# Efficacy of Epadel® (comprising not less than 98% eicosapentaenoic acid ethyl ester) for fibromyalgia

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本文

# Efficacy of Epadel® (comprising not less than 98% eicosapentaenoic acid ethyl ester) for fibromyalgia

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**Abstract** This study examined the efficacy of Epadel® (comprising not less than 98% eicosapentaenoic acid ethyl ester) for fibromyalgia (FM). Dosage of Epadel ® was gradually increased up to 2700 mg/day in patients with FM. During the administration of Epadel®, there were no new medicines added to the regimen and there were no changes in the dose of any other medication being co-administered. Subjective pain before administration of Epadel® was regarded as 10, and patients were then asked to estimate subjective pain after the administration of Epadel®. Twenty-nine patients with FM consisted of 26 females and 3 males ranging from 23 to 78 years of age (average: 48.1±14.9 years). Five patients (17.3%) discontinued medication due to adverse effects. The mean of total dosing period of Epadel ® was 39.3±19.4 days (range 21-119 days) in 24 patients who did not discontinue medication due to adverse effects. The mean dosing period of Epadel® 2700 mg/day was 17.8±7.8 days (range 7-39 days). Epadel® did not reduce pain in 13 patients (44.9%). Of the 13 patients, 2 suffered from adverse effects (weakness and fatigue). It reduced subjective pain in 11 patients (37.9%). Subjective pain after administration of Epadel® became 1 in two patients, 3 in two patients, 5 in one patient, 8 in four patients, and 9 in two patients. Of the 11 patients, 1 suffered from adverse effect (thirst sensation). Of the 11 patients, maximum dosage was 1800 mg/day in 1 patient.

## INTRODUCTION

Omega-3 fatty acids including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) reduced pain and fatigue in 12 patients with fibromyalgia (FM) in an uncontrolled study[1]. Ethyl icosapenpentate (EPA-E) is an EPA ethyl ester and it is mainly de-

esterified in the body. I examined efficacy of Epadel ® (comprising not less than 98% EPA-E) for FM.

**METHODS**

FM was diagnosed based on the 1990 criteria of the American College of Rheumatology[2]. Dosage of Epadel ® was gradually increased up to 2700 mg/day in patients with FM. During the administration of Epadel ®, there were no new medicines added to the regimen and there were no changes in the dose of any other medication being co-administered. Subjective pain before administration of Epadel ® was regarded as 10, and patients were asked estimated subjective pain after administration of Epadel®.

**RESULTS**

Twenty-nine patients with FM consisted of 26 females and 3 males ranging from 23 to 78 years of age (average: 48.1±14.9 years). Five patients (17.3%) discontinued medication due to adverse effects (weakness, nausea and dizziness, feeling of unwellness, diarrhea, and nausea). The mean of total dosing period of Epadel ® was 39.3±19.4 days (range 21-119 days) in 24 patients who did not discontinue medication due to adverse effects. The mean dosing period of Epadel ® 2700 mg/day was 17.8±7.8 days (range 7-39 days). Epadel® did not reduce pain in 13 patients (44.9%). Of the 13 patients, 2 suffered from adverse effects (weakness and fatigue). It reduced subjective pain in 11 patients (37.9%). Subjective pain after administration of Epadel ® became 1 in two patients, 3 in two patients, 5 in one patient, 8 in four patients, and 9 in two patients. Of the 11 patients, 1 suffered from adverse effect (thirst sensation). Of the 11 patients, maximum dosage was 1800 mg/day in 1 patient.

## Discussion

Epadel® is effective for hyperlipidemia. It is also effective for pain or ulcer due to arteriosclerosis obliterans. Epadel® 1800 mg/day reduced major coronary events by 18% in patients with hypercholesterolaemia [3].

Omega-3 fatty acids alleviated neuropathic pain[4], chronic nonspecific neck or back pain[5], and pain due to FM[1]. Maroon et al. performed an uncontrolled study[5]. Seventy-eight percent of patients with chronic nonspecific neck or back pain were taking 1200 mg of omega-3 fatty acids (EPA and DHA) and 22% were taking 2400 mg[5]. Fifty-nine percent discontinued to take their prescription non-steroidal anti-inflammatory

drugs for pain. Sixty percent stated that their overall pain was improved, and 60% stated that their joint pain had improved[5]. Ozgocmen et al. performed an uncontrolled study[1]. Fish oil capsules 1500 mg/day (EPA 18%, DHA 12%) were given three times to 12 female patients with FM for 4 weeks[1]. There were statistical significant beneficial changes from baseline for tender point counts, chest expansion measurements and pain severity, fatigue, depression scales that were evaluated using Fibromyalgia Impact Questionnaire[1].

However, omega-3 fatty acids are not widely administered in patients with FM. The greatest strength of omega-3 fatty acids is mild and rare adverse effects. Therefore, I have prescribed Epadel® in priority to milnacipran, duloxetine, and pregabalin in patients with FM. In Europe and the U.S., omega-3 fatty acids are available for hypertriglyceridemia and so on and New Drug Application for AMR101 (comprising not less than 96% ultra pure icosapent ethyl) has been accepted for filing by the U.S. Food and Drug Administration. Icosapent ethyl is identify with ethyl icosapenpentate.

Oxidative stress may play an important role in FM pathophysiology [6-7]. Omega-3 fatty acids are antioxidant agents[6-7]. It may be antinociceptive mechanisms of omega-3 fatty acids, however, the mechanisms remain unknown.

Dioxins level of generic medicines of EPA-E (0.012-0.030 pg TEQ/g) is 100-1000 times of that of brand-name medicine (Epadel®) of EPA-E (0.000081-0.00016 pg TEQ/g) [8]. Dioxins level of generic medicines of EPA-E is more than acceptable level of dioxins in tap water (0.001 pg TEQ/ml) [8]. Therefore, I recommend brand-name medicine (Epadel®) of EPA-E.

This study is a short-term uncontrolled study. A long-term double-blind study with EPA-E or omega-3 fatty acids is needed.

## Conclusions

Epadel® reduced subjective pain in 11 patients (37.9%). Epadel® did not reduce pain in 13 patients (44.9%). Five patients (17.3%) discontinued medication due to adverse effects.

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## 著者紹介

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