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건강기능식품의 기능성을 중심으로 한 오메가-3 지방산 함유유지의 혈행개선 효과에 대한 체계적 고찰*

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Systematic review of the effect of omega-3 fatty acids on improvement of blood flow while focused on evaluation of claims for health functional food*

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ABSTRACT

Omega-3 polyunsaturated fatty acids are essential fatty acids because humans cannot synthesize them de novo and must obtain them in their diet. Fish and fish oil are rich sources of omega-3 fatty acids, including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Significant evidence of the beneficial role of dietary intake of omega-3 fatty acids in blood flow has been reported and putative mechanisms for improvement of blood flow include anti-thrombotic effects, lowered blood pressure, improved endothelial function, and anti-atherogenic effects. Edible oils containing omega-3 fatty acids were registered as functional ingredients in the Korea Health Functional Food Code. Although omega-3 fatty acids have been evaluated by the Korea Food and Drug Administration (KFDA) based on scientific evidence, periodic re-evaluation may be needed because emerging data related to omega-3 fatty acids have accumulated. Therefore, in this study, we re-evaluated scientific evidence for the effect of omega-3 fatty acids as a functional ingredient in health functional food on improvement of blood flow. A comprehensive literature search was conducted for collection of relevant human studies using the Medline and Cochrane, KISS, and IBIDS databases for the years 1955−2012. Search keywords were used by combination of terms related to omega-3 fatty acids and blood flow. The search was limited to human studies published in Korean, English, and Japanese. Using the KFDA's evidence based evaluation system for scientific evaluation of health claims, 112 human studies were identified and reviewed in order to evaluate the strength of the evidence supporting a relation between omega-3 fatty acids and blood flow. Among 112 studies, significant effects on improvement of blood flow were reported in 84 studies and the daily intake amount was ranged from 0.1 to 15 g. According to this methodology of systematic review, we concluded that there was possible evidence to support a relation between omega-3 fatty acid intake and blood flow. However, because inconsistent results have recently been reported, future studies should be monitored. (J Nutr Health 2013; 46(3): 226 ~ 238)

KEY WORDS: systematic review, omega-3 fatty acids, blood flow, DHA, EPA, health functional food, re-evaluation.

서 론

오메가-3 지방산은 주로 식품을 통해 공급받을 수 있는 필수 지방산으로서 eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA)를 포함한다. 비록 EPA와 DHA의 전구체인 α-linolenic acid를 섭취할 경우 체내에서 EPA와 DHA가 합성되기는 하나 성인에서 α-linolenic acid가 DAH와 EPA로 전환되는 효율은 약 10~15 %, 어린이는 3~6%로 매우 낮기 때문에 DHA와 EPA가 풍부한 식품을 직접 섭취하는 것이 효과적

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인 것으로 알려져 있다.[1,2] 여러 연구들에 따르면 오메가-3 지방산이 혈전생성 억제, 죽상동맥경화를 유발시킬 수 있는 플라그의 생성 억제, 내피세포의 이완 촉진 등 혈행개선에 도움을 주는 것으로 보고되고 있으며,[3,4] 2004년부터 2007년까지 4년간 수행된 식품의약품안전처 고시형 건강기능식품 재평가 사업에서 EPA/DHA 함유제품의 경우 문헌검토만으로도 기능성에 대한 충분한 과학적 근거가 있다는 것이 확인된 바 있다. 하지만 재평가 사업 이후 새로운 연구들이 지속적으로 보고되고 있으며 특히 일부 인체적용시험에서는 오메가-3 지방산의 섭취가 혈행개선에 영향을 미치지 않는 것으로 보고되고 있어 최근의 연구 결과들을 포함하여 오메가-3 지방산의 혈행개선 기능성에 대해 재평가할 필요성이 있겠다. 이는 기능성 재평가에 대한 국제적 기류에 부합되는 것으로, 미국 FDA에서는 기평가된 health claim이나 qualified health claim의 재평가 필요성에 대해 Guideline에 언급하고 있으며,[5] 국제식품규격위원회 (Codex)에서도 기능성 표시의 재평가 필요성을 "Guidelines for use of nutrition and health claims-recommendations on the scientific substantiation of health claims"에서 강조하고 있다.[6]

따라서 본 연구에서는 식품의약품안전처에서 사용하고 있는 과학적 근거 중심의 체계적 고찰방법을 인체적용시험에 적합하도록 일부 변경하여 오메가-3 함유유지의 혈행개선 기능성에 대해 재평가를 수행하였다.

