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Diet in the prevention and treatment of depression - systematic review

Izabela Szulc, Szpital Praski P.W. Przemienienia Pańskiego in Warsaw, ORCID: 0000-0002-2262-6886, izabelaszulc4@gmail.com

Weronika Swacha, Mazowieckie Centrum Stomatologii in Warsaw, ORCID: 0000-0002-1865-5967, weronka6@gmail.com

Julia Kozłowska, Mazowieckie Centrum Stomatologii in Warsaw, ORCID: 0009-0005-1902-1615, jukoz01@gmail.com

Katarzyna Pacek, Centralny Szpital Kliniczny MSWiA in Warsaw, ORCID: 0000-0001-6947-558X, kasia.pacek1@gmail.com

Małgorzata Piekarska, Wojewódzki Szpital Specjalistyczny im. Stefana Kardynała Wyszyńskiego SPZOZ in Lublin, ORCID: 0000-0001-5055-4923, piekarska13@gmail.com

Radosław Kasperski, Wojewódzki Szpital Specjalistyczny im. Stefana Kardynała Wyszyńskiego SPZOZ in Lublin, ORCID: 0000-0002-7364-3205, r.kasperski95@gmail.com

Klaudia Jedlina, Centralny Szpital Kliniczny MSWiA in Warsaw, ORCID: 0000-0002-2363-2620, klaudiajedlina@gmail.com

Klaudia Rusin, Mazowieckie Centrum Stomatologii in Warsaw, ORCID: 0000-0001-8386-7053, klaudiarusin1911@gmail.com

Julia Budziłło, Uniwersyteckie Centrum Stomatologii in Warsaw, ORCID: 0000-0001-7994-6728, j.budzillo@gmail.com

Monika Lewandowska, Warszawski Uniwersytet Medyczny in Warsaw, ORCID: 0000-0001-7855-5995, lewandowska097@gmail.com

ABSTRACT

Introduction: Depression is one of the leading causes of disability worldwide. It affects, according to WHO, nearly 300 million people worldwide, a number close to 3,8 % of the world's population. Depression is not exclusively a mental disorder limited to psychiatry, nowadays it is present in all medical fields. It has a significant association with many comorbidities, as an example cardiovascular diseases and metabolic disorders. Additionally, depression often is manifested with psychosomatic symptoms. Both aspects lead clinicians to major diagnostic and therapeutic challenges.

Objectives: Due to the increasing number of depression diagnosis and regarding treatment difficulties and limitations of contemporary antidepressants, several recent studies focus on novel modifiable risk factors and promising future therapeutic tool. Today, mental health nutrition is an expanding field gaining considerable clinical attention in managing depression. Particularly in groups of children and elderly patients where we may meet concerns about traditional therapy.

Methods: This article is a wide systematic review of nutritional candidates that play an important role in both prevention and treatment of depression. We screened single diet elements (omega-3 fatty acids, zinc, selenium, iron, vitamin B12, vitamin D, folate, fiber, meat, creatine) along with entirety dietary patterns. Moreover, we

highlighted the importance of gut microbiota that is strongly connected with both diet and central nervous system.

Results: Each one of dietary element: omega-3 fatty acids, zinc, selenium, iron, vitamin B12, vitamin D, folate, creatine was found to correspond with mental health in patients and the level of mentioned diet components is negatively correlated with depression risk of individuals. Additionally, omega-3 fatty acids supplementation as well as zinc supplementation were established to promote a greater later respond to antidepressant in patient resistant to traditional pharmacotherapy. Moreover, all described elements broaden treatment possibilities. The evidence of this correlation generally is greater in risk groups for developing depression. It is worth emphasizing that, mainly seen in iron deficiency, type of consequences depends on the age when the deficiency occurred.

Regarding dietary patterns and meat consumption more complex interaction are noticed and the analysis requires considerable comprehensiveness. Nevertheless, we know that systemic inflammation has source in high consumption of processed food and red meat. Unhealthy diet leads also to deficiency of vitamin and minerals listed below with its implications.

