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REVIEW ARTICLE

Eicosapentaenoic Acid and Docosahexaenoic Acid in Endurance Performance and Cardiovascular Function

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PURPOSE: Fish oil contains omega-3 fatty acids, such as eicosapentaenoic acid (EPA; 20:5 n-3) and docosahexaenoic acid (DHA; 22:6 n-3). Consumption of EPA and DHA has been expected to improve fatigue recovery, endurance performance, antioxidant production, and anti-inflammatory responses. Therefore, this review aimed to evaluate the effects of omega-3 fatty acid on endurance performance as evaluated by human and animal studies and summarizes its effects on cardiovascular and endothelial functions.

METHODS: This review summarized the effects of EPA and DHA supplementation on the maximum oxygen uptake, exercise economy, muscle endurance performance, and cardiovascular and endothelial functions.

RESULTS: Effects of EPA and DHA supplementation on the maximum oxygen uptake are controversial. However, it has been suggested to improve the exercise economy and make the continuation of exercise easier. EPA and DHA supplementation could also improve endurance performance in the peripheral muscles. In addition, they may improve cardiovascular and vascular endothelial functions at rest and have positive effects on the heart rate, stroke volume, and cardiac output during a submaximal exercise.

CONCLUSIONS: This review concluded that EPA and DHA are considered effective in improving endurance performance in the peripheral muscles and cardiovascular function.

Key words: Nutritional supplementation, Endurance performance, Endothelial function, ω3, n-3, Unsaturated fatty acids

INTRODUCTION

Nutritional intake not only helps in improving and maintaining athletic performance, but also prevents exercise fatigue and promotes recovery from exhaustion. However, points regarding its actual effects and related mechanisms including the optimal dose, duration, and timing remain to be elucidated. Omega-3 fatty acids belong to the n-3 polyunsaturated fatty acid family and contain eicosapentaenoic acid (EPA; 20:5 n-3), docosahexaenoic acid (DHA; 22:6 n-3), α-linolenic acid, stearidonic acid, and docosapentaenoic acid. Omega-3 fatty acids first garnered attention when the heart disease rate became markedly low in the Greenland Eskimos, who consumed large amounts of these fatty acids [1,2]. Since then, many studies have been published, stating EPA and DHA are mainly found in fish oil and effective supplements in protecting the cardiovascular function, lowering blood pressure, and improving depression and cognitive function [3-11]. Regarding its involvement with exercise performance, EPA and DHA have been shown to improve fatigue recovery and endurance performance, as well as to maintain immune function [5,12,13]. Although there is no consensus among researchers regarding some points, EPA and DHA may possibly improve the exercise performance and cardiac function. This review focuses on the effects of EPA and DHA on endurance performance and cardiovascular function as evaluated by human and animal experiments.

1. EPA and DHA for endurance performance (Table 1)

EPA and DHA supplementation has been confirmed to alter the composition of red blood cells (RBCs) as well as the cell membrane in the myocardium and skeletal muscles in both humans and animals [14-16].

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Table 1. Summary of the effects of EPA/DHA supplementation on endurance performance and cardiovascular function

