First Edition

OREGANO

Nutrition Journal of Varastegan Institute for Medical Sciences

oregano

OREGANO
JOURNAL

By the spread of non-scientific content in society, there is a growing need for researchers in various fields to contribute to the growth of the scientific community by expanding content from valid scientific references. Accordingly, the Oregano journal is established to play a positive role in the scientific community. The Oregano authors attempted to bring the nutrition scientific community up to date by valid scientific content. All articles are provided in the form of a narrative review with practical figures. Despite all of the hardships of COVID-19 pandemic, the first edition of Oregano journal was finally published. Special thanks to Dr. Najmeh Seifi for all the constructive support that made the journal more impressive. Also, we appreciate Varastegan Institute for Medical Sciences for taking us this opportunity.

Best Regards

CONTENT

MEMBERS

The Effect of Human Milk Fortification With Extra Protein on The Growth Factors of Hospitalized Preterm Infants

Ali Ebrahimi Dabagh
Arvin Babaei

Introduction

Preterm is defined as the birth of a live baby at less than 37weeks' gestational age. The prevalence of preterm birth is reported to be 5- 18% of all births. Approximately 15 million babies are born prematurely each year and this number is growing every day (1).

The prevalence of preterm birth in Iran is 2.9% (2) and in the United States is 10% (3). In 2018, premature births and low birth weight accounted for 17% of infant mortality before the age of one (3). Survived infants may suffer from problems such as developmental delays, eating problems, respiratory problems, cerebral palsy, hearing problems, and vision problems if left untreated (3).

One way of feeding premature infants is through the feeding tube. Early feeding, especially in premature infants, has important effects on the long-term health of the infant, including brain development, cognitive function, linear growth, bone mineralization, infant health in the future life, and reducing the risk of diseases such as metabolic syndrome and cardiovascular diseases in adulthood (4).

Human milk, donor human milk (DM), preterm infant formulas (e.g., Human milk fortifier (HMF)), and transitional infant formulas are used in enteral infant feeding (5). The amount of energy required for premature infants is 110-135 kcal/kg/day and the amount of protein required for premature infants weighing less than 1 kg is equal to 4-4.5 g/kg /day and the amount of protein required for premature infants weighing 1 kg or more is equal to 3.5-4 g/kg /day (5,6).

The aim of this review study is investigating the effect of increasing the amount of protein in the diet of preterm infants compared to the recommended amount on growth and anthropometric indices.

Literature review

A single-center randomized clinical trial study was conducted by Quan et al in 2019 in China, which aimed to investigate the effect of a new individualized HMF method on improving the growth of premature infants. This method was based on periodic analysis of human milk (HM) protein concentration, preterm infant weight, and blood urea nitrogen. The results showed that the weight gain velocity of preterm infants in the third week after the enrollment was significantly higher than the standard group (P=0.022) (7).

A prospective cohort study of Shakeel et al was conducted in 2019 in the United States, that aimed to evaluate the tolerance of adding liquid protein (LP), providing 1g protein/6 ml, to fortified HM to improve protein intake and its effect on growth velocity in preterm infants.This study showed that the addition of LP up to 6ml/100ml to HM was well tolerated in premature very low birth weight (VLBW) infants. Although there was no significant difference between the two groups for growth velocity and anthropometric indices, weight and head circumference (HC) were higher in the LP group at discharge (8).

A randomized double-blind clinical trial study by Reid et al was conducted in 2018 in Australia. This study aimed to evaluate the effect of using high protein HMF in preterm

infants on the growth of these infants. This study showed that increasing protein intake from 1 to 1.8 g /100 ml of HM did not improve growth in infants born between 28-32 weeks of gestation. However, with increasing the protein intake, lean body mass was significantly (P=0.04) improved (9).

Maas et al in a single-blind randomized clinical trial study aimed to determine the different levels of protein intake through enteral feeding in premature infants fed HM. The results showed that an increase of 0.6 gr/kg/d of protein intake in VLBW infants had no significant effect on the growth increase. The number of infants in the high-protein group with weight, length, and HC less than the 10th percentile at the time of discharge were less than the low-protein group; But the difference was not significant (10).

A randomized clinical trial study by Bellagamba et al in 2016 in Italy aimed to investigate the effect of 1 extra gram of amino acid intake through parenteral nutrition (PN) and protein intake from enteral nutrition (EN) on the growth and improvement of the nervous system in extremely low birth weight (ELBW) infants. They showed that increasing the protein intake through EN and PN had no significant effect on the growth of ELBW premature infants (11).

Discussion

Based on the early protein hypothesis, higher protein consumption improves the circulating amino acid concentrations (e.g. branched-chain amino acids) which itself can increase the secretion of insulin and IGF-1 hormones, and consequently weight gain and deposition of fat in the body occur (12).Total IGF-1 is significantly associated with growth increase and it is one of the most important factors in bone formation in human beings (13) and has positive effects on linear growth (14).

Some theories about the fate of protein intake in preterm infants suggest that some HM proteins such as lactoferrin and immunoglobulin A (IgA) are excreted in large amounts in the feces; since these proteins are glycosylated in the gut and therefore making them indigestible (6). Another theory is that the intake of excess protein, in general, cannot reflect the intake of nitrogen-containing proteins, which are very important for growth (8). There is another theory that the amount of excess protein is absorbed, cannot be used for protein production but is metabolized to urea and eventually excreted (10).

Conclusion

As none of the available evidence can yet conclusively prove the ineffectiveness or effectiveness of intaking higher amounts of protein

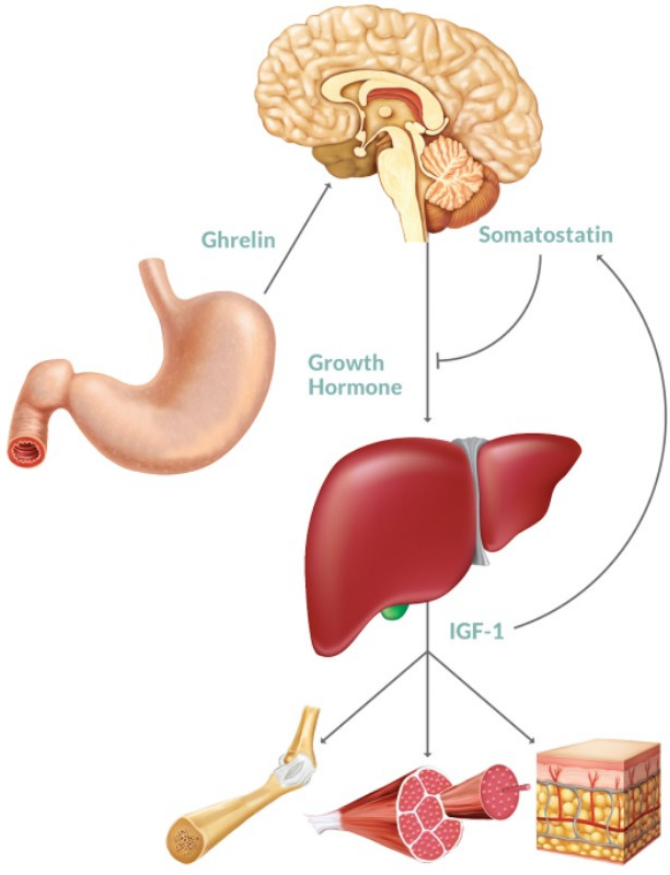


Figure 1. The mechanism of protein intake and IGF-1 on growth (15)

than guidelines, it can be concluded that increasing the protein intake more than the recommended amount in premature infants may not increase and improve the growth outcomes. Some studies showed that extra protein intake can play a positive role in increasing lean body mass in premature infants. However, larger and more multicenter studies are needed.

References

1. Preterm birth [Internet]. [cited 2021 Jul 31]. Available from: https://www.who.int/news-room/fact-sheets/detail/preterm-birth

2. Vakilian K, Ranjbaran M, Khorsandi M, Sharafkhani N, Khodadost M. Prevalence of preterm labor in Iran: A systematic review and meta-analysis. Int J Reprod Biomed [Internet]. 2015 Dec;13(12):743–8. Available from: https://pubmed.ncbi.nlm.nih.gov/27141533

3. Preterm Birth | Maternal and Infant Health | Reproductive Health | CDC [Internet]. [cited 2021 Jul 31]. Available from: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm

4. Riskin A. Meeting the nutritional needs of premature babies: their future is in our hands. Br J Hosp Med [Internet]. 2017 Dec 2;78(12):690–4. Available from: https://doi.org/10.12968/hmed.2017.78.12.690

5. Raymond JL, Morrow K. Krause and Mahan's Food & the Nutrition Care Process [Internet]. Elsevier Health Sciences; 2020. Available from: https://books.google.nl/books?id=51w3wQEACAAJ

6. Agostoni C, Buonocore G, Carnielli VP, De Curtis M, Darmaun D, Decsi T, et al. Enteral Nutrient Supply for Preterm Infants: Commentary From the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr [Internet]. 2010;50(1). Available from: https://journals.lww.com/jpgn/Fulltext/2010/01000/Enteral_Nutrient_Supply_for_Preterm_Infants_.21.aspx

7. Quan M, Wang D, Gou L, Sun Z, Ma J, Zhang L, et al. Individualized Human Milk Fortification to Improve the Growth of Hospitalized Preterm Infants. Nutr Clin Pract [Internet]. 2020 Aug 1;35(4):680–8. Available from: https://doi.org/10.1002/ncp.10366

8. Shakeel F, Newkirk M, Altoubah T, Martinez D, Amankwah EK. Tolerance of Hydrolyzed Liquid Protein Fortified Human Milk and Effect on Growth in Premature Infants. Nutr Clin Pract [Internet]. 2019 Jun 1;34(3):450–8. Available from: https://doi.org/10.1002/ncp.10193

9. Reid J, Makrides M, McPhee AJ, Stark MJ, Miller J, Collins CT. The Effect of Increasing the Protein Content of Human Milk Fortifier to 1.8 g/100 mL on Growth in Preterm Infants: A Randomised Controlled Trial. Nutrients [Internet]. 2018 May 17;10(5):634. Available from: https://pubmed.ncbi.nlm.nih.gov/29772833

10. Maas C, Mathes M, Bleeker C, Vek J, Bernhard W, Wiechers C, et al. Effect of Increased Enteral Protein Intake on Growth in Human Milk–Fed Preterm Infants: A Randomized Clinical Trial. JAMA Pediatr [Internet]. 2017 Jan 1;171(1):16–22. Available from: https://doi.org/10.1001/jamapediatrics.2016.2681

11. Bellagamba MP, Carmenati E, D'Ascenzo R, Malatesta M, Spagnoli C, Biagetti C, et al. One Extra Gram of Protein to Preterm Infants From Birth to 1800g: A Single-Blinded Randomized Clinical Trial. J Pediatr Gastroenterol Nutr [Internet]. 2016;62(6). Available from: https://journals.lww.com/jpgn/Fulltext/2016/06000/One_Extra_Gram_of_Protein_to_Preterm_Infants_From.20.aspx

12. Koletzko B, Demmelmair H, Grote V, Prell C, Weber M. High protein intake in young children and increased weight gain and obesity risk1. Am J Clin Nutr [Internet]. 2016 Feb 1;103(2):303–4. Available from: https://doi.org/10.3945/ajcn.115.128009

13. Langdahl, Kassem, Møller, Eriksen. The effects of IGF-I and IGF-II on proliferation and differentiation of human osteoblasts and interactions with growth hormone. Eur J Clin Invest [Internet]. 1998 Mar 1;28(3):176–83. Available from: https://doi.org/10.1046/-j.1365-2362.1998.00265.x

14. Tang M. Protein Intake during the First Two Years of Life and Its Association with Growth and Risk of Overweight. Int J Environ Res Public Health [Internet]. 2018 Aug 14;15(8):1742. Available from: https://pubmed.ncbi.nlm.nih.gov/30110887

15. Role of IGF-1 in the Growth Hormone/IGF Axis | ALPCO [Internet]. [cited 2021 Jul 31]. Available from: https://www.alpco.com/role-igf-1-growth-hormoneigf-axis

Small But Impressive: Alternations of Gut Microbiota in Hypothyroidism

Mohammad Amin Mohammadi

Introduction

The thyroid gland is a butterfly-shaped gland that has two lobes and is part of the endocrine system(1). Thyroid function is performed through the Hypothalamic-Pituitary-Thyroid (HPT) axis (2). Thyroid hormones play important roles in organs of the body such as heart, nervous system, adipose tissue, muscle tissue, bone, lipoprotein, intestine and etc (1). Types of thyroid disease include: hypothyroidism, Hyperthyroidism, goiter, graves' disease, hashimato, thyroiditis, and thyroid cancer (3).