연구방법

문헌검색

문헌검색은 2012년 5월 31일까지 출판된 문헌을 대상으로 실시하였다. 국외 문헌 검색은 Pubmed, Cochrane, IBIDS (International Bilbliographic Information on Dietary Supplements)을 이용하였고 국내 문헌은 KISS (Koreanstudies Information Service System)을 이용하여 검색하였다. 사용된 검색어는 오메가-3 지방산 관련 검색어 omega-3, DHA, EPA, eicosapentaenoic acid, docosahexaenoic acid와 혈행 관련 검색어 coagulation, platelet aggregation, prothrombin, thrombosis, blood flow, thrombotic, 혈행, 혈액응고를 조합하여 사용하였다. 문헌은 검색을 실시한 2012년 5월 31일까지 출판된 문헌만을 검토하였다.

이번 체계적 문헌고찰에 포함된 문헌 선정 기준은 다음과 같다: 1) 인체를 대상으로 한 인체적용시험, 2) 오메가-3 지방산 함유 유지의 혈행 개선효과를 평가한 연구, 3) 오메가-3 지방산 함유 유지를 경구로 섭취한 연구. 연구 제외기준은 다음과 같다: 1) 시험관시험 및 동물시험, 2) 경구 섭취 연구가 아닌 연구, 3) 섭취량, 섭취기간 등의 시험 관련 정보가 부재한 연구, 4) 오메가-3 지방산 함유 유지를 섭취하였으나 다른 성분들과 함께 섭취한 복합물 이용 연구, 5) 학회 초록이나 총설, 6) 한국어, 영어, 일본어 이외의 언어로 게재된 문헌. 자료의 추출과 1차 문헌 선정은 초록의 제목 혹은 전문을 보고 선정하였으며, 체계적 문헌 고찰의 경험이 많은 영양학 전문가가 각기 시행하여 Endnote와 Excel에 정리하여 중복된 문헌을 검색하여 제외하였다 (Fig. 1).

자료의 평가 방법

선정된 문헌에 대하여는 시험물질, 표준화 여부, 연구설계, 피험자, 피험자에 대한 기본 정보 제공 여부, 피험자수 산출 방법의 적절성, 피험자 선정 및 제외 기준에 대한 설명, 시험기간, 섭취량, 섭취 방법, 기초식이 조절, 생활습관의 조절, 탈락율, 통계분석, 결과 해석, 혼동요인 보정 여부 등의 항목으로 구분하여 질 평가를 실시하였다. 연구의 질 평가 방법은 식품의약품안전청에서 사용하고 있는 질평가 도구[7]에 FDA 평가 가이드라인[5]을 참조하여 변형된 방법을 이용하였다. 이 도구는 총 27개 문항으로 되어 있으며 각 항목당 질평가 점수는 -1점에서 1점 사이로 산출된다. 자료의 종합평가는 식품의약품안전처에서 사용하고 있는 방법을 사용하였다. 오메가-3 지방산 함유유지의 혈행개선 기능성을 연구한 자료의 양, 결과의 일관성, 활용성을 모두 고려하여 종합적으로 검토하였다.

결 과

문헌검색 결과

문헌검색을 통해서 검색된 논문은 총 4,486건이었다. 연구제목과 초록, 원문검토를 통해 오메가-3 지방산 함유유지의 기능성과 관련이 없는 문헌이 986건, 생체 외 실험이나 동물시험 등의 기반연구가 204건, 시험 관련한 정보가 부족한 문헌이 67건, 복합물의 기능성을 확인한 연구가 34건, 경구투여가 아닌 근육주사 또는 정맥주사 등의 경로로 오메가-3 지방산 함유유지를 투여한 연구가 18건, 초록 등의 2차 문헌이 417건, 한국어, 일본어, 영어 이외의 언어로 작성된 문헌이 49건으로 총 4117건의 문헌이 검토에서 제외되었다. 결과적으로 총 158편 (한 개 논문에서 2건 이상의 연구를 수행한 경우가 있어 연구 건수로는 총 164건)의 문헌이 오메가-3 지방산 함유유지의 혈행개선 기능성 검토에 사용되었다 (Fig. 1).

