Children's nutrition and the risk of developing neoplasms in childhood and adolescence.

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ABSTRACT

Background: The effect of children's eating habits on the development of cancers in childhood and adolescence has been of great concern to researchers in recent years. This literature review aims to present the foods that may be related to the prevention or the incidence of cancer at the children between 0-18 years of age.

Methods: A research on nutrition and the appearance of tumors in children and adolescents between the ages of 0-18 years old was done regardless of gender, educational level and nationality. A literature review was conducted using online databases and words, such as "Nutritional Habit", "Nutritional Status", "Diet'', "Adolescence'', "Childhood'', "Pediatric Cancer'', "Neoplasm'', "Carcinoma'', "Lymphoma'' and "Leukemia''. We collected and analyzed a total of 34 surveys, including three meta-analyses, ten case-control studies, one cross-sectional study and two research articles.

Results: Worldwide the results showed a protective interrelation between breastfeeding, and the consumption of fruits, vegetables and dairy products in the development of childhood cancer. In contrast, the consumption of meat, cured meats, smoked fish, vegetable oils, soft drinks such as cola, junk food, but also the exposure to heavy metals, stand as the risk factors for childhood cancer cases.

Conclusion: The Disease's prevention is associated with intrauterine life and the mother's diet during pregnancy. The nutrition of the child is crucial in the first years of life and eating habits then affect food choices at an older age. A Balanced children's nutrition is important and depends on the parents who should consult health care professionals. Finally, due to the constant appearance of new data, it is considered necessary to further study this field in Greece and cross-culturally.

Key Words: *Childhood, Adolescence, Cancer, Leukemia, Nutrition*

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Introduction

Cancer is the second most common cause of death in children aged 1-14 years after accidents. About 10,470 children in the United States under the age of 15 will be diagnosed with cancer in 2022, and the number of deaths is 1.050 children under the age of 15. Pediatric cancer rates have been rising more slowly in recent decades due to significant advances in treatment, resulting in 85% of children with cancer surviving 5 years or more. However, survival rates can vary depending on the type of cancer and other factors, such as the location of the tumor in the body, the stage of cancer, and its growth rate (1).

More specifically, the most common types of children's cancer are different from those adults suffer from, with the main ones being: leukemia, brain, and spinal cord tumors, neuroblastoma, Wilms tumor, lymphoma (including Hod and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma) (1).

Leukemia, a bone marrow and blood cancer, is the most common type of childhood cancer and accounts for about 28% of all cancers in children. The main symptoms are pain in the bones and joints, fatigue, weakness, pale skin, bleeding or bruising, fever, and weight loss. The most common types are acute lymphoblastic leukemia (ALL) and acute myelogenous leukemia (AML) (1), with ALL accounting for about 80% of pediatric leukemias, occurring in children 2-5 years of age, more common in boys where a poorer prognosis occurs, especially in Caucasian and Hispanic populations (2-4).

Risk factors for childhood cancer include genetic predisposition, syndromes such as Down Syndrome, exposure to viruses such as Epstein-Barr Virus (EBV), pesticides, dyes, air pollutants, petroleum solvents, ionizing radiation, parent's habits such as smoking and diet, and finally the nutrition of children from the time of birth (5,6). Specifically, the diet has been linked to the occurrence of various types of cancer in both children and adults (7). This is explained by biological mechanisms, like exposure to mutations that lead to a lack of nutrients and micronutrients. These dietary factors are necessary to protect against cancer by supporting cellular integrity, reducing inflammation, and improving the immune response (8-10).

