Proceedings of the 3rd International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/23/20231039

Analysis of the influence of ketogenic diet on cancer treatment

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Abstract. Cancer cells' metabolic Warburg effect behavior, in which they rely predominantly on aerobic glycolysis, offers a promising opportunity for focused intervention in tumor therapy. Since nutrient oxidation is linked to this metabolic pathway, manipulating one's diet may be a useful method for dealing with tumors. The high-fat, low-carbohydrate composition of the ketogenic diet causes a metabolic condition called ketosis, which is similar to the states of fasting and starvation on the body. The body is coerced into using fat for fuel, which in turn produces ketone bodies that can be used as alternative metabolites in the creation of aerobic energy. Weight loss, epilepsy therapy, and management of diabetes are just a few of the health benefits that have contributed to the ketogenic diet's meteoric rise in popularity. New studies are pointing to the ketogenic diet's promise in the treatment of cancer as well as its more traditional uses. To better utilize the ketogenic diet as a novel approach to cancer treatment and to refine and optimize the existing dietary protocol through scientific inquiry, this paper examines the ketogenic diet's use from an energy perspective and its potential implications in cancer treatment.

Keywords: ketogenic diet, cancer, ketone body, glycolysis.

1. Introduction

Cancer is now the second leading cause of death in the United States, making it a serious public health concern worldwide [1]. Given its catastrophic effects on both individuals and communities, cancer is the subject of intensive study in an effort to better understand its causes and to create more effective prevention, diagnosis, and treatment methods. There is constant development in oncology as scientists strive for better ways to treat cancer. Over the years, numerous therapies have been created and refined for the treatment of cancer, such as radiation therapy, surgery, chemotherapy, and proton therapy [2]. In addition to these conventional approaches, there is a rising interest in learning more about how food and nutrition might help prevent and treat cancer. Understanding the complex interplay between metabolic rate, nutritional availability, and tumor progression. The premise is that conventional cancer treatment could benefit from a boost in efficacy if it could impact tumor growth by manipulation of dietary intake and metabolic pathways.

In the 1990s, the ketogenic diet was found to be effective in treating epilepsy due to its capacity to alter the pathways cells use to get energy [3]. The mechanisms through which ketogenic diets mitigate chronic disease risk, including cancer, obesity, and cardiovascular disease, have been the subject of many studies. Inhibiting the metabolic process of glycolysis to provide energy, the ketogenic diet energizes cells through the oxidation of fat to form ketone bodies, which in turn inhibits the growth of cancer cells.

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The Warburg effect suggests that cancer cells preferentially proliferate using glycolysis-produced energy. Thus, from an energetic point of view, a ketogenic diet may be useful in preventing cancer cell proliferation.

Through a literature review and analysis, this study will examine the role of the ketogenic diet in cancer treatment and highlight the most recent findings in this area. Ketogenic diets have been shown to be a safe and effective strategy for cancer in clinical trials, and this has been further supported by preclinical research [4]. The potential for dietary treatments to decrease cancer cell development and treat cancer is encouraging. Patients experiencing distress from standard treatments like radiotherapy or surgery may find relief by adding these measures into their everyday diet. The financial burden associated with expensive medical treatments may be lessened if the patient opts for a nutritional approach to cancer therapy, which could benefit the patient's entire family. One potential cost-saving strategy for disease management is to replace some of the current pharmaceutical and treatment costs with food-based interventions.