자료의 평가

164건의 연구 중 낮은 평가를 받은 52건의 연구는 본 연구에서 제외하였다. 112건[8-115]의 연구는 모두 중재연구로서 88건이 무작위배정 대조군 비교 연구 (RCT)였고, 무작위 배정이 아

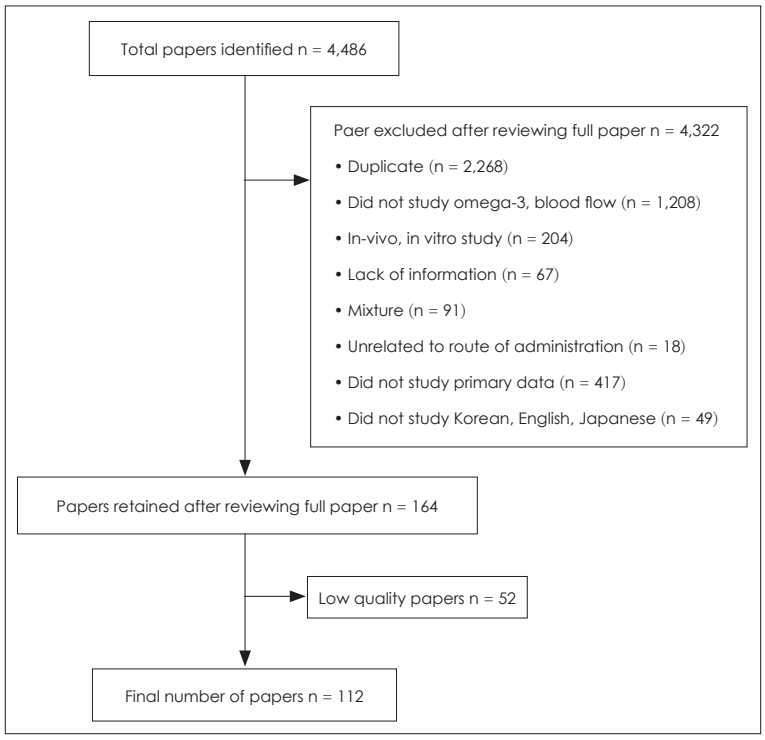

Fig. 3. Flow diagram of included and excluded studies.

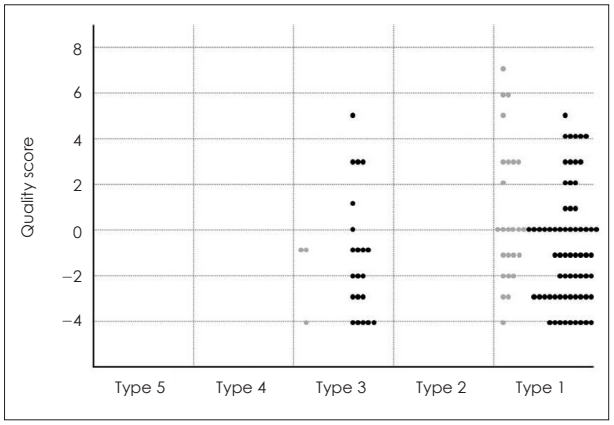

Fig. 2. Evidence table of systematic review for omega-3 fatty acids and effects on improvement of blood flow; (Type 1, RCT; Type 2, Cohort study; Type 3, non-RCT/case-control study etc; Type 4, animal study; Type 5, in vitro study; ●, significant improvement in the blood flow-related biomarkers; ●, no significant improvement in the blood flow-related biomarkers)

닌 연구 24건 중 17건[22-24,31,48,49,51-53,55,83-86,107-109]은 질 평가 결과 −1~−4점으로 점수가 낮았다 (Fig. 2). 총 112건 (5,536명) 중 84건 (3,910명)[8-18,20-79,81-86,112-114]의 연구에서 오메가-3 지방산 함유유지의 섭취로 인해 통계적으로 유의하게 혈행개선 효과가 나타났다 ($p < 0.05$). 또한 유의한 효과를 나타낸 84건의 연구 중 33건의 연구 (1,665명)[33,44,56-79,81-83,85,86]에서는 대조군과 섭취군간의 군간 차이를 보였으며, 대상자는 대부분 건강한 성인, 노인, 지질수준이 높은 사람들이었다. 질평가 점수 분포를 보면 평균 점수는 −0.48점 (−4~7점)으로 0점 이상의 높은 점수를 받은 50건의 연구들 중 유의한 개선효과를 보인 연구결과는 36건이었다. 총 112건의 연구 중 환자 대상 연구 52건 (2,980명)을 제외하고 건강한 성인을 대상으로 한 60건 (2,824명)의 연구를 검토한 결과 48건 (1,934명)의 연구[8-11,16,18,20,21,23-28,30-32,37-40,44-47,49,50,52-57,62-65,68,70,76,78,83,85,86,112,114]에서 통계적으로 유의한 개선효과를 보였다 ($p < 0.05$)(Table 1).

