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REVIEW ARTICLE

THE LEGITIMACY AND SAFETY OF USING ALTERNATIVE DIETS IN CANCER

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ABSTRACT

Alternative diets are used by cancer patients, especially among those who are not treated with conventional methods. Due to worrying data published by the World Health Organisation and its Agenda, the International Agency for Research on Cancer and the International Cancer Union, as well as epidemiological data from all over the world, it has been concluded that cancer will be the main cause of death in the world and that, therefore, the popularity of alternative diets among cancer patients may increase. The paper reviews the scientific literature and assesses the legitimacy and safety of selected alternative diets, as well as the description of research in terms of assumed anticancer efficacy in the following diets: ketogenic, Dr. *Budwig* and macrobiotic. The article also contains a summary of the analyzed scientific research and conclusions concerning the legitimacy of their use by cancer patients.

Key words: cancer, alternative diets, ketogenic diet, dr Budwig diet, macrobiotic diet, glucose metabolism

STRESZCZENIE

Diety alternatywne są stosowane przez pacjentów onkologicznych, szczególnie wśród osób, którym konwencjonalne metody leczenia nie przynoszą oczekiwanych efektów. Dane Światowej Organizacji Zdrowia oraz jej Agendy, Międzynarodowej Agencji Badań nad Rakiem oraz Międzynarodowej Unii Przeciwrakowej, a także dane epidemiologiczne z całego świata wskazują, że wkrótce nowotwory będą główną przyczyną zgonów na świecie. W związku z tym popularność diet alternatywnych wśród pacjentów onkologicznych może ulec zwiększeniu.

Dokonano przeglądu piśmiennictwa naukowego wraz z oceną zasadności i bezpieczeństwa stosowania następujących diet alternatywnych: ketogennej, dr *Budwig* i makrobiotycznej, w aspekcie ich zakładanej skuteczności przeciwnowotworowej.

Słowa kluczowe: choroby nowotworowe, diety alternatywne, dieta ketogenna, dieta dr Budwig, dieta makrobiotyczna, metabolizm glukozy

INTRODUCTION

Cancer and cardiovascular diseases are the commonest causes of death, accounting for 70% of deaths in Poland [6]. In 2013, cancer was diagnosed in over 155 thousand Poles [27]. According to the forecasts of WHO and its Agendas (IARC and UICC) and epidemiological data, in 10-20 years cancer will be the main cause of death worldwide. It is expected that during this period an increase in the incidence of the disease to about 26.5 million and an increase in the number of deaths to 17.1 million will be recorded. [37].

Currently, the following methods are used in cancer therapy: surgery, chemotherapy, radiotherapy,

immunotherapy and hormone therapy. Due to their ineffectiveness in many clinical cases, patients in advanced stages of the disease are interested in alternative methods, including special diets [59]. Still the authors of the study have not confirmed that the use of specialized diets or specific dietary models increase the chance of survival or cure. The relationship between diet and prognosis is still being studied and is still not entirely clear [50]. However, standard treatment and alternative therapies chosen by some patients may affect the effectiveness of conventional therapy and reduce its side effects on the patient [59].

There is no common knowledge about the validity and safety of their use. The aim of this study is to assess the validity of three alternative diets, i.e. ketogenic, Dr *Budwig* and macrobiotic in supporting cancer treatment, based on a review of the world literature.

CHARACTERISTICS OF ALTERNATIVE DIETS

Ketogenic diet

The ketogenic diet is successfully introduced in the treatment of drug-resistant epilepsy in children. Over time, it has been extended to patients with nodular sclerosis, brain tumors and neurodegenerative diseases such as *Alzheimer's* and *Parkinson's* disease. Many studies have also shown the neuroprotective properties of this diet [1, 5, 33, 52], binding it to molecular mechanisms and metabolism of ketone compounds and the ketosis they induce [33].

The ketogenic diet consists of high fat, moderate protein and very low carbohydrate content. This structure of the diet forces the patient's body to obtain energy from fat instead of glucose [1]. The ratio of fat, which accounts for 80% of energy requirements in a diet, to the sum of carbohydrates (5%) and protein (15%) is approximately 4:1. Ketosis can also be induced in the organism when the ratio of macro nutrients is 3:1 or 2:1, which is closely related to the patient's dietary tolerance and the expected results of the therapy. The main fat sources are long chain triglycerides (LTC) and medium chain triglycerides (MCT). A high MCT diet leads to higher ketosis, but at the same time causes more serious side effects for the patient (e.g. stomach pain) [10]. People who follow a ketogenic diet, fatty acid oxidation occurs in the liver, where is the absence of glucose, ketone compounds are formed, including: acetate, β-hydroxybutyrate and acetone. Low carbohydrate intake in the ketogenic diet may cause a slight decrease in blood glucose levels and support glycemic control resulting in lower level of A1c glycated haemoglobin (HbA1c) [59]. The effectiveness of the ketogenic diet can be controlled by testing the level of ketone compounds in blood serum and the β-hydroxybutyrate concentration in patient's urine [12].

Currently, research is also being conducted in the group of patients on the side effects of ketogenic diet and its importance in limiting the progression of disease [47]. However, the German Association of Urological Oncology (AUO), on the basis of a systematic review of the work on the use of a ketogenic diet, takes the view that a low-carbohydrate diet cannot be recommended to oncological patients because there are no prospective and randomized studies directly evidence of effectiveness [34].

Dr Budwig's diet

It was proposed in the 1950s by *Johanna Budwig* as a standard anti-hypertensive diet. However, the presented nutrition model is deficient in terms of iron and carbohydrate content. There is currently a lack of scientific researches on the safety and efficacy of this diet. The diet proposed by Dr *Johanna Budwig* does not support the development of correct eating habits according to current scientific guidelines. In addition, the use of this nutritional model over a longer period of time is unrealistic for the patient [26].