In addition, certain types of food, such as cured meats and smoked fish contain precursor forms of N-nitroso, leading to the formation of carcinogenic compounds N-nitroso in gastric acid (11).The molecular action of these compounds is inhibited by antioxidants such as vitamins C, E, flavonoids found in fresh fruits, vegetables, green tea, and soy (12-14). At the same time, the Mediterranean diet has a protective effect against chronic diseases including different types of cancer, through its anti-inflammatory and antioxidant action (15). Finally, breast milk contains several active immune components and multifactorial anti-inflammatory defense mechanisms, that affect the development of the immune system of the breastfed infant. A the same time, this type of feeding transfers to the newborn secretory IgA antibodies (6) and prebiotics (16). Biological mechanisms, such as the gut microbiome of the newborn, Natural Killer cells, and stem cells in breast milk can elucidate the inverse relationship between breastfeeding and leukemia. On the contrary, the introduction of infant formula into the child's diet modifies the intestinal microbiome and cannot mimic the protective properties of breast milk (6).

MATERIALS AND METHODS

A research algorithm was created in order to extract data on the effect of children's eating habits in the appearance of neoplasms in childhood and adolescence worldwide. Scientific online databases (PubMed and Google Scholar) were used to complete the research of this review. The main inclusion criteria were: a) age group:0-18, b) no geographical restrictions, c) type of study: cross-sectional, case-control, systematic reviews and meta-analyses and d) language: English. Finally, the authors collected and analyzed a total of 34 surveys, of which three meta-analysis, ten case-control studies, one cross-sectional study, and two research articles.

RESULTS

Breastfeeding

Starting with breastfeeding in a meta-analysis by Kwan et al. in 2004 (17) in the USA 14 case-control studies were studied and a negative correlation was found between long-term breastfeeding (> 6 months) and ALL as well as with AML. At the same time, short-term breastfeeding (<6 months) was found to be equally protective for the occurrence of ALL and AML in childhood, while the socioeconomic level as a confounding factor did not seem to affect the results. Another similar meta-analysis was conducted by Amitay et al. in 2015 (6), including 17 studies of cases and controls. The authors have concluded that compared to zero or less than 6 months of

breastfeeding, any for 6 months or more was associated with 20% fewer Odds for childhood leukemia, while continuous breastfeeding compared to the absence of it leads to 9% lower Odds.

In addition, in a case-control study by Schraw et al. involving 142 cases and 284 controls aged <14 years, the correlation between infant feeding practices and the age of solid food intake with a risk of acute lymphoblastic leukemia in childhood was studied. The results demonstrated that the longer duration of nutrition with formula and the delayed induction of solid food is not related to an increased risk of ALL (18). In contrast, in the case-control study by Greenop et al. (19) in 2015, 322 ALL cases, 679 ALL controls, 299 CBT cases, and 733 CBT controls participated and was found that breastfeeding, regardless of the duration, was linked to reduced risk of ALL. The study also showed that formula intake within 14 days of birth affected positively ALL, as was exclusive formula feeding for up to 6 months and found no significant difference between breastfeeding or formula feeding and the risk of brain tumor (30). Finally, in another study of Lupo et al. in 2014, 322 RMS cases and 322 controls participated and concluded that breastfeeding ≥12 months is significantly connected to a reduced risk of childhood retinoblastoma (RMS) (16).

Milk and Dairy Products

Other categories of food studied for association with ALL were meat and dairy products, as shown by a case-control study by Diamantaras et al. in 2013 in Greece. A total of 139 cases of infants' leukemia participated in this study, of which 121 were acute lymphoblastic leukemia and came from the Nationwide Registry for Childhood Hematological Malignancies. The same number of controls as the cases was used, from the same institution where the children were hospitalized for minor diseases and negative history of cancer or nutrition/metabolic disorders. The study was performed through interviews with the care givers and the children. A significant relation was found between the consumption of milk and dairy products and ALL, especially in the first year of life. This result arises probably from the action of vitamin D and the proteins that milk and dairy products contain. On the contrary, higher consumption of additional fats (butter, margarine, etc.) increased the risk of childhood leukemia, while a marginally statistically significant correlation with ALL was observed in macronutrient proteins. Finally, the study showed no statistically significant upregulation of risk between other foods and macronutrients studied with ALL (cereals, fruits, vegetables, meat, fish, and nuts) (20).

