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Review Article

Omega-3, Omega-6 EFAs and Cholesterol Good - The Bad - And the Ugly in Cancer Manifestation

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Abstract

Among the essential fatty acids the alpha linolenic acid Eicosapentaenoic acid (EPA) and Docosa-hexaenoic acid (DHA) are the highly unsaturated fatty acids of omega-3 category. Alongside these, the short chain butyric acid and Gamnalinolenic acid (GLA) and Dihomogamma linolenic acid are considered to be toxic and exert cytotoxic effects on cancer cells and modulate various cells proteins to bring apoptosis. On the contrary the linoleic acid palmitic acid arachidonic acids belonging to omega-6 category are pro-inflammatory in nature. Studies have revealed that the high omega-6 relative to omega-3 fatty acids may contribute to the cancer risk especially the breast cancer in women and prostate cancer in men. The omega-6 is thought to create a pro-inflammatory milieu interior in tissues so as to promote the carcinogenesis process. The survey on both omega-3 and omega-6 FFAs has revealed that their ratios remained as 1:20 or 1:25 in general population and 1:50 in western haplogroups in particular due to the nutritional pattern ad diets alongside augmenting factors like stress, alcohol and smoking etc. Besides these essential free fatty acids the total cholesterol represents the driving factors for more glucose absorption in cancer cells and induce the hormone responsive or driven cancers such as the prostate, breast, uterine, cervical cancers etc., Hence in our body lipid profile the omega-3, omega-6 and cholesterol constitute the good, the bad and the ugly components. Reversing the above pattern of lipid profile may prove to be a good augury of lipidomic therapy to the disease cancer.

Keywords: Carcinogenesis; Apoptosis; Omega-3; Omega-6 EFAs; Cholesterol

Introduction

Omega-3 and omega-6 fatty acids are said to be essential category of nutrients in the body lipid profile. Both of them are to be derived only from our nutrition and the tissues/cells lack the enzymes to synthesize these essential fatty acids from their own. Omega-6 EFAs are 20-25 times more in the tissues as compared to the omega-3s. These n-6 category of omega-6 are derived mostly from vegetable oils fried foods, eggs, milk, processed cereals, corn and soyabean oils etc.

Epidemiological findings have revealed that the ratio of omega-3 to omega-6 predetermines the cancer development. Higher the ratios better the survival without cancer. On the contrary lower ratios are the individuals are prone to cancer disease probabilities. Blasbalg., *et al.* [1] have revealed that in US population especially

in the women, the consumption of omega-6 fatty acids was higher compared to omega-3 fatty acids. Their higher n-6 fatty acids levels in the blood and breast tissue lipid profile are consistent with breast cancer. These studies have also revealed the risk of breast cancer due to the consumption of lower total omega-3 relative to omega-6 fatty acids. Prospective studies have also documented an inverse association between consumption of omega-3 fatty acids from fish and/or fish oil supplement and breast cancer incidence Indra and Ramalingam [2] have surveyed the fish eating population in kanyakumari district (T.N India) and revealed the low incidence of cancer in them.

Earlier studies have revealed that in clinical situation EFFAs deficiency caused changes in the cellular organization in the body that closely resembled the malignant changes of cancer Viz., a significant increase in the widening of the intercellular space., Loss or reduction of desmosomes and increased vascular permeability etc.

These earlier findings could not differentiate between the good and bad fatty acids. However in recent investigation the role of certain fatty acids in both the development of certain types cancers as well as in the regulation of cancer formation and metastasis has been delineated. For example the omega-3 fatty acids like alpha –linolenic aid (ALA), Eiscosapentaenoic acid (EPA) and docosahexaenoic acid DHA, are highly toxic to cancer cells. These fatty acids also decrease inflammation in tissues [3-5].

In carcinogenesis the formation of resistant metastatic cells and their migration through haematogenous and lymphagenous routes to distant organs is an important hallmark event. In the metastasis of cancer cells/resistant cells adhesion to the extra cellular matrix and matrix degradation enabled their migration to the contiguous regions in the same primary site and axillary lymph nodes.

Studies have revealed that GLA DHA and PHA the derivatives of linoleic (N-6) are reduced. The cancer cells adhesion to the matrix components such as types IV collagen, fibronectin, lminin, Vitronectin, and the basement membrane. [6] favour a metastasis.

Further, Jiang., *et al*. [7] have revealed that GLA inhibited the tyrosine phoshorylation of focal adhesion kinase (FAK) and Paxillin and cancer cells –matrix interaction.

In our observations on the fatty acids profile of various cancers tissues Viz., stomach Colon Rectum breast Uterine Cervix the low level of linolenic acid and the very high level of linoleic acd remain as an evidence to the fact that the tumours cell matrix attachment could have been facilitated by the absence of good EFAs like butyric acid, linolenic acid and its further conversion to EPA and DHA by the absence of their desaturases alongside the elongase and also due to higher linoleic acid and its failure to form the GLA and DGLA from it.

Moreover the EPA and GLA have been shown to inhibit the extra cellular matrix degeneration by the proteases of cancer cells [8].

Next to the omega-3 and mega-6 fatty acids being the good and bad lipids the level of cholesterol in blood and tissue constitute the ugly part of the lipid profile. The excess cholesterol deposition on cancer cell membranes in to special absorptive structures namely the “CAVEOLAE” for the most efficient absorption of glucose to feed the glycolytic function of cancer cells in anoxic or Hypoxic milieu implicate the above ugly functionality of cholesterol in cancer cells but it is the basic etiological bottom line of all cancers.

Thus it may be concluded that omega-3, omega-6 fatty acids and cholesterol represents the good, the bad and the ugly components in carcinogenesis respectively.

Cholesterol – the ugly

The direct evidence to the statement that cholesterol is the ugly inducer of cancer came from an American study conducted on 51529 men. It revealed that men who consumed more red meat (Cholestrol) had twice the greater risk of prostate cancer than those who consumed less. Similar to animal fats the dairy products like milk and their consumers revealed 1.5 to 5.5 times higher risk of getting prostate cancer than those who took none of these. The milk calcium brings a negative influence by reducing vitamin-D, the cancer fighting Vitamin and contributes to prostate cancer manifestation.

Omega-3 FAs-Good

The omega-3 rich flax seeds and its intake (30g/day) by 25 volunteers with cancer revealed that their tumors showed a slowdown in proliferation and increase in apoptosis of these cells. (Ramalingam 2019). Similarly in the lancet [9]; Swiss study

revealed that the omega-3 EFAs in such fishes as sardine tuna and salmon revealed anti-cancer effect and lower incidence of prostate cancer among 272 men followed for over 30 year [10].

Conclusion

Epidemiological studies and lipid profile of cancer tissues reveal that carcinogenesis is predetermined by the excess omega-6 essential fatty acids and cholesterol and omega-3. EFAs have a protective role in the manifestation of various cancers. Though ethnicity and haplo group genomes have implications to cancer frequency, metabolically the bad omega-6 EFAs and the ugly cholesterol plays a key role in cancer manifestation especially the hormone driven breast cancer in women and prostate cancer in men.

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