ASIA PACIFIC CENTER FOR EVIDENCE BASED HEALTHCARE

Should B Vitamins be used in the treatment of COVID-19?

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This rapid review summarizes the available evidence on the efficacy and safety of B vitamins in treating patients with COVID-19. This may change as new evidence emerges.

KEY FINDINGS

There is currently insufficient evidence regarding the effectiveness of B Vitamins in the treatment of COVID-19.

- **B vitamins are water-soluble vitamins that seems to play a major role in the body's immune system.**
- **There are currently no evidence for its use on COVID-19 patients, and no trials are ongoing to test its effects.**
- **B vitamins are generally considered safe as any excess is excreted in the urine, but still large doses should not be taken.**
- **There is no mention of B vitamins in the WHO Interim Guidance, US CDC Clinical Interim Guidelines and Chinese Clinical Guidance for COVID-19 management.**

BACKGROUND

B vitamins are as follows - B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), B7 (biotin), B9 (folic acid) and B12 (cobalamin). When all these are combined they are referred to as Vitamin B complex.

These water-soluble vitamins also contribute to cell functioning and plays a role in the energy metabolism to create and maintain healthy cells. It also seems to play a major role in the body's immune system.[1] Perhaps boosting of the immune system through B vitamin intake may translate into beneficial effects in the prevention and treatment of patients with COVID-19 infection.

Folic acid supplementation and multiple micro-nutrient supplementation have been studied well in maternal health and has been consistent in its benefits for pregnant women.[2] Vitamin B complexes have also been studied as part of food fortification to reduce anemia, showing that it may benefit the general population, but studies were of low quality and a high risk of bias cannot be discounted.[3] Supplementation with B vitamins were explored in terms of its effect on stress and anxiety for healthy and at-risk populations but benefit was only seen on stress, although quality assessment of the primary studies was not explicitly stated.[4] Niacin specifically, and B vitamins as well, have also been considered for the primary and secondary prevention of cardiovascular events, transient ischemic attacks or stroke. However in all of these studies, B vitamins did not show any benefit for patients whether low or high-risk for cardiovascular disease.[5,6,7,8]

Side effects can vary depending on what particular B vitamin is taken, but it is generally thought to be safe as the excess is excreted in the urine.[9] Niacin though has been associated with flushing, pruritus, rash, headache, gastrointestinal symptoms, and discontinuation of treatment due to those side effects.[5] In another study, the side effects observed were chiefly gastrointestinal disturbances, nausea and cutaneuos reactions in a few patients.[6]

METHODS

See General Methods Section.

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Articles were selected based on the following inclusion criteria:

- **Population:** COVID-19 patients of any age, with any co-morbidities, any severity
- **Intervention:** B vitamins, B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), B7 (biotin), B9 (folic acid) and B12 (cobalamin), Vitamin B complex, any dose, any duration, any type
- **Comparator:** placebo, any active control, no intervention
- **Outcomes:** mortality, clinical improvement, complications, respiratory distress, adverse events, length of hospitalization
- **Study designs:** randomized controlled trials (RCTs), non-randomized studies, observational studies

RESULTS

As of this date, there are no clinical trials specifically exploring the effect of B vitamins on patients infected with COVID-19. In 2016 there was a study by Kiel that showed that riboflavin and UV light effectively

reduced the titer of MERS-CoV in human plasma suggesting that this treatment may reduce the risk of transfusion transmission in both platelet and plasma products.[10] However, this was not a clinical trial.

There was a recently published systematic review on potential interventions for COVID-19 done in China, but upon assessment, the systematic review was not able to show how it conducted the search and if an appraisal method was done on the primary studies. In the review it was mentioned that a shortage of B vitamins may weaken host response and thus vitamin B supplementation may play a role in terms of enhancing a patients immune system.[1] The primary studies however were not clinical trials as it included Kiel's 2016 study as well as two animal studies on nicotinamide.

There are also no ongoing clinical trials on B vitamins use in COVID-19.

Recommendations from Other Guidelines

WHO interim guidance, US CDC interim clinical guidance, and Chinese clinical guidance does not mention vitamin B supplementaton for patients infected with COVID-19.

CONCLUSION

It has been said that a strong immune system can help prevent or treat COVID-19 infection, and the use of vitamins in general and B vitamins in particular might have an effect. However, there is currently insufficient evidence regarding the effectiveness of B vitamins in the prevention and treatment of patients with COVID-19.

Declaration of Conflict of Interest

No conflict of interest.

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Appendix 1. Literature search

DATABASE	SEARCH STRATEGY / SEARCH TERMS	DATE AND TIME OF SEARCH	RESULTS	
			Yield	Eligible
Medline	((((("severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) OR "Coronavirus"[Mesh]) OR (((((((covid-19) OR covid-19) OR covid19) OR SARS-COV-2) OR SARS COV 2) OR novel coronavirus) OR NCOV))) AND ((((((((((((((vitamin B1) OR vitamin B2) OR vitamin B3) OR vitamin B5) OR vitamin B6) OR vitamin B7) OR vitamin B9) OR vitamin B12)) OR ((((((((((("Thiamine"[Mesh]) OR "Riboflavin"[Mesh]) OR "Niacin"[Mesh]) OR "Niacinamide"[Mesh]) OR "Pantothenic Acid"[Mesh]) OR "Pyridoxine"[Mesh]) OR "Pyridoxal"[Mesh]) OR "Pyridoxamine"[Mesh]) OR "Biotin"[Mesh]) OR "Folic Acid"[Mesh]) OR "Hydroxocobalamin"[Mesh]) OR "mecobalamin" [Supplementary Concept])) OR ("Vitamin B 6"[Mesh] OR "Vitamin B 12"[Mesh] OR "Transcobalamins"[Mesh] OR "cyanocobalamin, pyridoxine, thiamine drug combination" [Supplementary Concept] OR "Thiamine"[Mesh] OR "Riboflavin"[Mesh] OR "Pantothenic Acid"[Mesh] OR "Niacinamide"[Mesh] OR "Cobamides"[Mesh] OR "Vitamin B Complex"[Mesh]))) OR ((B vitamin) OR B vitamins))) OR nicotinamide)	29 March 2020	34	0
CENTRAL	B vitamins [Mesh] AND coronavirus [Mesh]	29 March 2020	0	0
Trial Registries				
ClinicalTrials.gov	COVID-19 AND B vitamins	29 March 2020	0	0
Chinese Clinical Trial Registry	Vitamin B or B vitamins	29 March 2020	0	0