Meats

In a case-control study by Peters JM et al. in 1994, an attempt was made to determine the relationship between foods containing N-nitroso precursors or are inhibitors of the substance, and the occurrence of leukemia. The study included children aged 0-10 years living in Los Angeles, and the mother provided the researchers with information on the frequency of eating certain foods over a specific period. A significant effect was found with hot dog consumption, demonstrating that including more than 12 hot dogs per month in a child's diet significantly increases the risk of childhood leukemia (21). Sarasua S. et al. in 1994, conducted a case-control study regarding the effect of broiled and cured meat on childhood cancer. The study involved children aged 0-14 years and examined the frequency of consumption of ham, bacon, hot dogs, hamburgers, bologna, pastrami, corned beef, or salami and broiled food. The results showed that ALL was related to hamburger consumption, specifically eating more than one per week and a link was also demonstrated between brain tumors and feeding the child with ham, bacon, and sausage, and hot dogs, specifically more than 1 hot dog per week (22). At the same time, this study exhibited that the combination of no vitamin intake and meat consumption had a strong effect on ALL and brain neoplasms. A subsequent case-control study by Liu CY et al. in 2009, addressed the association between the consumption of cured/smoked meat and fish, which are the main sources of exposure to nitrites and nitrosamines, and the occurrence of acute childhood leukemia. The survey was aimed at people aged 2-20 years and a total of 179 cases and 475 controls participated. The questionnaire given could be completed either by the individual or by his/her mother and concerned the frequency of consumption of fruits, vegetables, bean-curd foods, tea alcohol-containing beverages, cured/smoked meat or fish, and pickled vegetables. This study displayed that eating cured meat and smoked fish more than once a week was related to an increased risk of ALL. No significant difference was found between consumption of tea, fruit, and pickled vegetables and acute childhood leukemia (23).

Oils

One category of food that has been of interest to researchers is vegetable oils. Particularly, an analysis with one variance of a case-control study by Lubin F.et al. in 2000, showed that high consumption of vegetable fat, carbohydrates, and vitamin E were significantly

correlated to the risk of brain tumors in children (24). Similar results were also shown in a study of cases and controls by Diamantaras AA et al. in 2013 in Greece, which studied the link between childhood leukemia with the consumption of macronutrients, various foods, energy intake, and the Mediterranean diet's consumption. In this study children aged 5-14 years were included and was found that higher consumption of added fats, such as seed oil and olive oil, was connected with an increased risk of childhood leukemia (20).

Junk Food

The scientific community has also shown particular interest in studying the effect of cola and junk food on childhood cancer. Specifically, a meta-analysis by Thomopoulos et al.in 2015 in Greece, with 12 case-control studies, concluded that the child's consumption of cola-type products did not correlate with the occurrence of ALL (25). On the other hand, a case-control study by Ayub et al. in 2020 found that the consumption of junk food and caffeinated beverages increased the risk of childhood leukemia, as children with a leukemia diagnosis who participated in the study had a higher consumption of these foods (26).

Fruits and Vegetables

Several studies have emphasized the effect of fruits and vegetables on the incidence of childhood leukemia, mainly because of their protective properties. A case-control study by Kwan ML et al. in 2004, attempted to highlight the relationship between the foods consumed by a child in the first two years of life and the development of leukemia. This study presented that frequent consumption of oranges and bananas, as well as orange juice, decreases the risk of childhood leukemia (27). Both fruits are important sources of vitamins and minerals, such as vitamin C and potassium, preventing carcinogenesis and protecting against DNA oxidation (28).