오메가-3 지방산의 일일 섭취량에 따른 연구 결과

유의한 개선 효과를 보인 연구에서 오메가-3 지방산 함유 유지의 섭취기간은 단회에서 2년까지였으며, 일일 섭취량은 0.1~15 g으로 건강기능식품공전에서 제시된 섭취량 기준 (0.5~2 g)에 포함되는 연구가 23건 (1,499명),[8,10-12,14,25,30,36,41,42,52,55,57,58,62,64,65,68,69,72,76,78,82] 기준 보다 낮은 경우가 5건 (114명),[28,39,47,49,61] 기준보다 높은 경우가 56건 (2,297명)[9,13,15-18,20-24,26,27,29,31-35,37,38,40,43-46,48,50,51,53,54,56,59,60,63,66,67,70,71,73-75,77,79-81,83-86,112-114]이었다 (Fig. 3). 오메가-3 섭취로 인한 심각한 부작용사례는 보고되지 않았다.

오메가-3 지방산 함유유지의 순도에 따른 결과

오메가-3 지방산 함유유지의 순도 (purity)를 저순도 (low purity)와 고순도 (high purity)로 구분하여 연구결과를 분석하였다. 순도가 낮은 오메가-3 지방산 함유유지를 사용한 연구가 98건으로 유의한 개선효과가 관찰된 연구가 72건이었으며, 고순도 오메가-3 지방산 함유유지를 사용한 14건의 연구 중에는 12건의 연구에서 유의한 개선효과가 나타났다 (Fig. 4).

Table 1. Characteristics of studies included for systematic review

Reference	Study type[1]	Target	Subject No.	Purity[2]	Dose (g)	Result[3]	Quality score
Baldassarre et al. 2006[8]	RCT	Healthy	64	Low	1.8	+	5
Blonk et al. 1990[9]	RCT	Healthy	45	Low	1.5, 3.0	+	3
Engler et al. 2004[10]	RCT	Healthy	20	High	1.2	+	−1
Fahs et al. 2010[11]	RCT	Healthy	20	High	0.9	+	−2
Finnegan et al. 2003[12]	RCT	Patients	150	Low	0.7, 1.5	+	−2
Green et al. 1990[13]	RCT	Patients	27	Low	4.32	+	−4
Grundt et al. 2004[14]	RCT	Patients	300	Low	0.882	+	0
Herrmann et al. 1995[15]	RCT	Patients	53	Low	9.12	+	4
Park et al. 2002[16]	RCT	Healthy	33	High	4	+	−3
Passfall et al. 1993[17]	RCT	Patients	12	Low	2.16	+	−1
Prisco et al. 1995[18]	RCT	Healthy	20	Low	3.44	+	2
Møller et al. 1992[19]	RCT	Healthy	40	Low	1.06	Ø	−3
Freese et al. 1997[20]	Non-RCT	Healthy	46	Low	5.2	+	0
Piolot et al. 2003[21]	Non-RCT	Healthy	32	Low	3	+	1
Rillaerts et al. 1989[22]	Non-RCT	Patients	12	Low	2.7	+	−2
Walser et al. 2006[23]	Non-RCT	Healthy	13	Low	5	+	−2
Haglund et al. 1990[24]	Non-RCT	Healthy	20	Low	4.5 mL	+	−3
Agren et al. 1988[25]	RCT	Healthy	62	Low	0.8	+	−1
Andrioli et al. 1999[26]	RCT	Healthy	60	Low	3.6	+	−4
Bach et al. 1989[27]	RCT	Healthy	30	Low	1.26, 2.52	+	−4
Coates et al. 2009[28]	RCT	Healthy	33	Low	0.2	+	4
Derosa et al. 2009[29]	RCT	Patients	333	High	3	+	4
Mann et al. 2010[30]	RCT	Healthy	30	Low	0.79, 1.02	+	0
Mann et al. 1997[31]	Non-RCT	Healthy	29	Low	2.894	+	−2
Mesa et al. 2004[32]	RCT	Healthy	42	Low	5.5, 5.7	+	−3
Mori et al. 1992[33]	RCT	Patients	32	Low	4.6	+	0
Myrup et al. 2001[34]	RCT	Patients	36	Low	2, 2.6	+	−2
Schmidt et al. 1988[35]	RCT	Patients	36	Low	4.5	+	−3
Serebruany et al. 2011[36]	RCT	Patients	30	Low	0.84, 1.62	+	−3
Tremoli et al. 1995[37]	RCT	Healthy	16	Low	2.25	+	−3
Tremoli et al.1994[38]	RCT	Healthy	29	Low	2.25	+	0
Véricel et al. 1999[39]	RCT	Healthy	20	Low	0.18	+	−1
von Schacky et al. 1985[40]	RCT	Healthy	7	High	6	+	−3
Westerveld et al. 1993[41]	RCT	Patients	24	High	0.9, 1.8	+	0
Woodcock et al. 1984[42]	RCT	Patients	19	Low	1.8	+	−4
Wright et al. 2008[43]	RCT	Patients	60	High	3	+	1
Zucker et al. 1988[44]	RCT	Healthy	9	Low	5.4	+	0
Zucker et al. 1988[44]	Non-RCT	Patients	6	Low	5.4	+	0
Zucker et al. 1988[44]	RCT	Patients	10	Low	5.4	+	0
Toft et al. 1997[45]	RCT	Healthy	78	Low	3.4	+	3
Cobiac et al. 1991[46]	Non-RCT	Healthy	31	Low	4.5	+	3
Croset et al. 1990[47]	Non-RCT	Healthy	16	High	0.1	+	5
De Caterina et al. 1993[48]	Non-RCT	Patients	14	Low	3.77	+	−1
Driss et al. 1984[49]	Non-RCT	Healthy	19	Low	0.15	+	−3
Grundt et al. 1999[50]	RCT	Healthy	57	Low	3.4	+	−1
Landgraf-Leurs et al. 1990[51]	Non-RCT	Patients	13	Low	7.7	+	−4
Okumura et al. 2002[52]	Non-RCT	Healthy	15	Low	1.8	+	−4
von Schacky et al. 1985[53]	Non-RCT	Healthy	6	Low	4.64 mL	+	−2

