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[Lau, Esther & Nissen, Lisa](#)
(2019)
Prenatal vitamin D for schizophrenia.
Australian Pharmacist, 38(8), pp. 82-83.

This file was downloaded from: <https://eprints.qut.edu.au/133146/>

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<https://www.australianpharmacist.com.au/prenatal-vitamin-d-for-schizophrenia/>

Prenatal vitamin D for schizophrenia

By Dr Esther Lau and Prof Lisa Nissen - September 17, 2019

The genetic and environmental factors behind schizophrenia are poorly understood, but research is increasingly finding links between maternal vitamin D status and the risk of schizophrenia.

An estimated one in 100 Australians live with schizophrenia, which is characterized by distortions in thinking, perception, emotions, language, sense of self and behaviour. The course of schizophrenia can vary, with 20-30% of people experiencing brief episodes (with complete or incomplete remission; or with progressive or stable deficits), while for others it is a chronic condition without temporary improvement.

Abnormalities in brain structure and function have been noted in people living with schizophrenia. In terms of function, dopamine imbalances in various parts of the brain are thought to be responsible for many symptoms of schizophrenia. For instance, increased dopamine in the mesolimbic pathway caused positive symptoms while a deficit in the mesocortical pathways were responsible for causing negative, and cognitive symptoms.

The updated theory now also considers changes and dysregulation to a range of neurotransmitter systems e.g. glutamate, serotonin, noradrenaline and other peptide neurotransmitters.

Antipsychotics, used to manage the symptoms are thought to be mediated (in part) by blockade of dopaminergic transmission (D2 receptors) in the brain, particularly the limbic system, making them effective for positive symptoms.

The differential blockade of D1 receptors, and antagonist activity at other receptors e.g. 5HT2 are thought to influence the effectiveness and adverse effects of the different antipsychotics. However, both the conventional and atypical antipsychotics are associated with significant side effects, and are ineffective/ limited in effectiveness for negative, cognitive, and mood symptoms.

Risk factors

Schizophrenia is a poorly understood heterogenous disorder with genetics and environmental exposures identified as causal factors. There has been interest in modifiable risk factors during prenatal periods and early life. Increased risk of schizophrenia has been noted to be associated with factors related to vitamin D deficiency e.g. winter/spring (as season of birth for schizophrenia), living in high latitude settings, urban residence in early life and migrant status – especially dark-skinned migrants to high latitude countries.

This led to the hypothesis of developmental vitamin D deficiency affecting areas of brain development since the vitamin D receptor is expressed in areas of the brain of interest to schizophrenia e.g. dopaminergic-rich regions. Animal studies have found transient prenatal vitamin D deficiency to be associated with neurochemical and behavioural changes.

A schizophrenia case-controlled study (n = 848) reported a relationship between neonatal vitamin D levels which is related maternal vitamin D status, and risk of schizophrenia. Subsequently, a larger scale Danish case-controlled study (n = 2602) investigated the association between neonatal vitamin D levels, and a diagnosis of schizophrenia in later life (identified from Danish psychiatric registers). The neonatal vitamin D levels were measured as the concentration of 25 hydroxyvitamin D [25(OH)D]

from neonatal dried blood samples, and reported in quintiles. Those in the lowest quintile (<20.4 nmol/L) had a significantly increased risk of schizophrenia compared to the reference fourth quintile i.e. 41-53.5 nmol/L (incidence rate ratio = 1.44, 95%CI: 1.12-1.85).

In Australia, neonatal vitamin D levels of <20.4 nmol/L is categorised as moderate deficiency, 30-49 nmol/L as mild deficiency, while >50 nmol/L is considered sufficient. Comparisons with the other quintiles were significantly different, and no significant interaction was noted between 25(OH)D and the schizophrenia polygenic risk score.

Next steps

Much more ongoing research with larger numbers is required to better understand the impact and interactions of genes vs the environment on the development of schizophrenia, particularly since collecting empirical evidence and accounting for confounders is difficult. The authors of the study point to future research to include e.g. investigating vitamin D levels at different time points from gestation through to early life when vitamin D deficiency may influence the risk of schizophrenia.

While vitamin D is the putative causal risk factor, it is important to investigate other confounding factors e.g. maternal risk factors that lead to vitamin D deficiency; and also the role of vitamin D supplementation in pregnant women.

As the authors also point out that it may be that correcting vitamin D deficiencies in pregnant women is effective as primary prevention of schizophrenia, akin to folate supplements for preventing spina bifida.

Useful references

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