



The Role of Nutrition in the Treatment of Depression

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Abstract

Depression is a mental disease that affects about 400 million people worldwide. Depression symptoms can be prevented and treated by many ways. Scientific evidence has proven that nutrition is related to mood and mental illnesses; nutritional therapy can be an effective treatment for depression symptoms. This paper reviews how the consumption of specific nutrients from natural food sources can play an integral role in the regulation of some brain hormones and neurotransmitters, which in turn affect depression. Some of these nutrients improve depression and some of them have anti-depressant effects. Carbohydrates, omega-3 polyunsaturated fatty acids, B-complex vitamins, vitamin D, magnesium, and zinc are all the most recognized nutrients to improve mood and treat depression. Thus, these nutrients effectiveness are discussed in this paper.

Keywords: Depression, Mental health, Nutrients, Carbohydrates, Polyunsaturated fatty acids (PUFAs), Amino acids (AAs), Zinc, Magnesium.

Introduction

Depression is a disease that affects people globally. The World Health Organization (WHO) predicted in 2012 that depression would affect about 350 million people around



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the world (Marcus, Yasamy, Ommeren, Chisholm, & Saxena, 2012). More surprisingly, an article that was published in 2014 by the same organization stated that depression affected about 400 million people around the world (World Health Organization (WHO), 2014). The World Mental Health survey, which involved seventeen countries, revealed that about 1 out of 20 people have had previous depression symptoms. Usually, depression symptoms happen at a young age and can recur. In addition, depression is considered a global disability disease because it can happen repeatedly (Marcus et al., 2012).

Depression can affect a person's life and leads to decreasing function at work, at school, and with the family; the worse the depression becomes, the more the person is prone to suicide. It is estimated the depression results in about one million suicides a year. The WHO is required to work on minimizing the increasing number of depression worldwide (WHO, 2012 a).

About 3 percent of the population in Japan and 16.9 percent of the population in the United States (US) are estimated to suffer from depression; most countries are between 8 percent to 12 percent. Some situations can make a person more prone to depression, as can belonging to certain demographics. For example, women are two to three times more prone to depression than men (WHO, 2012 b). In addition, there are some factors, which increase the prevalence of depression such as poverty, low education, violence, divorce (especially for men) and some chronic illnesses. Depression also has a genetic link (WHO, 2012 b).



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It is estimated that one out of every ten people will have depression in his or her lifetime and one of every five people already has suffered from depression (Christodoulou, 2012). However, it is expected that by 2020, depression will be the second primary reason of world disability and by 2030, it is likely to be the first cause for illness (Christodoulou, 2012).

Nutritional factors play an important role on depression. In fact, according to the American Psychiatric Association (APA), it was found that vitamin deficiency and/or consuming an unhealthy diet could contribute to depression (American Psychiatric Association (APA), n.d.). Thus, the aim of this paper is to address the most studied nutrients that have been proven by scientific evidences to have positive effects in the treatment of depression. In addition, a description of the effect of the different nutrients consumed from natural food on the regulation of hormones and the effect of them on depression and mood disorders will be discussed too.

What Is Depression?

Depression is defined as a mental disorder, which happens in combination with many other symptoms like sadness, loss of interest, low energy, guilty feelings or low self-worth, impaired sleeping, problems with appetite, and reduced concentration (Marcus, et al., 2012). Sometimes, when a person has blue symptoms or feels unhappy, it is normal and it takes a short time to go. On the other hand, people with depression feel interruption in their lives, which causes difficulties for them and for people who care about them. Usually, depressed people do not pursue treatment (National Institute of Mental Health, n.d.). Unfortunately, when symptoms are untreated, they can last for long



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time from weeks to years and this can lead to serious problems (The Brain & Behavior Research Foundation, n.d.). However, it is important to know that real depression is different from normal sadness or mood changes (WHO, 2012 a).

Types and Symptoms of Depression:

Symptoms of depression, according to WHO, can be divided into mild, moderate, or severe symptoms. As it was said before, the untreated depression can be severe in both types either for people who had depression before or for those who did not. In fact, there are two main types of depression: the bipolar mood disorder and unipolar depression. The bipolar depression is basically composed of both manic and depressive symptoms punctuated by some normal mood periods. The manic mood includes irritability, hyperactivity, stress of speech, over self-esteem, lower necessity of sleep (WHO, 2012 c).