Dr. Budwig's diet is rich in omega-3 fatty acids as well as vegetables, fruit and dietary fiber [26]. The basic and one of the most important component of the diet is linseed oil, which contains large amount of α-linolenic acid (ALA) [38]. The basic product is cottage cheese paste with linseed oil. Banned products in this food model include meat (especially fried), butter, margarines, mayonnaise, sugar and other oils [61]. Dr. Budwig believed that the cancer process in the human body is associated with a large amount of trans-fatty acids and a coexisting deficit of omega-3 and omega-6 fatty acids [18].

Macrobiotic diet

The term "macrobiotics" comes from the Greek word macros (large, long) and bios (life). This diet is considered to be conducive to maintaining general health, preventing cancer and other diseases [7]. A lifestyle based on observing the macrobiotic diet was spread by George Ohsawa (1893-1966), Japanese philosopher. Oshawa believed that a healthy diet would ensure peace and harmony on Earth. The macrobiotic diet achieved its greatest popularity in the United States in 1960 thanks to Michio Kushi, Oshawa student promoting health as a source of peace [22]. The classic macrobiotic diet provides ingredients that are adapted to age, gender, level of physical activity and the needs of the patient and environment [25]. Due to the individual approach to the patient, this model of nutrition is not characterized by strictly defined rulet [22]. The basic rule of the macrobiotic diet is its use in balance with the seasons, the needs of your body and nature. According to traditional Chinese medicine, the fundamental philosophy of macrobiotics is to identify and equalise the energy properties of all products consumed, which can be yin (cooled, moistened, expanded) or yang (heated, dried and shrunk) [2].

A standard macrobiotic diet is mainly characterised by a high content of complex carbohydrates and low fat content. The menus of 50 people on a macrobiotic diet were analysed. Fats constituted 23% of energy, carbohydrates 65% of energy [31], saturated fatty acids 4.5% of energy, while polyunsaturated fatty acids provided 7.1% of energy. Average cholesterol intake in the examined persons was 76 mg/d [29].

The macrobiotic nutrition model is not strictly vegetarian, it allows small amount of animal meat. The basis of the diet is natural and unprocessed food. The macrobiotic diet consists of 40-60% cereals, mainly brown rice, barley, millet, oats, wheat, maize, rye and buckwheat. Cereal grains can germinate and, from a macrobiotic point of view, are rich in "young energy" for clear thinking [2]. 20-30% of the daily energy requirement is provided by vegetables, mainly grown locally and prepared in different ways [29], but cooked is preferred because of their easier digestion [2]. Various types of beans (azuki, peas or lentils) and dishes made from them, e.g. tofu, tempech and natto, provide 5-10% of energy during the day. In addition, the macrobiotic diet consists of sea plants and fruit, white fish meat, seeds and nuts [25, 28].

In the classical macrobiotic diet a minimum proportion of meat (including poultry), animal fat (butter, lard), eggs, dairy products, refined sugar is allowed. It is recommended that genetically modified foods, sweeteners, food additive products [35] and purified grains that increase the risk of cancer are excluded from the diet [29]. People living in a moderate climate should resign from exotic fruits [42].

Michio Kushi has created a macrobiotic nutrition pyramid that takes into account the structure of the sea plant, which distinguishes the macrobiotic diet from vegetarian [16] and Mediterranean diets [58]. Due to the difficult access to natural food, time-consuming meal preparation and the high cost of unprocessed food, this diet is difficult to maintain for oncological patients [35].

THE IMPORTANCE OF ALTERNATIVE DIETS IN CANCER

Supporting conventional therapies

Relatively recently, researches have begun on ketogenic diet as a nutritional model to support cancer therapy. These studies were carried out both on animal models and by analyzing the medical records of patients who had chosen unconventional therapy [1].

Another, more detailed case report concerned a 65-year-old woman with multiform glioma treated with standard therapy and a ketogenic diet with limited energy value. The patient was temporarily starving before starting conventional therapy and then introduced a restrictive 4:1 ketogenic diet. The energy value of the dietary model used was about 600 kcal/day, additionally the patient was taking vitamin and mineral supplements. The ketogenic diet was observed simultaneously with the traditional treatment. During the therapy, steroid drugs (dexamethasone) were discontinued by doctors. After two months of treatment, the patient's body weight decreased by 20%, whereas magnetic

resonance imaging (MRI) and emission tomography with fluoro-deoxy-glucose (FDG-PET) did not detect cancer cells in the brain. In the patient's body, reduced blood glucose level and increased level of ketone compounds in urine were observed. MRI showed a recurrence of the tumor ten weeks after the suspension of strict dietary therapy [61].

The importance of ketogenic diet in cancer was also studied among pediatric oncological patients. At Cleveland University Hospital in the United States, research has been conducted to determine if the patient's ketosis condition reduces the availability of glucose to certain types of cancer, which could potentially disrupts tumor metabolism without adversely affecting the patient's overall nutritional status. Two girls with malignant stars at an advanced stage took part in the study. Patients have been on ambulatory observation for eight weeks. The state of ketosis was maintained by a diet consisting of 60% medium-chain fatty acids derived from oil. Metabolism of glucose in the tumor was evaluated with FDG-PET. Within seven days from the beginning of the ketogenic diet the blood glucose level of patients decreased to the lowest level of normal value, while the blood ketone concentration increased 20-30 fold. The results of the FDG-PET study showed a decrease in glucose uptake at the tumor site by an average of 28.7%. During the use of ketogenic diet by patients there was a 28.8% decrease in cancer standardized uptake values (SUV). In one of the patients participating in the study, a significant clinical improvement in the mood and development of new skills was observed. She continued her ketogenic diet for the next twelve months. During this period no progression of the disease was evident [39].