Reference (yr)	Population (age)	Dose (per day)	Duration	Exercise	Outcome
Raastad et al. (1997)	28 well- trained male soccer players (18 to 35 yr)	1.6 g EPA and 1.0 g DHA	10 weeks	Two trials on the treadmill to determine VO_{2max}, anaerobic threshold and running performance	VO_{2max} – Anaerobic threshold – Running performance –
Peoples et al. (2008)	16 trained cyclists (23.2 ± 1.2 yr)	0.80 g EPA and 2.4 g DHA	8 weeks	Peak O_2 consumption tests and sustained submaximal exercise test at 55% peak workload on a electronically braked	HR + VO_{2max} – Rate pressure product +
Żebrowska et al. (2015)	13 elite male cyclists (23.1 ± 5.4 yr)	0.66 g EPA and 0.44 g DHA	3 weeks	The regular cycling training and the mean individual monthly training volume was 655 ± 53 km	HR – Systolic blood pressure + Diastolic blood pressure – VO_{2max} + VO_2 +
Kawabata et al. (2014)	20 recreational male (Fish oil group: 23 ± 1 yr, Placebo group: 23 ± 0 yr)	0.914 g EPA and 0.399 g DHA	8 weeks	30-minute cycling exercise at 2-mM work load, followed by 30 minutes of cycling exercise at 3-mM work load, with a 10 minutes rest between the two sessions	HR – VO_{2max} - VO_2 + Ventilatory volume –
Ochi et al. (2019)	16 healthy male (EPA group: 20.1 ± 0.4 yr, placebo group: 20.5 ± 0.5 yr)	0.60 g EPA and 0.26 g DHA	8 weeks	Elbow flexor concentric contractions (6 sets of maximal 5 repetitions at a 30°/sec using the Biodex isokinetic dynamometer)	Peripheral muscle performance +
Clark et al. (2016)	14 health earlier males and females (25.0 ± 0.5 yr), 15 elderly males and females (63.5 ± 1.7 yr)	0.90 g EPA and DHA	12 weeks	15-second bouts of isometric handgrip at 10%, 30%, 50%, and 70% maximal voluntary contraction	Beat-to-beat systolic – Arterial blood pressure + HR –
Delodder et al. (2015)	4 healthy males and 4 healthy females (23 to 24.5 yr)	Intravenous administration; 0.12 g/kg EPA and 0.11 g/kg DHA, oral supplementation; 0.12 g EPA and 0.333 g DHA	Intravenous administration; 3 hours, Oral supplementation; 3 days	4 minutes at 50 W, the workload was increased by 25 W steps every 2 minutes. The test could be stopped voluntarily, or when the pedaling frequency could not be sustained or reaching 20 on the Borg scale	HR + Maximal power output + Peak blood lactate +
Ninio et al. (2008)	46 sedentary, overweight (BMI > 25 kg/m^2) adults with additional risk factors for CVD (25 to 65 yr)	0.36 g EPA and 1.56 g DHA	12 weeks	20-minute moderate walking speed on an electronic treadmill	HR variability + HR +
Logan and Spriet (2015)	24 health elderly females (66 ± 1 yr)	2.0 g EPA and 1.0 g DHA	12 weeks	30-minute low intensity cycling exercise	Resting metabolic rate + Energy expenditure + Rate of fat oxidation + Triglyceride + Timed Up and Go Test + Grip Strength - VO_2 + HR +
Buckley et al. (2009)	29 professional Australian football league players (Fish oil group: 21.7 ± 1.0 y, Placebo group: 23.2 ± 1.1 yr)	0.36 g EPA and 1.56 g DHA	5 weeks	A treadmill run to exhaustion	HR + Time to exhaustion –
Walser and Stebbins (2008)	21 healthy males and healthy females (37 ± 3 yr)	3.0 g EPA and 2.0 g DHA	6 weeks	20-minute pedaling at workload was increased by 25 W every 2 minutes on a recumbent bicycle ergometer	Stroke volume + Cardiac output + Systemic vascular resistance +
Macartney et al. (2014)	39 healthy males (18 to 40 yr)	0.14 g EPA and 0.56 g DHA	8 weeks	10-minute submaximal cycling at 125 W, 6 × 30 second Wingate cycling sprints/150 second recovery, and 5 minutes work capacity trial	Mean exercise HR+ Improved HR recovery + Peak HR –

(*Continued to the next page*)