The unipolar depression, which is known as the major depression, includes depressive, in which the person will feel depressed mood, loss of pleasure, lowering energy that leads to decreased activity for about more than two weeks. Additionally, in this type of depression a person might suffer from anxiety symptoms, upset sleeping, appetite problems, with also some feelings of guilt or low self-worth, reduced attention, and some other unreasonable symptoms. However, regarding the severity level of depression, a person with mild depressive symptoms will feel it hard to keep doing regular work or involving in social events, but she/he will not stop to operate completely. On the other hand, a person with severe depressive symptoms usually will not be able to continue the social activities or work with just a very limited ability to work (WHO, 2012 c).

Furthermore, there are some other types of depression that happen under specific



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circumstances. These types include psychotic depression, which makes the person see or hear, or think about things that other people do not see or hear. In addition, postpartum depression which women have after giving birth due to hormones confusion besides the new given responsibility about the baby. Additionally, there is the seasonal depression which usually happens during winter season (National Institute of Mental Health, n.d). There are also additional popular types of depression like Dementia which is a result of different diseases or injuries to the brain. In addition, some developmental disorders like autism are considered a type of depression too (WHO, 2014).

The Contributing Factors & Causes of Depression:

According to the WHO, there are many factors that might interfere with each other and lead to depression including social, psychological and biological aspects. In addition, there is a connection between depression and physical condition (WHO, 2012 c). According to APA 2014, depression can affect even people who live normal life without any surrounding problems. In contrast, the surrounding environment also can contribute to depression like violence, neglect, abuse, poverty, or medical condition such as vitamins deficiency besides unbalanced die. Moreover, depression can be initiated by factors like the body's biochemistry and genetics. Even more, the personality of a person like low self-esteem, intolerance of stress and pessimistic people are more susceptible to depression (APA, n.d.). However, depression itself can be a further indicator of more problems affecting depressed person negatively and makes depression more complicated (WHO, 2012 c).

Treatment and prevention of Depression:

Even though most depressed people do not seek treatments, depression could be treated



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by many ways (WHO, 2012 b). WHO has found that less than 25 percent of people seek treatment for depression around the world. In addition, as depression is considered an illness in the brain, it is important for a person to be aware of the illness and take care of him/herself through acceptable forms of prescribed treatment. It is recommended as part of the depression treatment to take action by exercising, relaxation techniques, maintaining normal sleep, reducing stress, managing work time properly, avoiding or limiting alcohol amount, being patient, making a daily schedule, and the most important part eating a healthy balanced diet (WHO, 2012 b).

Depression cannot just simply be treated for such a period of time; it is considered as the most treatable diseases among the mental disorders. The treatment of depression found to be effective and gives a relief from the symptoms (APA, n.d.). The first step in treating depression is to distinguish it and to seek a support. Depression can be treated effectively and can be diagnosed by health workers who are highly trained to deliver main health care. The basic treatment choices for depression include the support of psychosocial in combination with antidepressant medications and psychotherapy. However, medications are not the first-line treatment for moderate to severe depression or even for children and adolescents (WHO, 2012 c).

The Link between Nutrition and Depression

Hormonal Imbalances

Hormones play an imperative role in the severity of depression. In other words, the severity of depression depends on the level of these hormones in the body. Depression is associated with the abnormalities of these biochemicals like serotonin, epinephrine, norepinephrine, and Y-aminobutyric acid. For example, low serotonin levels are



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associated with the severe depression (Ross, 2010). Additionally, low melatonin levels are found to be associated with some mood disorders (Hardeland, 2012). Since biochemistry is one of the most important factors that play an imperative role in the initiation of depression, it includes the two most important hormones which are serotonin and norepinephrine located in the brain. These two hormonal abnormalities can cause some depression symptoms like anxiety, irritability, and fatigue (APA, n.d.).