The survival rate of patients with multiform glioma (GBM) treated with conventional methods is 8-15 months. Promising results, increasing survival, were obtained on animal models with GBM combining chemotherapy and radiotherapy with dietotherapy. Ketones have been reported to reduce oxidative stress, probably by improving mitochondrial function, which may also contribute to anticancer activity. Anticancer effects of ketones and ketogenic diet were observed on several models of rodents. The prescribed ketogenic diet was with a limited energy supply. In animals a decrease in growth of transplanted brain tumor cells was noticed. Mice on a ketogenic diet with limited energy supply had higher blood ketone concentration and reduced brain tumor growth associated with increased apoptosis. The ketogenic diet has also increased the effectiveness of metabolic inhibitors during the treatment of starlings in rodent models. A decrease in the growth of multiform glioma cells was shown on cell lines that were treated with β-hydroxybutyrate, the main ketone produced in the ketosis state. A reduced growth of brain cancer and higher animal survival were observed both in the group on a classical ketogenic diet and those enriched with MCT AIDS [47].

The effectiveness of different types of ketogenic diets was also analysed and compared. Standards of conduct during their application are being developed. In patients' blood, glucose and ketone levels must be monitored twice a day, and the patients' cooperation with a nutritionist is essential. Supporting GMB treatment with a ketogenic diet is possible during simultaneous radiotherapy and chemotherapy. The ketogenic model of nutrition was indicated as a complementary anticancer therapy for patients with malignant gliomas [47].

A research was also conducted to assess the toxicity and therapeutic efficacy of intranasally administered perillyn alcohol (POH) in combination with a ketogenic diet in patients with recurrent glioma. POH is a non-toxic, naturally occurring and hydroxylated monoterpene, showing cytotoxicity to glioma cells resistant to temosolomide. The study included 32 patients with recurrent GMB, 17 of the examined group were given a ketogenic diet and 15 were the control group. Each group received 55 mg POH four times a day for three months. Before the start of the clinical trial all patients were treated conventionally. After three months in the study group a partial response to treatment was observed in 77.8% (7 out of 9) of patients. They reported a reduction of the tumor in MRI, peritoneal oedema, as well as neurological stability, reduced demand for cicosteroids and general health improvement. Among the control group, a partial response to treatment was observed in 25.0% (2 out of 8) of patients, while the development of the disease occurred in 50.0% (4 out of 8) of patients. It appears that ketogenic diet with POH may be a form of complementary treatment in patients with recurrent multiform glioza [45].

In the therapy of breast cancer, caused by the overexpression of the human epidermal growth factor HER 2, transtuzumab (TRAS) is the first-line drug. This type of breast cancer belongs to the group of aggressive cancers, characterized by a high rate of metastases and difficulties in treatment. TRAS inhibits cancer growth in patients, but only in 12-26% of cases it causes cancer regression. Additionally, the response of patients' organisms to the therapy develops for one year, and in 5% of patients the drug is cardiotoxic. The aim of the study was to check whether combining a diet enriched with linseed oil with a low-dose TRAS could increase its therapeutic effectiveness. The study was carried out with mice that were given TRAS at a dose of 2.5 and 5 mg/kg body weight. The control diet contained 20% corn oil, and in turn the diet of study groups, cold-pressed linseed oil with 58% ALA. The control group tumors increased significantly in

size by 187% compared to zero week. Tumors in mice in the TRAS 2.5 group did not differ significantly in size. compared to the size of the tumor at the beginning of the study. In the case of TRAS 5 and TRAS 2.5 groups and TRAS 5 group additionally taking linseed oil, a significant regression of the tumor was noted by 75%, 89% and 84% respectively. The tumor area in the fourth week of the study was significantly lower in the TRAS 2.5 group on a linseed oil diet, compared to the group with the same dose of the drug, but on a control diet. This result was no different from that achieved by mice treated with double dose of the drug while taking linseed oil or on a control diet. The authors of the study noted that the combination of low-dose (2.5 mg/kg body weight) TRAS treatment with linseed oil supplementation was as effective as double-dose (5 mg/kg body weight) TRAS treatment [36].

Growth and tumor metastasis inhibition

Clinical trials are conducted using a ketogenic diet in support of treatment of oncological patients. It has been shown that diets with very low carbohydrate content contribute to the reduction of tumors located in the head and neck [28]. *Otto Warbung* [56] observed that cancer tumors absorb large amount of glucose as an energy source. On this basis, he put forward a thesis that the growth and metabolism of cancer cells are closely related to the process of glycolysis. Restricted access to the energy substrate causes impaired tumor growth. Additionally, thanks to the reduction of cachexia and increased tolerance to chemo- and radiotherapy, the patient's general condition improves [32].

The reduction of carbohydrate intake in the diet of an oncologic patient limits the formation of oxygen free radicals and inflammation of tissues, which contributes to the protection against the spread of cancer and has a preventive effect on healthy body tissues. The ketogenic diet, apart from a short period of starvation for the body's metabolic adaptation, has an appropriate energy value, which enables it to function and at the same time protects tissues and muscles from catabolism [32].

Brain tumors are one of the most common causes of death among children with cancer. Surgical resection followed by radiotherapy and/or chemotherapy was the standard therapy used for over fifty years. *Stafford* et al. [51] have proven that a ketogenic diet inhibits the development of gliomas, slows tumor growth and reduces the number of reactive oxygen species that usually promote tumor growth. The ketogenic diet does not work only by reducing the amount of easily accessible glucose, but its therapeutic effects are additionally associated with modulation of both the intracellular signal cascade and heomeostatic mechanisms. Healthy brain cells easily adjust their

metabolism to use ketones as an alternative source of energy, while cancer cells have a lower capacity to change their energy metabolizm [51]. Glycological cells, as well as most other types of cancer, cannot omit glycolysis and use ketone compounds in the Krebs cycle (TCA), their metabolism depends on the glycolytic pathway [4]. The data presented show that a ketogenic diet may contribute to the regression of brain tumours and may have neuroprotective effects on healthy brain cells during cancer treatment instead of chemotherapy. Additionally, in the cancer tissue there is an intensive cells growth accompanied by the formation of new blood vessels. However, the growth of cancer cells precedes angiogenesis, so that part of the hypertrophied tissue does not have enough oxygen. To continue growth, invasive tissue cells take energy from anaerobic glycolysis. Inhibition of glycolysis by a ketogenic diet may be a significant factor inhibiting the development of cancer cells [48].

