維生素 D 在降低 COVID-19 風險中的作用: 文獻綜述

威廉格蘭特博士;翻譯:田淑惠;審閱:成長

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The Role of Vitamin D in Reducing Risk of COVID-19: A Brief Survey of the Literature

by William B. Grant, PhD

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(2020年6月9號)維生素 D 水準升高與 Covid-19 發病率、嚴重程度和死亡風險降 低有因果關係的證據繼續增加,這份簡短的報告概述了到 2020 年六月初所瞭解到的情況, 並提供了一些關鍵參考資料的鏈接。

應該注意的是在發表證明維生素 D 補充的隨機對照實驗顯著降低 COVID-19 發病率或 死亡率的報導發表之前,可能無法接受維生素 D 補充的作用,一些關於維生素 D 補充和 COVID-19 發病率和結果的隨機對照試驗和觀察性研究正在規劃階段或進行中,需要研究 的明顯群體是那些風險最高的人群:生活在高海拔地區的深色皮膚的人,住在養老院或醫 療機構的人、囚犯、工廠工人,如美國肉類加工廠的工人,醫療保健工作者。一個主要的 問題是當權者認為維生素 D 對收入和利潤是一種威脅,因此他們使用"虛假資訊劇本" 來壓制維生素 D 的正面資訊。【1】

在四月初發表的一份綜述中,有人評論補充維生素 D 可以降低 Co ID-19 的風險,發現了兩種機制,1、通過維生素 D 刺激釋放的應激誘導的和防禦素,減少病毒存活和複製; 2、通過減少促炎細胞因數的產生,降低細胞因數風暴的風險。【2】

還提到了隨機對照實驗證明的補充維生素 D 可降低急性呼吸道感染的風險。【3】建 議補充維生素 D 的目的是增加血清 25 經維生素 D 水準至 40-60ng/毫升 (100-150 毫摩爾/ 升)納克,每天需要 4000-5000 國際單位/天維生素 D3 的劑量,由於維生素 D 轉化為不同 的代謝物需要鎂的存在,因此也應該補充鎂,也許是 400 毫克/天,這一建議是基於觀察 性研究的結果,如 Grassrootshealth.net 進行的一項關於流感樣病例的研究。【4】

最近有人建議,對於那些沒有補充維生素 D 的人,他們在一到兩周內開始補充大劑 量的維生素 D 幾十萬單位,基本原理是,如果沒有推注,身體將需要幾個月來達到最佳 水準。【5】也有人認為,雖然補充維生素 D 可以阻止 COVID-19 從症狀開始發展,它可 能在肺和器官發生急性損傷期後,不會有很大作用。最近的概述證據表明,在英格蘭的黑 人,亞洲和少數民族居民維生素 D 缺乏可以解釋更高的事件和死亡率的原因。【6】

References

 Grant WB. (2018) Vitamin D acceptance delayed by Big Pharma following the Disinformation Playbook. Orthomolecular Medicine News Service, Oct. 1, 2018. <u>http://orthomolecular.org/resources/omns/v14n22.shtml</u>

 Grant WB, Lahore H, McDonnell SL, et al. (2020) Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients April 2, 2020, 12, 988. <u>https://www.mdpi.com/2072-6643/12/4/988</u>

 Martineau AR, Jolliffe DA, Greenberg L, et al. (2017) Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ.
 356:i6583. https://www.bmj.com/content/356/bmj.i6583

4. Grant WB, Lahore H, McDonnell SL, et al., (2020) Vitamin D Supplementation Could Prevent

and Treat Influenza, Coronavirus, and Pneumonia Infections" Nutrients preprint, March 14,

2020 https://www.preprints.org/manuscript/202003.0235/v1

5. Grant WB, Baggerly CA, Lahore H. (2020) Response to Comments Regarding "Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths". Nutrients June 1, 2020, 12(6), 1620. <u>https://www.mdpi.com/2072-6643/12/6/1620</u>
6. Grant WB, Boucher BJ. (2020) Vitamin D deficiency due to skin pigmentation and diet may explain much of the higher rates of COVID-19 among BAME in England. BMJ comments, June 6, 2020. <u>https://www.bmj.com/content/369/bmj.m1548/rr-22</u>

Here are annotated links to related publications and preprints

"Of the 212 cases of COVID-19, majority had ordinary clinical outcome. Mean serum 25(OH)D level was 23.8 ng/ml. Serum 25(OH)D level was lowest in critical cases, but highest in mild cases. Serum 25(OH)D levels were statistically significant among clinical outcomes."

Alipio, MM. (2020) Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019 (COVID-2019); April 9,

2020. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3571484

"A lot of COVID-19 infected patients develop acute respiratory distress syndrome (ARDS), which may lead to multiple organ damage. These symptoms are associated with a cytokine storm syndrome. The aim of this letter is to note the 5 crucial points that vitamin D could have protective and therapeutic effects against COVID-19. For that reason, COVID-19 infection-induced multiple organ D." might be vitamin damage prevented by Aygun H. (2020) Vitamin D can prevent COVID-19 infection-induced multiple organ damage. Naunyn Schmiedebergs Arch Pharmacol. 2020 May 25:1-4. https://pubmed.ncbi.nlm.nih.gov/32451597

"Timely implementation of vitamin D supplementation programmes worldwide is critical; initial priority should be given to those who are at the highest risk, including the elderly, immobile, homebound, BAME and healthcare professionals. Population-wide vitamin D sufficiency could prevent seasonal respiratory epidemics, decrease our dependence on pharmaceutical solutions, reduce hospitalisations, and thus greatly lower healthcare costs while significantly increasing quality of life."