2. Analysis

2.1. The working principle of ketogenic diet

When compared to the typical diet's 45–65% carbohydrate, 20–35% fat, and 10–35% protein breakdown, the ketogenic diet's suggested macronutrient breakdown is closer to 75% fat, 20% protein, and 5% carbohydrate. The ketogenic metabolic state is induced by following this sequence. Healthy fats like avocados, almonds, and fatty fish make up the bulk of the ketogenic diet's calorie intake. Meat, poultry, and eggs, which are all high-protein foods, are eaten in moderation. Minimal amounts of carbohydrates, particularly those heavy in added sugars and grains, are allowed. This alternative eating plan pushes the body to use fat for fuel instead of carbohydrates. In 1921, Woodyatt hypothesized that acetone and beta-hydroxybutyric acid would be produced if a typical person underwent famine or consumed too much fat but not enough carbohydrates [3]. Therefore, the ketogenic diet was originally used as a treatment for epilepsy, and it remained so until the development of pharmaceutical alternatives. It became a possibility, especially for youngsters who did not react to standard treatments. The ketogenic diet causes a metabolic shift toward fat metabolism by simulating a state of metabolic famine. Instead of glucose, lipids are the predominant energy substrate in this eating plan. Fatty acids are metabolized in the liver into acetyl-CoA, and some of this acetyl-CoA is then broken down into ketones. An in-depth analysis of the ketogenic diet's unique methods of energy provision in humans has led to its investigation as a possible treatment for a wide range of illnesses. The capacity of the ketogenic diet to decrease cancer cell development has attracted a lot of study from the energy supply perspective. The ketogenic diet works to starve cancer cells and slow their multiplication by preventing them from getting the glucose they need for aerobic glycolysis. The ketogenic diet has the potential to improve cancer treatment tactics by targeting cancer cell development through energy manipulation, and continuing research is revealing its complex mechanics and therapeutic uses.

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2.2. *The principle of cancer cells growth*

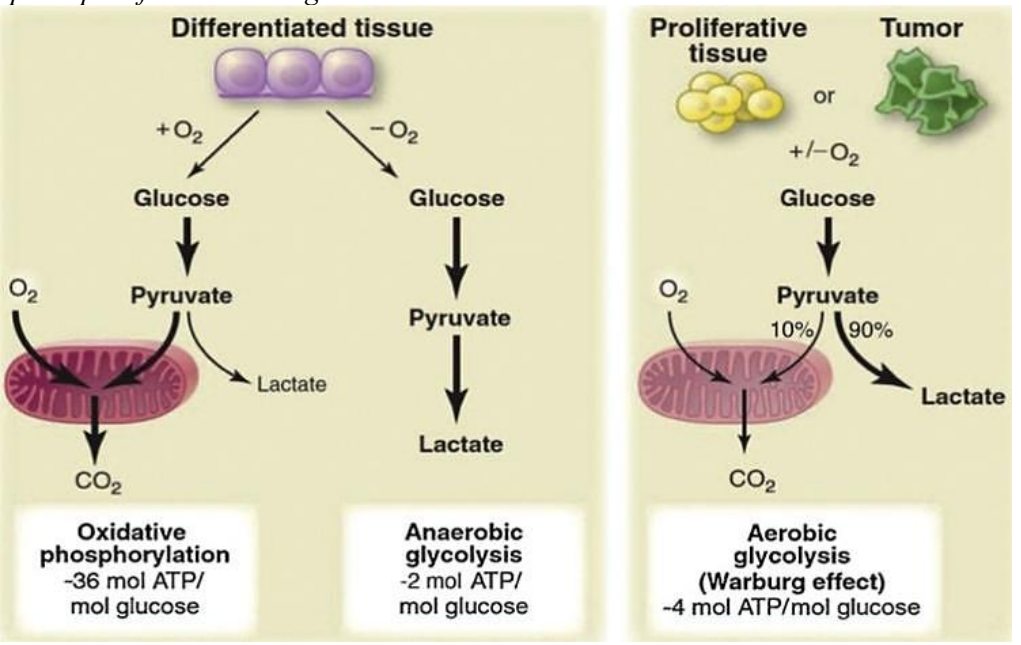

Figure 1. the metabolic pathways of differentiated cells and cancer cells [5].