Hypothyroidism is one of the most common endocrine disorders and it results from a deficiency of thyroid hormones, which can be congenital or acquired.

The incidence of hypothyroidism in the world is 1-2% in countries with sufficient iodineintake and accurate statistics are not available in Iran; However, based on the Tehran lipid and glucose study in 2011, the incidence was 7.1% and according to the Isfahan study in 2017, it was 0.5% (4).Problems with hypothyroidism include an increased risk of cardiovascular disease (Even heart failure), somatosensory and neurological symptoms, pregnancy and infertility problems, hyperlipidemia and goiter and its risk factors include: being female, family history, arbitrary drug use, age over 60, immune system deficiency and pregnancy. Causes of hypothyroidism include:

Autoimmune diseases, thyroid surgery, radiotherapy, medicine, congenital disease, pituitary disorder, pregnancy, iodine deficiency (3). Hypothyroidism can be diagnosed by clinical manifestations (noticeable and unexplained weight gain, excessive fatigue or depression, and abnormal dryness of the skin and hair) and laboratory examination (3)(5).

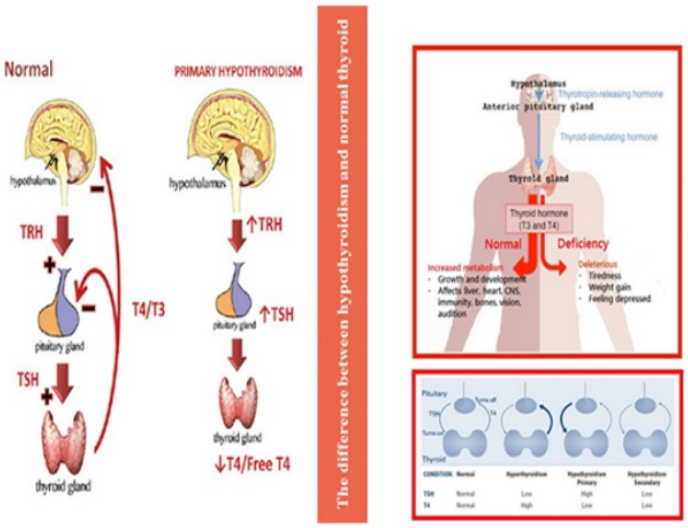


Figure 1.The Difference Between Hypothyroidism and Normal Thyroid(3)

For the treatment of hypothyroidism can be used 4 methods: 1- Medication 2- Diet therapy 3- Lifestyle changes 4- Supplementation (3) .

Probiotics are microorganisms located in different parts of the gastrointestinal tract that

are received through food and have health-promoting properties by maintaining and improving the balance of intestinal flora (6). Beneficial roles of probiotics in the body can be called the role in regulating inflammation, increasing the bioavailability of minerals, synthesis of metabolic hormones, blood sugar regulation, enzyme synthesis, vitamin synthesis, immune system regulation and etc. (7).

Studies show that the intestinal microflora of people with thyroid problems is dysbiosis; Therefore, the aim of the seminar is to investigate the effect of intestinal microbiota on thyroid function.

Literature review

According to a 2017 study by Spaggiari et al in Italy, a single-blind randomized prospective clinical trial of 71 patients with Levothyroxine-treated hypothyroidism, they were divided into control (n = 35) and intervention (n = 36) groups.

The intervention group received VSL#3 supplement in addition to Levothyroxine and the control group received only Levothyroxine. Based on the results of this study, there were no significant differences in thyroid function (TSH, FT3 and FT4) between the study and control groups (P> 0.05) and VSL#3 could not directly affect thyroid function (6).

In 2018, Zhao et al was done a cross-sectional study on 50 patients with hashimato and 27 healthy individuals as a control group. According to this study, by examining the stool samples of people with hashimato, dysbiosis of these people was proven, and also in people with Hashimato have an increased Firmicutes/Bacteroides ratio (8).

Based on a cross-sectional study by Wang et al in 2020 in China to examine the association between changes in the intestinal and oral flora thyroid function was done in pregnant women and its relationship with clinical features of mother and infant. Based on the results of this study, we observed a decrease in fetal head circumference (P=0.00001), body length of newborn (P= 7.0893E-7), FT4 (3.2351E-11).

In contrast, these parameters increased: weight gain during pregnancy (P=0.029), plasma CRP (P=1.2406E-10), amniotic fluid contamination (P=0.033), fetal distress (P=0.040) and TSH (0.001). The abundance of Gammaproteobacteria, Pasteuris and Privetella in hypothyroidism is higher than the control that all of them, are directly related to CRP and weight gain in pregnancy and are inversely related to FT4 (9).

According to a study by Talebi et al in 2020 in Iran (Isfahan), a double-blind randomized clinical trial was performed on 60 patients with hypothyroidism (synbiotic group (n = 30), placebo group (n = 30). The synbiotic and placebo groups received synbiotic (500 mg) and placebo supplements 2 hours after taking Levothyroxine, respectively. Based on 8 weeks of intervention, TSH (P=0.007) and fatigue severity scale (P=0.02) decreased and FT3 / TSH ratio increased (P=0.0001). However, these changes between placebo group and intervention group were not significant (4).

According to a 2020 cohort study in China conducted by Su et al, on the 52 patients with hypothyroidism and 40 healthy controls. Blood and fecal samples were taken and extracted microbiota and transferred to 20 mice, of which 10 mice received the control group microbiota (group A) and 10 mice received the hypothyroidism group microbiota (group B). butyryl-CoA transferase enzymes, lactoyl-CoA dehydratase, propionaldehyde dehydrogenase and methylmalonyl-CoA Decarboxylase significantly decreased in group B. TT4 levels decreased in the second, fourth, and sixth weeks of group B, with only significant changes in the sixth week (10).

Discussion

The intestinal microflora affects the thyroid by four mechanisms:

1- Iodine and Selenium Status: As we know, iodine is absorbed through the stomach and intestines and if the intestinal microflora becomes dysbiosis affects the absorption of iodine and selenium and reduces its. As a result, deiodinase activity decreases and thyroid hormones decrease (11). 2-Iodothyronines Metabolism: The intestinal microflora can bind to T3 and T4, which reabsorbs them from the intestine (11).

3- Thyroid Hormone Enterohepatic Circulation: Glucuronides and sulfates bind to iodothyronine in the liver and prevent their absorption they then enter the intestine through bile acids and are excreted in the feces. Intestinal bacteria, with the enzymes Beta-Glucuronidase and Sulfatase, break down these products, and iodothyronine is reabsorbed and returned to the blood (Figure 3) (11). 4- Levothyroxine Absorption: Levothyroxine is one of the main treatments for the thyroid and the gut microbiota plays an important role in its absorption. Levothyroxine must cross the intestinal barrier to enter the bloodstream for absorption; Intestinal microbiota modulates the absorption of oral levothyroxine by acting on intestinal mucosa, intestinal cell shape (enterocytes), and intestinal permeability. Therefore, intestinal dysbiosis can be one of the causes of oral levothyroxine malabsorption in thyroid patients (11).

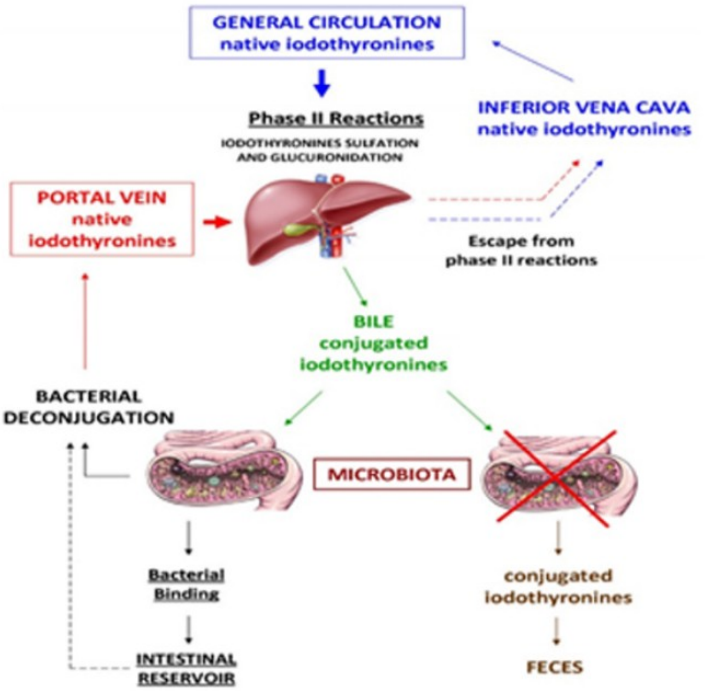


Figure 3.Thyroid Hormone Enterohepatic Circulation(12)

Conclusion

According to studies on the effect of beneficial intestinal microorganisms on thyroid function, it seems that daily consumption of probiotics at at least 109 CFU for 2 months, can be effective in improving the symptoms of hypothyroidism.

References

1. Khatawkar A V, Awati SM. Thyroid gland Embryology, Anatomy and Physiology [Internet]. 2015 [cited 2021 Apr 23]. Available from: http://iaimjournal.com/

2. Mendoza A, Hollenberg AN. New insights into thyroid hormone action [Internet]. Vol. 173, Pharmacology and Therapeutics. Elsevier Inc.; 2017 [cited 2021 Apr 23]. p. 135–45. Available from: https://pubmed.ncbi.nlm.nih.gov/28174093/

3. Krause and Mahan's Food & the Nutrition Care Process - 15th Edition [Internet]. [cited 2021 Apr 23]. Available from: https://www.elsevier.com/books/krause-and-mahans-food-and-the-nutrition-care-process/raymond/978-0-323-63655-1

4. Talebi S, Karimifar M, Heidari Z, Mohammadi H, Askari G. The effects of synbiotic supplementation on thyroid function and inflammation in hypothyroid patients: A randomized, double-blind, placebo-controlled trial. Complement Ther Med [Internet]. 2020 Jan 1 [cited 2021 Apr 23];48. Available from: https://pubmed.ncbi.nlm.nih.gov/31987229/

5. Kostoglou-Athanassiou I, Ntalles K. Hypothyroidism - New aspects of an old disease [Internet]. Vol. 14, Hippokratia. Hippokratio General Hospital of Thessaloniki; 2010 [cited 2021 Apr 23]. p. 82–7. Available from: /pmc/articles/PMC2895281/

6. Spaggiari G, Brigante G, Vincentis S De, Cattini U, Roli L, De Santis MC, et al. Probiotics ingestion does not directly affect thyroid hormonal parameters in hypothyroid patients on levothyroxine treatment. Front Endocrinol (Lausanne) [Internet]. 2017 Nov 14 [cited 2021 Apr 23];8(NOV):14. Available from: www.frontiersin.org

7. Calder PC. Nutrition, immunity and COVID-19. BMJ Nutr Prev Heal. 2020;3(1):74–92.

8. Zhao F, Feng J, Li J, Zhao L, Liu Y, Chen H, et al. Alterations of the gut microbiota in hashimoto's thyroiditis patients. Thyroid [Internet]. 2018 Feb 1 [cited 2021 Apr 23];28(2):175–86. Available from: https://www.liebertpub.com/doi/abs/10.1089/thy.2017.0395

9. Wang B, Xu Y, Zhang M, Zhang J, Hou X, Li J, et al. Oral and intestinal microbial features in pregnant women with hypothyroidism and their correlations with pregnancy outcomes. Am J Physiol - Endocrinol Metab [Internet]. 2020 Nov 30 [cited 2021 Apr 23];319(6):E1044–52. Available from: https://journals.physiology.org/doi/abs/10.1152/ajpendo.00234.2020

10. Su X, Zhao Y, Li Y, Ma S, Wang Z. Gut dysbiosis is associated with primary hypothyroidism with interaction on gut-thyroid axis. Clin Sci [Internet]. 2020 Jun 1 [cited 2021 Apr 23];134(12):1521–35. Available from: /clinsci/article/134/12/1521/225233/Gut-dysbiosis-is-associated-with-primary

11. Virili C, Centanni M. "With a little help from my friends" - The role of microbiota in thyroid hormone metabolism and enterohepatic recycling. Mol Cell Endocrinol. 2017 Dec 15;458:39–43.

