

Original

Importance of a balanced omega 6/omega 3 ratio for the maintenance of health. Nutritional recommendations

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Abstract

The modification of dietary patterns has led to a change in fatty acid consumption, with an increase in the consumption of ω -6 fatty acids and a marked reduction in the consumption of ω -3 fatty acids. This in turn has given rise to an imbalance in the ω -6/ ω -3 ratio, which is now very different from the original 1:1 ratio of humans in the past.

Given the involvement of ω -6 and ω -3 essential fatty acids in disease processes, the present article examines changes in dietary patterns that have led to the present reduction in the consumption of ω -3 essential fatty acids, and to study the importance of the ω -6/ ω -3 balance in maintaining good health. In addition, an assessment is made of the established recommendations for preventing a poor intake of ω -3 essential fatty acids, and the possible options for compensating the lack of these fatty acids in the diet.

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Key words: *Dietary omega 3 fatty acids. Balanced omega 6/omega 3. EPA. DHA.*

IMPORTANCIA DEL EQUILIBRIO DEL ÍNDICE OMEGA-6/OMEGA-3 EN EL MANTENIMIENTO DE UN BUEN ESTADO DE SALUD. RECOMENDACIONES NUTRICIONALES

Resumen

La modificación de los hábitos alimentarios ha llevado a un cambio en el consumo de ácidos grasos, con un aumento de los ácidos grasos ω -6 y una marcada reducción en el consumo de los ácidos grasos ω -3. Esto a su vez ha dado lugar a un desequilibrio en la relación ω -6/ ω -3, muy diferente de la proporción original 1:1 que tenían los seres humanos en el pasado.

Dada la importancia de la relación entre los ácidos grasos esenciales ω -6 y ω -3 en el desarrollo de diferentes enfermedades, en el presente artículo se examinan los cambios en los hábitos alimentarios que han llevado a la reducción en el consumo de ácidos grasos esenciales ω -3, y se estudia la importancia de este equilibrio en el mantenimiento de la salud. Además, se realiza una evaluación de las recomendaciones establecidas para prevenir una deficiencia en la ingesta de ácidos grasos esenciales ω -3, y las posibles opciones para compensar la falta de esos ácidos grasos en la dieta.

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Palabras clave: *Ácidos grasos omega 3. Balance omega 6/omega 3. EPA. DHA.*

Abbreviations

PUFAs: polyunsaturated fatty acids.
FAs: essential fatty acids.
LA: linoleic acid.
AA: arachidonic acid.
LNA: linolenic acid.

EPA: eicosapentaenoic acid.
DHA: docohexaenoic acid.

Introduction

In 1963 Arild Hansen and colleagues demonstrated for the first time that humans require the dietary intake of certain polyunsaturated fatty acids (PUFAs) that the body is unable to synthesize. These PUFAs are therefore referred to as essential fatty acids (FAs).¹

Since then there has been growing scientific interest in the role essential FAs may play in the human body, and research and discoveries in this field have expanded over time.

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It is presently known that the essential FAs of both the ω -6 series (especially linoleic acid [LA] and arachidonic acid [AA]) and the ω -3 series (the most important of which are linolenic acid [LNA], eicosapentaenoic acid [EPA] and docohexaenoic acid [DHA]) are essential for development and growth, and they play a key role in the prevention and management of coronary disease, hypertension, diabetes, arthritis, cancer and other inflammatory and autoimmune conditions.^{2,4}

The modification of dietary patterns over the last 100-150 years has led to a change in fatty acid consumption, with an increase in the consumption of ω -6 FAs and a marked reduction in the consumption of ω -3 FAs. This in turn has given rise to an imbalance in the ω -6/ ω -3 ratio, which is now very different from the original 1:1 ratio of humans in the past⁴.