Table 1. Continued

Reference (yr)	Population (age)	Dose (per day)	Duration	Exercise	Outcome
O'Keefe et al. (2006)	18 white male with a history of myocardial infarction and ejection fractions (67.8 ± 6.5 yr)	0.225 g EPA and 0.585 g DHA	4 months	Subjects were in the supine position for 8 minutes, followed by 8 minutes of standing and 60 minutes of sitting at rest	HR + Stroke volume + HR variability + HR recovery +
Da Boit et al. (2015)	37 healthy male and female, (25.8 ± 5.3 yr)	0.24 g EPA and 0.12 g DHA	6 weeks	Cycling time trial to fixed (70% of Wmax, 80 rpm)	HR – VO_2 –
Gray et al. (2012)	16 healthy male (24.0 ± 23.8 yr)	1.3 g EPA and 0.30 g DHA	6 weeks	1-hour cycling (70% VO_{2max})	HR – VO_2 –
Rontoyanni et al. (2012)	22 healthy males (23.0 ± 3.6 yr)	EPA group: 4.7g EPA and 1.1g DHA DHA group: 0.7g EPA and 4.7g DHA	1 time	12-minute multi-stage exercise stress test of moderate intensity on a programmable electrically braked cycle ergometer	Blood pressure – Cardiac output – Systemic vascular resistance + Stroke volume – HR –
Walser et al. (2006)	13 healthy males and females (26 to 57 yr)	3.0 g EPA and 2.0 g DHA	6 weeks	Two 90-second periods of handgrip exercise at 30% MVC and a rate of one contraction per second	Brachial artery diameter + Blood pressure – HR –

It has been demonstrated that 12 weeks of omega-3 fatty acid intake (EPA: 2.4 g/day; DHA: 1.2 g/day) increased the RBC deformability [16]. Because increased RBC deformability elevates oxygen supply through peripheral circulation to the skeletal muscles, it is thought to improve endurance performance [17]. Accordingly, EPA and DHA supplementation is assumed to improve endurance performance.

Raastad et al. [18] investigated male soccer players in a soccer league in Norway and found that intake of 1.6 g/day of EPA and 1.0 g/day of DHA for 10 weeks resulted in no change in the maximum oxygen uptake (VO_{2max}). Moreover, male cyclists who trained on a daily basis took 0.8 g/day of EPA and 2.4 g/day of DHA for 8 weeks, but the VO_{2max} did not increase [19]. Meanwhile, a recent study of elite male cyclists (VO_{2max} = 69.8 ± 4.9 mL·kg^{-1}·min^{-1}; mean individual monthly training volume = 655 ± 53 km) found that intake of 0.66 g/day of EPA and 0.44 g/day of DHA for 3 weeks resulted in a significant increase in the VO_{2max} [13]. In another study, 20 young untrained males were divided two groups. One group consisted of 10 subjects who ingested 0.914 g/day of EPA and 0.399 g/day of DHA for 8 weeks and another group of 10 subjects who ingested placebos containing medium-chain triglycerides. Their VO_{2max} was measured before and after supplement intake. The results indicated no difference in the VO_{2max} between the two groups [20]. The effects of EPA and DHA supplementation in improving the VO_{2max} are unclear based on these results to date.

On the other hand, EPA and DHA supplementation may have a role for exercise economy during exercise. EPA and DHA supplementations reduced oxygen consumption in skeletal muscle without changing the muscle work [21]. During steady-state exercise, submaximal oxygen uptake, an indicator of energy supply, is affected by both cardiac functions (cardiac output and oxygen carrying capacity) and skeletal muscle function (oxygen use by working muscle) [22,23]. Therefore, improvement of exercise economy by EPA and DHA supplementations could lead to improvement of the exercise economy of the whole body during submaximal exercise. In addition, exercise economy has been demonstrated to be correlated with endurance performance [24]. Kawabata et al. [20] tested the oxygen uptake under the submaximal exercise with the same lactic acid conditions and showed that the group that consumed EPA and DHA had less oxygen uptake during exercise than those in the placebo group [20]. Furthermore, oxygen uptake was negatively correlated with increased RBCs in this study. Thus, it has been suggested that EPA and DHA intake was related with increased RBCs to improve exercise economy. Moreover, in a group that consumed EPA and DHA, the rating of perceived exertion during exercise decreased [20]. Thus, EPA and DHA intake seemed to improve exercise economy and facilitated easy continuation of exercise. In fact, Huffman et al. [25] conducted a study on patients who consumed 0.3 g/day of EPA and 0.2 g/day of DHA for 4 weeks before a running exercise at 60% VO_{2max}. The results demonstrated that the exercise time until exhaustion in the EPA and DHA group was longer than that in the placebo group. Thus, although EPA and DHA intake may have limited effects for the maximum oxygen uptake, it is still effective in improving exercise economy and perceiving exertion during exercise.