In connection with gut microbiota and the soluble fiber the numerous interactions between it and central nervous system are intriguing and still unexplored. Beyond systemic inflammation plenty of others metabolic processes are involved including synthesis of neurotransmitters, hormones, BDNF and short-chain fatty acid. The qualitative and quantitative of microbiota composition is inextricably linked to mental health, especially to depression.

Conclusions: Each of the dietary aspect considered in the article has a significant correlation with depression disorder and might support the new multidisciplinary attitude toward it in mental health.

Key words: depression, diet, gut microbiota, dietary patterns, microelement

INTRODUCTION AND OBJECTIVES:

WHO reports that globally around 5% of adults suffer from depression. Furthermore, it is a leading cause of disability worldwide and is a major contributor to the overall Global Burden of Disease. The frequency of depression is rapidly growing nowadays. Depression is a complex disease that results from a combination of many factors including genes, social conditions, environment, lifestyle, biological and psychological wellbeing and the presence of low-grade systemic inflammation. It leads to fundamental reduction of the quality of life and as the most severe consequence to suicide. Multiple comorbidities such as anxiety disorders [1], cardiovascular [2] and autoimmune diseases appear to be related with depression. Depression is a heterogeneous syndrome and research nowadays call into question the monoamine hypothesis, an essential component of clinical approach to depression disorders in the past [3]. The fact that many patients despite the traditional treatment, that includes antidepressants and psychotherapy, are still experiencing the symptoms obliges us to search for other methods and factors that could help with the prevention and treatment of depression. We analyzed the link between depression and diet to demonstrate the role of nutrition in depression development together with its potential therapeutic properties.

MATERIALS AND METHODOLOGY:

All applicable English language databases such as Google Scholar and PubMed were searched for systematic reviews, meta-analysis and studies that include the depression pathogenesis and its correlation with nutrition. Most of the studies were published from 2019 to 2022.

RESULTS:

Omega-3 fatty acids

These polyunsaturated acids play a key role in central nervous system. They are considered as promising changeable factors in plenty of psychiatric disorders. The main evidence of the efficiency of omega-3 fatty acids use were found in depressive disorders, particularly major depression [4].

In 2019 International Society for Nutritional Psychiatry incorporate in the guideline using of omega-3 fatty acids, both pure eicosapentaenoic acid (EPA) or an EPA/docosahexaenoic acid (DHA) combination of a ratio higher than 2 (EPA/DHA >2), in major depressive disorder, an illness with unmet therapeutic needs [5].

A vast amount of the latest review studies and meta-analyses focus on omega-3 fatty acids as a novel approach in major depression field [6]. Systematic reviews and meta-analysis declined also the influence of omega-3 fatty acids on mental health in healthy individuals. The meta-analysis of 21 studies exposed the linear correlation

between higher fish consumption and lower depression odds with peak decreased risk of depression for 1.8 g/d intake of omega-3 fatty acids [7].

Omega-3 fatty acids are also an important promising treatment in some specific groups of patients. In this systematic review supplementation of omega-3-polyunsaturated fatty acids (PUFAs) was proved to provide positive effects in depressive group of elderly patients. Although no significant effect was noticed in well-being mental health group. Thus, the efficiency might be present mostly in groups of patients with mild to moderate symptoms [8].

A study of depressive disorders among children demonstrated that omega-3 fatty acids supplementation has a negative correlation with Children's Depression Inventory score via decrease of HDL-cholesterol (proatherogenic) and increase of large HDL subfractions (anti-atherogenic). Moreover, in this study the effect was not associated with omega-6 fatty acids intake [9].