Given the involvement of ω -6 and ω -3 FAs in disease processes, the aim of the present article is to examine changes in dietary patterns that have led to the present reduction in the consumption of ω -3 FAs, and to study the importance of the ω -6/ ω -3 balance in maintaining good health. In addition, an assessment is made of the established recommendations for preventing a poor intake of ω -3 FAs, and the possible options for compensating the lack of these fatty acids in the diet.

Changes in dietary patterns in the course of history

In the Palaeolithic period, the human diet was characterized by a low caloric intake in the form of fats (20-25%), a low intake of saturated fats (< 6%), and the trans-fatty acid intake was negligible.^{5,6} In addition, the diet of the human hunter-gatherer population of that time presented a balanced ω -6/ ω -3 ratio (1-2:1) as a result of the consumption of ω -3 FAs, which were found in large amounts in most food these individuals consumed: meat, plants, eggs, fish, nuts or berries. This situation made a significant contribution to human evolution, influencing and allowing the cerebral and cognitive development of the species.⁷

At present, the western diet has significant caloric content in the form of fats, above the recommended 30-35%. Specifically, the diet is characterized by a high proportion of saturated fats (> 10%), rich in ω -6 FAs and a low proportion of ω -3 FAs, resulting in ω -6/ ω -3 ratios in the range of 20-30:1. The dietary increase in trans-FAs has also been important.

These dietary changes have been a consequence of the socioeconomic changes during the last 100-150 years, i.e., the appearance of the industrial revolution. From that point onwards, saturated fat consumption began to increase exponentially. At the same time, the intake of ω -3 FAs began to decrease while the intake of ω -6 FAs increased slightly-quickly reaching very different levels from the original values. On the one hand, industrial interest in increasing food production since the 1940s-1950s has caused foods that were naturally

rich in ω -3 (meat, fish, poultry, etc.) to lose part of their ω -3 content as a result of the change in nutritional composition of the animal feed employed.⁴ In general, the percentage of saturated fats increased due to confinement and the excessive energy content of the diet fed to livestock. In addition, the ω -6 FAs content increased considerably as a result of the increment (up to 70%) in ω -6-rich grain and also the addition of vegetable oil.⁸ On the other hand, ω -3 has practically disappeared, since green leaves and the insects that feed on them are no longer consumed. For these reasons the ω -6/ ω -3 balance which animals maintained in their natural environment was lost, causing the products derived from them to have large amounts of ω -6 and small amounts of ω -3 FAs.^{9,10} In addition to changes in livestock production, there has been an indiscriminate substitution of saturated fat in food with ω -6 FAs, designed to obtain benefits in terms of a reduction in serum cholesterol concentration.

It also must be taken into account that the ω -3 intake is much lower today as a consequence of the reduction in fish consumption¹⁰. Another factor of relevance is the fact that most of the fish now consumed comes from fish farms, where the feed mainly employed contains less ω -3 FAs.

Biochemistry and metabolism of ω -6 and ω -3 fatty acids

The PUFAs consumed with the diet are absorbed by intestinal cells, and subsequently give rise to their different metabolites. On hand, elongation and desaturation reactions transform PUFAs into long-chain PUFAs.⁹ "Retroconversion" resulting in a shortening of two carbon units of the longest LA and LNA derivatives. On the other hand, cyclooxygenases (COX) and lipoxygenases (LOX) generate different prostanoids from EPA and AA (prostaglandins (PG), leukotrienes (LT), thromboxanes (TX), etc.).

Figure 1 shows the most important steps in the transformation of LA and LNA into their principal derivatives (AA, EPA, DHA and prostanoids).

All these derivatives are important to maintain a healthy status. The long-chain PUFAs (AA, EPA, DHA) are incorporated into the cell membranes, particularly into the lipid bilayer of the plasma membrane. Depending on the proportion of each present in the membranes, the latter undergo changes in fluidity and therefore in their capacity to house different enzymes, receptors, channels and pores-thus allowing improved adaptation of cell functions to physiological needs.¹¹ On the other hand, the prostanoids, play a key role as mediators of the local symptoms of inflammation: vasoconstriction, vasodilatation, coagulation, pain and fever. And the inflammation constitutes the basis of many chronic illnesses such as cardiovascular disease, obesity, diabetes, arthritis, mental illness, cancer and autoimmune conditions.

