Nutrition 32 (2016) 1165–1170

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

Combinations of distinct long-chain polyunsaturated fatty acid species for improved dietary treatment against allergic bronchial asthma

Christopher Beermann Ph.D. [a,*], Sandy Neumann M.Sc. [a], Daniela Fußbroich M.Sc. [a], Stefan Zielen M.D. [b], Ralf Schubert Ph.D. [b]

[a] Food Technology, Department of Biotechnology, University of Applied Sciences, Fulda, Germany
[b] Pediatric Pulmonology and Allergology, Children's Hospital I, Goethe-University, Frankfurt/Main, Germany

ARTICLE INFO

Article history:
Received 2 March 2016
Accepted 11 April 2016

Keywords:
Arachidonic acid
Allergic disease
Eicosapentaenoic acid
Fat metabolism
Inflammation
Pulmonology

ABSTRACT

Allergic bronchial asthma is a chronic inflammatory disease of the airways with an increasing incidence in Western societies. Exposure to allergens provokes recurrent attacks of breathlessness, airway hyperreactivity, wheezing, and coughing. For the early phase and milder forms of allergic asthma, dietary supplementation with long-chain polyunsaturated fatty acids (LCPUFA), predominantly fish oil–associated eicosapentaenoic (C20:5 ω-3) and docosahexaenoic acid (C22:6 ω-3), and distinct crop oil–derived fatty acids might provide a sustainable treatment strategy, as discussed in several studies. In addition to immune-controlling prostaglandins, leukotrienes, and thromboxanes, specialized proresolving mediators, such as lipoxins, resolvins, protectins, and maresins, are metabolized from different LCPUFA, which actively resolve inflammation. The aim of this review was to discuss the possible synergistic effects of ω-3 and ω-6 LCPUFA combinations concerning rebuilding fatty acid homeostasis in cellular membranes, modifying eicosanoid metabolic pathways, controlling inflammatory processes by focusing on resolving inflammation in the bronchoalveolar system on the cellular level, and helping to control clinical symptoms in bronchial asthma.

Introduction

Bronchial asthma is a chronic inflammatory disease of the airways, with an increasing incidence in Western societies [1]. To date, several asthma treatment concepts, like bronchodilating beta-2 receptor agonists, leukotriene (LT) receptor antagonists, anti-inflammatory glucocorticoids, and monoclonal anti-immunoglobulin (Ig)E are available, which are associated with total resistance or receptor-desensitizing caused loss of effectiveness with long-term therapy [2,3]. As a possible therapeutically supportive or even an alternative treatment concept, ω-3 and ω-6 long-chain polyunsaturated fatty acids (LCPUFA), especially eicosapentaenoic acid (EPA; C20:5 ω-3), docosahexaenoic acid (DHA; C22:6 ω-3), and dihomo-γ-linolenic acid (DGLA; C20:3 ω-6), have been suggested by many studies to possess immunomodulatory effects in acute or chronic pneumonia [4–6].

Since the late 1970s, studies have promoted the immunomodulatory potential of marine ω-3 PUFA. Since then, the controversial discussion on the truth of the health promoting effects of EPA and DHA has continued [7]. Currently, fish, plants, algae, and fungi containing LCPUFA, as well as modern oil processes for refining dietary oils, have enabled the creation of complex oil blends with specific LCPUFA profiles. Several distinct species of ω-3 and ω-6 LCPUFA have been shown to have wide beneficial effects in the control of inflammatory processes [7–11].

The resolution phase of inflammation is a strongly regulated, energetic, and complex program that fails in asthma and therefore becomes a key point of intervention [4]. This review investigates the possible synergistic combinations of ω-3 and ω-6 LCPUFA species in allergic bronchial asthma, focusing on resolving inflammation by metabolically associated specialized proresolving mediators (SPM).

* Corresponding author. Tel.: +49 661 964 9506; fax: +49 661 964 0505.
E-mail address: Christopher.beermann@lt.hs-fulda.de (C. Beermann).

http://dx.doi.org/10.1016/j.nut.2016.04.004
0899-9007/

LCPUFA connects fat metabolism with immune reactions in asthma

Asthma is defined as a chronic inflammatory disease characterized by chronic inflammation and remodeling of airways, reversible airflow limitation, eosinophil and leukocyte tissue infiltration, and airway hyperactivity [12]. Furthermore, asthma is associated with hyperresponsiveness (e.g., triggered by allergens and/or enhanced by low temperatures and exercise) [13]. Figure 1 shows the immunologic processes in asthma related to ω-3 and ω-6 fatty acids and their derivatives. The allergic response is generally mediated by a T-helper cell type-2 immune response characterized by the secretion of interleukin (IL)-4, IL-5, IL-9, and IL-13, which promote eosinophilic inflammation and IgE production by plasma cells. In the early phase of the asthmatic response, allergen recognition by specific IgE on mast cells triggers the release of mediators (i.e., histamine and LCPUFA-derived lipid-mediatory eicosanoids) [14]. In asthma, eicosanoids derived from arachidonic acid (AA), such as the cysteinyl leukotrienes, induce bronchospasm, edema, and mucous hypersecretion [15]. Additionally, these mediators released during the early phase of an immune response also gradually initiate and support a late-phase asthmatic response configured around T-helper cell type-2 cells and eosinophils [16].