Additionally, the ratio between omega-6 fatty acids and omega-3 fatty acids appears to be an important factor in mental health. Young individuals with ultra-high-risk phenotype of mood disorders were tested for 7-years and the results showed that high ratio of omega-6 fatty acids and omega-3 fatty acids indicates greater risk of developing mood correlated psychiatric disorders. Furthermore, no other psychiatric diseases were found to have this correlation. It suggests that the ratio between omega-6 fatty acids and omega-3 fatty acids might be specific for mood disorders [10]. This study among the children showed a greater positive effect of omega-3 fatty acids on depressive disorders in comparison with mixed anxiety and depressive disorder. Moreover, it confirmed that high ratio omega-6 fatty acids/omega-3 fatty acids corresponds with severity of symptoms [11].

Among perinatal women the omega-3 fatty acids monotherapy efficiency and safety was studied. The result showed the superior antidepressant effect over placebo group. In addition, the beneficial effect was discovered in postpartum depressive symptoms as well. The effect probably had a correlation with higher EPA/DHA ratio. No significant side effects were noticed [12].

Considering separately Docosahexaenoic acid and Eicosapentaenoic acid both levels correspond with depression. The lower level of DHA [13] and lower level of EPA as a compound of erythrocytes plasma and membranes were correlated with increased severity of depressive syndromes [14].

The importance of DHA and EPA in depressive patients is undeniable as a predictor and an additional treatment opportunity for patient. The conclusion is compatible with study results that demonstrated a greater later antidepressant response among patients with higher baseline of omega-3 fatty acids [15].

Zinc

Zinc is a crucial cofactor for many enzymes and an essential chemical element for prenatal and postnatal development. Zinc appears to be strongly linked with depression status. It was found to reduce the risk of depression development and relieve depressive symptoms. The abnormal zinc level was found among depressed patients [16]. What's more the supplementation of zinc reduced significantly risk of depression development [17]. It is also considered as an additional tool for antidepressant therapy. Furthermore, this metal was also studied in group of patients with lack of effectiveness in traditional treatment. Zinc occurred to enhance the response of individual for antidepressant treatment. In meta-analysis zinc supplementation in patient resistant to antidepressant therapy decreased depression score and favored treatment [18]. Zinc appears not only to promote effectiveness of antidepressant drugs but may also act as an antidepressant in monotherapy [16].

Selenium

Selenium is a trace element in diet that forms selenocysteine and many selenoproteins necessary for our cellular functions. Selenium is recently a subject of many studies concerning mental health, due to its regulation of immune system and antioxidant effects. Recently published systematic review and meta-analysis, where both interventional and observational studies were included, demonstrated that selenium supplementation decreased the severity of depressive symptoms in patients. Moreover, selenium intake played an important role in postpartum depression prevention. Although correlation of selenium level with depression odds was not confirmed [19]. However, in this study high selenium intake correspond with lower prevalence of depression [20]. Low serum selenium level was also reported to increased Hamilton Depression Rating Scale together with Beck Anxiety Inventory in patients with correct level of thyroid hormones [21]. Selenium intake and odds for depressive symptoms appeared to have an inverse association [22]. A study performed on a sample of 9354 participants revealed strong report between selenium and depression probability. Selenium intake was found to have the strongest link with depression among all the dietary factors considered [23].

Iron

Iron is a crucial mineral for growth, development and healthy functioning of our body. According to WHO iron deficiency is the leading nutritional disorder globally. Groups in greater risk of iron deficiency are children, young women with severe menstrual bleeding and as a common comorbidity it is found in patient with gastrointestinal bleeding and with heart failure.

The difference in iron deficiency between vegetarian and non-vegetarian appear not to be evident however applying vegan/vegetarian diet it could be necessary to control and supply iron in individuals with additional risk factor as an example pregnant women [24] [25].

In pediatric patients' iron deficiency was reported to affect central nervous system development. Its influence begins in embryonic phase of development and can cause consequences during all lifetime of individuals. The structural changes in hippocampus, corpus striatum were identified. The authors mentioned: depression, anxiety, sleep and psychotic disorders [26]. In another study among children, secondary to iron deficiency, specific wariness and hesitance, lack of positive affect, diminished social engagement were present, due to alteration of mesolimbic pathways [27]. The importance of iron level during intrauterine development and the time of deficiency is confirmed to remain consequences besides iron supplementation later in lifetime.

