

Importance of Lipids in Management of Breast Cancer

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Abstract: *Most recent research for breast cancer is being conducted on the basis of lifestyle and supplementary diet. The abnormal and unlimited differentiation of cells leads to a deadly disease known as cancer. Everyone is so familiar with word cancer because each one of us will explore cancer patient in their family or close relations. Lipids are the naturally occurring organic bio-molecule containing diverse range of compounds which play important role at cellular role including signaling and hormone regulation. Fats are the major regulators of cancer metabolism and progression in breast cancer. Findings from literature studies has also confirmed that occurrence of cancer is generally depended on the type of lipid you consumed instead of amount of lipid consumed. There are number of major switches which control the progression and proliferation of breast cancer. Omega-3 fatty acids are cancer inhibitor whereas omega-6 and saturated fatty acids are cancer promoters. Hence there is a need to find the exact amount of fat required by the body to fight and control cancer progression further. This article deals with current studies on lipids, its metabolism and its connection with cancer progression and inhibition.*

Keywords: Lipids, dietary fats, cancer

1. Introduction

According to global cancer statistics every 1 in 10 women is affected by breast cancer and is the most common problem among women in both developed and developing nations [1]. Healthy diet and lifestyle can reduce the risk of breast cancer by 40% and in addition to that if breast cancer is diagnosed at early stages survival rate is really high as 98% [2]. Breast cancer is manageable at initial stages of treatment as compared to other cancer types but treatment strategies are not successful as expected. There is need to conduct more research in understanding the pattern of disease in terms of age, lifestyle, diet habits, geographical conditions, history of patient etc. Unfortunately, even after massive advancements in medical technology, Breast cancer patients are increasing around the world [3]. As the disease progresses and cancer cells multiply continuously, the pain amplifies severely along with multiple side effects which lead to both physical and psychological damage [3]. Talking in terms of number, developed nations have more number of breast cancer patients as compared to developing nations [4]. It is expected that the count of breast cancer patients to increase by 70% till 2020 in developing nations by 2020 [5]. It has been stated that there is constant increase in pain even after surgical treatments specifically among young women [6]. Literature has estimated the 50% known risk factors for breast cancer i.e., age, family history, hormonal imbalance, obesity etc but the other 50% is still not yet known [7].

Lipids are the insoluble compounds which are involved in various processes both at organism and cellular levels. Literature studies have found the evidence that lipid metabolism and lipid type intake may affect the activity of cancer cells and alter the progression of cancer [8]. Also some of the specific lipids extracted from marine algae and fish like DHA have shown a synergic effect to enhance the activity of anti-cancer agents [9]. Lipid supplementation plays a very important role in inhibition of cancer cell growth. Intake of polyunsaturated fatty acids specifically N-3 PUFA has shown to inhibit the growth of colorectal cancer

whereas intake of N-6 polyunsaturated fats and animal fats are associated with the development of various cancer types [10]. Olive oil rich in Monounsaturated Fatty acids (MUFA) is considered to be the efficient and safe oil. In one of the research conducted by Garcia et.al, 2006 studied the protective role of olive in breast cancer in the Canary Islands women [11]. The fundamental mechanism which makes olive oil efficient cancer fighter is its polyphenol composition and fatty acid structure which neutralizes the effect of oxidative stress. Minimum 25-30% of cancers are related to diet, lifestyle and environmental factors [12]. Breast cancer is also related to the type of dietary fat consumption both in terms of quantity and quality. But there is no detailed study or research on individual fatty acids and its role in cancer inhibition or progression [13].

2. Lipids and its Synthesis in Mammalian Cell

Lipids are one of the major principal components in eukaryotic cells that play an important role in various cellular processes. They are divided into two major groups: polar and non polar lipids. Polar lipids are phospholipids whereas non polar lipids are classified into neutral, storage and sphingolipids. Phospholipids protect the cell from outside stress and harsh conditions by forming the biological membrane bilayer. Triacylglycerol are stored lipids which are retrieved during energy crisis conditions in eukaryotic cells like the savings account in bank which can be used during money crisis. There is great interest in increasing vegetable oil yield and varying its fatty oil composition for widening array of specialty applications such as lipid based formulations used in drug delivery, lipid coated micro-bubble and various other industrial uses.

3. Fundamentals of Lipid Structure and its Distribution

They belong to group of organic compounds which consists of fats, oils, waxes, cholesterol, phospholipids, steroids, and fat-soluble vitamins which are soluble in ethanol and

chloroform and rarely soluble in aqueous solution. The tail of lipids is long chain fatty acids which is hydrophobic in nature and have a carboxyl 'polar' head.