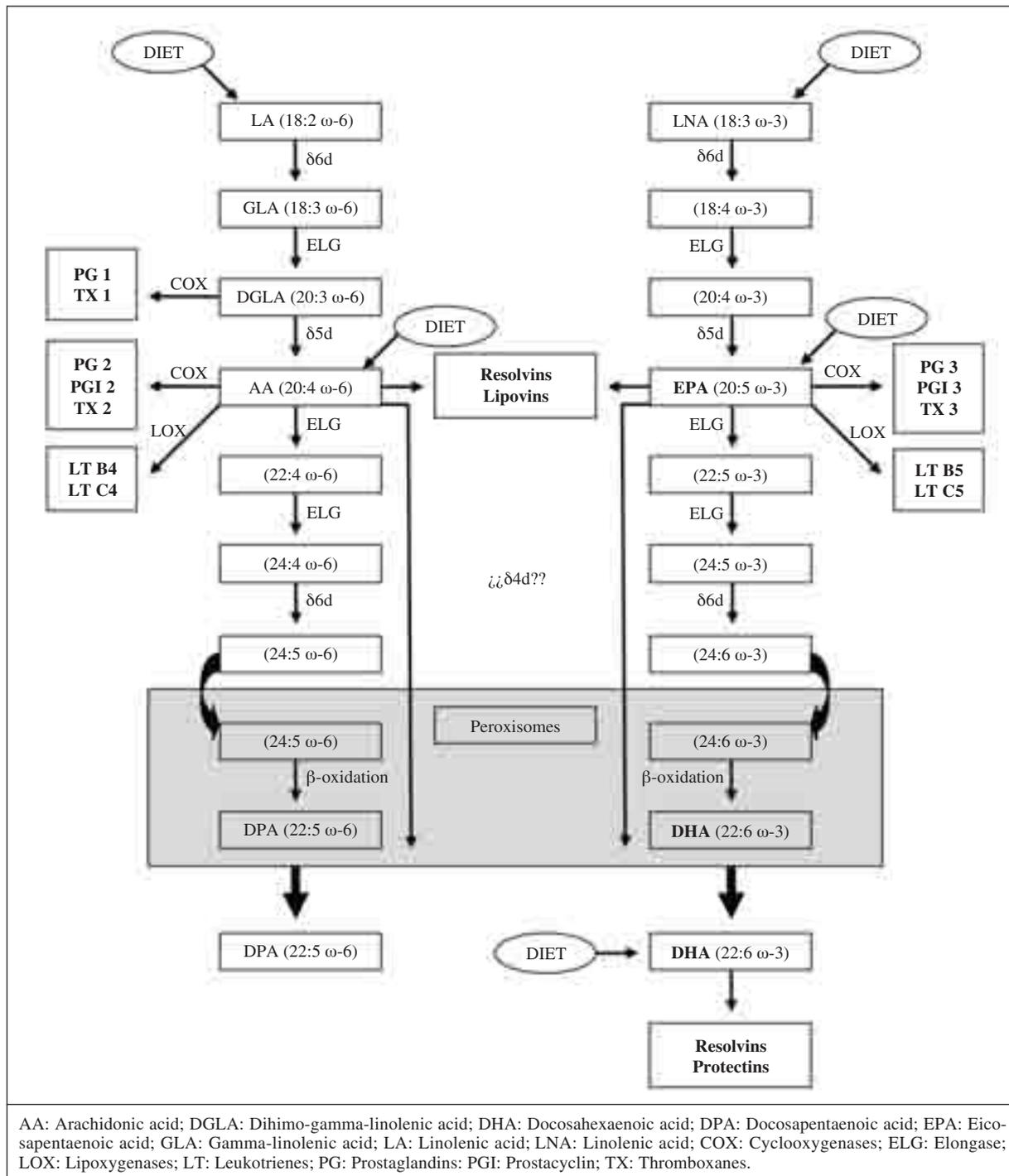


Fig. 1.—Biochemistry of omega 6 and omega 3 fatty acids.