Evaluating The Association Between Dietary Isofelavons and The Risk of Prostate Cancer

Arezoo RastegarMoghadam-Ebrahimian

Introduction

Prostate Cancer (PCa) is the most common cancer in men and includes the highest number of new diagnoses among men's cancers (20%) and is the second leading cause of death in men with cancer (10%) (1,2). The incident rate of PCa varies in different parts of the world. Concerning the statistics, this rate is the highest in Oceania. In Iran, as indicated by the report in 2013, 9.11 persons per 100000 were diagnosed with PCa (3,4).The exact cause of PCa is unclear, but there are many possible risk factors including old age, race, family history, lifestyle, smoking, obesity and high BMI, type of diet and medications (5,6,7). PCa is rare among men under the age of 45 years, but more common after the age of 50 years. Studies have shown that a diet rich in red meat or high-fat dairy products increases a person's risk of developing PCa. (5,6,7,8,15).

There are usually no symptoms during the early stages of PCa. However, if symptoms do appear, they usually include: Frequent need to urinate, difficulty commencing and maintaining urination, blood in the urine, painful urination and ejaculation, difficulty achieving or maintaining an erection. Diagnosis includes physical examination and collecting the patient's medical history. If the patient has symptoms or abnormally high Prostate-specific antigen (PSA) levels,further examinations may be requested (8). When PCa is suspected, tissue biopsy remains the standard of care for diagnosis.Surgery and radiation continue to be curative treatments for a localized disease but have adverse effects such as urinary symptoms and sexual dysfunction that can negatively affect the quality of life. For metastatic disease, chemotherapy as initial treatment now appears to extend survival (8,9).

Multiple preclinical and observational studies have observed that diet, exercise, and lifestyle interventions may play a role in mitigating disease progression, mortality, and overall disease burden for high-grade and fatal PCa. Especially phytoestrogens which are a large group of plant secondary metabolites have a significant protective effect against the development of PCa due to their structural/functional similarity to 17b-estradiol and the resulting competitive binding to estrogen receptors (7).Additionally, the lower rates of hormone-sensitive cancers like PCa among Asian populations, known for their regular consumption of phytoestrogen-rich foods, suggest that the consumption of phytoestrogens and especially Isoflavones in the Western diet may decrease cancer risk (7,14).This study aims to investigate the relationship between the consumption of dietary isoflavones and the risk of PCa.

Literature review

Phytoestrogens have been shown to have estrogenic and antiestrogenic activity and the ability to modify other steroid hormones and hormone-binding proteins. The classification and some types of phytoestrogens are shown in Figure 1 (6).

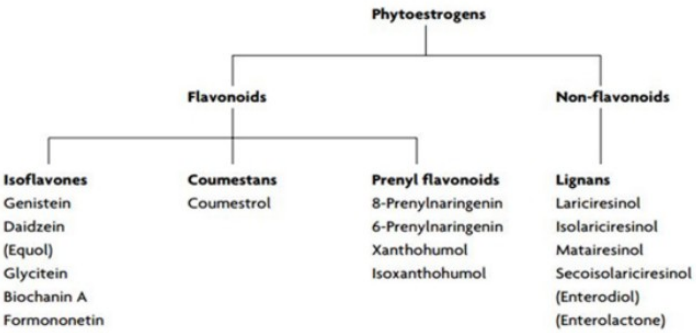


Figure 1.The classification and some types of phytoestrogens (6)

The highest levels of dietary phytoestrogens have been found in soy and soy fermented products (11).

Wu,Y et al. examined the association between plasma genistein, epidemiological factors, and PCa in a Chinese population in 2015. Totally, 100 men over the age of 40 underwent prostate biopsy for PCa. The results of this study indicate that increasing the level of genistein reduces the incidence of PCa (P<0.005) (5).

Russo G.I et al. investigated the association between dietary phytoestrogen consumption and PCa in a sample of southern Italian individuals in 2017. In this study, a total of 118 histopathological-verified PCa cases and a total of 222 controls were collected. They found an inverse association between dietary isoflavone intake and PCa (P<0.01), while a positive association was found with lignans intake (16).Reger M.K, et al. was done a prospective cohort study in this field in 2018 in America. Their study investigates whether intake of phytoestrogens may influence PCa risk in human populations or not. During a median follow up of 11.5 years, 2,598 cases of PCa (including 287 advanced cases) have been identified among 27,004 men with prostate, lung, colorectal. Dietary intake of phytoestrogens (excluding lignans) was assessed with a food frequency questionnaire. This study showed that consumption of isoflavones in the diet was associated with an increased risk of advanced PCa, but no statistically significant association was found between consumption of "total isoflavones and phytoestrogens" and "non-advanced and total PCa (P=0.002) (6).

In a prospective study in 2020 in Japan, Sawada N, et al. investigated the association between soy, soy products and isoflavones intake and PCa mortality. They conducted a population-based prospective study in 43,580 Japanese men with no history of cancer or cardiovascular disease (aged 45-74 years). Participants completed a validated questionnaire which included 138 food items. During 16.9 years of follow-up, they registered 221 deaths from PCa. Their study suggested that high intake of soy and isoflavones might increase the risk of PCa mortality (P for trend=0.04) (16).

Zhang, M et al, was done a meta-analysis study that examined the association between phytoestrogen consumption and risk of PCa by of published data in 2016. They retrieved 507 papers, and 29 studies were ultimately confirmed as eligible. The meta-analysis showed that phytoestrogen intake was significantly associated

with a reduced risk of PCa, (OR= 0.77 , P=0.000) (7).

Discussion

In this study we reviewed the association between Isoflavone intake and PCa. Many studies show that Isoflavones affect the body through various mechanisms.

It has been shown that increased genistein's plasma levels induce its attachment to ER-β receptors on cell surface resulting in inhibition of some cellular pathways such as cell growth, angiogenesis, oxidativestress and mitogen activated protein kinase and induces apoptosis and autophagic cell death (Figure 2) (5,15).However, another study has shown that high levels of genistein in people with PCa can lead to proliferation and metastasis of cancer cells by increasing phosphorylation of epidermal growth factor receptor (6).

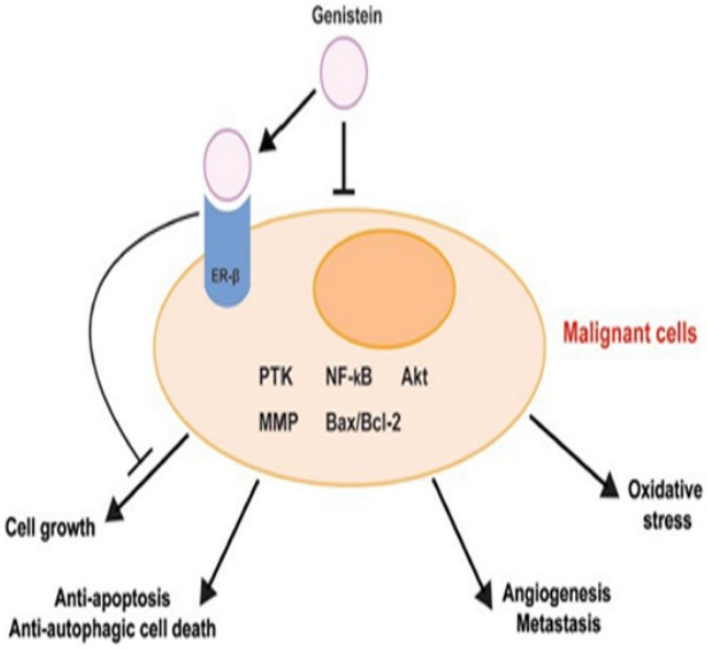


Figure 2.Genistein and its influence on cellular fate (6)

On the other hand, Isoflavones reduce testosterone levels by inhibiting the activity of the 5-alpha reductase enzyme, which ultimately prevents the prostate gland from enlarging (15).Soy isoflavones are structurally similar to 17b-estradiol and can bind to estrogen receptors beta (ER-b). This is considered to be one of the mechanisms of their preventive effects on PCa. (Figure 3 , 4) (16).

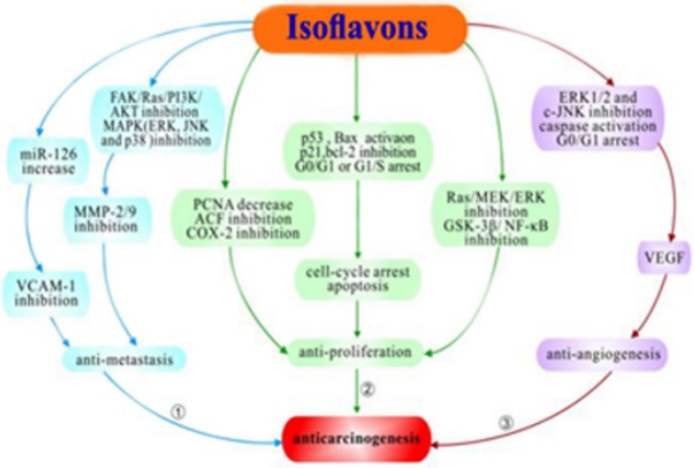


Figure 3.The effect of Isoflavons of different signaling pathways (17)

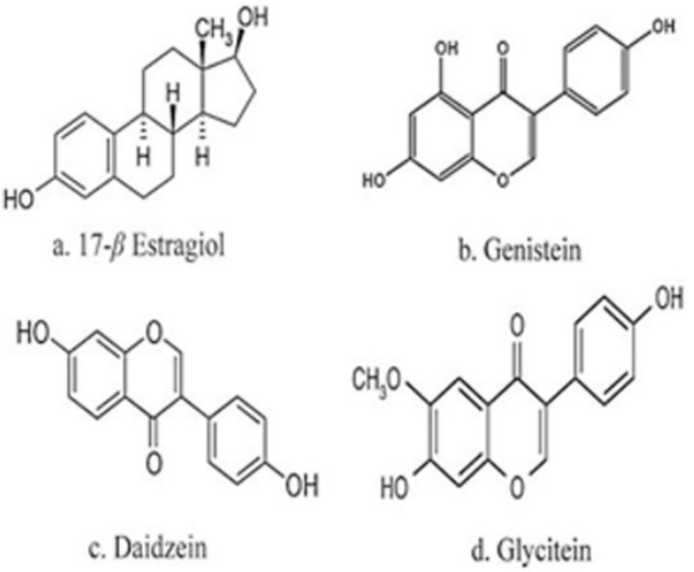


Figure 4.The chemical structure of 17b-estradiol, Gentistein, Daidzein and Glycitein (17)

Another mechanism involves gut microflora. Variation in individual metabolism of phytoestrogens due to differences in gut microflora may

influence the serum concentration of phytoestrogens and their biological effects (15).