Phospholipids are the membrane lipids and plays very important role in signaling pathways which can change overall functioning biological life as their composition decides the fate of membrane stability and signaling. Recent studies have shown that enzymes present in the membrane region are involved in signaling mechanism and also promotes various interactions such as lipid-lipid and protein-lipid [14]. All these mechanisms are depended on enzyme activity. Major enzymes which are involved in lipid metabolism are as follows:-

Acetyl CoA carboxylase (Acetyl-CoA) is involved in initiation of fatty acid synthesis and formation of malonyl-CoA by carboxylation [15]. Experimental studies have confirmed that regulating the activity of this enzyme might give the desired result as it is an initiating enzyme [16]. Fatty acid synthase complex (FAS) is multi-protein complex involved in acyl transfer; carbon addition is 2 steps and termination of the reaction. Long chain of fatty oils are synthesized *de novo* using common constituent like stored carbon sources- Carbohydrates. Then the use of complex enzyme system comes i.e. Acetyl-CoA and FAS to start synthesizing the long chain fatty acids such as Palmitate and Stearate. The reactions to form unsaturated fatty acids and very long chain fatty acids are done by Desaturases and Elongases respectively.

Various studies prove that lipid diet may promote or inhibit breast cancer through interfering in various molecular pathways and interrupting hormone signalling.

4. Genetic Linkage between Lipids and Cancer and Dietary Fats Role in Tumor Development

Some forms of lipids are known to have an extraordinary therapeutic value for cancer patients. Past studies says that consumption of high fat diet leads to initiation of cancer specifically breast, colon, pancreatic and prostate cancer [17]. Researchers are still working on the molecular mechanisms and metabolism of lipids in cancer progression or inhibition. These studies are crucial to understand the key reasons behind cancer mortality. Various mechanisms involved in fat linked breast cancer are as follows:-

1. Peroxidation of conjugated double bond in PUFAs leading to oxidative stress which ultimately leads to DNA damage.
2. Conversion of essential fatty acids to eicasonoids, short lived hormone like lipid derived primarily from dietary linolenic acid.
3. Interaction of fatty acids with signal transduction between high dietary PUFAs intake and oestrogen catabolism [13].

Increased peroxidation of PUFA and cellular oxidative stress damages the cell membrane and intracellular signaling pathways which initiates the process of malignancy. Lipid peroxidation produces several products such as trans-4-

hydroxy-2-nonenal and malondialdehyde which form DNA adducts in human cells. Literature studies strongly support the research that products obtained from lipid peroxidation and oxidative damage are related with breast cancer progression. Also the research on lipid extracts from breast tissue also indicated the presence of genotoxic substances which are involved in carcinogenesis. Further research studies on mice model have shown that dietary fats are linked with every step of tumor development [18].

10% of breast cancer patients are related to irregular gene expression of BRCA1 (BReast Cancer gene one) and BRCA2 (BReast Cancer gene two) gene. Some patients with breast cancer usually have a history of cancer patients with defected BRCA1 or BRCA2 gene but in some cases they do not have any family history of cancer patients with defected gene [19]. In one of the recent experimentation conducted to study changing biochemical parameters in breast tissue with BRCA1 mutation. Correlated spectroscopy (COSY) was used to assess various factors like lipid unsaturation and triglyceride levels in breast cancer tissue and healthy subjects. There was increase in unsaturation and triglyceride level in BRCA1 and BRCA2 samples compared to cellular cholesterol level [20].

5. Lipid Biosynthesis and Cancer

In early 1950s research conducted by Medes et al., reported that cancer cells show lipid production by *de novo* pathway whereas they also consume lipids from the tissue environment [21].

There are many reports supporting the relation between lipid alteration and cancer progression at different stages like proliferation, differentiation, apoptosis, inflammation, autophagy, motility and membrane homeostasis. Lipid biosynthesis has very important role in development of organism cell membrane and overall development therefore it is important to study all the regulatory elements associated with lipid biosynthesis [22]. Fatty acid Synthase (FASN) is a multi enzyme complex involved in fatty acid synthesis and cancer pathogenesis, some of the cancer types like breast and prostate have shown up-regulation of FASN [23]. Literature studies also confirm that malignant cells have increased Fatty acid synthesis and also switch off of normal metabolic activity i.e. less intake of exogenous FAs to meet the energy requirements [24]. Lipid metabolism has been reported to play an important role in many breast cancer subtypes whereas over expression of FASN has also been reported in MCF10A and HBL100 breast epithelial cells [25]. As fatty oil are considered to be most important for cell integrity and development, which makes it very important to study lipids metabolism in cancerous tissue and also metabolism of transformed cells to check if it has the potential to spread to secondary sites [26].

6. Conclusion

Hypothesis generated from literature studies about lipids and breast cancer suggests that fat diet regulates breast cancer. Therefore cancer progression or inhibition depends on the type of fats, quality and quantity we are consuming. Studies in various animal models stated that consumption of omega-

6 fatty acids in large amount triggers the proliferation of cancer in some stages due to oxidative damage whereas consumption of omega-3 fatty acids inhibits the progression of cancer. This concludes that diet and lifestyle play key role in cancer patient's life. Therefore there is a need to design better dietary lipids and along with other fundamental biomolecules. Fatty oils and their metabolites have major impact on many industries like pharmaceuticals, food supplements and renewable source of energy. Some countries have sense their importance and have already started to take initiatives to use dietary lipids for medical requirements. With the evidence of changing fatty oil composition in different species it has been proved that they have different use and varied requirements. Though the basic pathways of lipid metabolism are well studied but the complex pathways are yet to be discovered. With a view to current studies and evidences, food scientists and medical biotechnologist have to explore the new pathways and exact lipid composition that could fulfill the precise requirements of a breast cancer patient.

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