The authors of 62 studies recognized the use of a low carbohydrate diet as a supportive therapy in the treatment of various diseases, 11 were concerned with anticancer therapy. In Germany, at the University of Würzburg, patients whose conventional cancer treatments had been ineffective were included in the research on the effectiveness of a ketogenic diet. Preliminary reports indicate that patients who were able to continue their ketogenic diet therapy for more than three months have improved with stable physical condition and tumor contraction or slowing down its growth. However, the authors of the study cannot statistically determine the impact of this diet on cancer cells due to the small number of people who took part in the study and their heterogeneity. Pilot data from the study suggest that ketogenic diet may be effective even in patients with advanced metastatic cancer [46].

Gabor and Abraham [9] in their study showed the strengthening effect of linoleic acid (C18=2) and the growth of mammary gland tumor cells transplanted in rodents [9]. However, a study conducted by Kamalia et al. [23] showed that a diet rich in eicosapentaenoic acid (EPA) and decosahexaenoic acid (DHA) gave the opposite effect [23]. In another study in mice with breast cancer with metastases it was found that a diet with linseed oil rich in α -linolenic acid was more effective in inhibiting tumor growth and its metastases to the lungs than a diet rich in fish oil. In a different study on an animal model it was observed that linseed oil did not show any suppressing effect on the growth of cancer cells and their spread to other organs [8].

It was examined whether n-3 fatty acids derived from linseed oil will affect the cytolytic capacity of macrophages and eicosanoids production. Mice were fed a diet of 10% linseed oil or fish oil from herring or saffron oil for three weeks. In *vitro* and in *vivo* activated macrophages selected functions were

evaluated. As predicted by the authors of the study, macrophages from mice fed on linseed oil and herring fish oil produced significantly less both prostaglandin and leukotrienes compared to macrophages from mice fed on saffron oil. Furthermore, macrophages from these mice were able to synthesise additional EPA leukotrien. However, the effect caused by linseed oil on mouse models was not as spectacular as with fish oil. For specific functions, macrophages from mice consuming linseed oil did not have an altered cytolytic capacity compared to macrophages from mice eating fish oil. The specific binding of macrophages to tumours, the production of nitric oxide and the production of tumour necrosis factor did not change after intake of linseed oil, which was observed after consumption of fish oil [19].

The aim of another study, carried out in the 1990s, was to determine if dietary supplementation with flax seeds, their ligan or oil fractions, starting from the thirteenth week after the cancer invasion, would reduce the size of nipple tumors (in the early stages of the disease) and the appearance of new tumors in rats. Ligands are diphenolic compounds present in products with high fibre content. They are assigned anticancer, antioxidant, low estrogenic (or anti-estrogenic) and anti-angiogenic properties. That suggests a diet rich in ligan precursors in mammals could protect them from cancer. Linseed is a good source of leagunes, both in vivo and in vitro researches. The authors of the study divided the animals into five groups. The control group received a diet with 20% corn oil, the next groups a diet with the addition of 2200 nmol/d of the ligano precursor sekoisodiol-diglycoside (S.D.) or 1.82% linseed oil, or 2.5% linseed or 5% linseed. After seven weeks it was found that the tumor volume was more than 50% lower in all therapeutic groups compared to control. Tumour volumes were smaller in groups on a diet with S.D. and 2.5% and 5% of linseed compared to groups whose diet was enriched with linseed oil. The authors of the study consider that taking S.D. present in linseed is beneficial in the phase of carcinogenesis promotion, while the effectiveness of linseed oil is observed after the growth of a tumor in the body. The beneficial effect of linseed oil on the cancer is attributed to its high ALA kontent [54].

In another study, it was evaluated which component of linseed reduces growth and metastases of human breast cancer in mice. The authors of the study wanted to determine whether the cancer inhibitory effect was caused by linseed oil, liganeskolaroglycol diglycoside or both at once. Eight weeks after the injection of cancer cells, an appropriate dietary model was introduced to the laboratory animals. Five different diets were used, a control diet with 20% corn oil and tested with 10% freshly milled linseed or with linseed oil or liganoescolaroglycol diglycoside or two at the

same time. Each of the prepared diets was isocaloric and high-fat. Noticeably lower tumor growth rate was observed in groups taking a diet with freshly ground linseed, linseed oil and two components simultaneously. However, there were no significant differences in the rate of cancer growth between the other two groups. Compared to the control group, the frequency of lung metastases decreased by 50.1%, 30.1%, 16.3% and 70.1%, respectively, in groups taking supplementation with freshly milled linseed, ligano-seskolaroglycol diglycoside, linseed oil and two components simultaneously. Among the study groups, only the group taking supplementation of both linseed components simultaneously had the lowest incidence of lung metastases. On the other hand, considering the occurrence of metastases to lymph nodes, only in the group supplemented with linseed oil a significant reduction of 52.5% was noted compared to the control group. The incidence of metastases in other organs, such as liver, bones, kidneys and abdominal cavity, decreased in all therapeutic groups, but in the group taking linseed oil and linseed oil with liganeskolaroglycol diglycoside metastases did not occur at all. The authors of the study believe that linseed oil, or linseed oil with liganeskolaroglycol diglycoside, contributes to the inhibitory tumour growth caused by the consumption of freshly ground linseed. Additionally, in the groups of mice taking linseed oil and two supplements at the same time, significantly lower proliferation of cancer cells was observed compared to the group of mice eating only freshly ground linseed, which suggests that both of these components increased the effect of freshly ground linseed causing reduced tumor growth rate [55].