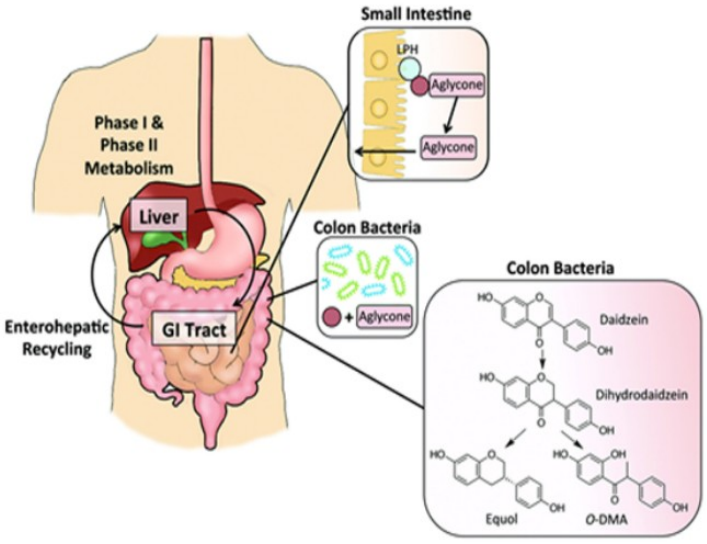


Figure 5.The effect of gut microflora on serum concentration of phytoestrogen (16)

The last mechanism we discuss here includes the study of Bravo (1998) which reported that flavonoids effectively scavenge oxidizing molecules, suggesting that flavonoids confer protection against cancers by inhibiting DNA damage induced by singlet oxygen and free radicals. Conversely, flavonols have been shown to inhibit CP450 enzymes of the CYP1A family (Ciolino et al., 1999; Kang et al., 1999; Muto et al., 2001; Lautraite et al., 2002) (7).

Conclusion

According to the studies, we concluded that there is a direct relationship between consumption of soy and dietary isoflavones (especially genistein) and the risk of advanced PCa, but in non-advanced PCa, this relationship is inverse. In other words, the use of isoflavones in people who have not been diagnosed with PCa or a non-advanced form of it can have a protective effect and help in the healing process.

But in people with metastatic advanced PCa, overuse of isoflavones can lead to disease progression and increased mortality due to the decreased number of ER-β receptors.

References

1-Siegel, R. L., Miller, K. D., &Jemal, A . Cancer statistics. CA: A Cancer Journal for Clinicians 2019 . 69(1), 7–34

2- https://prostatecancerfree.org/ accessed 23 DES 2020

3- Askari, F., M. K. Parizi, and B. Rashidkhani. Dietary patterns and PC: a case-control study. Iranian Journal of Nutrition Sciences & Food Technology.2013; 8.3 : 17-25.

4- Rawla, P. Epidemiology of PC. World journal of oncology. 2019; 10.2:63

5- Wu, Y., Zhang, L., Na, R., Xu, J., Xiong, Z., Zhang et al. Plasma genistein and risk of PC in Chinese population. International urology and nephrology. 2015; 47(6): 965-970

6- Reger, M. K., Zollinger, T. W., Liu, Z., Jones, J. F., & Zhang, J. Dietary intake of isoflavones and coumestrol and the risk of PC in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. International journal of cancer. 2017;142(4: 719-728

7- Zhang, M., Wang, K., Chen, L., Yin, B., & Song, Y. Is phytoestrogen intake associated with decreased risk of PC? A systematic review of epidemiological studies based on 17,546 cases. Andrology.2016;4(4): 745-756

8- https://www.can.org.na/ Accessed 28 DES 2020

9- Litwin, M. S., & Tan, H. J. The diagnosis and treatment of PC: a review. Jama.2017; 317(24): 2532-2542

10- Ballon-Landa, E., & Parsons, J. K. Nutrition, physical activity, and lifestyle factors in PC prevention.Current Opinion in Urology.2018; 28(1): 55-61

11- USDA-lowa University isoflavones database (1999)

12- Garg, S., Lule, V. K., Malik, R. K., &Tomar, S. K. Soy Bioactive components in functional perspective: A review.International Journal of Food Properties.2016; 19(11): 2550-2574

13- Matsushita, M., Fujita, K., &Nonomura, N. Influence of diet and nutrition on PC. International Journal of Molecular Sciences.2020; 21(4):1447

14-Adlercreutz, H., & Mazur, W. Phyto-oestrogens and Western diseases. Annals of medicine.1997; 29(2): 95-120

15- . Russo, G. I., Di Mauro, M., Regis, F., Reale, G., Campisi, D., Marranzano, M et al. Association between dietary phytoestrogens intakes and PC risk in Sicily. The Aging Male.2018; 21(1): 48-54

16-Sawada, N., Iwasaki, M., Yamaji, T., Shimazu, T., Inoue, M., Tsugane, S et al. Soy and isoflavone consumption and subsequent risk of PC mortality: the Japan Public Health Center-based Prospective Study. International Journal of Epidemiology.2020; 49(5): 1553-1561

Waist Circumference and Risk of Liver Cancer

Khashayar Khanizadeh

Introduction

The liver is the body's largest solid organ. On average, it weighs around 3 pounds in adult (1). The liver has two large sections, called the right and the left lobes. The gallbladder sits under the liver, along with parts of the pancreas and intestines. The liver's main job is to filter the blood coming from the digestive tract, before passing it to the rest of the body. The liver also detoxifies chemicals and metabolizes drugs (2).

The gallbladder stores bile, a combination of fluids, fat, and cholesterol. Bile helps break down fat from food in the intestine. The gallbladder delivers bile into the small intestine. This allows fat-soluble vitamins and nutrients to be more easily absorbed into the bloodstream(3).

Liver cancer is the sixth most common type of cancer worldwide, with more than 840,000 new cases in 2018. Men are in a higher risk of developing the disease than women (4).

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer-derived from hepatocytes and it accounts for 85-90% of all primary liver cancers worldwide; followed by biliary tract cancer, which includes cancer of the bile ducts and gallbladder (5).

Tumors of the bile ducts can be classified as extrahepatic bile duct cancer (EBDC) and intrahepatic bile duct cancer (IBDC). The average age in patients diagnosed with liver cancer has risen, and the proportion of female patients with liver cancer has been slightly increasing. The disease has poor survival rates, and in Europe the mean age-standardized survival rate at 5 years is 12%.

Approximately 80% of the cases occur in less developed countries such as Asia and Africa, while Europe and Latin America, and the Caribbean report the lowest incidences (4).

Some studies indicated an association between measures of adiposity such as waist circumference (WC), Waist-to-hip ratio, and body mass index (BMI), and liver cancer. WC is a more accurate predictor of abdominal fat compared to BMI in males. WC is measured at the midpoint between the lowest rib margin and the iliac crest. Central adiposity was defined by WC as ≥90 cm (in men) or ≥ 80 cm (in women) (4).

Literature review

In 2012, Schlesinger et al conducted a nested case-control study to examine the relationship between weight, BMI, Waist-to-hip ratio (WHR), and Waist-to-height ratio (WHtR) with HCC, EBDC, IBDC, and gallbladder cancer. A positive association between obesity (especially abdominal obesity) and the risk of liver cell cancer and gallbladder cancer was observed (6).

According to a study by Campbell et al in the U.S.A., a nested case-control on patients with a variety of liver cancers. They were divided into control (n=547) and case group (n=220). The correlation of BMI, WHtR, WHR, and Weight changes in adulthood with risk of liver and bile duct cancer in the American adult community were assessed. A significant relationship was observed between increased waist size and risk of liver cancer (7).

A case-control in Europe by Baumeister et al, on 275 HCC, 93 Intrahepatic bile duct cancer (IHBC), and 164 Non-gallbladders extrahepatic

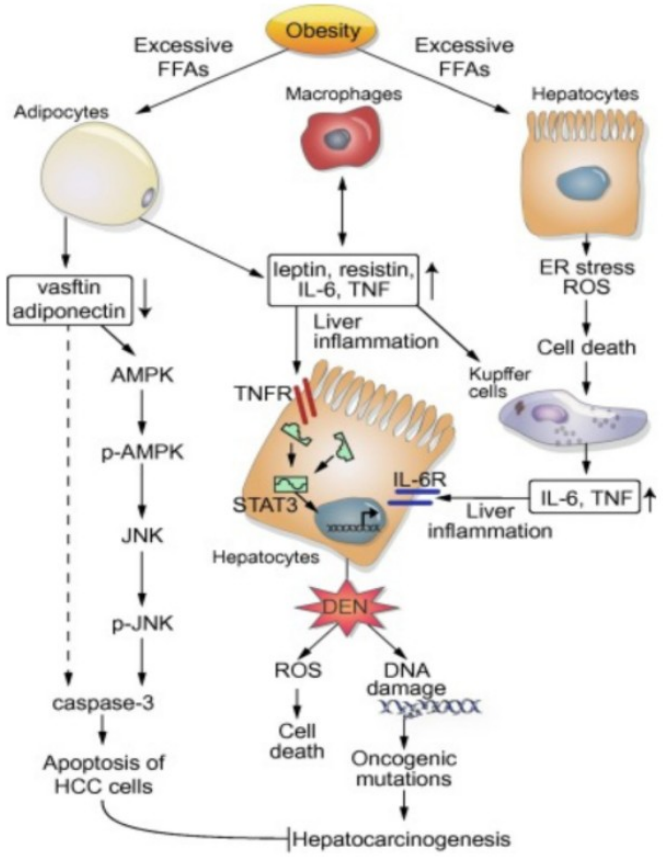


Figure 1. Mechanism of action of free fatty acids on the occurrence of liver cancer (9)

bile duct cancer (NGBC) was done to investigate the relationship between physical activity and the risk of liver-biliary cancers. they concluded that there was an inverse relationship between physical activity and the risk of liver cancer, which is potentially mediated by obesity (5).

A prospective study by Pang et al in 2019 was done in China, on 512713 people. They examined the association between central obesity with risk of liver cancer. Based on the results of this study, general obesity poses a lower risk of liver cancer than central obesity, and WC was reported to be a better parameter for liver cancer risk than BMI (8).

Systematic review and meta-analysis by Rahmani et al in 2019, examined the association between waist circumference and risk of liver cancer. According to the results, increased waist size has a linear and significant relationship with increased risk of liver cancer (4).

Discussion

During obesity, the amount of free fatty acids increases and affects the liver cells. Adipose tissue causes the secretion of cytokines, which increases inflammation. The cytokines secretion also stimulates macrophages to produce cytokines, which in turn causes inflammation of the liver. Accumulation of free fatty acids in the liver causes the death of liver cells or damage to DNA, which is followed by carcinogenic mutations and liver cancer (9).

Conclusion

In conclusion, we found a positive association between WC and the risk of liver cancer. According to the results of the articles, every 5 cm increase in waist circumference, increases the risk of liver cancer by 11% (8).

References

1. https://www.healthline.com/human-body-maps/liver
2. https://www.webmd.com/digestive-disorders/picture-of-the-liver
3. https://www.webmd.com/digestive-disorders/picture-of-the-gall-bladder
4. Rahmani J, Kord Varkaneh H, Kontogiannis V, Ryan PM, Bawadi H, Fatahi S, et al. Waist Circumference and Risk of Liver Cancer: A Systematic Review and Meta-Analysis of over 2 Million Cohort Study Participants [Internet]. Vol. 9, Liver Cancer. S. Karger AG; 2020 [cited 2021 Jun 30]. p. 6–14. Available from: www.karger.com/licwww.karger.com/lic
5. Baumeister SE, Schlesinger S, Aleksandrova K, Jochem C, Jenab M, Gunter MJ, et al. Association between physical activity and risk of hepatobiliary cancers: A multinational cohort study. J Hepatol. 2019 May 1;70(5):885–92.
6. Schlesinger S, Aleksandrova K, Pischon T, Fedirko V, Jenab M, Trepo E, et al. Abdominal obesity, weight gain during adulthood and risk of liver and biliary tract cancer in a European cohort. Int J Cancer [Internet]. 2013 Feb 1 [cited 2021 Jun 30];132(3):645–57. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.27645
7. Campbell PT, Newton CC, Freedman ND, Koshiol J, Alavanja MC, Freeman LEB, et al. Body mass index, waist circumference, diabetes, and risk of liver cancer for U.S. adults. Cancer Res [Internet]. 2016 Oct 15 [cited 2021 Jul 1];76(20):6076–83. Available from: http://cancerres.aacrjournals.org/
8. Pang Y, Kartsonaki C, Guo Y, Chen Y, Yang L, Bian Z, et al. Central adiposity in relation to risk of liver cancer in Chinese adults: A prospective study of 0.5 million people. Int J Cancer [Internet]. 2019 Sep 1 [cited 2021 Jul 1];145(5):1245–53. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.32148
9. Sun B, Karin M. Obesity, inflammation, and liver cancer. Vol. 56, Journal of Hepatology. Elsevier; 2012. p. 704–13.