The role of nutrition in the treatment of depression

Nutrition plays a significant role in treating depression; it helps to ease depression symptoms. More specifically, vitamins and minerals, just until the last decade, were found to be beneficial when used to treat the mental illnesses (Rucklidge, 2013). A study was conducted to find the effect of the dietary consumption on the mental health like depression and anxiety. The researchers used a composite measure assessment to assess the dietary intake of fruits, vegetables, beef, lamb, fish, and whole grain that participants were consuming in the study. The results exhibited that this dietary pattern was linked with lower levels of depression and anxiety in comparison with the unhealthy food such as processed food, which was associated with higher probability of these mental illnesses (Jacka, Pasco, Mykletun, Williams, Hodge, O'Reilly, Nicholson, 2010).

In addition, in the *Journal of Child and Adolescent Behavior*, there was a case report of a child aged 13 years old having eating disorder, diabetes, and depression; however, it was recommended for this child to set a nutritional plan as an important approach of the treatment plan (Puri & Littlefield, 2014). However, people, in general, connect more easily between nutritional deficiency and illness than connecting between nutrition and depression. In fact, nutrition plays a significant role in the harshness and the period of



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depression. Many eating patterns affect depression. The nutritional neuroscience confirms that nutritional issues interfere with a person's intellectuality, behavior, and feelings. There are some nutrients that are related to mental health, such as carbohydrates, proteins, essential fatty acids containing omega-3 fatty acids, vitamins like B-complex vitamins, B12, folate, and minerals like calcium, chromium, iodine, iron, lithium, selenium, and zinc (Rao, Asha, Ramesh, & Rao, 2008).

In addition, folic acid, B12, and B6 are important for the methylation and decarboxylation which rule DNA and DNA synthesis, proteins, phospholipids, and neurotransmitters like catecholamine and monoamine. Moreover, vitamins like vitamin C is the greatest abundant antioxidant in the brain; it has an imperative role in the process of neural maturation, neuroprotection, and neurotransmission. Additionally, minerals like magnesium, zinc, and calcium are important for the function of Central Nervous System (CNS) in addition to their roles in myelination, the synthesis of neurotransmitter, and modification of activity in both neurotransmitters which are the dopaminergic and adenosinergic (Kennedy, Veasey, Watson, Dodd, Jones, Maggini, Haskell, 2010).

Carbohydrates

Tryptophan levels in human plasma have been found effective in increasing serotonin levels which help with depression. A 1997 Cambridge University study found that consuming carbohydrates stimulates the secretion of insulin and increases tryptophan, which is a protein, plasma level while decreasing the levels of competing amino acids. Thus, increasing tryptophan will lead to an increase in serotonin levels causing a high level of both in the brain. However, protein consumption will provide the plasma with amino acids which increase the ratio of amino acids than tryptophan; tryptophan



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concentration then will not increase that much by protein consumption in comparison with increasing amino acids. In addition, insulin secretion that resulted from consuming protein can affect the ranks of tryptophan and serotonin in the brain. In fact, the level of these two neurotransmitters could remain the same or change depending on the type of the protein consumed and its portion in comparison with the carbohydrates (Fernstrom & R.Wurtman, 1997).

The tryptophan was found to increase the level of serotonin in the brain with a difference found between it and the consumption of the amino acids. Not only that, but also carbohydrate consumption was found to raise the brain serotonin level. Additionally, consuming carbohydrates-rich and protein-free formula diets were found to raise brain serotonin level; on the other hand, the high protein diet was found to decrease it. A study was conducted to investigate the influence of carbohydrate-rich and protein-rich breakfasts, which are normally consumed by Americans, on the tryptophan and the other large neutral amino acids (LNAA) plasma levels ratio and to see the response of tyrosine, which is a precursor of brain dopamine and norepinephrine (Wurtman, Wurtman, Regan, McDermot, Tsay, Breu, 2003).

In this study, the participants consumed during 3 to 7 separate days after overnight fasting either a carbohydrate-rich meal with a low amount of protein or rich protein meal with a low amount carbohydrates. The blood samples were collected at baseline and subsequent intervals after the consumption of either meals to measure the tryptophan, tyrosine, five LNAA, and insulin. The results found that there was a significant difference between the two-meal consumption on tryptophan-LNAA plasma levels and tyrosine-LNAA by



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showing the higher median for tryptophan:LNAA 54 percent in comparison with just 28 percent for tyrosine:LNAA. In addition, the results showed that after the carbohydrate consumption, the insulin level increased significantly in comparison to protein consumption (Wurtman et al., 2003).