Table 1. Continued

Reference	Study type[1]	Target	Subject No.	Purity[2]	Dose (g)	Result[3]	Quality score
Sanders et al. 1983[54]	RCT	Healthy	5	Low	1.63, 3.28, 6550	+	−4
Sanders et al. 1983[54]	RCT	Healthy	5	Low	5.96 mL	+	−4
Haglund et al. 1994[55]	Non-RCT	Healthy	12	Low	0.96	+	−3
Fumeron et al. 1991[56]	RCT	Healthy	36	Low	6	+	−4
Goyens et al. 2006[57]	RCT	Healthy	37	Low	1.6	+	3
Green et al. 1985[58]	RCT	Patients	18	Low	1.8	+	0
Hansen et al. 1993[59]	RCT	Patients	31	Low	3.4, 3.6	+	0
Hendra et al. 1990[60]	RCT	Patients	80	Low	3	+	0
Pirich et al. 1999[61]	RCT	Patients	26	Low	0.354	+	1
Rizza et al. 2009[62]	RCT	Healthy	50	Low	1.7	+	0
Vognild et al. 1998[63]	RCT	Healthy	266	Low	3.45 mL	+	−1
Phang et al. 2012[64]	Non-RCT	Healthy	30	High	2	+	3
Phang et al. 2012[65]	Non-RCT	Healthy	30	High	2	+	3
Axelrod et al. 1994[66]	RCT	Patients	20	Low	2.6	+	−1
Berrettini et al. 1996[67]	RCT	Patients	40	Low	2.58	+	2
Flaten et al. 1990[68]	RCT	Healthy	64	Low	1.4	+	−3
Haberka et al. 2011[69]	RCT	Patients	40	Low	0.84	+	−3
Honstra et al. 1990[70]	RCT	Healthy	84	Low	4.7	+	−4
Lau et al. 1995[71]	RCT	Patients	45	Low	2.8	+	−2
Lindman et al. 2004[72]	RCT	Patients	219	Low	1.44	+	−2
McVeigh et al. 1994[73]	RCT	Patients	20	Low	3	+	−3
Mehta et al. 1988[74]	RCT	Patients	8	Low	5.4	+	0
Moertl et al. 2011[75]	RCT	Patients	49	Low	0.882, 3.528	+	−1
Mori et al. 1997[76]	RCT	Healthy	138	Low	0.8, 1.6	+	2
Solomon et al. 1990[77]	RCT	Patients	10	Low	4.6	+	0
Wensing et al. 1999[78]	RCT	Healthy	67	Low	1.2	+	−1
Woodman et al. 2003[79]	RCT	Patients	59	High	4	+	1
Grundt et al. 2003[80]	RCT	Patients	300	Low	0.882	Ø	−3
Johansen et al. 1999[81]	RCT	Patients	54	Low	2.42	+	−4
Krishnan et al. 2007[82]	RCT	Patients	60	Low	0.6	+	−4
Brox et al. 1981[83]	Non-RCT	Healthy	10	Low	25 mL	+	−4
Mehta et al. 1988[84]	Non-RCT	Patients	8	Low	5.4	+	−4
Nordøy et al. 1994[85]	Non-RCT	Healthy	6	Low	4.86	+	−1
Wojenski et al. 1991[86]	Non-RCT	Healthy	9	High	3, 4	+	−1
Agren et al. 1997[87]	RCT	Healthy	55	Low	1.05, 1.68, 2.28	Ø	0
Almdahl et al. 1993[88]	RCT	Patients	18	Low	5.04	Ø	−2
Conquer et al. 1996[89]	RCT	Healthy	24	Low	1.62	Ø	5
Conquer et al. 1999[90]	RCT	Healthy	20	Low	3	Ø	6
Demke et al. 1988[91]	RCT	Patients	31	Low	1.7	Ø	3
Donnelly et al. 1992[92]	RCT	Patients	16	Low	1.08	Ø	3
Gajos et al. 2011[93]	RCT	Patients	54	Low	0.84	Ø	−1
Goodfellow et al. 2000[94]	RCT	Patients	28	Low	1.7	Ø	0
Grundt et al. 2003[95]	RCT	Patients	300	Low	0.882	Ø	−2
Hagve et al. 1993[96]	RCT	Healthy	16	Low	5.1	Ø	−4
Haines et al. 1986[97]	RCT	Patients	41	Low	4.6	Ø	−2
Hellsten et al. 1993[98]	RCT	Healthy	41	Low	2	Ø	−1
Montegaard et al. 2010[99]	RCT	Patients	8	Low	0.74, 3.84	Ø	−3
Neff et al. 2011[100]	RCT	Healthy	49	Low	2	Ø	0

