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Short Communication

The Effect of N-3 Polyunsaturated Fatty Acids on Lung Function and use of Medication in Athletes with Asthma. A Pilot Trial

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Abstract

Asthma is the most frequent chronic disease among young adults, not least in the western societies, with an even higher frequency among elite athletes. Asthma consists of airway inflammation and smooth muscle contraction, normally treated with anti-asthma therapy, some of which have side effects. n-3 LCPUFA in fish oil (FO) has anti-inflammatory effects, and some studies have shown clinical effects of FO on asthma. We aimed to study if FO has an anti-asthma effect in elite athletes with asthma.

The study was a randomized, double-blinded clinical trial. Ten elite athletes with a medical certificate allowing the use of asthma medication, age 15-46 years, were recruited among elite athletes supported by the Team Denmark Organization. All subjects had a positive mannitol test prior to enrollment. Depending on whether they used inhaled corticosteroids or not, the subjects were randomly assigned in pairs to either FO (2 g EPA and 1.3 g DHA) or soy oil capsules (SO) for 8 weeks. Change in forced expiratory volume (FEV_1) after exercise, NO excretion, sputum cell count and use of medication were measured before and after intervention.

There was a slight trend towards increased exercise-induced decrease in lung function, use of asthma medication and respiratory inflammation in the FO-group, but the changes were neither significant nor clinically relevant.

ABBREVIATIONS

FO: Fishoil; SO: Soyoil; PUFA: Poly-Unsaturatedfattyacids; N-3 LCPUFA: Long-Chain N-3 PUFA; SFA: Saturated Fatty Acids; MUFA: Mono-Saturated Fatty Acids; FEV_1: Forced Expiratory Volume In 1 Second

INTRODUCTION

Asthma is a chronic lung disease diagnosed in 7-11% of the adult population in Denmark [1] with a higher prevalence among elite athletes (16-20%) [2]. Inflammation and airway hyperresponsiveness are basal characteristics of asthma. The inflammation in asthma is in general a Th2 driven, dominated by eosinophilic granulocytes and mast cells, which when provoked release mediators inducing bronchoconstriction. However, in elite athletes the cellular inflammation tends to be more disperse with a variety of cells [3]. Persisting asthma is typically treated with regular inhaled corticosteroids as controller treatment and inhaled short-acting beta-2-agonistsas-needed reliever medication.

Long-chainpoly-unsaturatedn-3fattyacids(n-3LCPUFA)have anti-inflammatory effects, and several studies [4-6] have shown a beneficial effect of dietary n-3 LCPUFA on exercise-induced asthma, but no convincing effects have been demonstrated in chronic asthma. In two double-blinded, randomized trials with a cross-over design a significant improvement of the lung function in asthma provoked by exercise was found as well as a decreased

use of bronchodilating medicine after doses of eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) of about 5 g/day for three weeks [7,8]. Based on these results we wanted to investigate the effect of n-3 LCPUFA on the lung function after exercise in elite athletes with asthma.

MATERIALS AND METHODS

All athletes (113 athletes from 21 different sports) in the Danish national center for elite sports (Team Denmark) with a certificate to use asthma medications during competitions were invited to participate. Seventy-six (67 %) responded and 30 of these wanted to participate. Eighteen subjects were excluded due to a negative mannitol test, two changed their mind about participation, leaving 10 participants in the pilot study (Table 1).The athletes were from eight different sports: swimming (n=3), cycling (n=1), rowing (n=1), cross country running (n=1), handball (n=1), taekwondo (n=1), curling (n=1) and golf (n=1). All participants were found to have a positive mannitol test prior to enrollment, and continued their medication principles during the investigation.

Depending on whether they used inhaled corticosteroids or not, the subjects were randomly assigned in pairs to either fish oil (FO) (2 g EPA and 1.3 g DHA) or soy oil capsules (SO) for 8 weeks. Compliance was assessed by erythrocytecontent of n-3 LCPUFA [9,10] (Table 2) before and after the intervention.

Forced expiratory volume during 1 second (FEV_1) was measured before and 1, 3, 5, 7, 10, 15 and 20 minutes after an exercise test on a treadmill was performed at a speed of 9-16 km/h, 80-90% of maximal pulse and aimed at exhaustion after six-eight minutes, supervised by an experienced physiologist and in accordance with the standard at the Team Denmark Test Center. Time to exhaustion and maximal uptake of oxygen (VO_2-max) was used to measure performance. Plasma lactate was measured two minutes after the treadmill test. Fractionated exhaled nitric oxide (FeNO) was measured according to ATS/ERS recommendations with an NO analyser (NIOX MINO®, Aerocrine, Stockholm, Sweden) at a flow of 50 ml/s [11] before and after the intervention, but not in relation to the max-test. Sputum was induced by inhalation of increasing doses of hypertonic saline (3%, 4% and 5%) via an ultrasonic nebulizer (Easyneb II, Flaemnuova®, Italy) for three consecutive 7-minute periods after being pre-treated with 0.2 mg salbutamol [12].Antropometrics, amount of training and use of reliever medications was registered.