Furthermore, there was a study conducted in Harvard School of Public Health for 12 years to determine the connection between carbohydrates intake and depression. Some 43,000 women who had no history of depression participated in the study and they were asked about their diets. The results showed that women who were consuming red meat, pasta, bread, and chips they were 29 to 41 percent more likely to have depression. On the other hand, the women who consumed olive oil, wine, and fish were at a low probability to have depression. Based on this study, in fact, it is unknown if carbohydrates lead to depression or when people feel low mood they crave carbs (Innes, 2013).

However, some researchers say that people usually crave carbohydrates when the level of serotonin, the feel-good hormone, is low in our brain. In addition, other researchers disagree with that and say that when people are already depressed; just then, they start to eat carbohydrates to give them the feeling of relief. It is important to mention that in the earlier study participants stated that eating sugary food provides a quick fix for the mood, but this is not good because after a while the sugar level will crash, which makes the person not feel as good as he/she was. However, to avoid depression it is recommended to eat complex carbohydrates, which makes the blood level steady and gives energy to the brain for a long time (Innes, 2013).

Polyunsaturated Fatty Acids



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Fatty acids include both omega-3 and omega-6 polyunsaturated fatty acids (PUFAs). They come either from the diet or can be synthesized from the essential fatty acids α -linolenic Acid (ALA) in addition to Linoleic Acid (LA). The food sources for omega-3 PUFAs are oily fish like salmon, mackerel, and sardines. Fatty acids are important components of cell membranes (Bloch & Hannestad, 2012). There are studies found that PUFAs have an important role in depression treatment. This mechanism is simply identified in reducing the neuro inflammation. In fact, low-rank inflammatory reaction and stimulation in the cell mediated immunity, with higher oxidative and nitrosative is linked to depression. However, the pro-inflammatory cytokines effect on depression mechanism is poorly understood (Mendes, 2014).

Initial data findings conclude that the inhibition of the pro-inflammatory cytokines or the signals might recover depression and rises up the response for the treatment of antidepressants (Mendes, 2014). It was found that high omega-3 levels decrease the making of pro-inflammatory cytokines and depression symptoms; on the other hand, low ranks of both omega-3 and omega-6 PUFAs can lead to depression and suicide. Also, if there are low levels of the Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) which are compounds found in omega-3 fatty acids, that will cause phospholipase A2 and cyclooxygenase 2 genetic irregularities which in turn would lead to severe depression (Mendes, 2014).

High omega-3 PUFAs in the diet might function by changing the cell membrane fluidity and phospholipid structure in CNS. This increasing of omega-3 PUFAs levels in cell membranes was found to increase serotonin and dopamine neurotransmission (Bloch &



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Hannestad, 2012). The deficiency of omega-3 PUFAs can change many neurotransmitters because of its important role in the membrane flexibility; such as in the serotonergic and dopaminergic system. Thus, omega-3 PUFAs in addition to selective serotonin uptake inhibitors were recommended to treat people suffering from depression symptoms. That is because omega-3 can progress the dopamine neuron survival and decreases the oxidation of cortical monoamine. In addition, omega-3 deficiency was found to be associated with decreasing the brain glucose intake and reduces the action of cytochrome oxidation; both are signs for the function and action of neuronal. Moreover, omega-3 was found to be involved in the formation of Brain-Derived Neurotrophic Factor (BDNF) which is found in the hippocampus and the ruling of hypothalamic-pituitary-adrenal alliance (Mendes, 2014).

A 2011 study of postpartum depression showed that low ranks of omega-3 PUFAs, especially DHA found to be related to postpartum depression. That is because DHA could be loss from the tissues and the brain during pregnancy and lactation periods especially with low intake of omega-3 PUFAs. Thus, the low intake of omega-3 PUFAs lead to decreasing DHA which causes depression and this situation is found predominantly in postpartum depression. Actually, postpartum depression symptoms might lead to severe consequences for the infant development or sometimes to maternal suicide (Levant, 2011).

In a literature paper collected many studies in PubMed from 1964 to 2010 examining the effect of pregnancy and lactation periods on the status of omega-3 (n-3) PUFAs in both humans and animals and the association between n-3 PUFAs and postpartum depression.