The effects of EPA and DHA intake on endurance performance in

peripheral muscles have only been investigated in animals. It showed that three bouts of electrical muscle contractions (10 minutes) for the ankle plantar flexor muscles with 30-minute intervals inhibit the muscle force deficit with the 8-week ingestion of EPA and DHA compared with that of saturated fatty acid or omega-6 fatty acid [21]. Furthermore, the recovery rate in the muscle force between one and three bouts was significantly higher in the group that consumed EPA and DHA [21]. In addition, oxygen consumption during exercise was smaller in the EPA and DHA group than that in other groups [21]. These results suggest that one of the mechanisms of endurance performance improvement with EPA and DHA is caused by reduction of oxygen cost for muscle contraction (oxygen availability). However, no investigations have examined the effects of EPA and DHA intake on local muscle endurance in humans. Therefore, their effects on muscle endurance performance of the elbow flexors after consuming 0.6 g/day of EPA and 0.26 g/day of DHA for 8 weeks were recently verified. Our results showed that the decrease in work output for EPA and DHA group during muscle contractions are lower than that in the placebo group [26] (Figure 1). Since EPA and DHA supplementations reduce oxygen consumption in skeletal muscle [21], we speculate that saving oxygen consumption plays an important role for peripheral muscular performance. Further studies should investigate to clarify the mechanism regarding EPA and DHA supplementation on muscular performance. Accordingly, although the effects of EPA and DHA supplementation in improving the VO_{2max} are unclear, EPA and DHA supplementation appears to improve endurance performance in the peripheral muscles.

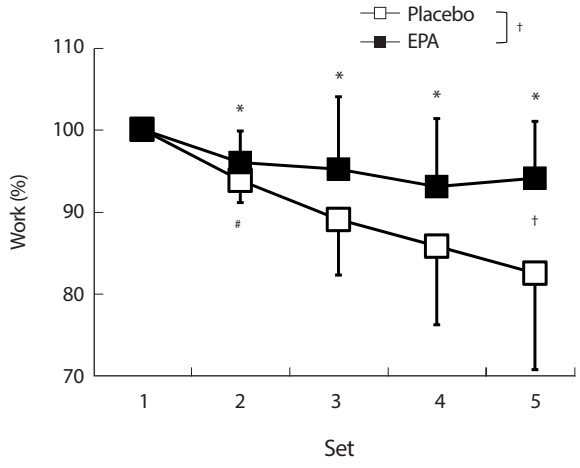

Fig. 1. Changes (mean±SD) in work output over five sets of six maximal concentric contractions in placebo and EPA group. †(p<.05); a significant difference between groups, #(p<.05); a significant difference from first set in EPA group, *(p<.05); a significant difference from first set in placebo group (data are from Ochi et al., 2019).

2. EPA and DHA for cardiovascular function (Table 1)

EPA and DHA intake has been clarified to improve the cardiovascular function [4,27]. In particular, previous reports have found that EPA and DHA supplementation affects the heart rate (HR) [28-30]. Logan and Sprient [27] reported that elderly individuals (aged 60-74 years) who took 2.0 g/day of EPA and 1.0 g/day of DHA for 12 weeks had decreased HR at rest. Similarly, they showed that Australian football players who took 0.36 g/day of EPA and 1.56 g/day of DHA for 5 weeks had decreased HR at rest and during a submaximal exercise [9]. Walser and Stebbins [31] found that trained subjects who took 3.0 g/day of EPA and 2.0 g/day of DHA for 6 weeks had increased stroke volume and cardiac output during a 20-minute cycling (starting from 25 W and increasing by 25 W every 2 minute). Therefore, an increased stroke volume and cardiac output seem to play a role in decreasing HR due to EPA and DHA intake. Bicycle pedaling exercise with 0.14 g/day of EPA and 0.56 g/day of DHA for 8 weeks has been shown to immediately improve the HR recovery [12]. Similarly, O'Keefe et al. [32] found that patients with myocardial infarctions and depressed ejection fractions improved post-exercise HR recovery with 0.225 g/day of EPA and 0.585 g/day of DHA daily for 4 months. Conversely, EPA and DHA intake exhibited no changes in HR at rest or during a submaximal exercise [33-35]. Thus, although improvement of cardiac function can be assumed because of EPA and DHA intake, factors such as intake volume, period, and exercise load should be investigated in more detail in the future.