Association Beetween Overweight and Obesity with Obstructive Sleep Apnea

Zohreh Hoseini

Introduction

People with obesity are more likely to have sleep apnea, a potentially serious disorder in which breathing repeatedly stops and starts during sleep (1). Nearly 1 billion adults aged 30–69 years worldwide were estimated to have obstructive sleep apnoea, with or without symptoms.

Sleep apnea has three types:

1. Obstructive Sleep Apnea (OSA): It is the most common sleep apnea. This type of apnea occurs when your throat muscles intermittently relax and block your airway during sleep.
2. Central Sleep Apnea: In this type a part of the brainstem that controls breathing is hurt.
3. Complex Sleep Apnea: It is a complex situation and occurs when both obstructive sleep apnea and central sleep apnea happens at the same time (1).

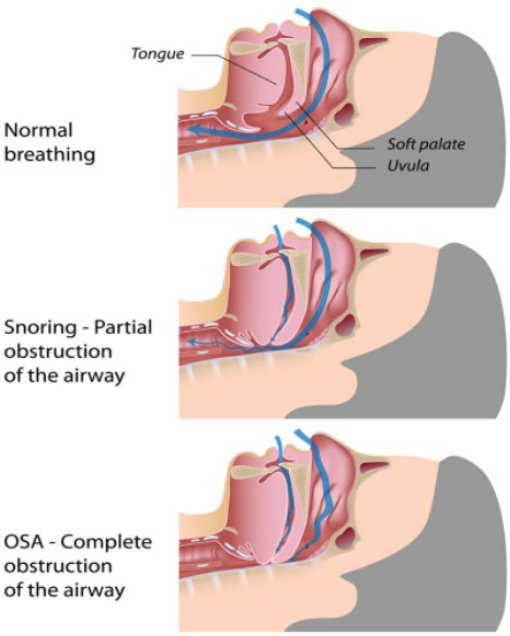


Figure 1. Differences between normal breathing, snoring, and OSA (7)

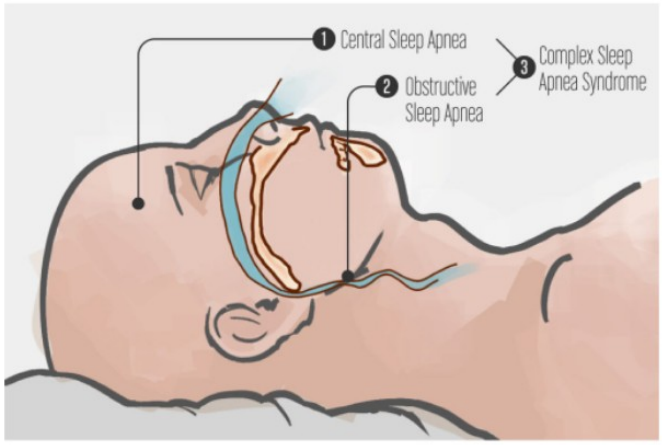


Figure 2. Types of apnea (8)

Some risk factors predispose to OSA, including obesity, neck circumference, male gender, old ages, a family history of sleep apnea, smoking and alcohol, narrowed airway and also some chronic diseases (1).

The symptoms of OSA include excessive daytime sleepiness, loud snoring, awakening with a dry mouth or sore throat, morning headache, difficulty concentrating during the day, nighttime sweating(1).

This disease has some side-efects too, including fatigue during the day, experiencing mood changes such as depression or irritability, high blood pressure, cardiovascular diseases, diabetes type 2, metabolic syndrome, heart attack, stroke, and sudden death (1).

Literature review

Genio et al. examined the long-term effect of sleeve gastrectomy on upper respiratory tract

physiology on 36 OSA patients in the age range of 18-60 years in Itlay in 2015. This study demonstrated that sleeve gastrectomy surgery is effective in weight loss and OSA improvement(2).

Galilolghadr et al. compared sleep structure and OSA in obese children with and without metabolic syndrome aged 8-16 years in Iran in 2015. The case group composed of 42 children with metabolic syndrome and 38 children without metabolic syndrome were assigned to the control group. They concluded that OSA was more severe in children with metabolic syndrome than children without metabolic syndrome(3).

Bazzano et al. examined the relationship between childhood overweight and obesity and the risk of developing OSA in middle age. They followed up 844 children aged 4-18 years till they reached middle age (1975-2010) in the USA in 2015. They concluded that over weight and obesity was associated with excess OSA in middle-age(4).

Scott et al. compared the clinical parameters and polysomnography in children with normal weight, overweight, obesity in 290 children aged 2-18 years in the U.S.A. in 2016. They also aimed to identify factors exacerbating the severity of sleep apnea. They concluded that the severity of OSA is associated with greater age and weight(5).

Dong et al. aimed to investigate the relationship between obesity and OSA in different demographic groups on 3214 Participants in China in 2020. Their conclusion was that overweight and obesity are important risk factors for OSA in children and adults(6).

Discussion

The main reason and mechanism for this disorder is fat accumulation in the neck and stomach. Indeed, fat accumulation in the neck leads to airway narrowing. As a result, air can not pass through the airway easily. Fat accumalation in stomach also leads to increased pressure to the diaphragm and so decreases respiratory volume (figure 3).

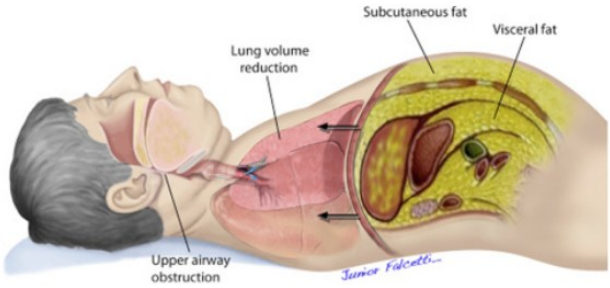


Figure 3. Obesity is linked to obstructive sleep apnea (OSA) (9).

Conclusion

Overweight and obesity are important risk factors for OSA. Weight managment can decrease the risk of developing OSA.

References

1. Mayo Clinic - Mayo Clinic [Internet]. [cited 2021 Jul 4]. Available from: https://www.mayoclinic.org/
2. Del Genio G, Limongelli P, Del Genio F, Motta G, Docimo L, Testa D. Sleeve gastrectomy improves obstructive sleep apnea syndrome (OSAS): 5 year longitudinal study. Surg Obes Relat Dis. 2016 Jan 1;12(1):70–4.
3. Jalilolghadr S, Yazdi Z, Mahram M, Babaei F, Esmailzadehha N, Nozari H, et al. Sleep architecture and obstructive sleep apnea in obese children with and without metabolic syndrome: a case control study. Sleep Breath [Internet]. 2016 May 1 [cited 2021 Jul 5];20(2):845–51. Available from: https://link.springer.com/article/10.1007/s11325-015-1291-y
4. Bazzano LA, Hu T, Bertisch SM, Yao L, Harville EW, Gustat J, et al. Childhood obesity patterns and relation to middle-age sleep apnoea risk: The Bogalusa heart study. Pediatr Obes [Internet]. 2016 Dec 1 [cited 2021 Jul 5];11(6):535–42. Available from: https://onlinelibrary.wiley.com/doi/-full/10.1111/ijpo.12103
5. Scott B, Johnson RF, Mitchell RB. Obstructive Sleep Apnea: Differences between Normal-Weight, Overweight, Obese, and Morbidly Obese Children. Otolaryngol - Head Neck Surg (United States) [Internet]. 2016 May 1 [cited 2021 Jul 5];154(5):936–43. Available from: https://journals.sagepub.com/doi/abs/10.1177/0194599816636626
6. Dong Z, Xu X, Wang C, Cartledge S, Maddison R, Shariful Islam SM. Association of overweight and obesity with obstructive sleep apnoea: A systematic review and meta-analysis. Obes Med. 2020 Mar 1;17:100185.
7. Snoring and Obstructive Sleep Apnea (OSA) - Fort Worth ENT & Sinus [Internet]. [cited 2021 Jul 31]. Available from: https://fortworth-ent.net/ear-nose-throat/snoring-obstructive-sleep-apnea-osa/
8. 9 Signs You May Have Sleep Apnea - Help You Rest [Internet]. [cited 2021 Jul 31]. Available from: https://helpyourest.com/9-signs-you-may-have-sleep-apnea/
9. Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G. Obstructive Sleep Apnea: A Cardiometabolic Risk in Obesity and the Metabolic Syndrome. J Am Coll Cardiol [Internet]. 2013;62(7):569–76. Available from: https://www.sciencedirect.com/science/article/pii/S0735109713022481

The Use of Glycomacropeptide in Dietary Management of Phenylketonuria

Fatemeh Teymoori
Maryam Yousefi

Introduction

Phenylketonuria (PKU) is a genetic metabolic disorder. Due to a mutation in the gene encoding the enzyme phenylalanine hydroxylase, the amino acid phenylalanine (Phe) is not converted into tyrosine in the body of a PKU patient, unlike in a healthy individual. If left untreated, the buildup of phenylalanine in the body and its metabolites can cause some symptoms and side effects (1), like hyperactivity, skin rashes (eczema), Microcephaly (abnormally small head), neurological problems, musty odor in the breath, urine and skin, Pale skin, and blue eyes (2).

The global prevalence of PKU is 1 per 1000-1500 live births and in Iran is 1 per 4698 live births (3,4). The primary treatment for PKU is a low-protein diet with limited sources of the amino acid phenylalanine. The goal of the treatment is to lower the blood phenylalanine level to the normal range (5).

Unauthorized food includes all kinds of meat products containing aspartame, milk, and dairy products, eggs, nuts, beans, products containing wheat. Permitted food includes fruits and vegetables, sugar, formulas, and special products for these patients. The main formula for treating these patients is amino acid medical foods (AA-MF) (6,7,4). AA-MF are the main source of protein for these patients and are completely free of phenylalanine and enriched with a series of vitamins and minerals. However, several problems such as bone problems, digestive problems, and kidney dysfunction have been reported in the use of these formulas. Therefore, it is necessary to have an alternative to these formulas. Glycomacropeptide medical food (GMP-MF) can be an alternative to these formulas.

Glycomacropeptide (GMP) is a polar Glycophosphopeptide with 64 amino acids and is a by-product of cheese production from Whey protein and contains a small amount of Phe.

Essential amino acids constitutes 47% of GMP weight. However, Glycomacropeptide lacks some amino acids and needs to be enriched with the amino acids Histidine, Leucine, Methionine, Tryptophan, and Tyrosine (Tyr) (6,8).

The potential benefits of having GMP in the PKU diet are greater feelings of fullness, better taste, gastrointestinal health, lower osmolarity, and affordable price (5,8).

The aim of this study is to make a comparison between MP-MF and AA-MF in terms of safety and dietary effectiveness in PKU patient.