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The results in general found that consuming fish oil, DHA, EPA either alone or in combination improves the depression symptoms significantly. Even though some studies did not find significant results, most studies found that consuming omega-3 PUFAs have antidepressant effects (Levant, 2011). Also, a study conducted on pregnant women to assess if the low omega-3 during pregnancy could contribute to postpartum depression. The results showed that a low omega-3 level lately during pregnancy is connected to higher depression (Markhus, Skotheim, Graff, Frøyland, Braarud, Stormark, & Malde, 2013).

Folate or Folic Acid and B12

Folate (vitamin B9) and cobalamin (vitamin B12) deficiency are associated with depression, particularly in older people. In addition to the association with depression, folate found to be important in the cognitive function and low B12 is connected to dementia and cognitive weakening. Many studies indicated that folate and vitamin B12 play an significant role in the function of the CNS. The impaired intake of these vitamins found in many cases resulted in severe negative effects like mental retardation, psychiatric, seizures, and myelopathy (Bottiglieri, 2013).

Many epidemiologic, observational, and case-control studies found a relationship between functional folate deficiency and depression signs, the harshness, and the results of the treatment in the old population. It was found that in depressed people folate is lower than in people with psychiatric disorders. Also, low folate levels are connected with low response to antidepressant. Furthermore, high levels of B12 have been linked to better results in the treatment of depression. In fact, B12 is reported to have stronger effect on depression than folate even though low folate was found to delay the recovery



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from depression in comparison with normal level of folate (Roberts, Bedson, & Tranter, 2010).

With more research done on the supplementation of the B vitamins than dietary intake of this vitamin, high consumption of folate and high folate level is linked to low occurrence of depression among men but not the other B vitamins such as B12, B6, B2 (riboflavin). On the other hand, low folate and low B12 consumption are linked to depression in women. Low B12 particularly has been linked to cause severe depression in older women. However, the deficiencies in B12, B6, and folate in the older population are associated with the physiological changes with absorption in the older population. Thus, supplementation might be necessary for this population. Even though a study was conducted on older population suggests that folate is not necessarily related to depression either the dietary intake or supplementation, vitamin B12 was found to have a strong antidepressant effect either from the diet or supplementation. Additionally, just the B6 supplementation, not the diet, found to be effective against depression (Roberts, Bedson, & Tranter, 2010).

Talking about the relationship between depression and folate consumption, there was a 2012 study of Japanese workers conducted regarding the socioeconomic status (SES) and job tension. Folate consumption through diet was measured in addition to the depression symptoms in Japanese workers. The study found a significant inverse relationship between folate intake and depression in Japanese workers regarding the SES and job stress issues (Miyaki, Song, Htun, Tsutsumi, Hashimoto, Kawakami, Takahashi, Shimazu, Inoue, Kurioka, & Shimbo, 2012).



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When dihydro-folate, found in foods, is converted to 5-methyltetrahydrofolate (L-methylfolate), this L-methylfolate is used in methionine synthetase by converting homocysteine into L-methionine. Here comes the role of B12 to simplify this action. Methionine connects with ATP forming S-adenosylmethionine (S-AdoMet) which is most abundant in the CNS. S-AdoMet assists the synthesis of the neurotransmitters dopamine, norepinephrine, and serotonin which have antidepressant function (Nelson, 2012).

Unfortunately, there are many causes for folate deficiency like various drugs, malabsorption conditions, chronic illnesses, alcoholism, and nutritional deficiency. Thus, the U.S. Food and Drug Administration (FDA) in 1998 requested to fortify grain foods with folic acid which massively reduced the prevalence of deficiency in the United States. Because of that, folate is better to be consumed in its different forms to fight depression like folate supplementation rather than folate replacement (Nelson, 2012).

As there is a relationship between depression, anorexia, and weight loss, it is important to know if low folate causes depression or vice versa. Actually, depression is known to minimize the appetite and leads to dietary restraint and decreases the folate as a result and worsens depression. There is also a concern that the deficiency of B12 is always hidden with folate (Nelson, 2012). However, even though some studies did not find significant results for the good effect of B vitamins on depression, a lot of studies found that vitamin B-complex is a good treatment for depression as proved by many studies.