Thus, the relationship between derivatives is very important to maintain homeostasis.

The enzyme δ-6 desaturase (fig. 1) plays a key role, since it has greater affinity for LNA than for LA – competitively inhibiting the formation of its unsaturated derivatives. Accordingly, a 10-fold greater proportion of LA is needed versus LNA in order to inhibit the formation of LNA derivatives. In other words, in order to block

the transformation of LA into AA by 50%, LNA would have to be present in amounts equivalent to 0.5% of the caloric content. In contrast, the reduction of LNA transformation into EPA requires an energy supply in the form of LA equivalent to approximately 7% of the caloric content of the diet. In this context, experimental evidence indicates that the optimum ratio between these acids should be close to 4:1-5:1, and should not exceed 10:1.⁹

Also, both EPA and DHA play a vital role in many metabolic processes, but the LNA conversion process in humans is not efficient – only 5-10% are converted to EPA, and a mere 2-5% to DHA.¹¹ The conversion process appears to be more efficient in females.¹²

Therefore, there are many specific mechanisms of action that contribute to maintain body homeostasis.^{4,13}

Importance of ω -3 and ω -6 balance in the genesis and course of various diseases

Many epidemiological studies and clinical trials have shown the relationship between the intake of ω -3 FAs and beneficial effects in different diseases: cardiovascular disorders, different cancers (breast, colorectal, prostate, etc.), asthma, inflammatory bowel disease, rheumatoid arthritis and osteoporosis, among others. Such evidence will be expanded in the future.

Another important and more controversial aspect is the relationship between the intake of ω -3 and ω -6 FAs in all these diseases.

Regarding the influence of the ω -6/ ω -3 ratio, Simopoulos considers an adequate ratio or balance between ω -6 and ω -3 FAs to be important for the prevention and treatment of cardiovascular diseases.⁴ For the secondary prevention of cardiovascular disease, a ratio of 4:1 has been associated with a 70% reduction in total mortality.

On the other hand, Griffin et al. in the OPTILIP study,¹⁴ concluded that the ω -6/ ω -3 ratio is practically of no use in predicting changes in cardiovascular risk. However, it must be taken into account that in this study, the ω -6/ ω -3 ratios of the patient groups were 3:1-5:1, and that the control group presented a ratio of 10:1 – these values are not very different from the optimum ratio of 4:1-5:1 without exceeding 10:1.⁹

In this context, García-Ríos et al. in 2009,¹⁵ considered that treatment with both types of fatty acid on an individualized basis, ensuring an adequate daily intake, appeared to be more reasonable than analyzing their ratio – since the ingestion of either of them, and fundamentally of ω -3 (mainly EPA and DHA), is deficient in the great majority of the current western population.

It can be stated that an adequate intake of both FAs, ω -6 and ω -3, is essential for good health and for reducing the percentage of cardiovascular diseases – though it is not clear whether the ratio between them is of any use.¹⁶ During the 1960s-1970s, an increase in ω -6 consumption proved central to dietetic counseling, in view of the effects observed in lowering LDL-cholesterol. The consumption of ω -6 doubled, and mortality due to coronary disease decreased 50%. Recently, the American Heart Association (AHA) published a review recommending the amount of ω -6 to represent between 5-10% of total energy consumed. The AHA indicates that the consumption of ω -6 from vegetable oils, nuts and seeds is beneficial when forming part of a healthy diet plan in which saturated and trans-fats are replaced by PUFAs.¹⁷