The authors of the next study report that 80% of breast cancer patients use complementary or alternative therapy, including dietary supplements [3]. Linseed is the third most commonly used supplement. Linseed oil, which is rich in fatty acids from the n-3 family, is popularly used by patients with breast cancer because of its potential anticancer effects [36].

It was also found that these properties and principles of the macrobiotic diet, to some extent, contribute to the carcinogenic and therapeutic effects of diet on the patient's body [22].

Effects on patients' well-being and quality of life

The authors of clinical trials conducted among people at the terminal stage of the disease showed good tolerance of ketogenic diet by patients and its beneficial effect on their well-being, with no serious side effects [37, 48] (mainly constipation), even improved the emotional state of patients and reduced insomnia [48]. The ketogenic model of nutrition may additionally improve the quality of patients' life and

their blood parameters [46]. However, other researchers report that side effects of radio and chemotherapy (nausea, vomiting or other stomach problems) can be further exacerbated by a ketogenic diet [47]. In one of the patients participating in the *Nebeling* et al. [39] study was observed to have a significant clinical improvement in mood and development of new skills [39].

Macrobiotic diet for people with cancer can result in weight loss, making it unsuitable for devastated oncological patients. Dietary enthusiasts believe that it improves health, but can cause nutrient deficiencies when the patient's food selection is too radical. The food chosen by patients should provide many nutrients, but there is a risk that the energy value of the diet, protein and fluid content may be insufficient [22].

Cancer protection

The American Institute for Cancer Research and the World Cancer Research Fund have prepared dietary recommendations on cancer prevention. The authors of the report suggest that a diet based on plant products, which simultaneously minimizes the consumption of red and processed meat and is rich in whole-grain cereal products, reduces the risk of cancer [20, 21]. Many components of the macrobiotic diet have been found to have an anti-cancer effect. Whole grain products belong to the basic group of food products in the macrobiotic diet. The importance of unprocessed grains in the prevention of cancer is not only attributed to the presence of increased amount of dietary fiber, but also includes their impact on the metabolism of estrogen, glucose, insulin and oxidative processes in the body [49]. The influence of regular consumption of various vegetables on reducing the risk of cancer was also appreciated [11]. An increase in the consumption of fruit and vegetables from 250 g to 400 g per day can reduce the risk of cancer by 23%. It has also been pointed out that sea vegetables included in the macrobiotic diet may reduce the risk of breast cancer [53, 60] and endometrial cancer [13]. Brown seaweed contains fucoiudan, a polysaccharide sulphate characteristic of this variety [19], and fucoxanthin, a carotenoid causing brown colouring of plants which are known to have anticancer properties [40, 41].

Legumes, whose daily supply in a macrobiotic diet should be about 5-10% of the daily energy intake. They can reduce the risk of cancer through the presence of inhibitors and saponins. Additionally, the phytoestrogens - ganistein and daidzein found in the seeds show antioxidant antiangiogenetic effects. Isoflavonoids can also affect signal transduction and inhibit the action of DNA topoisomerases [29].

The anticancer effect of the macrobiotic diet is also associated with minimizing the consumption of foods with a pro-cancerogenic effect on the human body [30]. With the exception of fish, the macrobiotic feeding model minimises the consumption of red meat, which increases the risk of colon and rectal cancer [44], as well as prostate [49] and pancreatic cancer [16]. Moreover, the macrobiotic diet is based on natural and organic food, which is associated with a reduction in the body's exposure to pro-cancerogenic pesticides or artificial plant fertilizers [22].

At the beginning of the 21st century it has been shown that the increased consumption of whole-grain cereal products, soybean products and legumes causes a decrease in testosterone levels in patients. This is associated with a lower incidence of breast cancer in postmenopausal women. In addition, these products are conducive to weight normalization in overweight or obese patients [43].

Researchers from the Nutritional Data System for Research (NDSR) compared the nutrient and anti-inflammatory content of the macrobiotic and customary American diet (2009-2010 NHANES data) and the USDA recommendations and standards. The authors of the study used the previously developed indicator of dietary inflammation to compare nutritional models. The energy value, macronutrient content, 28 microelements and the score of the inflammatory index of the diet were analysed. In the study conducted in the next edition of the NHANES study, the macrobiotic diet was characterized by a lower percentage of energy from fat, a higher daily supply of dietary fiber and a higher content of most of the studied microelements. With the exception of vitamins D and B₁₇ and calcium, the nutrients filled or exceeded the RDA recommendations. Macrobiotic diet has also been shown to have an anti-inflammatory effect due to its nutrient profile. It prevents diseases and supports their treatment. Additionally, the authors of the study observed a strong antibacterial effect of the diet, compared to the typical diet of Americans. The results of studies on cancer prevention showed a significant reduction of inflammation in the body of patients while eating foods with strong antiinflammatory properties, which were included in the macrobiotic diet [15].

SUMMARY

Most of the scientific research in which cancer patients participated concerned the use of ketogenic diet. The authors of the study have observed the regression of neoplastic lesions after applying a strict low-carbohydrate diet, in patients who do not respond to conventional methods of treatment. It has been noticed that chronic hyperglycaemia is a risk factor for the development of cancer, as well as worsens the prognosis in already suffering patients and shortens

the survival period. Cancer cells do not use ketone compounds as a source of energy as opposed to healthy cells. It suggests that the ketogenic diet could be used in the future as a therapy to support traditional methods of treatment. Due to insufficient number of studies with a large number of homogeneous cancer patients, ketogenic diet can still not be considered as anticancer dietary therapy.