Table 1. Continued

Reference	Study type[1)]	Target	Subject No.	Purity[2)]	Dose (g)	Result[3)]	Quality score
Nilsen et al. 1991[101)]	RCT	Patients	20	Low	5.04	Ø	−1
Poppitt et al. 2009[102)]	RCT	Patients	102	Low	1	Ø	2
Prisco et al. 1994[103)]	RCT	Healthy	20	Low	3.44	Ø	3
Saifullah et al. 2007[104)]	RCT	Patients	27	Low	0.671	Ø	6
Sanders et al. 2011[105)]	RCT	Healthy	367	High	0.45, 0.9, 1.8	Ø	7
Sirtori et al. 1992[106)]	RCT	Patients	12	Low	4.5	Ø	−1
DeCaterina et al. 1990[107)]	Non-RCT	Patients	30	Low	4.3	Ø	−1
Din et al. 2008[108)]	Non-RCT	Healthy	28	Low	0.7	Ø	−1
Nelson et al. 1997[109)]	Non-RCT	Healthy	12	Low	6	Ø	−4
Boberg et al. 1992[110)]	RCT	Patients	14	Low	3	Ø	0
Park et al. 2009[111)]	RCT	Healthy	158	Low	0.135, 0.27, 0.54	Ø	0
Brox et al. 2001[112)]	RCT	Healthy	120	Low	2.6, 3.3	+	3
Brox et al. 1983[113)]	RCT	Patients	17	Low	30 mL	+	−2
Hwang et al. 1997[114)]	RCT	Healthy	32	Low	9	+	4
Hwang et al. 1997[114)]	RCT	Healthy	36	Low	6, 15	+	4
Gajos et al. 2010[115)]	RCT	Patients	63	High	0.84	Ø	3

1) RCT: randomized clinical trial 2) Low: purity < 90%, high: purity ≥ 90% 3) +: significant improvement in blood flow-related biomarkers, Ø: no significant improvement in blood flow-related biomarkers