RESULTS AND DISCUSSION

Compliance was fairly good with an increase in all erythrocyte n-3 PUFA and a concomitant decrease in SFA, MUFA and n-6 PUFA in the FO-group (Table 2), but no convincing effects on the lung function were observed (Table 3). If any changes at all, the best results were observed in the control group (SO-group). We found no differences in FeNO or cytological variables related to inflammation between the two groups. Likewise, no differences were seen in relation to performance judged by VO_2-maxand p-Lactate after exercise, or the amount of training (Table 4). There was a slight reduction in the use of broncho-dilatator in the SO-group, but this was neither significant nor considered to be clinically relevant.

Table 1: Baseline characteristics of elite athletes with asthma treated with Soy-oil (SO) or Fish-oil (FO). Median and range. No significant differences between the groups.

	SO (n=5)	FO (n=5)
Age,yrs	21 (20-39)	25 (15-46)
Sex, M/F	2-Mar	1-Apr
BMI, kg/m^2	23.2 (20.8-24.2)	22.5 (20.0-25.2)
Atopics, n	4	2
Daily use of medications, n	3	3
Use of bronchodilators, number of doses/2 wks	12 (0-24)	0 (0-4)
Lung function (FEV_1),liter	4.6 (3.6-5.6)	3.9 (3.6-4.6)
Lung function (FEV_1, % of predicted)	95 (86-128)	94 (87-102)
Lung function (FVC), liter	5.5 (4.2-7.0)	5.5 (4.5-5.7)
Lung function (FVC, % of predicted)	97 (92-119)	108 (92-123)
EIB, n	2	2
↑ sputum eosinofiles(>1 %), n	3	4
↑ sputum neutrofiles(>35 %),n	2	4
FeNO, ppb	18.5 (11.1-119)	39.1 (14.5-104)
Training, hours/week	20.0 (20-25)	16.5 (8-26)
VO_2max, l/min	4.1 (3.7-5.3)	4.7 (3.9-5.3)
Max-heart rate, beats/min	183 (173-196)	194 (184-206)
Fish ingestion, g/day	30 (22-136)	29 (11-43)
n-3 LCPUFA ingestion, mg/day	835 (89-2105)	529 (305-944)

Abbreviations: BMI: Body Mass Index; FEV_1: Forced expiratory volume in 1sec; FVC: Forced vital capacity; EIB: Exercise-Induced bronchoconstriction; FeNO: Exhaled nitric oxide, ppb: Parts Per Billion; VO_2max: Maximal Uptake Of Oxygen; n-3 LCPUFA: Long-Chain Poly-Unsaturated N-3 Fatty Acids.

Table 2: Erythrocyte fatty acid composition in Soy-oil (SO) or Fish-oil (FO) treated elite athletes with asthma. Mean ± SD.

	FO(n=5)	SO (n=5)
SFA total (%)		
Before	39.8 ±3.4	40.7 ±1.8
After	36.3 ±3.3	38.2 ±2.7
Δ	-3.5 ± 2.2	-2.3 ± 1.5
MUFA total (%)		
Before	20.9 ± 0.8	21.4 ± 1.2
After	19.3 ± 0.6	20.0 ± 1.8
Δ	-1.5 ± 1.2	-1.3 ± 2.3
n-6 PUFA (%)		
Before	27.4 ± 2.4	25.9 ± 1.2
After	25.2 ± 3.3	28.1 ± 1.8
Δ	-1.9 ± 2.4	2.3 ± 0.9
n-3 PUFA (%)		
Before	7.8 ± 1.4	7.8 ± 1.3
After	15.0± 0.8	9.9 ± 3.3
Δ	7.0 ± 1.3	1.8 ± 2.5
EPA (20:5n-3) (%)		
Before	0.7 ±0.2	0.9 ± 0.4
After	3.7 ±0.2	1.4 ± 0.9
Δ	3.0 ± 0.3	0.4± 0.7
DHA (22:6n-3) (%)		
Before	4.5 ± 0.1	4.5 ± 0.9
After	7.4 ± 0.7	5.7 ± 1.8
Δ	2.7 ± 0.8	1.0 ± 1.5

Abbreviations: SFA: Saturated fatty acids; MUFA: Mono-Unsaturated Fatty Acids; n-6 PUFA: N-6 Poly-Unsaturated Fatty Acids; n-3 PUFA: N-3 Poly-Unsaturated Fatty Acids; EPA: Eicosapentaenoic Acid; DHA: Docosahexaenoic Acid.