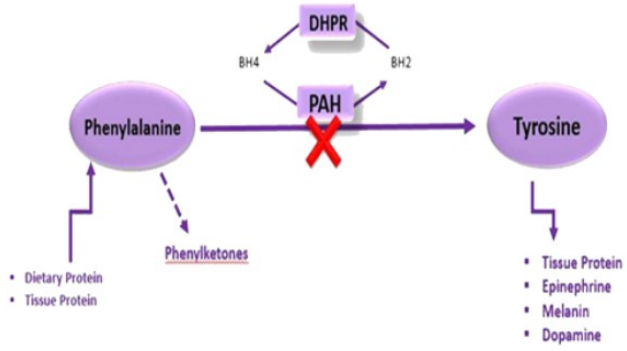


Figure 1. Pathogenesis of PKU

Literature review

Pinto et al conducted a retrospective ,longitudinal study and reported the nutritional status of 11 PKU patients taking AA and GMP in 2017. The result showed that the median blood Phe did not significantly change during the study (P=0.594). Median blood Tyr increased (P=0.033), and all biochemical markers remained stable, except for a lower A1C haemo-

globin (P=0.011). Also, Anthropometry and body composition measurements remained unchanged. Partial GMP contribution to total protein substitute intake did not affect nutritional status in patients with PKU (8).

Daly A. et al conducted a prospective 6-month pilot study in 2017, In order to evaluate the effect of phenylalanine content of CGMP-amino acid (CGMP-AA) in 22 PKU subjects in two groups. In the CGMP-AA group, there was a significant increase in blood phenylalanine concentrations (P=0.02), a decrease in tyrosine concentrations(P=0.03) and and an increase in Phe :Tyr ratios(P=0.02) (9).

A clinical trial, crossover study that conducted by Stroup et al in 2017 hypothesized that AA-MF provide a high dietary acid load, subsequently increasing urinary excretion of renal net acid, calcium, and magnesium, compared to GMP-MF in 8 PKU participants. Based on food record, 24-hr urine sample, calculating potential renal acid load (PRAL) of AA-MF and GMP-MF, It was concluded that AA-MF provided 1.5–2.5-fold higher PRAL and resulted in 3-fold greater renal net acid excretion compared to GMP-MF (P=0.002). GMP-MF significantly reduced urinary excretion of calcium by 40% (P=0.012) and magnesium by 30% (P=0.029) (1).

Zaki et al conducted a prospective clinical trial study in 2016. They aimed to study the feasibility of use of GMP for partial replacement of artificial formula in treatment of children with PKU on 10 patients with PKU in 2 phases. Results demonstrated that the median and interquartiles of Phe levels were not significantly different in phases I and II, 376 µmol/L versus 490 µmol/L, respectively and other laboratory data showed no significant difference between the two phases.(5)

A 2-stage randomized, crossover trial study conducted by Ney et al in 2016. They investigated the efficacy and safety of a low-Phe diet combined with GMP-MFs or AA-MFs that providing the same quantity of protein equivalents in subjects with phenylketonuria. It was concluded that significant increase in Phe intake from GMPMFs observed (P=0.026) .Subjects rated GMP-MFs as more acceptable than AA-MFs and noted improved gastrointestinal symptoms and less hunger with GMP-MFs (6).

Discussion

GMP-MF leads to lower level of appetite stimulating hormone (ghrelin) and a better satiety. So as a result of increased satiety, the consumption of other foods and the level of phenylalanin decrease (figure 2).

Figure 2. The effect of GMP-MF on Phe level

GMP-MF are also considered as prebiotic and increasing normal gut flora and decreasing patogenes. So, they increase appetite stimulating hormones like CCK, PYY, and GLP-1. As a result GMP-MF adjusts appetite and energy (figure 3). GMP-MF also decreases dietary acid load which decreases urinary calcium excretion, and likely contributing to lower skeletal fragility and decreasing osteoprosis in PKU (figure 4).

GMP-MF has high concentrations of the amino acids like Threonine, Leucine, and Isolecine that compete with phenylalanine in absorption via L-acyle transferase-2. Consequently, phenylalanine absorption decreases (figure 5-A).

GMP-MF contains leucine. leucine stimulates muscle protein synthesis. Following the synthesis of muscle proteins, phenylalanine is consumed in the body and its blood level decreases (figure 5-B).

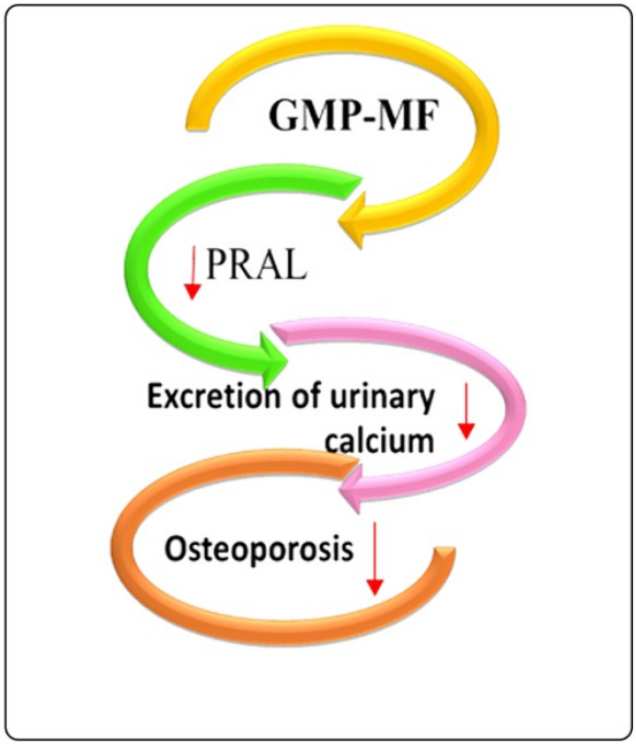


Figure 4. The effect of GMP-MF on osteoporosis

GMP-MF decreases inflammatory cytokine and act of osteoclasts, so it reduces bone resorption.

GMP-MF as a protein source causes higher muscle-bone interaction and reduces the risk of fracture. GMP-MF as a prebiotic, increases bioavailability of minerals and ossification (figure 6).

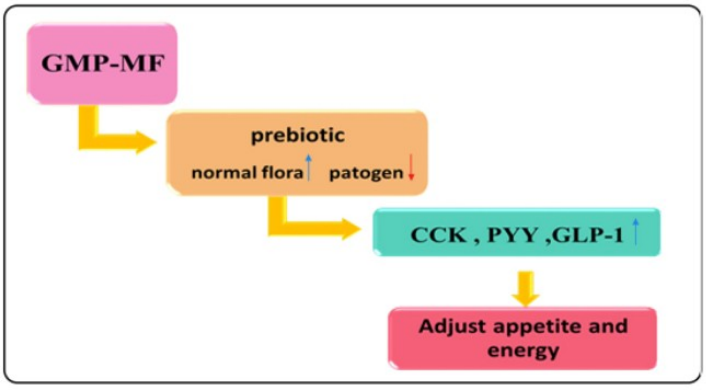


Figure 3. The effect of GMP-MF on appetite and energy adjustment

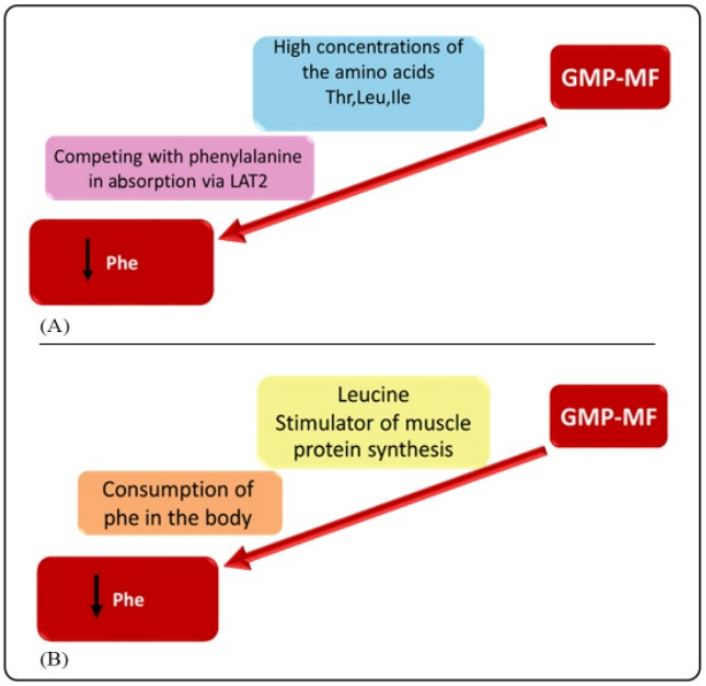


Figure 5. The effect of GMP-MF on Phe level

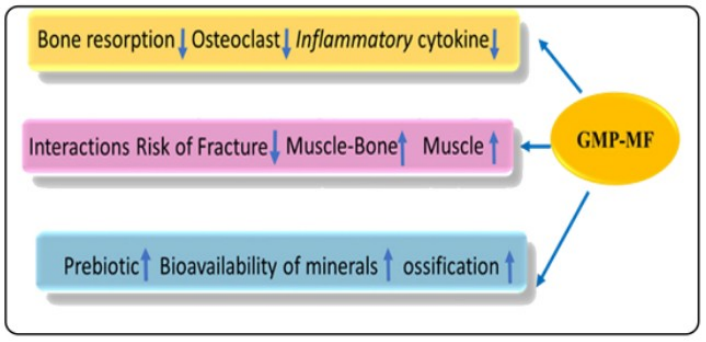


Figure 6. The effect of GMP-MF on bone

Conclusion

Generally, articles comparing GMP-MF and AA-MF in terms of efficacy and patient acceptance in the diet of patients with PKU led to the following results:

1. GMP (Glycomacropeptide) can be present as all or part of the protein in a PKU patient's diet and has no adverse effects on nutritional status. 2. GMP leads to increased blood Tyr levels and decreased Phe/Tyr ratio, which is good for the patient. 3. rises in PRAL and RNAE by AA-MF increases urinary excretion of calcium and magnesium and thus increases the risk of bone fractures. As a result of reducing urinary excretion of Ca and Mg by consuming GMP-MF, the risk of bone fractures decreases.

All in all, Adding 50% GMP to food and short-term use is safe and has few side effects. GMP-AA is preferred by patients because of its better taste and texture and less digestive problems and hunger.

References

1. Stroup BM, Sawin EA, Murali SG, Binkley N, Hansen KE, Ney DM. Amino Acid Medical Foods Provide a High Dietary Acid Load and Increase Urinary Excretion of Renal Net Acid, Calcium, and Magnesium Compared with Glycomacropeptide Medical Foods in Phenylketonuria. J Nutr Metab. 2017;2017.

2. Symptoms - Symptoms - Mayo Clinic [Internet]. [cited 2021 Jun 29]. Available from: https://www.mayoclinic.org/symptoms

3. Morovatdar N, Badiee Aval S, Hosseini Yazdi SMR, Norouzi F, Mina T. Epidemiology and clinical study of phenylketonuria (PKU) patients in Khorasan Province; Norteast Iran. Iran J Neonatol IJN [Internet]. 2015 Mar 1 [cited 2021 Jun 29];6(1):18–22. Available from: https://ijn.mums.ac.ir/article_4151.html

4. Healthline: Medical information and health advice you can trust. [Internet]. [cited 2021 Jul 30]. Available from: https://www.healthline.com/

5. Zaki OK, El-Wakeel L, Ebeid Y, Ez Elarab HS, Moustafa A, Abdulazim N, et al. The Use of Glycomacropeptide in Dietary Management of Phenylketonuria. J Nutr Metab. 2016;2016.