Furthermore, among pregnant women iron was connected to postpartum depression, stress and was found to be effective as a therapy for mentioned disorders [28].

In adulthood the iron deficit is related with depression, anxiety and sleep disorders. The study with 2000 individuals older than 64 years showed the correlation between depressive symptoms and lower serum hemoglobin and ferritin levels [29].

The patients with iron deficiency anemia (IDA) were in greater risk of psychiatric disorder, and additionally the difference increased over time of deficiency. Moreover, its supplementation is related to a considerably lower risk of this psychiatric disorders compared to non-iron supplementation patient, but IDA patients who were receiving supplementation were still at greater risk compared to non-IDA group [30].

Vitamin B12, folate, vitamin D

Vitamin B12 and folate is strongly connected with well-functioning nervous system, vitamin D plays an important role in calcium and phosphorus homeostasis. Furthermore, levels of three of them were found to have negative correlation with depression disorders [31] [32]. Moreover, in a study where depression odds were measured in two group divided according to healthy and unhealthy dietary patterns, the odds of depression were lower in healthy dietary patterns group via increased serum B12 and folate level. What's more the correlation was confirmed by adding B12 and folate to regression model, when considerable association between dietary patterns and depression was excluded [33]. Vitamin D supplementation in elderly depressive patients was exposed as a factor contributing to improvement of depression score [34].

Creatine

Creatine, an amino acid accumulated mostly in muscle is recently studied due to its potential correlation with depression development in some patients. The explanation of its important role might relate to cellular (particularly in brain cells) metabolism and energy homeostasis in which it plays an important role. It was showed a significant negative correlation between dietary creatine intake and depression odds [35]. Additionally benefits of creatine supplementation as a promising adjunctive treatment are recent subject of many studies [36] [37]. Sex-based impact is a relevant aspect of the link between creatine and depression. Results were stronger demonstrated among females [38].

The gut microbiota

The gut microbiota according to research influences the depression development via no less than two mechanisms: regulation of systemic inflammatory and metabolism of neurotransmitters and hormones.

Higher incidence of pro-inflammatory types of microorganisms in gastrointestinal tract, stimulated by food-driven antigens supply occurred to be strongly associated with depression disorder [39]. Additionally, this imbalance leads to elevated permeability of intestinal wall and as a result to consequent auto immunities.

Furthermore, exists also the correlation between lower number of bacteria able to produce lower short-chain fatty acid and BDNF-brain-derived neurotrophic factor, the key neurotrophic factor that maintains survival of neurons and synaptic plasticity, and was showed to be decreased in depressed patients. [40] [41] [42].

Gut-brain axis also impacts the production and metabolism of neurotransmitters like serotonin, GABA. More research showed the connection between the gut imbalance and hyperactivity of hypothalamic-pituitary-adrenal

(HPA) axis. Mentioned increased HPA activity along with chronic stress play a great role in progression of depressive disorder [43].

Some studies suggest that gut microbiota could be considered not only in prevention but also as a composed treatment element. Submission of probiotics have showed a considerable improvement in patient with depression, the anti-inflammatory mechanism occurs to be likely [44] [45] [46]. There were also conducted animal studies as an example Bifidobacterium longum and Bifidobacterium breve administration to mice improved expression of Tph1 and secretion of 5-hydroxytryptophan (5-HTP) in RIN14B cells, also elevated the level of 5-HTP and BDNF in brain. Simultaneously decreased the serum cortisone level. Both metabolic effects had an implication on less depressive behaviors of mice and underlined an anti-depressive feature [47].

Soluble dietary fiber

Beneficial influence of the fiber on human health seems to be an obvious fact but it's worth to underline that precisely soluble dietary fiber is the one that regulates positively the gut microbiota and reduces the low-grade systemic inflammation as a result. Animals' studies demonstrated that 57% of variety of the total gut microbiota is explained by diet and only 12% of variety is genes-related [48]. Therefore, in nutrition choices the importance both of amount and type of fiber is relevant.