For this reason, Willet suggests that despite the fact that the ω -6/ ω -3 ratio has been described as important due to the opposing action exerted upon inflammatory activity, the existing scientific evidence is inconclusive, and in humans a high ω -6 intake has not been correlated with high inflammatory marker levels.¹⁶

In conclusion, regarding the ω -6/ ω -3 ratio in cardiovascular disease, various studies agree that the ratio must be improved, though there are controversial data on its usefulness as a cardiovascular risk marker. While some researchers point to the need to reduce ω -6 consumption in order to improve the ratio, other authors stress that the important issue is to increase the consumption of ω -3, and particularly of EPA and DHA – seeking alternatives that, beyond the adoption of nutritional educational measures designed to increase fish consumption, are able to compensate for deficiencies in the consumption of this fatty acid, at least in reference to cardiovascular disease.

Cancer is another disease that has generated great interest in evaluating the usefulness of ω -3 supplementation and establishing the optimum ω -6/ ω -3 ratio. Many experimental studies have shown the role played by ω -3 (DHA and EPA) in suppressing the development of most cancer processes, including breast, colon, prostate, liver and pancreatic cancers.^{3,4,18-23} Furthermore, ω -3 FAs reduce inflammation, favour apoptosis and exert antiproliferative effects. In addition, there is evidence that EPA and DHA exert a potent antiangiogenic effect, inhibiting the production of some of the main angiogenic mediators²⁴. This explains the great interest in establishing fatty acid ingestion in adequate proportions. There is agreement regarding the need to lower the ω -6/ ω -3 ratio, and according to some authors the ideal ratio may be 1:1 or 2:1.²⁵

In the case of bronchial asthma, the data are contradictory. In 2004, Kompauer et al. evaluated 740 adults between 20-64 years of age and reported no association between the ω -6/ ω -3 ratio and serum phospholipids and allergic sensitization in adults.²⁶ Other authors likewise found no association, concluding that the mentioned ratio exerts no protective effect against asthma.^{27,28} In contrast to these findings, other authors have reported a protective effect of the ω -6/ ω -3 ratio.^{29,30} In 2009, Simopoulos suggested that a ω -6/ ω -3 ratio of 5:1 exerts beneficial effects upon asthma, while a ratio of 10:1 has adverse effects.⁴

Another disorder associated with inflammation and in which the ω -6/ ω -3 ratio may be of great interest is inflammatory bowel disease (IBD). A range of applications for this ratio have been explored, both in relation to the measurement of inflammatory marker levels and as it refers to local mucosal inflammatory reduction and lessening of the pain patients suffer.³¹⁻³³

In reference to rheumatoid arthritis, various authors have suggested the potential benefits that could be obtained by combining drug treatment with an adequate ω -6/ ω -3 ratio, reporting significant changes particularly in inflammatory markers.^{4,34}

Regarding bone diseases, studies in animals have shown that the ingestion of long-chain ω -3 FAs could influence bone formation and resorption.^{35,36} The influence of the ω -6/ ω -3 ratio upon bone mineral density in elderly adults was assessed by Weiss et al. in 2005.³⁷ An increase in the ratio was seen to be significantly and independently correlated with increased bone mineral density of the hip in all participating women, and of the spine in women receiving hormone therapy. Similar results have been obtained in other studies.³⁸

There is also evidence that the pathophysiology of major depression is influenced by changes in fatty acid intake. In 2009, Dinan et al. evaluated the levels of arachidonic acid, IL-6 and TNF α in depressed responders and non-responders to antidepressive treatment.³⁹ Arachidonic acid and IL-6 were found increased in both responders and non-responders, and although no differences in terms of TNF α were noted, there were significant differences in the EPA and arachidonic acid ratio between controls and responders versus non-responders. Other studies likewise reinforce these observations in major depression and bipolar disorder, and low DHA levels and high ω -6/ ω -3 ratios may even predict suicidal behaviour.⁴⁰⁻⁴²