6. Ney DM, Stroup BM, Clayton MK, Murali SG, Rice GM, Rohr F, et al. Glycomacropeptide for nutritional management of phenylketonuria: A randomized, controlled, crossover trial. Am J Clin Nutr [Internet]. 2016 Aug 1 [cited 2021 Jun 29];104(2):334–45. Available from: https://academic.oup.com/ajcn/article/104/2/334/4668552

7. van Calcar SC, Ney DM. Food Products Made with Glycomacropeptide, a Low-Phenylalanine Whey Protein, Provide a New Alternative to Amino Acid-Based Medical Foods for Nutrition Management of Phenylketonuria. J Acad Nutr Diet. 2012 Aug 1;112(8):1201–10.

8. Pinto A, Almeida MF, Ramos PC, Rocha S, Guimas A, Ribeiro R, et al. Nutritional status in patients with phenylketonuria using glycomacropeptide as their major protein source. Eur J Clin Nutr [Internet]. 2017 Oct 1 [cited 2021 Jun 29];71(10):1230–4. Available from: https://www.nature.com/articles/ejcn201738

9. Daly A, Evans S, Chahal S, Santra S, MacDonald A. Glycomacropeptide in children with phenylketonuria: does its phenylalanine content affect blood phenylalanine control? J Hum Nutr Diet [Internet]. 2017 Aug 1 [cited 2021 Jun 29];30(4):515–23. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/jhn.12438

10. Figure 3 | Physiological Effect of Ghrelin on Body Systems [Internet]. [cited 2021 Jun 29]. Available from: https://www.hindawi.com/journals/ije/2020/1385138/fig3/

11. Kondrashina A, Brodkorb A, Giblin L. Dairy-derived peptides for satiety. J Funct Foods. 2020 Mar 1;66:103801.

12. Córdova-Dávalos LE, Jiménez M, Salinas E. Glycomacropeptide bioactivity and health: A review highlighting action mechanisms and signaling pathways [Internet]. Vol. 11, Nutrients. MDPI AG; 2019 [cited 2021 Jun 29]. p. 598. Available from: www.mdpi.com/journal/nutrients

13. Daly A, Evans S, Pinto A, Jackson R, Ashmore C, Rocha JC, et al. The impact of the use of glycomacropeptide on satiety and dietary intake in phenylketonuria. Nutrients [Internet]. 2020 Sep 1 [cited 2021 Jun 29];12(9):1–13. Available from: www.mdpi.com/journal/nutrients

14. Osuna-Padilla IA, Leal-Escobar G, Garza-García CA, Rodríguez-Castellanos FE. Carga ácida de la dieta; mecanismos y evidencia de sus repercusiones en la salud. Nefrología. 2019 Jul 1;39(4):343–54.

15. Daly A, Evans S, Chahal S, Santra S, Pinto A, Jackson R, et al. Glycomacropeptide: Long-term use and impact on blood phenylalanine, growth and nutritional status in children with PKU. Orphanet J Rare Dis [Internet]. 2019 Feb 15 [cited 2021 Jun 29];14(1):1–12. Available from: https://doi.org/10.1186/s13023-019-1011-y

Effect of Low Glycemic Index Treatment in Epileptic Patients

Patro Soltani

Introduction

Epilepsy is a central nervous system (neurological) disorder in which brain activity becomes abnormal, causing seizures or periods of unusual behavior, sensations, and sometimes loss of awareness. Epilepsy affects both males and females of all races, ethnic backgrounds and ages (1). More than 50 million people are living with epilepsy globally (2).

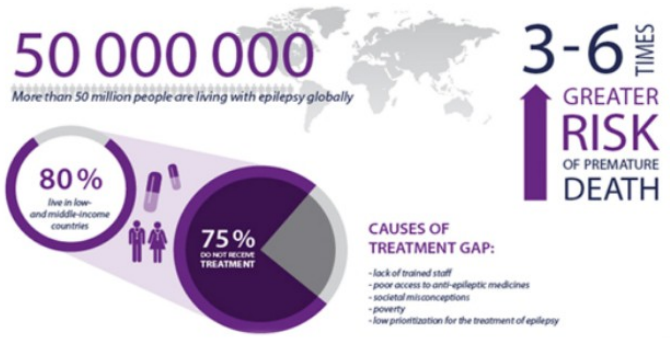


Figure 1 .Impact of epilepsy (2)

Certain factors may increase risk of epilepsy such as family history, head injuries, stroke and other vascular diseases, dementia and brain infections. Seizure symptoms can vary widely. Some people with epilepsy simply stare blankly for a few seconds during a seizure, while others repeatedly twitch their arms or legs. Treatment with medications or sometimes surgery can control seizures for the majority of people with epilepsy (2). Since biblical times, dietary therapy has been used to alleviate seizures. Hippocrates believed that fasting would help to purify the epileptic body and this purification was associated with a reduction in seizure activity.The ketogenic diet (KD), a specific form of dietary therapy created at the Mayo Clinic in 1924, works to establish a state similar to fasting to control seizures. The ketogenic diet results in an increased circulation of ketone bodies in the blood, which serve as a major energy source for the brain. This shift in metabolism has been shown to reduce seizure activity (2).

The low glycemic index treatment (LGIT), which was developed at the Center for Dietary Therapy of Epilepsy at the Massachusetts General Hospital (MGH), is similar to the ketogenic diet, but allows for more dietary freedom. The LGIT does not require a specific meal plan, focusing specifically on glycemic index and portion size, rather than strict ratios of fat to carbohydrates and protein. The LGIT aims for an intake of 40–60 g of carbohydrates per day. Those carbohydrates that are consumed, however, must have a low glycemic index (GI<50) (3). Considering that following LGIT for 1 month has been reported to reduce epileptic seizures by an average of 50% compared to other ketogenic treatment regimens, in this seminar we will examine the effect of LGIT in improving epilepsy.

Literature review

Sondhi et al, conducted a randomized controlled trial to determine whether the Modified Atkins Diet (MAD) and LGIT diet are better than KD among children with drug-resistant epilepsy. The results of this study demonstrated that LGIT diet makes a better balance between seizure reduction and relatively fewer adverse events compared with the KD and MAD (4).

From March 2014 to February 2015, 36 patients received LGIT at Severance Children's Hospital by Kim et al, to determine the efficacy and tolerability of LGIT. After 3 months of therapy, 20 patients (56%) experienced a 50% or greater reduction in seizure frequency (5).

Grocott et al, conducted a retrospective medical record review of 23 subjects who utilized the LGIT at the Clinic and Center for Dietary Therapy of Epilepsy at the Massachusetts General Hospital. This study aimed to assess the effectiveness of the low glycemic index treatment for seizure control in Angelman syndrome (AS). This cohort was composed of 23 subjects with AS aged 2 to 31 years. 22% of them became seizure-free after LGIT. Grocott et al found that the high level of seizure control and lower rate of side effects make the low glycemic index diet a viable treatment for seizures in Angelman syndrome(6).

Karimzade et al studied 42 children with refractory epilepsy aged 1.5-17 years, to determine the efficacy and tolerability of LGIT. More than 50% seizure reduction was observed in 71.4% of the patients after the second week (7).

Discussion

One of the mechanisms through which ketone bodies can lead to seizure reduction in epilepsy patients is through more efficient glutamate recycling (Figure 1). Metabolism of acetyl-CoA generated from a high-fat diet requires the consumption of oxaloacetate in the Krebs-cycle. Reduced availability of oxaloacetate along with increased availability of α-ketoglutarate leads to low aspartate levels and high glutamate levels. This higher availability of glutamate allows glutamic acid decarboxylase to produce more c-aminobutyric acid (GABA), an inhibitory neurotransmitter and an important anti-seizure agent (8).

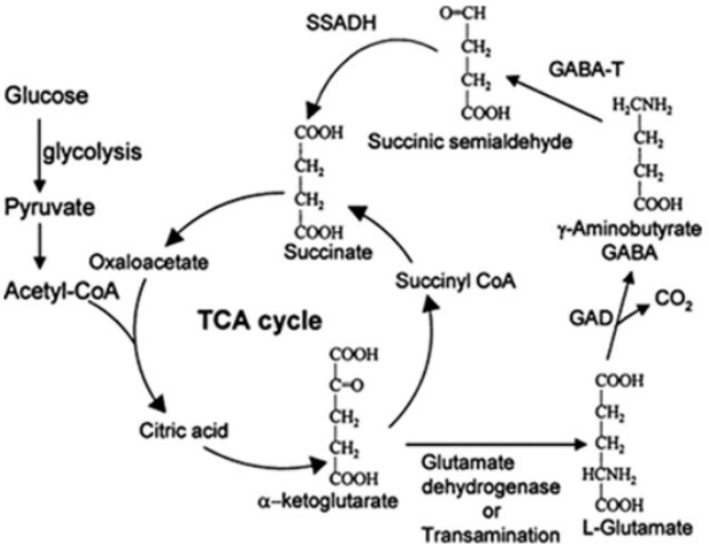


Figure 2 .efficient glutamate recycling is a mechanism by which ketone bodies can reduce seizures in epileptic patients. (8)

Conclusion

The result of the current study reveals that LGIT has a beneficial effect in patients with intractable epilepsy. LGIT has several advantages over other kinds of KD. First, the adverse effect of LGIT is lower than other kinds.

Second, LGIT is the most liberalized kind of KD that puts it as more palatable KD for adolescents and adults. Although, due to the paucity of strong evidence, more high-quality studies are required to determine the efficacy and adverse effects of LGIT in patients with intractable epilepsy.

References

1. Epilepsy - Symptoms and causes - Mayo Clinic [Internet]. [cited 2021 Jun 29]. Available from: https://www.mayoclinic.org/diseases-conditions/epilepsy/symptoms-causes/syc-20350093

2. Epilepsy - Diagnosis and treatment - Mayo Clinic [Internet]. [cited 2021 Jun 29]. Available from: https://www.mayoclinic.org/diseases-conditions/epilepsy/diagnosis-treatment/drc-20350098

3. Low Glycemic Index Treatment | Epilepsy Foundation [Internet]. [cited 2021 Jun 29]. Available from: https://www.epilepsy.com/learn/treating-seizures-and-epilepsy/dietary-therapies/low-glycemic-index-treatment

4. Sondhi V, Agarwala A, Pandey RM, Chakrabarty B, Jauhari P, Lodha R, et al. Efficacy of Ketogenic Diet, Modified Atkins Diet, and Low Glycemic Index Therapy Diet among Children with Drug-Resistant Epilepsy: A Randomized Clinical Trial. JAMA Pediatr [Internet]. 2020 Oct 1 [cited 2021 Jun 29];174(10):944–51. Available from: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2769074

5. Kim SH, Kang HC, Lee EJ, Lee JS, Kim HD. Low glycemic index treatment in patients with drug-resistant epilepsy. Brain Dev. 2017 Sep 1;39(8):687–92.

6. Grocott OR, Herrington KS, Pfeifer HH, Thiele EA, Thibert RL. Low glycemic index treatment for seizure control in Angelman syndrome: A case series from the Center for Dietary Therapy of Epilepsy at the Massachusetts General Hospital. Epilepsy Behav. 2017 Mar 1;68:45–50.

7. Karimzadeh P, Sedighi M, Beheshti M, Azargashb E, Ghofrani M, Abdollahe-Gorgi F. Low Glycemic Index Treatment in pediatric refractory epilepsy: The first Middle East report. Seizure. 2014 Aug 1;23(7):570–2.

8. Sadeghifar F, Penry VB. Mechanisms and Uses of Dietary Therapy as a Treatment for Epilepsy: A Review. Glob Adv Heal Med [Internet]. 2019 Jan 11 [cited 2021 Jun 29];8:2164956119874784. Available from: http://www.ncbi.nlm.nih.gov-/pubmed/31548917

Effects of Media on Children's Food Choices

Yeganeh Behnam

Introduction

Media is the communication outlets or tools used to store and deliver information or data. The term refers to components of the mass media communications industry, such as print media, publishing, news, media, photography, cinema, broadcasting, digital media and advertising (1). Every day, people often think media influences as negative, such as exposure to violence leading to antisocial behavior. But the media also has a positive impact. We can learn all kinds of useful things by reading newspapers, magazines, books, and websites. Media technology has made viewing increasingly easier as time has passed throughout history (1).

