

Effect of omega 3 fatty acids on C-reactive protein and interleukin-6 in patients with advanced nonsmall cell lung cancer

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Abstract

This study investigated the anti-inflammatory effects of omega 3 fatty acids (O3FAs) for patients with advanced nonsmall cell lung cancer (ANSCLC).

A total of 137 patients with ANSCLC were included in this study. Of those, 77 patients underwent O3FA and were assigned to a treatment group, while 60 patients did not receive it, and were assigned to a control group. C-reactive protein (CRP), and interleukin (IL)-6 levels, as well as the levels of tumor necrosis factor-alpha (TNF α) and prostaglandin E2 (PGE₂) were checked. In addition, nutritional status and quality of life were also evaluated. All patients in the treatment group received a total of 6 weeks treatment.

After 6 weeks treatment, patients in the treatment group exerted better outcomes in CRP and IL-6, although no significant differences were found in nutritional status, as well as the quality, compared with patients in the control group.

The results of this retrospective study found that O3FA may change levels of CRP and IL-6, except the nutritional status and quality of life.

Abbreviations: ANSCLC = advanced non-small cell lung cancer, BMI = body mass index, CRP = C-reactive protein, ECOG = Eastern Cooperative Oncology Group, EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer quality of life questionnaire, FFM = fat-free mass, IL-6 = interleukin-6, MUAC = mid-upper arm circumference, O3FA = omega 3 fatty acids, PGE₂ = prostaglandin E2, TNF-a = tumor necrosis factor-a.

Keywords: advanced nonsmall cell lung cancer, effect, omega 3 fatty acids

1. Introduction

Lung cancer is the most leading cause of cancer mortality around the world.^[1–4] It has been reported that the 5-year survival rate of patients with lung cancer is about 15% for all stages, although patients at an earlier stage have a longer survival.^[5,6] Of all types of lung cancers, nonsmall cell lung cancer (NSCLC) is the most common type, and accounts for 80% of all lung cancers.^[4,7]

Presently, chemoradiotherapy is used as a first-line treatment for patients with NSCLC. It has promising efficacy, and also helps for the rehabilitation and recovery process in patients with this condition.^[8–10] Unfortunately, it is also accompanied with lots of toxicities, such as nausea, vomiting, poor appetite, and also

anorexia, anemia, and weight loss.^[8,11–13] In addition, such kinds of toxicities often lead to a poor nutritional status and quality of life.^[8] Moreover, it can also result in treatment-related morbidity and mortality.^[14] If this condition cannot be treated very well, it may result in cancer cachexia.^[15,16]

Several studies have reported that cancer cachexia is associated with anti-inflammatory factors, such as the levels of C-reactive protein (C-RP), interleukin-6 (IL-6), tumor necrosis factor-a (TNF-a), and prostaglandin E2 (PGE₂).^[17,18] It is also reported that omega 3 fatty acids (O3FAs) can treat such condition effectively.^[19–24] However, limited data are still available for O3FA in patients with NSCLC among Chinese population. In this retrospective study, we analyzed the effect and adverse events of O3FA in patients with NSCLC among Chinese population.

2. Materials and methods

2.1. Ethics

This study was approved by the Medical Ethical Committee of The First People's Hospital of Xiaochang. The written informed consent was obtained from all patients.

2.2. Design

This study was conducted at The First People's Hospital of Xiaochang between January 2015 and November 2016. A total of 137 patients with stage IIIA and IIIB NSCLC were included in this study. Of those, 77 patients received O3FA, and were assigned to a treatment group, while 60 patients did not receive O3FA, and were assigned to a control group. The clinical characteristics of all included patients are listed in Table 1. All patients in the treatment group received O3FA for a total of

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The author (s) of this work have nothing to disclose and have no conflicts of interest.

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Table 1
Characteristics of all included patients in both groups.

