Effect of vitamin d on mental health

Vitamin D and mental health

Fat-soluble Vitamin D is produced when exposed to sunshine or from diet and pregnant women with darker skins have lower plasma vitamin D level when compared with lighter skins [1] .

Vitamin D might play a role in genetic transcription, and inflammatory system in the brain. Recently the association of vitamin D intake and mental health has been focused. It is associated with numerous psychiatric disorders, such as schizophrenia, depression and etc. The reason might be that vitamin D could stimulate genes that produce neurotransmitters such as dopamine and serotonin, affecting brain function. 1, 25-dihydroxyvitamin D (1, 25(OH) $_2$ D) might have an impact on brain serotonin by regulating the expression of tryptophan hydroxylase 2 [2] and on plasma calcium level [3] . High level of calcium level in the brain is actually regulated indirectly by low serum 25-Hydroxyvitamin D (25(OH)D) level. Furthermore, 1 alpha-hydroxylase and vitamin D receptors (VDR), involved with the production of 1, 25(OH) $_2$ D, could be generated in neurons of the brain. Besides, the regions of the brain, such as dopaminergic–rich regions, governing depression have their own VDR [4, 5] .

Besides, Vitamin D deficiency has been defined as serum 25(OH)D level lower than 12 ng/mL or 30nmol/L [6] , measured by the Institute of Medicine, while vitamin D insufficiency is defined as 12-20 ng/mL or 30-50 nmol/L. It still remains discrepancy of various subjects as for Recommended Dietary Allowance (RDA) on their vitamin D intake, including infants (400 international units (IU) /d), pregnant women (600 IU/d) and elderly (> 50

years, 600-800IU/d) [6, 7] . This paper will mainly focus on the relationship between vitamin D level and three main mental disorders, autism, schizophrenia and depression. The author will reveal the association between low vitamin D intake and the risk of these diseases, then discuss if vitamin D supplementation will be efficient in the treatment of these three diseases, and further provide implications of the importance of maintaining adequate vitamin D level among pregnant women.

Autism Spectrum Disorder (ASD)

Adequate Vitamin D could be beneficial to bone mineral density and neuronal differentiation, or it will cause an increased risk of autism behavior. ASD is a common mental disorder, manifested in impaired communication abilities and social behaviors and specific behaviors. A cross-sectional study has revealed a high affinity of low vitamin D with a high prevalence of ASD among children (n= 122) [8] . It has also been proved in a recent cohort study [9] among large population-4229 mothers and their children with the symptoms of autism-related traits at 6 years old. The level of 25(OH)D was assessed both in maternal mid-gestation serum and infant sera (core blood at birth) first. Samples who have vitamin D insufficiency take (serum level of 25(OH)D < 25 nmol/L) hold a higher social responsiveness scale(SRS)-scored in children at 6 years old, suggesting that vitamin D deficiency might be related to high risk of autism-related traits. However, poor communications might also be associated with ASD.

For the rescue therapy, it might be improved under high doses of vitamin D intake among children, which has been reported in a cross-sectional study [8] .

A Randomized Controlled Trial (RCT) study [10] also revealed that supplemented with vitamin D3 300 IU/kg/d for four months in children (3-10 years old, n= 120) might improve their ASD symptoms, measured by CARS and Aberrant Behavior Checklist (ABC), SRS. In the future, a larger scale study should be conducted to prove the efficacy of vitamin D supplementation among Children with ASD. Another study further strengthened the importance of taking vitamin D3 supplementation in the treatment of ASD among 500 children (215- ASD). Results have shown a decrease in scores of the autism behavior checklist(ABC) and the Childhood Autism Rating Scale (CARS) after receiving VD3 supplementation for 3 months, indicating the improved symptoms of ASD [11] .

Besides, pregnant women might also have a large effect on the risk of ASD. Lower risk of ASD or autism-related traits might occur when intake adequate vitamin D during the midterm gestation [9, 12] . Topics like the early stage or the full term of vitamin D deficiency and brain development could be focused on in the future.

Therefore, it might be an effective therapy for children to improve the symptoms of ASD by receiving vitamin D supplementation for at most three months (< 30IU/kg/d), or an optimal preventing the high risk of ASD by maintaining adequate vitamin D level among pregnant moms.