This relationship has also been extensively studied in postpartum depression. During the last three months of pregnancy, the fetus accumulates an average of 67 mg/day of DHA through the placenta, and then through breast milk – a situation that would favor depletion and the risk of postpartum depression.⁴³

It has been shown that DHA content in brain tissue is decreased in patients with neuronal alterations, as in Alzheimer's disease. Recent studies have also underscored the importance of arachidonic acid, due to its influence upon membrane plasticity and fluidity preservation in the hippocampus, and its protective action against oxidative stress.⁴⁴ The balance between ω -3 and ω -6 allows cell membranes to develop with flexibility and fluidity for transmitting signals between neurons, thereby proving decisive for physical and mental wellbeing. As a result, an appropriate diet affording a ω -6/ ω -3 ratio of 4:1 may be effective and necessary for meeting the body's requirements and for promoting health and longevity.⁴⁵

Nutritional recommendations for the consumption of ω -3 fatty acids and the ω -6/ ω -3 ratio

As we have seen, there are a number of pathologies in which the ω -3 and ω -6 FAs play an important role, thus reflecting the importance of ensuring their adequate dietary intake, particularly when considering the variations there have been in the human diet and that have resulted in a change in ω -6/ ω -3 ratio from 1-2:1 to 20:1.

The estimations of ω -3 ingestion are mainly based on information obtained on food consumption and from the chemical analysis of diets. The approximate

consumption of LNA in European countries varies from 0.6-2.5 g/day. However, few data are available on the ingestion of DHA and EPA in Europe, due to a lack of reliable information. An approximate estimation of the consumption of ω -3 FAs in Europe is 0.1-0.5 g/day. These figures are high in comparison to the estimated intake of DHA and EPA in the United States (0.1-0.2 g/day), but low in comparison with the data corresponding to Japan (up to 2 g/day), where fish is one of the most commonly consumed foods.⁴⁶ In Spain, a recent study carried out by the Ministry of Agriculture, Fisheries and Food, showed that despite the fact that the Spanish population consumes levels of ω -3 close to the recommended level (1.52 g/day), the ω -6/ ω -3 ratio is very high (16:1), due to a high intake of ω -6.⁴⁷ In addition, the percentage of energy contributed by EPA+DHA with respect to total energy in the diet was found to be lower than the recommended value (0.5%).

At present, there are a series of recommendations regarding the consumption of ω -3 FAs, developed by scientific societies and national and international organizations, though there is still insufficient evidence to set a maximum tolerable dose of ω -3 and ω -6.⁴⁸

On comparing the recommendations for ω -3 consumption and the ω -6/ ω -3 ratio of the different organizations and the existing consumption data, the results show that the consumption of these FAs is generally low, and that the ω -6/ ω -3 ratio should be lower than the ratio currently found.

Many countries have recommended daily EPA and DHA intake levels ranging from 500 mg/day in France to 1-2 g/day in Norway. As regards international organizations, the World Health Organization (WHO) recommends the consumption of between 0.3-0.5 g/day, while the International Society for the Study of Fatty Acids and Lipids (ISSFAL) advocates 500 mg/day, and the North Atlantic Treaty Organization (NATO) recommends 800 mg/day.

The most recent recommendations of the American Heart Association (AHA) are that adults should consume fish at least twice a week. Likewise, patients with coronary disease should consume 1 g of EPA+DHA daily; while patients with hypertriglyceridemia should consume 2-4 g/day of EPA+DHA.²¹ The AHA postulates that fish oil supplementing is an option for securing an intake of approximately 1 g/day of ω -3 FAs.²¹

A recent publication by the European Food Safety Authority (EFSA) postulates that the amount of EPA+DHA required to lower triglyceride levels is 2-4 g/day, and 3 g/day to lower blood pressure.⁴⁹

Taking the above into account, the recommended amounts and the ideal fatty acid ratio must be adjusted according to the findings of additional research designed to determine the specific needs for the different diseases, and other important dietary factors, as well as possible genetic factors that may condition the requirements of these nutrients.