Heavy Metals

Researchers have focused also in recent years on the effect of heavy metals in the development of childhood cancers, both through their intake through the digestive tract, and through the air and percutaneous contact (29). A study conducted off the coast of China showed that farmed scallops contained significant amounts of heavy metals. In particular, high levels of cadmium (Cd), arsenic (As), and nickel (Ni) were found, being public health concern due to the increased risk of cancer if consumed (30). Another study in Nigerian communities with heavy artisanal mining activity looked at the health risks of eating heavy metal-contaminated vegetables. More precisely, consumption of vegetables contaminated with cadmium (Cd) and chromium (Cr) can lead to an upregulated risk of childhood cancer (31).

DISCUSSION

The main goal of this research was to examine the possible foods that may influence the occurrence of childhood cancer. More specifically, the eating habits that appeared to protect against childhood cancer were breastfeeding for at least 6 months (6,16,17,19), consumption of dairy products (20), as well as fruits, vegetables (27) and tofu (23). Some studies have shown that formula feeding leads to an increased risk of childhood cancer (6,19), while in a study of cases and controls, longer duration of formula feeding and delayed introduction of solid food were not associated with an increased risk. On the other hand, the types of food which were associated with childhood neoplasms were hot dogs (21,22), hamburgers (22), cured meats, smoked fish (23), and high amounts of vegetable (24) and added fats (20). Also, high-risk are considered to be caffeinated beverages and junk food (26), as well as the intake of heavy metals through food (29-31).

The prevention of cancer's development commences in the endometrial life and with the diet of the mother during pregnancy. The children's diet during the first years of their life plays an important role, as according to scientific studies, eating habits are established in the first years of life and affect food choices at an older age. For this reason, it is vital for parents, in cooperation with health professionals, to introduce solid foods and potential allergens into the child's diet promptly and encourage children to consume a variety of foods, especially foods rich in iron and zinc (32).

In regard to breastfeeding, the guidance of the World Health Organization is to follow exclusive breastfeeding for the first 6 months of life, to achieve the optimal growth, development, and health of the infant. Newborns who are not breastfed or have mixed feeding are considered a high-risk group for malnutrition, morbidity and mortality (33). Finally, according to the recommendations of experts, soft drinks containing caffeine, as well as honey and unpasteurized foods should be avoided at ages younger than two years (32).

CONCLUSION

In summary, the model of nutrition followed during infa-

-ncy and adolescence, as well as the habits and knowledge available to caregivers, are of great importance. Some eating habits that protect the appearance of cancer in childhood and adolescence, are the consumption of fruits and vegetables, legumes, and cereals. The reduced intake of foods with a high percentage of sugar and salt, soft drinks and alcohol, as well as red meat is also considered protective(34).

The contribution of society and government in taking measures to promote and support healthy eating can be particularly beneficial. Specifically, it is essential that young parents can receive objective and comprehensive information in appropriate feeding practices, without the influence of advertising. Moreover, it is necessary to support young mothers, both socially and professionally, so that breastfeeding and childcare can continue unhindered even after their return to paid employment. It may also be beneficial to create support networks among mothers in the community, to interact with each other, and involve counsellors to whom mothers can be referred from hospitals and clinics. Finally, it is extremely important to ensure that the quality of products placed in the market follows health protocols and is suitable for feeding infants and young children (33).

It is also necessary to educate and raise awareness among children and adolescents, parents and grandparents, as in many cases they seem to have a negative impact on the eating habits of their grandchildren (35). High attention should be given to specific social groups, which appear to be more vulnerable and exhibit high-risk behaviors, such as sexual minorities (36). Studies have shown that obesity and overweight problems, physical inactivity, diets low in fruit and vegetables are significantly more prevalent among sexual minority individuals than heterosexual women. In addition, care is also reserved for families of low socioeconomic level, for whom government programs in the U.S. have been put in place so that they have access to nutritious meals and educational activities that support the healthy eating habits of children and adolescents (32). In Greece though, young parents can visit specific sites to get consultation on proper children's nutrition from the time of birth to adulthood to establish proper eating behaviors (37).

In conclusion, this literature review summarizes the foods that may protect or lead to children's cancer but future research is needed to establish all the types of food that may be related to pediatric neoplasms.

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