Vitamin D and schizophrenia or schizoaffective disorder

Schizophrenia is a chronic but severe mental disorder manifested in impaired cognition ability, social behaviors and loss of interaction with reality. schizoaffective disorder, a similar mental problem as schizophrenia, is

characterized by psychotic symptoms such as delusions and mood disorders. The incidence of schizophrenia might be affected by a low level of vitamin D interacted with genetic factor and other environmental factors, such as areas of higher latitude with limited sun exposure.

Neonatal vitamin D deficiency (serum 25(OH)D level < 20. 4 nmol/L), especially born in winter and spring has been associated with increased risk of schizophrenia [13] . This case-control study has strengthened the significance for pregnant women to maintain an adequate level of vitamin D level in decreasing the risk of schizophrenia. Nevertheless, it is still highly needed to illuminate the relationship between low level of vitamin D intake and the risk of schizophrenia from four aspects, a larger sample scale of research or RCTs, 25OHD level form different pregnancy stage, unmeasured vulnerable factors to the risk of schizophrenia.

Similar results have been also found in elderly that, low plasma level of vitamin D might be highly related to patients with schizophrenia or schizoaffective disorder, which has been proved in a cross-sectional study ($25(OH)D_3 + 25(OH)D_2$ <19. 9 ng/mL) [14] and an RCT (< 75 nmol/L) [15] . In the former cross-sectional study, 149 Patients (around 47 years old) with schizophrenia or schizoaffective disorder, receiving flexible assertive community treatment (FACT), were tested by Diagnostic and Statistical Manual of Mental Disorder (DSM-IV). Results might indicate that vitamin D could possibly act as a cause of schizophrenia or schizoaffective disorder. However, some bias has not been eliminated to obtain the accurate association between vitamin D level and schizophrenia such as daily sun

exposure and BMI, therefore, a strict assessment system is suggested to be applied in a larger scale of research in future.

As for the efficacy of vitamin D supplementation used for the treatment of schizophrenia, none improvement of schizophrenia has been found in two recent RCTs. A recent RCT has shown that vitamin D supplementation (14, 000 IU/week) might not improve schizophrenia symptoms of patients (39-49 years old) treated with Clozapine, however, with a mild improved cognitive function among a small portion of samples (n= 17). Here, eight weeks intervention among 23 patients [15,] have beenmeasured by Montreal Cognitive Assessment (MoCA). Another RCT [16] has also proved it amongpatients with vitamin D deficiency (< 30 ng/mL) injected with 2 x 300, 000IU/mL (n= 120) within a four-month intervention. It might be hard to rescue schizophrenia of a later stage-among elderly, instead, one of the hypothesis might be that vitamin D supplementation might be efficient in infants or pregnant moms, an early stage of this type of disease. Furthermore, it still remains unknown about the efficacy of vitamin D supplementation for schizophrenia, including its optimal doses, vitamin D supplementation time for this disease and if it would be more efficient when combined with other therapy.

Vitamin D and depression

Depression, a common but serious mood disorder and has an impact on your thinking

and perception and reality. A cross-sectional study among 770 Malay and Indian female teachers (41 years old) has shown that, lower vitamin D intake (25(OH)D serum level <20 ng/ml or <50 nmol/l) might have high affinity to the incidence of depression [17] . They used the Anxiety and Stress Scale (DASS-21) to measure the level of depression.

A random controlled trial (RCT) among 230 participants (30-75 years old) and a large cohort study among 902 participants (18-65 years old) has proved that low level of 25(OH)D could be used as a biomarker of the presence and severity of depression [18, 19] .

Different types of depressions (postpartum depression, common depression and etc.) might have varied susceptible to vitamin D supplementation. As for the treatment of depression by vitamin D supplementation, it still remains controversial about the effect of vitamin D supplementation on depression from the perspective of short-term and long-term or intervention with other anti-drugs. It might be beneficial to take vitamin D (1500 IU/d) and fluoxetine when compared with fluoxetine for 2 months in the treatment of depression. In this study, 40 patients (18-65 years old) were found to have a significant decrease in their depression symptoms at their second week of intervention, which was tested with Hamilton Depression Rating Scale and Beck Depression Inventory [20] .