Table 3: Exercise-induced changes in FEV_1 in elite athletes with asthma before and after the intervention with Soy-oil (SO) or Fish-oil (FO). Median (range).

	SO			FO		
	Before (n=5)	**After (n=4)**	**Δ (n=4)**	**Before (n=5)**	**After (n=4)**	**Δ (n=4)**
FEV_1 (time 0), liter	4.6	4.4	-0.1	3.9	4.1	0.2
	(3.6-5.6)	(3.5-5.6)	(-0.1-0.1)	(3.6-4.6)	(3.6-5.0)	(-0.2-0.7)
Minimum FEV_1 after exercise, litre	4	4.2	0.2	3.6	3.4	-0.1
	(3.1-4.9)	(3.4-5.6)	(-0.1-0.5)	(3.1-4.7)	(3.0-4.8)	(-0.2-0.1)
Exercise-induced decrease in FEV_1, litre	-0.4	-0.1	0.2	-0.3	-0.3	-0.1
	(-0.6 -0.1)	(-0.3-0.0)	(-0.1-0.5)	(-0.8-0.5)	(-1.6- -0.3)	(-0.8-0.0)
Difference FEV_1 %	-6.7	-2.6	3.2	**-7**	-6.9	-2.7
	(-13.9- -2.8)	(-4.9-0.0)	(-1.5-13.9)	(-27.4-1.1)	(-34-.0 -4.0)	(-13.5 -0.1)

Work test performed on a tread mill. Two of the participants were injured at the time of the test after the intervention. No significant changes found.
Abbreviations: FEV_1: Forced Expiratory Volume in the 1st second.

The dominating weakness in this study is the limited number of participants, but they were highly selected, and all had severe asthma. Even in a small sample like this, one would have expected an indication of an improvement, but if any, the indications pointed in the opposite direction. It was estimated that it would require convincing, positive effects of FO compared to SO in the next 16 patients entering the trial to reach a statistically significant positive effect of the fish-oil supplementation (Mann-Whitney rank-sum-test). Accordingly, we were not able to confirm the promising results by Mickelborough et al. [7,8].

CONCLUSION

We conclude that FO is unlikely to have a clinically relevant effect on asthma in elite athletes.

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Table 4: Performance on the tread-mill test in Soy-oil (SO) or fish-oil (FO) treated elite athletes with asthma. Median (range).

	SO			FO		
	Before (n=5)	**After (n=4)**	**Δ (n=4)**	**Before (n=5)**	**After (n=4)**	**Δ (n=4)**
Test-time, min	7.2	6.5	-0.2	7	6.5	-0.8
	(6.1-7.3)	(6.2-7.0)	(-1.1-0.7)	(5.4-9.1)	(6.2-7.1)	(-1.6- - 0.2)
VO_2max,l O_2/min	4.1	4.2	0.1	4.7	4.3 (n=3)	-0.2 (n=3)
	(3.7-5.3)	(3.8-5.1)	(-0.3-0.5)	(3.9-5.3)	(3.7-5.1)	(-0.5- -0.2)
p-Lactate, mmol/l	12.6	10.7	-0.8	10.3	8.9	-0.6
	(9.4-14.9)	(7.3-14.3)	(-2.1- -0.6)	(6.1-12.2)	(6.5-9.7)	(-2.5-0.4)
Weight, kg	73.4	68.2	1.1	69.8	70.6	-0.4
	(60.8-86.4)	(62.2-88.0)	(-0.1-1.6)	(60.6-80.3)	(61.3-77.3)	(-3.0-0.7)
FFM %	83.5	79	-0.7	87	85.6	0.3
	(73.3-89.4)	(71.5-89.8)	(-1.9-0.6)	(79.2-92.0)	(79.2-90.6)	(-1.4-1.3)
Training, h/wk	20.4	10.3	-5.6	10.6	8.8	-4.1
	(5.8-29.3)	(7.7-18.5)	(-20.3-2.7)	(4.9-25.6)	(4.7-12.9)	(-12.7-0.0)

No significant differences between the groups.
Abbreviations: FFM: Fat Free Mass

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