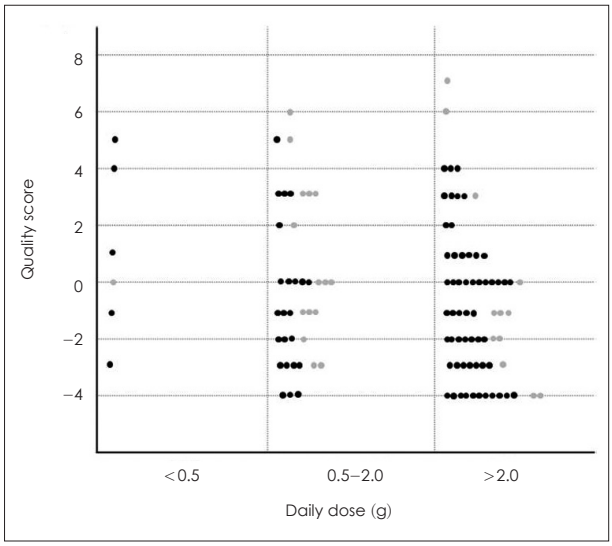

Fig. 3. Effects of omega-3 fatty acids on improvement of blood flow according to daily dose (●, significant improvement in the blood flow-related biomarkers; ●, no significant improvement in the blood flow-related biomarkers).

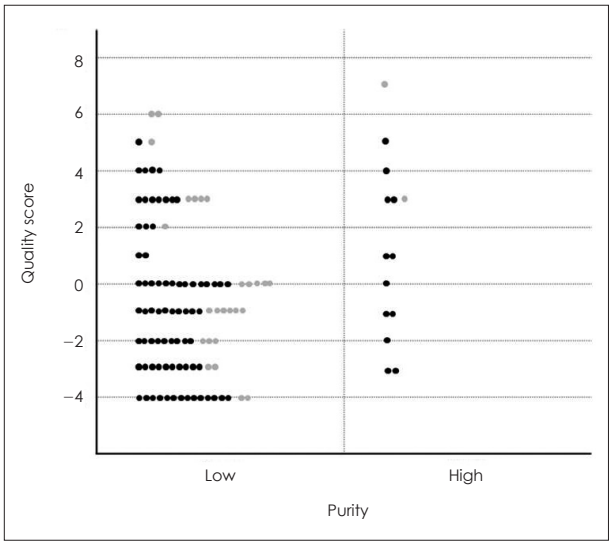

Fig. 4. Effects of omega-3 fatty acids on improvement of blood flow according to purity (Low: purity <90%; high: purity ≥ 90%; ●, significant improvement in the blood flow-related biomarkers; ●, no significant improvement in the blood flow-related biomarkers).

재평가 이후 출판된 연구들의 결과

오메가-3 지방산 함유유지의 건강기능식품 개별인정등록 이후에 출판된 연구 결과를 검토한 결과 2007년 이후 발표된 연구는 총 21건 (2007년 2건, 2008년 2건, 2009년 5건, 2010년 4건, 2011년 6건, 2012년 2건)[11,28-30,36,43,62,64,65,69,75,82,93,99,100,102,104,105,108,111,115]으로 이 중 12건의 연구 (765명)[11,28-30,36,43,62,64,65,69,75,82]에서 통계적으로 유의한 혈행개선 효과가 나타났으며 ($p < 0.05$), 9건의 연구 (856명)[93,99,100,102,104,105,108,111,115]에서는 개선효과가 관찰되지 않았다.

고 찰

건강기능식품의 기능성은 근거중심평가방법에 의해 평가시점에서의 모든 연구결과들을 종합하여 평가한다. 체계적 고찰방법이라고도 불리는 이 방법은 연구자의 편견이나 견해를 최대한 배제하여 좀 더 객관적이고 정확하게 현재까지의 연구결과들을 종합할 수 있다는 장점이 있다. 하지만 체계적 고찰방

법에 의해 평가되는 경우에도 평가된 시점 이후 새로운 과학적 증거들이 보고된다면 이에 기반한 재평가가 다시 수행되어야 할 것이다. 따라서 본 연구에서는 오메가-3 지방산 함유유지의 혈행개선 기능성을 재평가하기 위해 식약청에서 기능성 평가에 사용하고 있는 방법을 인체적용시험의 평가에 적합하도록 일부 보완한 체계적인 고찰 방법으로 재평가를 실시하였다. 문헌검색을 통해 총 112건의 연구를 선별하였고 각각의 연구에 대하여 질평가를 수행하였다. 질평가는 피험자, 시험디자인, 혼동요인, 순응도, 표준화된 시험물질 사용 여부, 측정한 바이오마커, 통계분석 방법의 항목에 대해 구분한 후 실시하였다. 개별평가에 따라 질평가 점수가 낮았던 52건[24,55,116-165]의 연구는 이후의 평가에서 제외되었다. 질평가 점수가 낮았던 연구들은 대부분 피험자의 선정/제외 기준에 대한 설명이 없거나, 무작위배정이 아니거나, 기초 식이조사를 실시하지 않은 등 시험 설계와 관련하여 중요한 정보가 기재되어 있지 않은 연구들 이었다

