. Alvarez Campano CG, Macleod MJ, Aucott L, Thies F. Marine-derived n-3 fatty acids therapy for stroke. Cochrane Database of Systematic Reviews 2019, Issue 6. Art. No.: CD012815. DOI: 0.1002/14651858.CD012815. <http://dx.doi.org/10.1002/14651858.CD012815>

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