Today children are encouraged to use media tools in school and are expected to have a general understanding of the various technologies available. The internet is arguably one of the most effective tools in media for communication tools (1). Food advertising is aimed to reach a wide range of people and age levels through various sources and platforms. Advertising can easily influence the choice of people, especially teenagers and younger children. There is strong evidence that food advertising influences children's demand for food. There are significant associations between television viewing, diet quality, blood cholesterol levels, and obesity (2).

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. Globally, 38 million children under the age of 5 were overweight or obese in 2019, and over 340 million children and adolescents aged 5-19 were overweight or obese in 2016 (3).

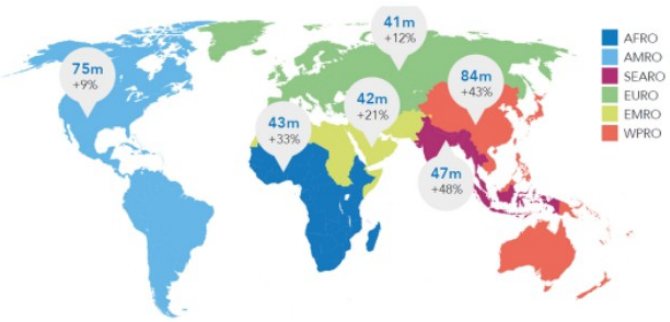


Figure 1 .Number of children aged 5-19 living with overweight or obesity in 2016,And the increase in prevalence from 2010 to 2016, by WHO region (3)

Obesity is a leading cause of death worldwide, with rates increasing in adults and children. Obesity in children also increases the risk of physical and mental illnesses such as metabolic syndrome, precocious puberty, respiratory disorders, etc. (3).

The main treatment for obesity consists of weight loss via calorie-restricted dieting and physical exercise. Dieting, as part of a lifestyle change, produces sustained weight loss, despite slow weight regain over time (3).

This study aimed to investigate how food commercials influence children's food choices.

Literature review

Bruce et al. examined the effects of food advertising on 23 children (8-14 years) in the U.S in 2016. This study concluded that children exposed to advertisements prefer branded foods at much greater rates than children not similarly exposed. Television advertising impacts food consumption and eating behaviors as well. Behavioral studies show the relationship between food advertising acceptance and the amount of food consumed. For example, snack and sweet food intake increases during or after commercial viewing in children. Children who are overweight may be more responsive to food branding and therefore at greater risk for marketing persuasion. There is some behavioral and epidemiologic research that demonstrates an association between marketing for unhealthy foods and increased risk for childhood obesity (4).

Also, Giese et al. explored the relationship between exposure to unhealthy and healthy food TV commercials, and food intake on 2851 children (8-21 years) in three European Countries in 2015. In this study, participants indicated higher exposure to unhealthy compared to healthy food advertisements. Also, unhealthy food advertisement exposure was positively associated with unhealthy food intake. Studies in children and adolescents consistently revealed a positive relationship between hours of TV viewing and daily sweets, and soft drink consumption as well as a negative relationship with fruit and vegetable consumption.The consumption of unhealthy food items increases when children watch more TV. One explanation is that the advertisements children are exposed to while watching TV might change the incentive value of the promoted foods (5).

According to articles that have been reviewed, food marketing is cited as a significant environmental factor implicated in food choices, overeating, and ultimately, obesity. Television advertising and branding affect both food familiarity and preference.

Discussion

When observing food brand logos, obese children demonstrate reduced neurofunctional reactivity in the prefrontal cortex, a cortical region known to be associated with self-control.For brain analyses, the primary focus was on the brain region most active during reward valuation the ventromedial prefrontal cortex (vmPFC). Researchers hypothesized that, after the children viewed food commercials, activity in their vmPFC would increase while they made specific food choices (4).

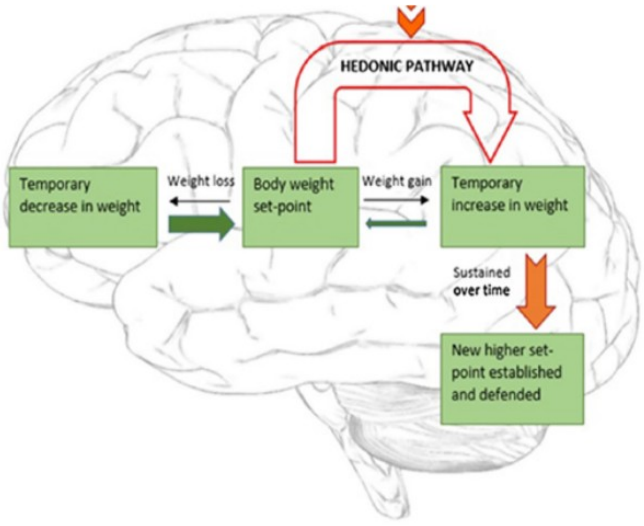


Figure 2 .The role of the hedonic system in obesity (8)

Also watching food commercials changes the way children consider the importance of taste when making food choices. Children did not use health values for their food choices, indicating children's decisions were largely driven by hedonic, immediate rewards (i.e. "tastiness"). However, children pay more attention to taste after watching food commercials compared with non-food commercials. The ventromedial prefrontal cortex, a reward valuation brain region, showed increased activity during food choices after watching food commercials compared with after watching non-food commercials (4).

Conclusion

Overall, our results suggest that watching food commercials before making food choices may bias children's decisions based solely on taste, and that food marketing may systematically alter the psychological and neurobiological mechanisms of children's food decisions (4). Increasing the promotion of healthy foods on social media may not be an effective strategy to encourage healthy dietary behaviors in children. More research is needed to understand the impact of digital food marketing and inform appropriate policy action (7).

References

1. Chassiakos YR, Radesky J, Christakis D, Moreno MA, Cross C, Hill D, et al. Children and adolescents, and digital media. Pediatrics [Internet]. 2016 Nov 1 [cited 2021 Jul 1];138(5). Available from: www.aappublications.org/news

2. Norman J, Kelly B, McMahon AT, Boyland E, Baur LA, Chapman K, et al. Sustained impact of energy-dense TV and online food advertising on children's dietary intake: A within-subject, randomised, crossover, counter-balanced trial. Int J Behav Nutr Phys Act [Internet]. 2018 Apr 12 [cited 2021 Jul 1];15(1):1–11. Available from: https://doi.org/10.1186/s12966-018-0672-6

3. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

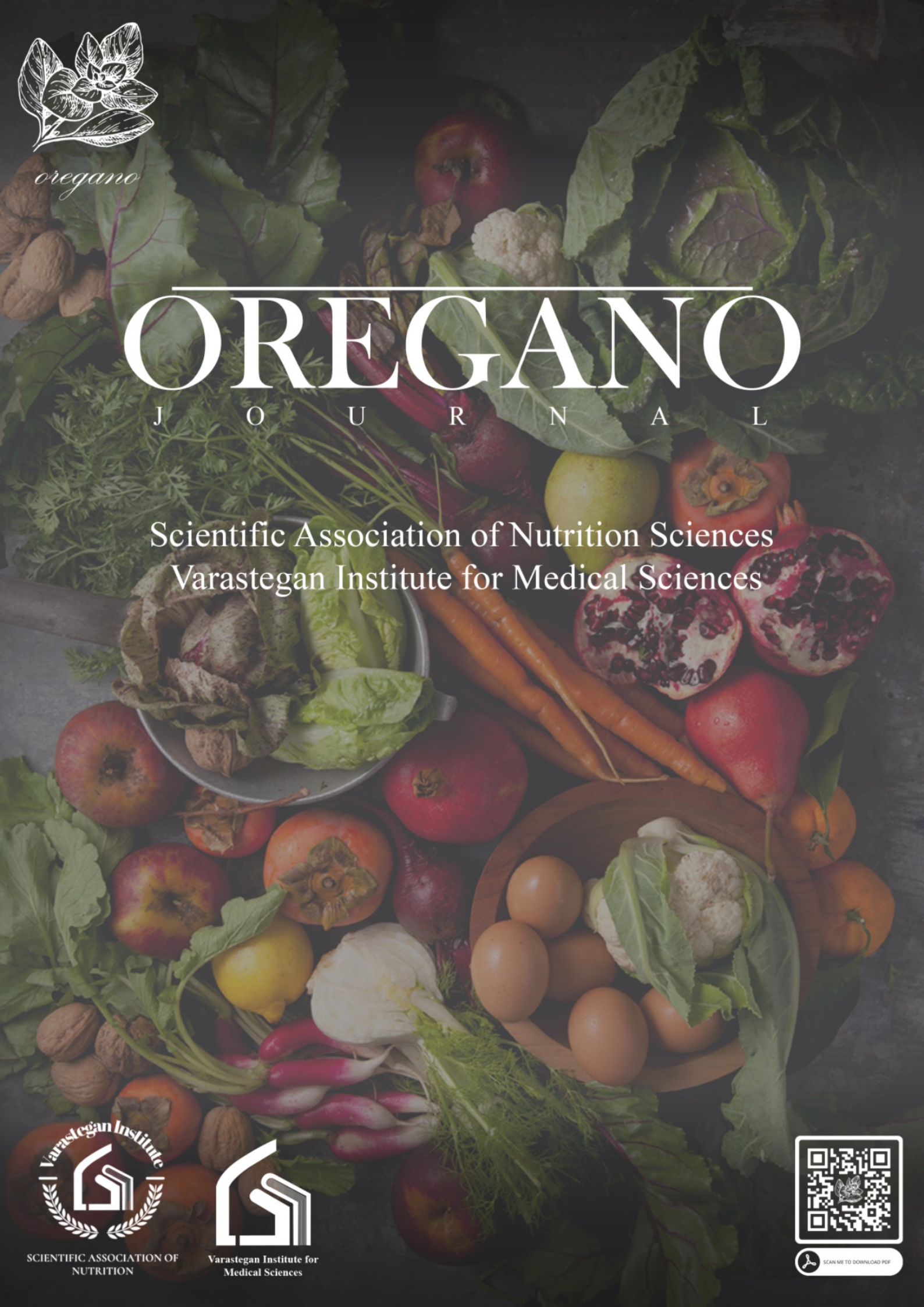
4. Bruce AS, Pruitt SW, Ha OR, Cherry JBC, Smith TR, Bruce JM, et al. The Influence of Televised Food Commercials on Children's Food Choices: Evidence from Ventromedial Prefrontal Cortex Activations. J Pediatr. 2016 Oct;177:27-32.e1.

5. Giese H, König LM, Tăut D, Ollila H, Băban A, Absetz P, et al. Exploring the association between television advertising of healthy and unhealthy foods, self-control, and food intake in three European countries. Appl Psychol Heal Well-Being. 2015 Mar;7(1):41–62.

6. Onaolapo AY, Onaolapo OJ. Food additives, food and the concept of 'food addiction': Is stimulation of the brain reward circuit by food sufficient to trigger addiction? Vol. 25, Pathophysiology. Elsevier B.V.; 2018. p. 263–76.

7. Coates AE, Hardman CA, Halford JCG, Christiansen P, Boyland EJ. Social media influencer marketing and children's food intake: A randomized trial. Pediatrics. 2019 Apr;143(4):20182554.

8. PC L, JB D. Food for Thought: Reward Mechanisms and Hedonic Overeating in Obesity. Curr Obes Rep [Internet]. 2017 Dec 1 [cited 2021 Jul 31];6(4):353–61. Available from: https://europepmc.org/article/med/29052153



oregano

OREGANO

JOURNAL

Scientific Association of Nutrition Sciences
Varastegan Institute for Medical Sciences

Varastegan Institute

SCIENTIFIC ASSOCIATION OF NUTRITION

Varastegan Institute for Medical Sciences

SCAN ME TO DOWNLOAD PDF