Davies G, Garami AR, Byers J. (2020) Evidence Supports a Causal Model for Vitamin D in COVID-19 Outcomes. 1 May, updated 3 June,

2020. https://www.medrxiv.org/content/10.1101/2020.05.01.20087965v2.full.pdf

"We retrospectively investigated the 25-hydroxyvitamin D (25(OH)D) concentrations in plasma obtained from a cohort of patients from Switzerland. In this cohort, significantly lower 25(OH)D levels (p = 0.004) were found in PCR-positive for SARS-CoV-2 (median value 11.1 ng/mL) patients compared with negative patients (24.6 ng/mL)."

D'Avolio A, Avataneo V, Manca A, et al. (2020) 25-Hydroxyvitamin D Concentrations Are Lower in Patients with Positive PCR for SARS-CoV-2. Nutrients. 2020 May

9;12(5):E1359. https://pubmed.ncbi.nlm.nih.gov/32397511

"COVID-19 patients showed lower median 25(OH)D (18.6 ng/mL, IQR 12.6-25.3, versus 21.5 ng/mL, IQR 13.9-30.8; P=0.0016) and higher vitamin D deficiency rates (58.6% versus 45.2%, P=0.0005). Surprisingly, this difference was restricted to male COVID-19 patients who had markedly higher deficiency rates than male controls (67.0% versus 49.2%, P=0.0006) that increased with advancing radiological stage and were not confounded vitamin D-impacted comorbidities." De Smet D, De Smet K, Herroelen P, et al. (2020) (2020) Vitamin D deficiency as risk factor for COVID-19: convergence of pandemics, May 5, severe а two 2020. https://www.medrxiv.org/content/10.1101/2020.05.01.20079376v2

"The RAS, which includes ACE and ACE2, is a complex network that has a major role in various biological functions 31. Chronic vitamin D deficiency may induce RAS activation lung fibrosis through activation of the RAS 35; therefore, increasing evidence indicates that 1,25(OH)2D3 may also be a negative endocrine regulator of the RAS. Inducing the expression of renin, ACE, Ang II and AT1R, and inhibiting ACE2 expression could result in acute lung injury. Vitamin D inhibits renin, ACE and Ang II expression, and induces ACE2 levels in ALI."

Ghavideldarestani M, Honardoost M, Khamseh ME. (2020) Role of Vitamin D in Pathogenesis and Severity of COVID-19 Infection https://www.preprints.org/manuscript/202004.0355/v1 "We performed a retrospective study in two tertiary medical centers in South Asia. The medical records of COVID19 patients were reviewed and a total of 176 subjects included were the elderly whose age is at least 60 years, We reported that majority of the subjects had 25(OH)D level below 30 ng/ml, most of them were male, had diabetes, and were classified as severe. Most of the male and female subjects had 25(OH)D level below 30 ng/ml."

Glicio, EJ.(2020) Vitamin D Level of Mild and Severe Elderly Cases of COVID-19: A Preliminary Report (May 5, 2020). SSRN: https://ssrn.com/abstract=3593258

Several recent publications and preprints report multi-country studies based of COVID-19 case or death rates with respect to country mean 25(OH)D concentration. One concern regarding such studies is that the 25(OH)D concentrations used are probably not related to those most likely to develop COVID-19 at the time of incidence. However, a more serious problem is that life

expectancy has a much stronger correlation (direct) than does 25(OH)D as discussed in this preprint. I have confirmed their findings using more recent COVID-19 case and death rate data. Kumar V, Srivastaa A. (2020) Spurious Correlation? A review of the relationship between Vitamin D and Covid-19 infection and

mortality. https://www.medrxiv.org/content/10.1101/2020.05.25.20110338v1.full.pdf

This article presents retrospective results for 780 patients in Indonesia. Compared to 25(OH)D >30 ng/ml, 25(OH)D between 20 and 30 ng/ml had an odds ratio for death of 7.6 (P<0.001), while 25(OH)D <20 ng/ml odds ratio for death 10.1 (P<0.001). had an of Raharusun, P, Priambada S, Budiart C, Agung E, Budi C. (2020) Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study (April 26, revised 6 May, 2020). SSRN. https://ssrn.com/abstract=3585561

JoAnn E. Manson, MD, DrPH, (2020) Does Vitamin D Protect Against COVID-19? MEDSCAPE, May 11, 2020

The recommended dietary allowance of vitamin D is 600-800 IU/daily, but during this period, | a multivitamin or supplement containing 1000-2000 IU/daily of vitamin D would be

reasonable. https://www.medscape.com/viewarticle/930152

Other resources on vitamin D and COVID-19
<u>https://www.grassrootshealth.net/</u>

https://vitamindwiki.com/

(Dr. William Grant is director of the Sunlight, Nutrition, and Health Research Center <u>http://www.sunarc.org</u> wbgrant@infionline.net)

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