Vitamin D

Vitamin D is known for its association with bone health. In addition to that, low serum vitamin D became associated with many other chronic diseases. The vitamin D deficiency



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problems results are hard to determine due to the individual differences and its association with calcium intake (Thacher & Clarke, 2011). Many people in the U.S. who have depression or other mental illness are deficient in this vitamin. This deficiency is either due to low dietary consumption or the lifestyle like low exposure to the sunshine (Penckofer, Kouba, Byrn, & Ferrans, 2010). Unfortunately, it is not absolute if lacking vitamin D leads to depression or if vitamin D consumption is an operative treatment for depression (Howland, 2011). However, it was found that the treatment for mental illness and depression with vitamin D is an operative way and a worthwhile therapy which results in improving the long-term health and well-being of patients (Penckofer, Kouba, Byrn, & Ferrans, 2010).

Furthermore, the mechanism of how vitamin D relates to mood and how it affects the brain was not completely known. In other words, it was not known how vitamin D works is the response to stress in the monoamine system and on the hypothalamic-pituitary-adrenal axis. Also, it was not known if vitamin D can help people with moderate to severe depression or if enough vitamin D has an antidepressant effect (Johnson & Elizabeth, 2009). However, the influence of vitamin D on depression is really controversial. The only mechanism that was known for vitamin D was its association with calcium metabolism and bone health (Spedding, 2014).

Recently, the mechanism of action of vitamin D is found to be related to vitamin D receptors (VDR) in the endocrine, paracrine and autocrine. This mechanism affects the physiological system with the brain. In addition, enzymes those are important to convert hydroxylation of 25hydroxyvitamin D (25OHD) to 1,25dihydroxyvitamin D, which is the



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active form, are located in the hypothalamus, cerebellum, and substantia nigra. More specifically, vitamin D action is described as regulating the hypothalamic-pituitary-adrenal axis, controlling adrenaline, noradrenaline and the dopamine creation via VDR which is in the adrenal cortex. This will work against the reduction of dopamine and serotonin. Thus, this biologic character of vitamin D in depression has started (Spedding, 2014).

Recent data suggests that low vitamin D ranks are connected with 8 percent to 14 percent rise in depression and 50 percent rise in suicide (Spedding, 2014). The results of a systematic review and meta-analysis of observational studies and randomized controlled trials showed that there was a low level of vitamin D among depression people in comparison with the control group. In addition, there was a high ratio of depression in the lowermost vitamin D in comparison with the uppermost vitamin D ratio in the cross-sectional studies. Additionally, there was a significant increase ratio of severe depression in the lowermost vitamin D in comparison with the uppermost vitamin D classifications in the cohort studies. So, the results of these studies conclude that low vitamin D ranks are linked with depression (Anglin, Samaan, Walter, & McDonald, 2013).

Furthermore, a cross-sectional study was conducted; the serum 25-hydroxyvitamin D [25(OH)D] was examined and depression score was measured as a Center for Epidemiologic Studies Depression Scale (CES-D) with score of 10 or more. Participants were divided into two groups with and without depression history regarding the CES-D scores. The results showed that higher vitamin D is related to lower depression



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constructed on CES-D score. Additionally, the results were stronger in individuals with a history of depression and on the other hand not significant in individuals with no depression history. So, these results indicate propose that individuals with depression history might be a good population to measure the level of vitamin D (Hoang, DeFina, Willis, Leonard, Weiner, & Brown, 2011).

Magnesium

Magnesium is the second major intracellular cation and it is involved in the function of more than 300 enzymes (Derom, Sayón-Orea, Martínez-Ortega, & Martínez-González, 2013). In many people, magnesium dietary intake is usually not enough and this leads to health problems like hypertension, cardiovascular disease (CVD), and type 2 diabetes. Also, magnesium deficiency might be associated with depression. Magnesium also has a biological effect and is involved in some pathways in the pathophysiology of depression. Magnesium is an opponent for calcium; it impairs the incoming of the calcium into the neuron. Through this action, magnesium might gain neuro-protective assets which protect the neuron from the death of the cells. High calcium levels ions and glutamate with low magnesium might free the brain cell synaptic action and lead to depression and mood illnesses (Derom, Sayón-Orea, Martínez-Ortega, & Martínez-González, 2013).