Figure 1 shows two possible scenarios for the metabolic pathways of differentiated cells, one with oxygen and one without. Oxidative phosphorylation is a highly efficient process that differentiated cells use to generate ATP (adenosine triphosphate) from energy generation when oxygen is present. In the process of oxidative phosphorylation, pyruvate is metabolized in the mitochondrial TCA (tricarboxylic acid) cycle to generate ATP and carbon dioxide. However, when oxygen levels are low, cells switch to anaerobic glycolysis to generate energy [5]. Although anaerobic glycolysis is less effective than oxidative phosphorylation, it does allow cells to keep producing ATP even in low-oxygen environments. The notion of the "Warburg effect" posits, however, that cancer cells engage in a form of aerobic glycolysis, as depicted in Figure 1 on the left. Despite the presence of oxygen, cancer cells primarily rely on the conversion of pyruvate to lactate for energy production, in contrast to most differentiated cells, which favor oxidative glycolysis. Because of this metabolic switch, cancer cells are able to rapidly absorb ATP and grab additional glucose to fuel their rapid multiplication [6]. It is believed that cancer cells gain a number of benefits from favoring aerobic glycolysis. First, it facilitates the rapid generation of ATP, which is required to meet the substantial energy needs of cancer cell growth and division. In addition, NAD+ (nicotinamide adenine dinucleotide) molecules, which are needed for glycolysis to continue at an accelerated rate, are regenerated as a result of the redirection of pyruvate towards lactate synthesis. The development of tailored cancer medicines relies heavily on our ability to identify and exploit metabolic abnormalities between cancer cells and normal cells. Researchers can investigate new ways to specifically stop the growth of cancer cells by interfering with their energy metabolism by capitalizing on the cells' specific metabolic weaknesses. Inhibiting enzymes critical for aerobic glycolysis or encouraging the use of alternate energy sources like ketones can deprive cancer cells of glucose and slow their growth.

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2.3. *The influence of ketogenic diet on cancer cells*

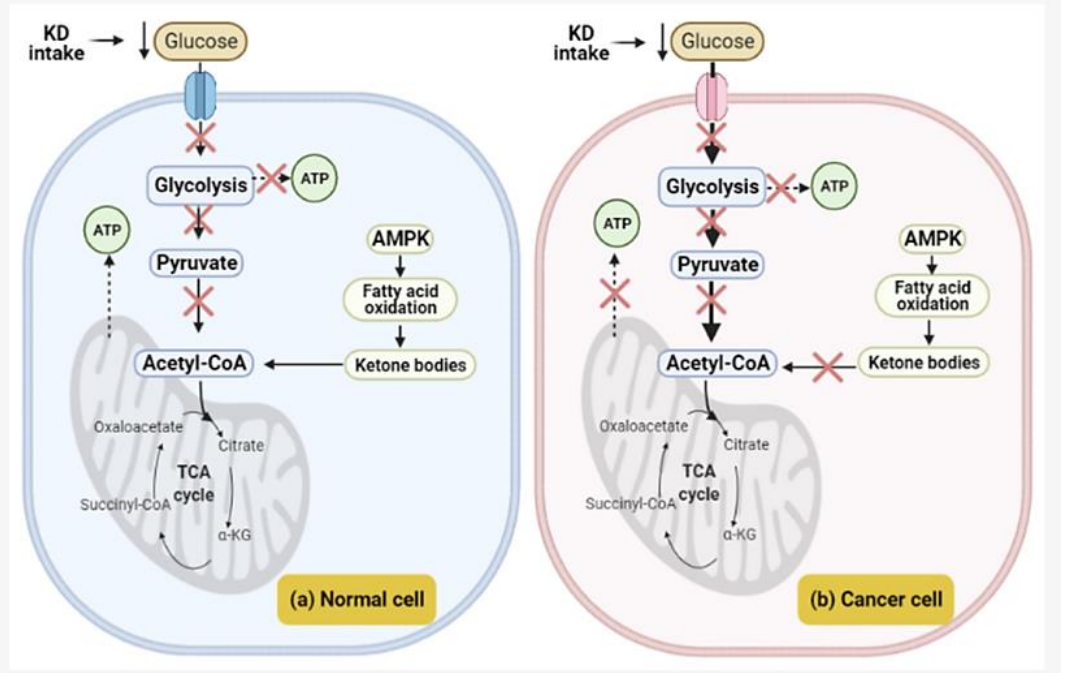

Figure 2. Normal cell (a) and Cancer cell (b) [7]