It seems like vitamin D supplementation could be effective in the treatment of ASD only combined with other therapy or within a short-term intervention. Some other researches have proved this theory in their studies that, it is hard to get improvement in ASD within a long period interval or vitamin D

supplementation. An RCT has proved it among 230 participants with low 25(OH)D serum level (<55 nmol/L) who were treated with six months intervention of 40, 000 IU vitamin D3/ week [19] . It also suggested that a low serum level of 25(OH)D might be a result or co-factor rather than a cause of the incidence of depression. Another recent randomized double-blind study [21] also proved it among a small portion of patients with depression. Here, 23 patients (18-65 years old) with depression and low plasma 25(OH)D level (< 50 nmol/L) were assigned to take D supplementation 7 mg/d for three months, meanwhile, they were tested by the Hamilton Rating Scale for Depression (HAM-D17) and Major Depression Inventory (MDI) at their 3 and 6 months. As a result, none reduction in Depression scores have been assessed. For this study, a larger scale of the sample in the future is still highly suggested for a supportive conclusion.

However, this theory cannot be applied among pregnant women because vitamin D supplementation might ameliorate the severity of their depression, which has been reported in a recent single-blind RCT [22] . Here, pregnant women with low plasma 25(OH)D level (< 30nmol/L), receiving vitamin D supplementation of 2000 IU/d during their third trimester of pregnancy, might decrease the level of maternal depression, including their pregnant late stage and postpartum stage. Since exclusion standard of depression level > 13 has been applied in this study, so it could only show a mild depression score of parental depression. In order to obtain an optimal therapy of vitamin D (doses, duration) on varied levels of depression among pregnant women, a larger scale with an accurate depression measurement tools should be used in a further study. Overall, vitamin D supplementation

might improve depression symptoms, especially among pregnant moms (eg. postpartum depression) or a short-term interval combined with other therapy.

Conclusion

This paper mainly focuses on the relationship between vitamin D level and three main mental disorders, autism, schizophrenia and depression. The author has clarified the association between low vitamin D intake and the risk of these diseases, then discuss the efficacy of vitamin D supplementation in the treatment of these three diseases, and further provide suggestions of maintaining adequate vitamin D level among the specific population, especially among pregnant women.

For ASD, gestational or children vitamin D deficiency has high affinity with a high incidence of autism-related traits or ASD [8, 9] . ASD might be prevented from pregnant women by taking adequate vitamin D3 and might be rescued among children by receiving at most three months for less than 30 IU/kg/d, however, none studies have shown the preventing therapy of vitamin D in a later stage- children. Besides, the threshold of vitamin D deficiency remains to be established in children and varied efficient vitamin D supplementation doses and duration of intervention need to be further studied.

As for schizophrenia, neonatal vitamin D deficiency seems to be highly related to a high risk of schizophrenia, meanwhile, elderly vitamin D deficiency might act as a cause of schizophrenia among patients with schizophrenia. It might be hard to rescue schizophrenia of a later stage- among elderly. However, it is possible for pregnant women to maintain an

adequate level of vitamin D level in decreasing the risk of schizophrenia [13] . In all, it still remains unclear about the efficacy of vitamin D supplementation for schizophrenia, including its optimal doses and duration time for this disease among pregnant women and if it would be more efficient when combined with other therapy in elderly.

Lastly for depression, lower 25(OH)D serum level (<20 ng/ml or <50 nmol/l) might have a high affinity to the incidence of depression. Although it might not be a consensus on the efficacy of vitamin D supplementation applied in preventing depression, vitamin D supplementation could be effective in a certain population such as pregnant moms (eg. postpartum depression) or a certain situation, a short-term interval combined with other therapy.

Overall, Low vitamin D level has been associated with high risk or incidence of ASD, schizophrenia, and depression. In order to lower the risk of these diseases, it’s better to maintain adequate serum 25(OH)D level (> 20 ng/mL) from pregnancy by taking vitamin D rich-food, such as olive oil, almond and etc., or increased sun exposure. As for the treatment of these diseases, ASD symptoms might be improved among children, while schizophrenia and depression not. Therefore, more RCTs are suggested to be performed for obtaining strong conclusions.

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