In human studies, there are evidences showing that magnesium is a crucial treatment for depression. A systematic review of 27 studies was conducted to observe the link between magnesium and depression in human adults. Credible depression scales were used and the studies that included other elements used with magnesium were excluded from the study. The results showed a significant effect of dietary intake of magnesium to reduce depression symptoms. Even though some studies proved that magnesium was a helpful



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treatment and a protective for depression, more studies are needed to investigate to what extent magnesium is beneficial in the treatment of depression (Derom, Sayón-Orea, Martínez-Ortega, & Martínez-González, 2013).

There is a 2013 study of magnesium consumption was conducted to investigate the influence of magnesium dietary intake on depression symptoms in students since depression in students is related to endless problems. Even though some medications can be used to treat depression, it may cause some side effects. Thus, researchers aim to find natural ways to prevent depression before it happens in college students. An example of these methods is appropriate nutrients intake like magnesium, especially because it plays an important role in depression. The results showed that magnesium that was consumed from food over 12 months has an inverse association with depression symptoms regarding, age, sex, body mass index, monthly expenses, living on campus, close friends, physical activity, smoking, education, and marital status (Yary, Aazami, & Soleimannejad, 2013).

Additionally, it has been hypothesized that magnesium deficiency can lead to treatment-resistant depression (TRD). A clinical trial study showed the effective result of magnesium in treating depressed diabetics people because magnesium was used as the tricyclic anti-depressant imipramine which did not cause any adverse effects. Unfortunately, removing magnesium from processed food negatively affects the brain. On the other hand, additives like calcium, glutamate, and aspartate might develop disorders. So, taking these two together will lead to insufficient dietary magnesium intake which is the main leading cause for TRD; thus, magnesium must be prescribed to treat TRD. As it



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is known that low brain magnesium will reduce serotonin levels and on the other hand anti-depressants increase brain magnesium, so it is thought that magnesium is an actual treatment for all types of depression, not just TRD (Eby & Eby, 2009).

Zinc

A reduction in the neurogenesis and an increase in the neurodegeneration have been associated with depression which is caused by inflammatory processes. Many scientific evidences suggested that changes associated with aging like decreases in brain function, cognitive efficacy, and neurodegeneration might be associated with the zinc ion convenience. In fact, many studies revealed that depression is affected by the serum level of hypozincemia and using antidepressant can regulate this situation. It was found that depressed people have a low zinc serum level and this is linked with activating immune system markers which may be caused by changes in the immune-inflammatory system associated with depression. In addition, some studies revealed the efficiency of zinc supplementation as an antidepressant in treating resistant and non-resistant patients. In addition to that, zinc was found to have antidepressant efficacy on many depression models and the zinc deficiency was associated with developing depression symptoms. This process involves a decrease in the neurogenesis and the neuronal existence or affects learning and memory efficacy (Szewczyk, Kubera, & Nowak, 2011).

Actually, as zinc has the effect of an antidepressant, there is a study conducted to assess the effect of antidepressant zinc on chronic to mild stress (CMS), models of depression, and zinc treatment on brain-derived neurotrophic factor (BDNF) protein and on the level of messenger RNA. The results demonstrated that there was a quick effect of zinc antidepressant-like on CMS action. Also, there was an increase in the BDNF mRNA and



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the level of protein in the hippocampus after the zinc enduring treatment (Sowa-Kućma, Legutko, Szewczyk, Novak, Znojek, Poleszak, Papp, Pilc, & Nowak, 2008). This hippocampal zinc availability helps the synaptic flexibility like the long-term effect and the cognitive function (Takeda, 2011).

Another study was conducted to observe the association between zinc consumption and depression signs in postgraduate students. That is because postgraduate students are prone to depression because of the heavy stress they face. The study included 402 participants, and out of them 173 were women and 229 were men. The results showed an inverse relationship between zinc consumption and depression. Even after considering other factors like age, sex, education, smoking, and activity level, the results were consistent showing that long-term zinc consumption regulates depression symptoms (Yary & Aazami, 2012).

Furthermore, regarding the gender-specific pathophysiological mechanisms difference in a population-based epidemiological survey, another study was conducted to investigate the link between low zinc consumption and depression symptoms in women. The results showed that zinc was related to depression in women, but not men. In addition, low dietary zinc consumption was linked with higher probability of having depression (Maserejian, Hall, & McKinlay, 2012). Therefore, as was shown in all this scientific evidence, zinc intake is an effective treatment for depression symptoms and it improves the memory and cognitive functions.