A review of the literature has revealed many contradictory information concerning the actual effect of Dr. Budwig's diet on carcinogenesis. The cited scientific research evaluating the influence of linseed oil on cancer cells was conducted mainly on animal models. Some of the results collected are contradictory, but several quoted studies have shown that taking linseed oil together with conventional cancer therapy results in a faster reaction of the rodent organism to the treatment received, compared to laboratory animals taking only traditional treatment. Additionally, the authors of the study noticed that it is possible to reduce the dose of anticancer drugs (even by half) with simultaneous supplementation with linseed oil (or linseed) obtaining identical treatment results as with a higher dose of therapists. The authors of the study attributed beneficial changes caused by linseed oil supplementation in the examined mammals to ALA. Mice and rats are characterized by a different metabolism than humans, which does not allow for an unambiguous assessment of the effectiveness of the dietary model proposed by Dr. Budwig.

The analysis of the quoted literature on diet of *George Ohsawa* indicates that the macrobiotic dietary model is recommended primarily as prevention of cancer. For people with a diagnosis of cancer, a macrobiotic diet can have an adverse effect on their nutrition and health. Macrobiotic nutrition can contribute to weight loss and nutrient deficiencies, which excludes its use in oncological patients.

Alternative diets are very popular among oncologic patients, however, in the light of current and quoted studies, their use cannot be clearly considered as justified. However, numerous indications of their high effectiveness in supporting conventional therapy are very promising.

REFERENCES

- 1. Allen B.G., Bhatia S.K. Anderon C.M., Eichenberger-Gilmore J.M., Sibenaller Z.A., Mapuskar K. A., Schoenfeld J. D., Buatti J. M., Spitz D. R., A. Fath M. A.: Ketogenic diets as an adjuvant cancer therapy: History and potential mechanizm. Redox Biol 2014;2:963-970 doi: 10.1016/j.redox.2014.08.002.
- 2. Ashton A.: The macrobiotic diet. Nat Health 2011;41:42-47.
- 3. Boon H. S., Olatunde F., Zick S. M.: Trends in complementary/alternative medicine use by breast

- cancer survivors: comparing survey data from 1998 and 2005. BMC Women's Health 2007;7:4 doi: 10.1186/1472-6874-7-4.
- 4. *Cahill G.F. Jr.*: Fuel metabolism in starvation. Annu Rev Nutr 2006;26:1–22.
- 5. Choragiewicz T., Zarnowska I., Gąsior M., Żarnowski T.: Przeciwdrgawkowe i neuroprotekcyjne działanie diety ketogennej [Anticonvulsant and neuroprotective effects of ketogenic diet]. Przegl Lek 2010;67(3):205-212 (in Polish).
- 6. Cierniak-Piotrowska M., Marciniak G., Stańczak J.: Statystyka zgonów i umieralności z powodu chorób układu krążenia. [w:] Strzelecki Z., Szymborski J.: Zachorowalność i umieralność na choroby układu krążenia a sytuacja demograficzna Polski [The statistics of deaths and mortality from cardiovascular diseases, [in:] Strzelecki Z., Szymborski J.: Morbidity and mortality from cardiovascular diseases and the demographic situation of Poland]. Warszawa, Rządowa Rada Ludnościowa 2015; 46-80 (in Polish).
- 7. Cunningham RS., Herbert V.: Nutrition as a component of alternative therapy. Semin Oncol Nurs 2000;16(2):163-169
- 8. Fritsche K.L., Johnston P.V.: Effect of dietary a-linolenic acid on growth, metastasis, fatty acid profile and prostaglandin production of two murine mammary adenocarcinomas. J Nutr 1990;120:1601-1609.
- 9. Gabor H., Abraham S.: Effect of dietary menhaden oil on tumor cell loss and the accumulation of mass of a transplantable mammary adenocarcinoma in BALB/c mice. J Natl Cancer Inst 1986;76(6):1223-1229.
- 10. Gasior M., Rogawski M.A., Hartman A.L.: Neuroprotective and disease-modifying effects of the ketogenic diet. Behav Pharmacol 2006;17(5-6):431–439 doi:10.1097/00008877-200609000-00009.
- 11. Glade M. J.: Food, nutrition and the prevention of cancer: a global perspective. American Institute for Cancer Research/World Cancer Research Fund, American Institute for Cancer Research, 1997. Nutrition 1999;15(6):523-526 doi:10.1016/s0899-9007(99)00021-0
- 12. *Glibert D.L.*, *Pyzik P.L.*, *Freeman J.M.*: The ketogenic diet: seizure control correlates better with serum β-hydroxybutyratethanwithurineketones, JChild Neurol 2000;15(12):787-790 doi: 10.1177/088307380001501203.
- 13. Goodman M.T., Wilkens L.R., Hankin J.H., Lyu L. Ch., Wu A. H., Kolone L. N.: Association of soy and fiber consumption with the risk of endometrial cancer. Am J Epidemol 1997;146(4):294-306.
- 14. *Haddad H., Sabate J, Whitten C.G.*: Vegetarian food guide pyramid: a conceptual framework. Am J Clin Nutr 1999;70(3Suppl):615-619 doi: 10.1093/ajcn/70.3.615s.
- 15. Harmon B.E., Carter M., Hurley T.G., Shivappa N., Teas J., Hébert J. R.: Nutrient composition and anti-inflammatory potential of a prescribed macrobiotic diet. Nutr Cancer 2015;67(6):933-940 doi: 10.1080/01635581.2015.1055369.
- 16. *Howe G.R.*, *Burch J.D.*: Nutrition and pancreatic cancer. Cancer Causes Control 1996;7:69-82.