Characteristics	Treatment group (n=77)	Control group (n=60)	P
Age, y	63.8 (6.4)	62.9 (7.1)	.44
Sex			
Male	43 (55.8)	33 (55.0)	.92
Female	34 (44.2)	27 (45.0)	.92
BMI, kg/m ²	23.5 (2.1)	23.9 (2.4)	.31
Nutritional status			
Body weight, kg	67.2 (11.5)	70.1 (12.3)	.16
MUAC, mm	276.8 (31.4)	285.9 (34.6)	.11
FFM, kg	54.3 (7.7)	56.9 (8.1)	.09
Histology			
Squamous cell carcinoma	21 (27.3)	17 (28.3)	.89
Adenocarcinoma	56 (72.7)	43 (71.7)	.89
ECOG			
0	35 (45.5)	28 (46.7)	.90
1	42 (54.5)	32 (53.3)	.90
Stage of disease			
IIIa	46 (59.7)	35 (58.3)	.87
IIIb	31 (40.3)	25 (41.7)	.87
Karnofsky performance status	82.1 (10.9)	84.9 (11.4)	.15
Chemotherapy			
Cisplatin	27 (35.1)	21 (35.0)	.99
Cisplatin and docetaxel	46 (59.7)	37 (61.7)	.82
Cisplatin and bevacizumab	4 (5.2)	2 (38.6)	.60
Inflammatory parameters			
CRP, mg/L	13.5 (3.9)	12.7 (3.5)	.21
IL-6, mg/mL	10.5 (4.2)	11.3 (3.7)	.24
TNF- α , pg/mL	3.7 (1.5)	3.3 (1.2)	.08
PGE ₂ , mg/mL	15.8 (2.9)	16.5 (3.2)	.19
EORTCQLQC30	55.7 (22.4)	59.2 (24.3)	.40

Data are present as mean \pm standard deviation or number (%).

BMI=body mass index, CRP=C-reactive protein, ECOG=Eastern Cooperative Oncology Group, EORTC QLQ-C30=European Organization for Research and Treatment of Cancer quality of life questionnaire, FFM=fat-free mass, IL-6=interleukin-6, MUAC=mid-upper arm circumference, PGE₂=prostaglandin E₂, TNF- α =tumor necrosis factor- α .

6 weeks. All outcome measurements were analyzed before and after 6 weeks treatment.

2.3. Patients

All patients were between 20 and 75 years of age. All of them were eligible for chemoradiotherapy, and had adequate hematologic, renal, and liver function. Patients were excluded if they received surgery; had severe comorbidities; and were pregnancy or breastfeeding. In addition, the subjects were excluded if the cases had insufficient information, such as characteristics and outcome data.

2.4. Treatments

Patients in a treatment group received orally O3FA capsules [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] for a total of 6 weeks. The EPA 510 mg and DHA 200 mg were taken once daily throughout the period of whole chemoradiotherapy treatment. Patients in a control group did not receive O3FA intervention.

2.5. Outcomes

The outcome measurements included the plasma levels of CRP, IL-6, TNF- α , and PGE₂. We obtained the plasma and

erythrocytes by centrifuging venous blood at 3000g for 5 minutes at 4°C. It was performed by centrifuge J6M (Beckman, Palo Alto, CA). The samples were stored at -80°C until use. The levels of CRP, IL-6, TNF- α , and PGE₂ were measured by ELISA kits (R&D systems, Minneapolis, MN).

In addition, nutritional status and quality of life were also evaluated in this study. The nutritional status was measured by the body weight, mid-upper arm circumference (MUAC), and fat-free mass (FFM). The quality of life was also assessed by the European Organization for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30). This scale varies from 0 to 100, with a higher score indicating better quality of life. All outcomes were measured before and after 6 weeks treatment. Furthermore, any kinds of adverse events related to the treatment were also recorded in this study.

2.6. Statistical analysis

In this retrospective study, SPSS software (SPSS V.18.0; IBM Corp., Armonk, NY) was used to analyze all the outcome data. *t* test was used to analyze the continuous data between 2 groups. Chi-square test was used to analyze the dichotomous data between 2 groups. All *P* values were 2-sided at a significance of *P* < .05.

3. Results

The characteristics of all included patients in both groups are summarized in Table 1. The comparisons of all characteristic values did not significantly differ between the 2 groups (Table 1).

After 6 weeks intervention, patients who underwent O3FA found significant changes in CRP (*P* < .01, Table 2) and IL-6 (*P* < .01, Table 2), except the TNF- α (*P* = .19, Table 2) and PGE₂ (*P* = .31, Table 2), when compared with patients who did not receive it.