Generally, linoleic acid (LA; C18:2 ω-6) and α-linolenic acid (ALA; C18:3 ω-3) are essential fatty acids and precursors of LCPUFA, such as EPA, DHA, or AA [17]. They are synthesized through a series of elongation and desaturation steps within the same enzymatic metabolic pathway [18,19]. LCPUFA integrated into the cell membrane phospholipids of immune cells are released by phospholipase A_2 in response to appropriate triggers and are transformed by specific lipoxygenases (LOX) and cyclooxygenases (COX) into hormone-like immune regulatory eicosanoids, which are involved in the pathogenesis of asthma [7,20].

There is evidence that airway inflammation and airway hyper-responsiveness are influenced by the ratio of ω-6 to ω-3 LCPUFA in tissues and cells [21,22]. One study showed that decreased inflammation could be partially due to reduced ω-6 PUFA-derived lipid mediator formation as a result of competitive inhibition or downregulation of COX or LOX [21]. The LCPUFA profiles of cell and organelle membranes strongly influence its functions and numerous cellular processes such as cell survival and death [20,23]. Several studies have clearly demonstrated that dietary LCPUFA supplementation can affect the fatty acid composition of these membranes [24,25]. Thus, the already reported association between asthma and dietary LCPUFA intake is reasonable [26–28]. Concerning the immune response, T-cell function is modulated by this directly through effects on cell signaling and gene transcription [29]. Again, ω-3 and ω-6 LCPUFA are ligands and/or modulators for the nuclear factor (NF)-κB and peroxisome proliferator-activated receptors (PPAR), which control various genes of immune response regulation, whereas especially ω-3 LCPUFA downregulate proinflammatory genes [20]. Taking this into consideration, it might be possible to precisely ameliorate or even resolve the inflammation by dietary interventions with preformed LCPUFA. Based on this knowledge of the associated disease-specific immunologic mechanisms, the dietary rebuilding of LCPUFA homeostasis has been shown to improve asthma control, lung function, and inflammatory markers in children with asthma [30,31].

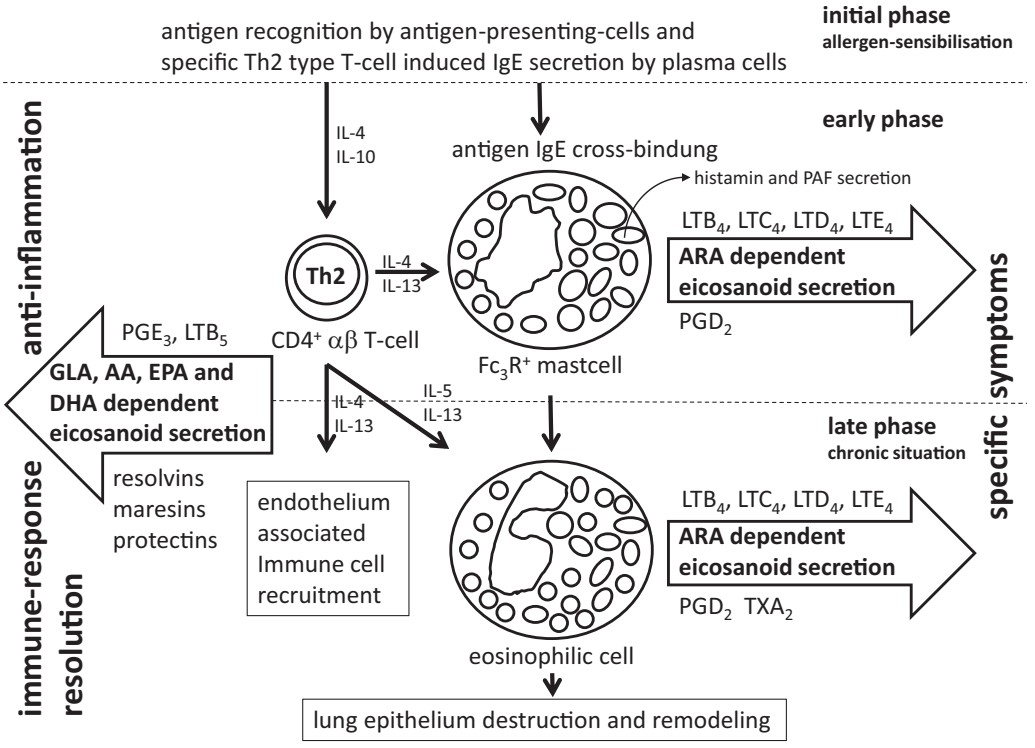

Fig. 1. The developmental process of allergic asthma and the regulatory function of LCPUFA-derived eicosanoids. AA, arachidonic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GLA, γ-linolenic acid; LCPUFA, long-chain polyunsaturated fatty acid; Ig, immunoglobulin; IL, interleukin; LT, leukotriene; PAF, platelet-activating factor; PG, prostaglandin; Th, T helper; TX, thromboxane.