- 17. *Hubbard N.E., Chapkin R.S., Erickson K.L.*: Effect of dietary linseed oil on tumoricidal activity and eicosanoid production in murine macrophages. Lipids 1994;29(9):651-655.
- 18. Huebner J., Marienfeld S., Abbenhardt C., Ulrich C., Muenstedt K., Micke O., Muecke R., Loeser C.: Counseling patients on cancer diets: a review of the literature and recommendations for clinical practice. Anticancer Res 2014;34(1):39-48.
- 19. Itoh H., Noda H., Amano H., Zhuaug C., Mizuno T., Ito H.: Antitumor activity and immunological properties of marine algal polysaccharides, especially fucoidan, prepared from Sargassum thunbergii of Phaeophyceae. Anticancer Res 1993;13(6A):2045-2052.
- 20. *Jacobs D.R.*, *Marquart L.*, *Slavin J.*, *Kushi L. H.*: Wholegrain intake and cancer: an expanded review and meta-analysis. Nutr cancer 1998;30(2):85-96.
- 21. Jacobs D.R., Meyer K.A., Kushi L.H. Folsom A. R.: Is whole grain intake associated with reduced total and cause-specific death rates in older women? The Iowa Women's Health Study. Am J Public Health 1999;89(3):322-329.
- 22. Kardasz M., Pawłowska D.: Dyskusyjne metody terapii alternatywnej u osób z chorobą nowotworową [Questionable methods of alternative therapy in persons with cancer]. Nowa Med 2008;2:16-25 (in Polish).
- 23. *Karmali R.A., Marsh J., Fuchs Ch.*: Effect of omega-3 fatty acids on growth of a rat mammary tumor. J Natl Cancer Inst 1984;73(2):457-461.
- 24. Kiedrowski M., Gajewska D.: Co powinien wiedzieć lekarz rodzinny o popularnych "dietach odchudzających" i samym odchudzaniu? [What should the general practitioner know about popular "slimming diets" and weight loss?]. Med Rodz 2013;3:95-98 (in Polish).
- 25. Kishi M., Jack A.: The book of Macrobiotics: The uniwersal way of health, happiness and peace. Tokyo and New Yourk, Japan Publications 1986.
- 26. Klement R.J.: Restricting carbohydrates to fight head and neck cancer—is this realistic?. Cancer Biol Med 2014;11(3):145-161 doi: 10.7497/j.issn.2095-3941.2014.03.001.
- 27. Krajowy Rejestr Nowotworów [National Cancer Register]. Available http://onkologia.org.pl/nowotwory-zlosliwe-ogolem-2/ (Accessed 12.12.2017) (in Polish).
- 28. Kushi K., Jack A.: The cancer prevention diet: Michio Kushi's macrobiotic blueprint for the prevention and relief of disease. New York, St. Martin's Griffin 1993.
- 29. Kushi L.H., Cunningham J.E., Hebert J.R., Lerman R. H., Bandera E. V., Teas J.: The macrobiotic diet in cancer. J Nutr 2001;131(11 Suppl):3056-3064.
- 30. Kushi L.H., Meyer K.A., Jacobs D.R.: Cereals, legumes and chronic disease risk reduction: evidence from epidemiologic students. Am J Clin Nutr 1999;70(3Suppl):451-458 doi:10.1093/ajcn/70.3.451s.
- 31. Kushi L.H., Samands K.W., Lacey J.M. Brown P. T., Bergan J. G., Sacks F. M.: The association of dietary fat with serum cholesterol in vegetarians: the effect of dietary assessment on the correlation coefficient. Am J Epidemol 1988;128(5):1054-1064.

- 32. Lee Ch., Raffaghello L., Brandhorst S., Safdie F. M., Bianchi G., Martin-Montalvo A., Pistoia V., Wei M., Hwang S., Merlino A., Emionite L., de Cabo R., Longo V. D.: Fasting cycles retard growth of tumors and sensitize a range of cacer cell types to chemotherapy. Sci Transl Med 2012;4(124):124-127 doi: 10.1126/scitranslmed.3003293.
- 33. Liśkiewicz A., Jędrzejowska-Szypułka H., Lewin-Kowalik J.: Characteristics of ketogenic diet and its therapeutic properties in central nervous system disorders. Ann. Acad. Med. Siles 2012;66(6):66–76.
- 34. Maisch P., Gschwend JE., Retz M.: Efficacy of a ketogenic diet in urological cancers patients: a systematic review. Urologe 2018;57(3):307-313. doi: 10.1007/s00120-017-0563-5.
- 35. Martiness C., Small S., Waltz-Hill M.: Alternative nutrition therapies in cancer patients. Semin Oncol Nurs 2005;21(3):173-176.
- 36. Mason J.K., Chen J., Thompson L.U.: Flaxseed oil—trastuzumab interaction in breast cancer. Food Chem Toxicol 2010:48(8-9);2223-2226.
- 37. Meder J.: Rak głównym zabójcą ludzi XXI wieku. Narodowy program zwalczania chorób nowotworowych, [w:] Potrynkowska A., Strzelecki Z., Szymborski J. i wsp.: Zachorowalność i umieralność na nowotwory a sytuacja demograficzna Polski [Cancer is the main killer of 21st century people. National Programme for Combating Cancer, [in:] Potrynkowska A., Strzelecki Z., Szymborski J. et al.: Zachoralność i umieletność na nowotworowych a sytuację demograficzna Polski]. Warszawa, Rządowa Rada Ludnościowa 2014; 50-57 (in Polish).
- 38. Mińskowski K., Grześkiewicz S., Krupska A.: Zastosowanie metody HS-SPME_GC/FID do wykrywania wczesnych zmian oksydacyjnych oleju lnianego [Application of HS-SPME_GC/FID method to detect early oxidative changes in flax oil]. Żywn Nauka Technol Jakość 2012;19(6):93-102 (in Polish).
- 39. Nebeling L.C., Miraldi F., Shurin S.B., Lerner E.: Effects of a ketogenic diet on tumor metabolism and nutritional status in pediatric oncology patients: two case reports. J Am Coll Nutr 1995;14(2):202-208.
- 40. *Nishino H.*: Cancer prevention by carotonoids. Mutat Res 1998;402(1-2):159-163.
- 41. Okuzumi J., Nishino H., Murakoshi M., Iwashima A., Tanaka Y., Yamane T., Fujita Y., Takahashi T.: Inhibitory effect of fucoxanthin, a natural carotenoid, on N-myc expression and cel cycle progression in human malignant tumor cells Cancer Lett 1990;55(1):75-81 doi:10.1016/0304-3835(90)90068-9.
- 42. Questionable methods of cancer management: "Nutritional" therapies. CA Cancer J Clin 1993;43(5):309-319.
- 43. Rezash V: Can a macrobiotic diet cure cancer? Clin J Oncol Nurs 2008;12(5):807-808 doi: 10.1188/08. CJON.807-808.
- 44. Sandhu M.S., White J.R., McPherson K.: Systematic review of the prospective cohort studies on meat consumption and colorectal cancer risk: a meta-