As regards the recommended ω -3/ ω -6 ratio, it is difficult to establish an ideal balance between the FAs,

though it seems clear that ω -3 must be present at least in the amounts found today in the Spanish diet, and preferably in higher amounts. Alternatives are needed for improving the ω -6/ ω -3 ratio. In this sense, an increase in ω -3 (EPA and DHA) in the diet may be regarded as a valuable strategy. From the above we can deduce that a considerable increase in fish consumption is required, or alternatively strategies must be sought to reach the recommended minimum amounts of EPA and DHA, and an adequate balance between the latter and ω -6.

Alternatives for increasing ω -3 fatty acid consumption in the population

Increased ω -3 fatty acid consumption can come from changes in diet, with an increase in fish consumption, though western societies tend to include very little fish in their diet. The scarcity of fish and its high cost, together with consumer concerns about the presence of contaminants, often cause people to prefer more convenient and less expensive foods.

An alternative for increasing consumption would be to supplement with ω -3 daily foodstuffs such as margarine, eggs and their products, pasta, sauces, juices, meat and milk and dairy products; the so-called functional foods. In relation to these products, the Food Standards Agency of the United Kingdom has warned that current regulation of these products does not distinguish between ω -3 of plant origin (linolenic acid) and those of fish origin (EPA and DHA). As mentioned previously, the conversion rate of linolenic acid to EPA and DHA is very low, and only the consumption of fish ω -3 is able to guarantee adequate amounts of EPA and DHA. In addition, an important issue when adding ω -3 FAs to foods is that these FAs are highly vulnerable to oxidation, and quickly react when exposed to oxidizing agents such as the oxygen in air. Furthermore, despite the great number of ω -3 enriched foods available on the market, the health effects of their regular consumption have not yet been demonstrated. This is an area of research which undoubtedly will continue to expand in the coming years.

Dietary supplements are a clear option for contributing to meet the established recommendations. The introduction of such supplements in population groups that do not receive sufficient amounts through the diet, or that present cardiometabolic risk factors, may help reach the required doses in an easy and rapid manner. However, the consumption of ω -3 supplements can be limited by the presence of different contaminants (methylmercury, polychlorinated biphenyls or dioxins) – some of which have prolonged half-lives and can accumulate within the body. In turn, it must be mentioned that the mean EPA and DHA concentration in many dietary supplements is only 30%, and there are important variations between brands and even within one same commercial brand. In this context, it is important to use certified and validated products with

formulations of defined quality and purity. These formulations moreover must be free of contaminants and must involve a standardized manufacturing process ensuring a consistent supply of EPA and DHA.

An even less studied field is that of transgenic foods. In the future it will be possible to enrich meat and an endless range of manufactured foodstuffs (milk, beverages, eggs, etc.) with DHA and/or EPA. Such technological advances will offer a unique tool and new opportunities for research.⁵⁰

Conclusion

In conclusion, most studies indicate that the ω -6/ ω -3 ratio should be lower than that presently found in the general population, with a view to improving general health and reducing the risk of disease. Nevertheless, further studies are needed to confirm and consolidate this idea, and to shed light on the more controversial aspects that have arisen in relation to this subject. On the other hand, institutions and organizations working in nutrition and health should establish a firm consensus regarding their recommendations. This would offer guidelines for both professionals and the general population, with a view to establishing and following balanced diets.

Along these lines, it is necessary to promote nutritional education programs stressing the need to increase the consumption of food rich in ω -3 FAs (particularly EPA and DHA), or even to incorporate functional foods or dietary supplements where required, though always in the form of certified and validated products with purity and quality guarantees, to be consumed in the context of a balanced diet.

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