Regarding the effects of EPA and DHA intake on the vascular function, 3.0 g/day of EPA and 2.0 g/day of DHA for 6 weeks increased the blood vessel diameter and vascular blood flow by gripping exercise at 30%MVC [36]. Hypertensive patients (systolic phase blood pressure: 138.7±5.0 mmHg) who took 0.9 g/day of EPA and 1.5 g/day of DHA for 24 months had decreased systolic phase blood pressure by 2.6±2.5 mmHg [37]. In addition, a meta-analysis verifying the effects of EPA and DHA intake on the vascular endothelial function according to flow-mediated dilatation (FMD) testing revealed improvement by 1.4% [38]. However, whether EPA and DHA supplementation can be used to enhance muscular endurance remained unclear. Therefore, we recently investigated the effects of 8-week supplementation of 0.6 g/day of EPA and 0.26 g/day of DHA on the muscular fatigue caused by numerous muscle contractions. The results show that DHA and EPA supplementation did not attenuate the reduction of muscle work output in response to muscle con-

tractions.

In addition, prolonged sitting impairs leg endothelial function, and this impairment is thought to be mediated by a sustained reduction in FMD. An increase in nitric oxide (NO) bioavailability appears to be a proposed mechanism by which EPA and DHA supplementation enhances endothelial function [39-43]. Therefore, we recently examined whether EPA (0.6 g/day) and DHA (0.26 g/day) supplementation could be an effective strategy for preventing vascular dysfunction of sitting. Specifically, we rationalized that improved NO bioavailability by EPA and DHA supplementation would preserve endothelial function. The results exhibited that EPA and DHA supplementation is not effective in preventing the detrimental effects of prolonged sitting on the leg endothelial function [44]. Thus, EPA and DHA supplementation has positive effects for cardiovascular function at rest in patients and during a submaximal exercise, and these effects for young healthy subjects may be limited.

CONCLUSION

In conclusion, no consensus has been reached regarding whether EPA and DHA supplementation can effectively increase the maximum oxygen uptake; however, it may improve the exercise economy and perceived exertion during exercise. In addition, EPA and DHA may improve cardiovascular and vascular endothelial functions at rest and have positive effects on the HR, stroke volume, and cardiac output during submaximal exercise.

As mentioned above, EPA and DHA may be summarized to have several positive roles during exercise performance. Unfortunately, the optimal periods and dosage of EPA and DHA remain unclear. Therefore, appropriate conditions, such as age, sex, exercise experience, and diseases, should be considered. EPA and DHA intake for 30-60 days may result in human myocardial membrane uptake [45] and for 3-4 months increased RBC deformability in patients with angina and claudication [46,47]. Regarding the dosage, the amount of EPA and DHA should be limited to a total of 3 g/day for safety in humans according to the natural medicine comprehensive database [48]. Simopoulos mentioned that a majority of athletes, especially at the leisure level, should consume approximately 1 to 2 g/day of EPA and DHA as a general guideline. Otherwise, the suggested intake ratio between EPA and DHA of approximately 2:1 has been suggested to be beneficial for the overall health of an athlete [17,49]. In the future, the duration, doses, either EPA or DHA, or the synergistic effects of the simultaneous ingestion of both should be investigated in other interventions. Interestingly, recent studies reported that the positive relationship between EPA/DHA and muscle strength [50], muscle protein synthesis, enhanced rapamycin [51], peak torque development [52], and reduced eicosanoids and pro-inflammatory cytokines [53]. These recent findings may constitute basic data that could be useful for not only improving sports performance, but also improve clinical conditions and promoting health.

CONFLICT OF INTEREST

No conflicts of interest, financial or otherwise, are declared by the authors.

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