- analytical approach. Cancer Epidemiol Biomark Prev 2001;10(5):439-446.
- 45. Santos J.G., Da Cruz W.M.S., Schönthal A.H., Salazar M. D., Fontes C. A. P., Quirico-Santos T, Da Fonseca C. O.: Efficacy of a ketogenic diet with concomitant intranasal perillyl alcohol as a novel strategy for the therapy of recurrent glioblastoma. Oncol Lett 2018;15(1):1263-1270 doi: 10.3892/ol.2017.7362.
- 46. Schmidt M., Pfetzer N., Schwab M. Strauss I., Kämmerer U.: Effects of a ketogenic diet on the quality of life in 16 patients with advanced cancer: a pilot trial. Nutr Metab (Lond) 2011;8(1):54-67 doi: 10.1186/1743-7075-8-54.
- 47. Schwartz KA, Noel M, Nikolai M., Chang H. T.: Investigating the ketogenic diet as treatment for primary aggressive brain cancer: challenges and lessons learned. Front Nutr 2018;5:11 doi: 10.3389/fnut.2018.00011.
- 48. Seyfried T.N., Sanderson T.M., El-abbadi M.M., McGowan R., Mukherjee P.: Role of glucose and ketone bodies in the metabolic control of experimental brain cancer. Br J Cancer 2003;89(7):1375-1382.
- 49. *Slavin J.L.*: Mechanisms for the impact of whole grain foods on cancer risk. J Am Coll Nutr 2000;19(3Suppl):300-307.
- 50. Stachowiak U.: Dieta a nowotwór. Poradnik dla Pacjentów [Diet and cancer. Patient guide]. Wielkopolskie Centrum Onkologii; 18-21. Available https://www.wco.pl/wp-content/uploads/2015/08/dieta_a_nowotwor.pdf (Accessed 22.02.2018) (in Polish).
- 51. Stafford P., Abdelwahab M.G., Kim D.Y., Preul M. C., Rho J. M., Scheck A. C.: The ketogenic diet reverses gene expression patterns and reduces reactive oxygen species levels when used as an adjuvant therapy for glioza. Nutr Med (Lond) 2010;7:74-85 doi: 10.1186/1743-7075-7-74.
- 52. Stafstrom C.E., Rho J.M.: The ketogenic diet as a treatment paradigm for diverse neurological disorders, Front. Pharmacol. 2012;3 Available https://doi.org/10.3389/fphar.2012.00059 (Accessed 19.03.2018).
- 53. *Teas J., Herbison M.L., Gelman R.S.*: Dietary seaweed (laminaria) and mammary carcinogenesis in rats. Cancer Res 1984;44(7):2758-2761.
- 54. Thompson L.U., Rickard S.E., Orcheson L.J., Seidl M. M.: Flaxseed and its lignan and oil components reduce mammary tumor growth at a late stage of carcinogenesis. Carcinogenesis 1996;17(6):1373-1376.
- 55. Wang L., Chen J., Thompson L.U.: The inhibitory effect of flaxseed on the growth and metastasis of estrogen receptor negative human breast cancer xenograftsis attributed to both its lignan and oil components. Int J Cancer 2005;116(5):793-798.
- 56. Warburg O.: On the origin of cancer cells. Science 1956;123:309-314.
- 57. Westman E.C., Yancy W.S. Jr, Mavropoulos J.C. Marquart M., McDuffie J.R.: The effect of a low-carbohydrate, ketogenic diet versus a low-glicemic index diet on glycemic control in type 2 diabetes mellitus. Nutr Metab (Lond) 2008;19(5):36 doi: 10.1186/1743-7075-5-36.
- 58. Willet W.C., Sacks F., Trichopoulon A., Drescher G., Ferro-Luzzi A., Helsing E., Trichopoulos D.:

- Mediterranean diet pyramid: a cultural model for healthy heating. Am J Clin Nutr 1995;61(6Suppl):1402-1406 doi: 10.1093/ajcn/61.6.1402S.
- 59. Woźniak-Holecka J., Zborowska K., Holecki T.: Alternative medicine as a complementary form of treatment in the oncological patients' opinion. Psychoonkologia 2010;14(1):21-28.
- 60. Yamamoto I., Maruyama H., Moriguchi M.: The effect of dietary seaweeds on 7,12-dimethylbenz[a]anthracene induced mammary tumorigenesis in rats. Cancer Lett 1987;35(2):109-118 doi:10.1016/0304-3835(87)90033-4.
- 61. Zuccoli G., Marcello N., Pisanello A., Servadei F., Vaccaro S., Mukherjee P., Seyfried T.N.: Metabolic management of glioblastoma multiforme using standard therapy together with a restricted ketogenic diet: case report. Nutr Metab (Lond) 2010;7:33-39 doi: 10.1186/1743-7075-7-33.

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