After 6 weeks treatment, patients who received O3FA neither enhanced the nutritious status (body weight, *P* = .44; MUAC, *P* = .13; and FFM, *P* = .19, Table 3), nor improved quality of life,

Table 2
Inflammatory parameters after 6 weeks treatment (change from baseline).

Outcome	Treatment group (n=77)	Control group (n=60)	Difference	P
CRP, mg/L	-2.2 (-5.7, -0.8)	9.4 (6.8, 11.3)	-11.5 (-14.6, -8.7)	<.01
IL-6, pg/mL	-4.1 (-7.4, -2.5)	5.8 (2.9, 8.0)	-9.8 (-12.6, -7.3)	<.01
TNF- α , pg/mL	1.8 (0.9, 2.7)	2.7 (1.1, 4.3)	-0.9 (-1.7, -0.3)	.19
PGE ₂ , pg/mL	-1.5 (-2.9, -0.4)	-0.7 (-1.4, -0.2)	-0.7 (-1.2, -0.2)	.31

Data are present as mean \pm standard deviation or number (%).

CRP=C-reactive protein, IL-6=interleukin-6, PGE₂=prostaglandin E₂, TNF- α =tumor necrosis factor- α .

Table 3
Nutritional status after 6 weeks treatment (change from baseline).

Nutritional status	Treatment group (n=77)	Control group (n=60)	Difference	P
Body weight, kg	1.5 (0.6, 2.7)	0.8 (0.3, 1.6)	0.7 (0.3, 1.1)	.44
MUAC, mm	12.1 (6.3, 17.4)	6.2 (3.0, 9.7)	6.0 (4.2, 7.7)	.13
FFM, kg	3.5 (1.9, 5.6)	1.8 (1.1, 3.2)	1.7 (1.2, 2.4)	.19

Data are present as mean and range.

FFM=fat-free mass, MUAC=mid-upper arm circumference.

Table 4**Comparison of quality of life after 6 weeks treatment.**

EORTC QLQ-C30	Treatment group (n = 77)	Control group (n = 60)
Difference from before treatment	15.7 (10.1, 26.8)	7.7 (2.4, 13.9)
<i>P</i>	<.01	.08
Difference between groups		8.1 (3.9, 12.0)
<i>P</i>		.38

Data are present as mean and range.

EORTC QLQ-C30=European Organization for Research and Treatment of Cancer quality of life questionnaire.

measured by EORTC QLQ-C30 ($P=.38$, Table 4), compared with patients who did not receive it.

As for adverse events, no treatment-related adverse events occurred in the treatment group. No death-related therapy occurred in the treatment group.

4. Discussion

Patients with lung cancer often suffer from cancer cachexia.^[25] It has been found that this condition (often manifested with weight loss, decreased lean body mass, and hypermetabolism) is often associated with some inflammatory factors. Furthermore, these factors often consisted of CRP, IL-6, TNF- α , and PGE₂.^[17]

Although several studies have investigated the anti-inflammatory effects of O3FA for patients with lung cancer, the results are still inconsistent.^[21,26,27] One study found that continual assumption of EPA and DHA can benefit the cachectic therapy in patients with lung cancer.^[21] The results of other 2 studies demonstrated that O3FA may beneficially impact nutritional status, quality of life, as well as the physical activity in patients with NSCLC receiving multimodality treatment.^[26,27]

The results of this study are partly consistent with the previous studies.^[21,26] In this study, we found that O3FA can significantly change the serum levels of CRP and IL-6, which is consistent with the previous study. However, the results of this study did not show better outcomes in the improvement of nutritional status and quality of life.

This study has following limitations. First of all, this study collected the patient cases from 1 center only, which may affect the generalization of these results to other hospitals. Second, the outcome measurements may be not comprehensive in this study, especially for the nutritional status, and quality of life assessment, because the data analysis of the results was only based on the current available data. Third, the duration of the treatment period may be insufficient, which may also affect the results of this study. Future studies should avoid these limitations.

5. Conclusion

The results of this study demonstrated that the O3FA may impact the serum levels of CRP and IL-6. However, it may be not help to improve nutritional status and quality of life in patients with ANSCLC.

Author contributions

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