총 112건 연구 중 84건[8-18,20-79,81-86,112-114]에서 유의한 혈행개선 효과가 확인되었으며 피험자 수로 환산하면 총 5,804명의 피험자 중 2/3가 넘는 3,910명의 연구에서 오메가-3 지방산 함유유지 섭취로 유의한 혈행개선 효과가 나타난 것으로 평가되었다 ($p < 0.05$). 유의하게 개선된 바이오마커를 보면 bleeding time, platelet adhesion, platelet aggregation, thromboxane A2, plasma fibrinogen level, platelet count 등으로 확인되었다. 또한 건강인을 대상으로 한 60건의 연구를 분석한 결과에서는 2/3 이상인 48건의 연구 결과에서 유의한 혈행개선 효과를 보임이 확인되었다.

오메가-3 지방산의 일일 섭취량은 0.1~15 g으로 유의한 개선효과를 보인 연구들을 보면 건강기능식품공전에서 제시된 섭취량 기준 (0.5~2 g)에 포함되는 연구가 23건 (1,499명), 기준 보다 낮은 경우가 5건 (114명), 기준보다 높은 경우가 56건 (2,297명)[9,13,15-18,20-24,26,27,29,31-35,37,38,40,43-46,48,50,51,53,54,56,59,60,63,66,67,70,71,73-75,77,79-81,83-86,112-114]이었다. 오메가-3 지방산 함유유지의 순도에 따라 층화분석한 결과 저순도 (low purity) 오메가-3 지방산 함유유지를 사용한 98건의 연구 중 72건에서 유의한 결과가 관찰되었으며, 고순도 (high purity) 함유유지를 사용한 14건의 연구 중 12건에서 유의적인 개선효과가 나타났다.

오메가-3 지방산 함유유지가 건강기능식품으로 인정받은 이후에 출판된 논문들만을 분석한 결과에서도 총 21건[11,28-30,36,43,62,64,65,69,75,82,93,99,100,102,104,105,108,111,115] 중 12건의 연구[11,28-30,36,43,62,64,65,69,75,82]에서 통계적으로 유의한 혈행개선 효과가 나타났으며, 개선효과가 없었던 연구를 보면 시험식품을 단회투여한 연구가 1건,[99] 혈행개선에 적합하지 않은 대상자에게서 효과를 확인한 연구가 3건,[93,102,104] 대상자의 특성을 파악할 수 없는 연구가 1건,[115] 피험자들의 식이조절이 잘 이루어지지 않은 연구가 3건[83,102,111]이었다. 이들 연구들은 본 연구에서 실시하는 오메가-3 지방산 함유 유지의 혈행개선 기능 재평가 결과에 영향을 주지는 않았으나 오메가-3 지방산 함유유지의 혈행개선 기능성에 대한 일관성을 약화시켰으므로 향후 연구 결과 추이를 지켜볼 필요가 있을 것으로 판단된다.

요약 및 결론

오메가-3 지방산 함유유지의 혈행개선 기능성을 건강기능식품 재평가 기준에 맞추어 체계적 고찰을 실시하였다. 2012년 5월 기준 DB 검색을 통해 4,486건의 자료를 수집하여, 선정/제외 기준에 따라 선별한 결과 총 112건의 연구가 평가되었다. 112건 (5,804명) 중 84건 (3,910명)의 연구에서 통계적으로 유의한 개선 효과 나타났으며 ($p < 0.05$), 일일 섭취량은 0.1~15 g으로 공전에서 제시되어 있는 섭취량 (0.5~2 g) 기준을 포함하였다. 건강인을 대상으로 한 60건의 연구를 검토한 결과 48건의 연구에서 유의한 개선 효과를 보였다. 이들 문헌 중 건강기능식품 개별인정 등록 후 발표된 연구는 21건으로서 종합평가에 의하면 오메가-3 지방산 함유유지 섭취는 혈행개선 기능성을 나타낼 수 있는 것으로 판단되었다. 따라서 현재시점에서 건강기능식품인 오메가-3 지방산 함유유지의 혈행개선 기능성은 인정될 것으로 판단되나 일부 연구에서 개선효과가 없는 것으로 보고되고 있으므로 향후 연구결과 추이를 지속적으로 지켜볼 필요가 있을 것이다.

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