Meat

The correlation between meat consumption and depression is still unclear however nowadays great amount of research focuses on this argument.

Different diet often happens to be followed by diverse socio-economical level and lifestyle. Vegetarians and vegans are considered to have generally healthier habits including nutrition and physical activity, however vegetarians also more often present concerns regarding environmental issues. These factors are possible to interfere with studies results regarding meat consumption.

Higher consumption of red meat is associated with higher risk of psychiatric disorders depression included, probably due to inflammatory reactions. Red meat delivers precursors for inflammatory mediators and favors pro-inflammatory types of microorganisms in gastrointestinal tract [49].

In the meanwhile, systematic review of 18 studies demonstrated prevalent of greater risk of developing depression, anxiety and related symptoms among meat-abstinent, though the results of studies analyzed were various [50].

An interesting study from 2020 was performed to explore the correspondence between meat consumption and depression risk. The main goal of the study was to distinguish whether the nutrition patterns or the psychological conflict connected to meat consumption issues influence depression development. Three groups took part: meat-eater, vegans/vegetarians and meat-reducers. Results showed the highest depression scores among the meat-reducers who can experience a cognitive dissonance regarding willingness to avoid meat and at the same time face a difficulty to abandon eating it [51].

In study where two groups with healthy and unhealthy dietary patterns were analyzed in the context of depression odds, the healthy diet had a low meat consumption and unhealthy one was composed with red meat and processed meat. The healthy dietary patterns were correlated with lower depression odds, providing sufficient level of vitamin B12 [52].

Although it is still uncertain the correlation between meat consumption and depression, from analyzed studies we can conclude that high red meat consumption can lead to depression. However, whether low meat-consumption or meat-elimination diet is more likely to correspond with depression is still unclear.

Dietary patterns

Nowadays the number of studies that focus on whole dietary patterns instead of a single nutrition element is rising. The complexity of both pathogenesis of depression and interaction between nutritional elements allows to confirm the correctness of this tendency. Although the healthy dietary patterns have wide range of diversity there are some repetitive components like high number of fruits, vegetables and whole grains. These studies are compatible with negative correlation between healthy dietary patterns and depression odds [53].

Interesting perspective was showed in study where 3 dietary patterns were analyzed for depression odds: traditional diet (vegetables, fruit, beef, lamb, fish, whole-grain foods), modern diet (fruit and salads, fish, tofu, beans, nuts, yogurt, red wine), and western diet (meat pies, processed meats, pizza, chips, hamburgers, white bread, sugar, flavored milk drinks, beer). Although positive correlation in western diet and negative correlation in traditional one was compatible with other studies, there was an unexpected result regarding the modern dietary pattern. The modern diet tended to increase risk of depression rather than decrease it. The reason of this is unknown and needs further studies [54].

Diet rich in saturated fat and refined sugar interferes with central nervous system. The molecular changes in the brain where exposed in animal study where rats fed with these components after 2 months already had decreased level of BDNF, further with consumption of saturated fat and refined sugar metabolism of other important molecules, necessary for neuronal plasticity, and learning capacities were disturbed [55].

CONCLUSIONS:

Undeniably treatment for depression requires multidisciplinary approach and greater focus on active prevention. Nourishment is one of the fields where many notable correlations with depression were found during last years. Latest studies demonstrated plenty of promising nutritional candidate that alleviates depressive syndromes, may provide an additional therapeutic element for depression and moreover may play an important role in prevention of depression.

Taking into consideration the complexity of both alimentation and pathophysiology of depression further studies are still required to define the consensus on nutrition-based interventions as prevention, additional therapy or monotherapy in managing depression. However, the importance of diet is unquestionable and should constitute a significant part of the holistic approach towards mental health in particular depression.

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