Those on a ketogenic diet consume far fewer carbohydrates than they would on a standard diet, leading to lowered blood sugar levels. There are serious consequences for cellular metabolism as a result of the decreased availability of glucose. The rate at which glucose is broken down by glycolysis is slowed because of the reduced availability of glucose. Because of this drop in ATP generation, pyruvate stores are becoming depleted. Cancer cells, as was said in the previous paragraph, exhibit a unique metabolic behavior characterized by their high glucose intake and dependence on glucose for their metabolic demands. A ketogenic diet, on the other hand, reduces glucose levels while simultaneously increasing levels of the ketone body. Cancer cells are unable to effectively use ketone molecules like beta-hydroxybutyrate and acetoacetate to generate ATP [7]. Ketone bodies can be synthesized by normal cells via fatty acid oxidation even when glucose utilization is blocked, as shown in Figure 2a. The next step involves converting these ketone molecules into acetyl-CoA, which is then used in the TCA cycle to produce ATP. As a result, a ketogenic diet can promote proper cell growth since it provides an alternate energy source. Cancer cells, as shown in Figure 2b, are unable to use ketone bodies as a source of energy because of the metabolic alterations they undergo. Since cancer cells cannot use ketone bodies as a source of energy by converting them into acetyl-CoA, a ketogenic diet starves them. The ketogenic diet's potent anti-cancer effects can be traced back in large part to this energy principle [7].

3. Discussion

Ketogenic diets, in addition to traditional cancer treatments like chemotherapy and radiation, have been the subject of a growing body of preclinical and clinical research in recent years. There are a few variations on the ketogenic diet, with the most common being the classical ketogenic diet (CKD), followed by the modified Atkins diet (MAD), the medium-chain triglyceride (MCT) diet, and finally the very-low-calorie ketogenic diet (VLCKD) [8]. Both the ketogenic diet alone and the ketogenic diet in combination with conventional therapy have varying degrees of therapeutic efficacy for various tumor types. A natural ketogenic diet is doable for breast cancer patients undergoing severe radiation therapy [9]. Glioblastoma treatment looks to be more effective and has no major negative effects in glioma treatment. But the ketogenic diet is less beneficial in treating glioblastoma that has returned [8].

The ketogenic diet may be an effective tool in the fight against cancers, especially when combined with standard treatments[8]. Although the ketogenic diet has many potential health benefits, it is also

associated with certain undesirable side effects. When determining whether or not to use the ketogenic diet on a larger scale for clinical therapy, these negative effects must be taken into account. Research into the diet's anti-cancer mechanisms, improvements to its therapy protocols, and the mitigation of any potential adverse effects should continue. Researchers can address the limitations and modify the method, making the ketogenic diet a more feasible and sustainable alternative for cancer patients, if they examine the advantages and hazards of the diet in depth. Therefore, attaining its full therapeutic potential and supporting informed clinical decision-making necessitates ongoing research into the safety, efficacy, and long-term implications of the ketogenic diet.

4. Conclusion

From a metabolic point of view, the ketogenic diet appears to be a viable strategy for halting cancer cell development. Clinical studies examining the effects of the ketogenic diet, which emphasizes protein and fat consumption while severely restricting carbohydrates, have recently become popular. Instead of presenting a thorough analysis of the ketogenic diet's effects on many common cancers, including particular experimental data and a detailed conclusion, this study concentrates on stating the theoretical underpinning of research into its usage in the treatment of cancer. While certain clinical trials have shown promise in using the diet to treat cancer, the vast bulk of these efforts has focused on individuals with brain tumors [6]. However, the ketogenic diet is not without its flaws, and there is a need for improvement and greater customization in the context of adopting the diet to cure disorders.

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