Discussion

According to WHO, in 2014, depression affected 400 million people around the world.



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Also, depression is considered as a disease of disability because it could happen again and it takes years while having it. Depression also could affect a person's quality of life, impair the normal daily activities, and it could lead to suicide. Moreover, depression prevalence is huge around the world with about 16.9 percent of the population in the United States, for example, suffering from it. Some groups are more prone to depression, like women and those who live in poverty, have a low level of education, divorce, violence, or suffer from chronic illnesses all are factors increase the prevalence of depression. By 2020, depression is expected to be the second leading disease of disability and by 2030; it is expected to be the first cause of illnesses.

Depression is a mental disorder with symptoms such as sadness, loss of pleasure, low energy, guilty feeling, low self-worth, reduced quality of sleep, appetite problems, and low concentration. However, depression is different from the normal sadness feelings. Untreated depression can lead to serious problems for a person. Symptoms of depression are divided into mild, moderate, or severe symptoms, which is common with the untreated situations. Depression can be subdivided into bipolar mood disorder and unipolar depression, which is the major depression. In addition, other types of depression include psychotic depression, postpartum depression, seasonal depression, dementia, and autism. Depression can be caused by social, psychological, and biological aspects. Even though depression can be treated by many ways, people often do not seek treatments. A depressed person must take care of him/herself and a balanced diet plays an important role in hormonal regulation, which affects mood and depression.

Carbohydrates were found to have an effective role for a quick fix for mood disorder by



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increasing serotonin levels in the brain. To have this effect, consuming complex carbohydrates is the best choice to make insulin levels sustainable in the blood and brain. In addition, PUFAs have been found to reduce the neuro inflammation, the oxidative stress, and inhibit the pro-inflammatories, which are associated with depression. Also, omega-3 PUFAs have been effective in the treatment of postpartum depression. Moreover, deficiencies in B-complex vitamins B6, B12, and folate have been linked to depression, especially in older adults. B12 and folate were found to be effective in improving cognitive function and the treatment of such conditions as dementia, CNS, mental retardation, psychiatric, seizures, and myelopathy. In addition, vitamin D was found to be associated with depression, not just bone health. Vitamin D has been found to play an imperative role in the physiological system in the brain and enhancing dopamine and serotonin activation.

Furthermore, magnesium deficiency found to be associated with depression, especially in college students. Magnesium found to prevent the brain cell death which if happens will lead to depression and mood illnesses. In addition, it has an anti-depressant effect and can increase serotonin level. Additionally, zinc deficiency found to be associated with depression by having an antidepressant effect. That is because low zinc serum levels are related to changes in immune-inflammatory system. Ultimately, eating a healthy balanced diet is strongly recommended because nutrient consumption from food not just will improve a person's overall health, but also will improve mental health.

Conclusion

Depression is a disease and affects a person's quality of life, impairing daily normal activities, and might lead to suicide. Female gender, poverty, low educational level,



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genetics, violence, divorce, and severe illnesses are all factors which contribute to depression. Depression symptoms include loss of pleasure, reduced energy, low self-worth, reduced quality of sleep, appetite problems, loss of concentrations, and feelings of sadness and guilt; however, sadness feeling is different from real depression. When symptoms are not treated, they can become even worse. It is necessary to seek treatment for all types of depression.

One important area of depression treatment is the nutritional approach. This is by eating a healthy well-balanced diet that includes different nutrients which play an important role in hormonal regulation and improving mood and depression. Nutrients consumed through food that were proven by scientific evidence to have a positive effect on depression are carbohydrates, proteins, essential fatty acids that including omega-3 and omega-6 fatty acids, vitamins like B-complex (B12, folate, B6), vitamin C, and minerals like calcium, magnesium, iodine, iron, lithium, selenium, and zinc. However, this paper discusses just six nutrients that were found in the top popular nutrients to have a strong effect on depression like carbohydrates, polyunsaturated fatty acids, B-complex vitamins (B6, B12, folate, & folic acid), Vitamin D, magnesium, and zinc. Obviously, more research is needed on other nutrients that were found to be effective on mental health to confirm their effects through consumption from food not from nutritional supplementations. These nutrients include minerals like calcium, chromium, iodine, iron, lithium, and selenium.



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