

Vitamin D supplementation to prevent COVID-19 in older people

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To the Editor—Since the review on the immune modulating effects of vitamin D in coronavirus disease 2019 (COVID-19) infection by Kaler et al¹ last year, there has been an open-label trial showing positive effects of vitamin D supplementation in COVID-19 patients in Spain. Out of 838 COVID-19 in patients, 447 were routinely given calcifediol (25-hydroxycholecalciferol) 532 µg on admission, and 266 µg on day 3,7,15 and 30. The treatment group had very significantly lower rates of intensive care unit admission (4.5% vs 21%) and death (4.7% vs 15.9%).² In contrast, two randomised trials of a single large dose of vitamin D3 on admission in moderate to severe COVID-19 patients have showed no significant benefits.³ The discrepant results may be due to differences in vitamin D formulations. As compared with vitamin D3, calcifediol does not require hydroxylation in liver which is often impaired in acute illness. Therefore, vitamin D supplementation should preferably be started before exposure to COVID-19. Older people who seldom go outside, especially those in old age homes, have high prevalence of vitamin D deficiency. Indeed, an expert group recommended routine use of vitamin D3 1000 units daily in old age homes.⁴ A randomised trial of vitamin D3 in older people showed that doses up to 2000 units daily for four months was very safe.⁵ In the midst of the pandemic, I recommend vitamin D3 2000 units once daily in homebound older people to prevent COVID-19 infection and its complications, especially those who are not fully vaccinated.

Author contributions

The author contributed to the Letter, approved the final version

for publication, and takes responsibility for its accuracy and integrity.

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Timothy Kwok*, MD

Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong

* Corresponding author: tkwok@cuhk.edu.hk

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Liver injury associated with the use of health supplement HemoHIM

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To the Editor—A recent press release issued by the Department of Health of the Hong Kong SAR Government urged public not to buy or consume an oral health supplement “HemoHIM”.¹ This product has been withdrawn from the market in Hong Kong, Taiwan and Singapore. In Hong Kong, from April to September 2021, four women presented to public hospitals because of acute hepatitis (Table).² All patients had consumed a health supplement named HemoHIM (Atomy; Gongju, South Korea) and liver function improved after cessation of use. No alternative medical causes were identified. A sample of HemoHIM was analysed by high-performance liquid chromatography with diode-array detection and liquid chromatography–tandem mass spectrometry, revealing the presence of methoxsalen,

psoralen, and benign herbal markers. Subsequent analysis of additional samples from different sources showed consistent laboratory findings. Methoxsalen (also known as 8-methoxypsoralen, 8-MOP) and psoralen are naturally occurring furocoumarins. They can be found in a number of plant species at various concentrations and are collectively referred to as psoralens. Psoralens have photosensitising property, thus methoxsalen is formulated as drugs used in PUVA (Psoralen and ultraviolet light UVA) treatment for psoriasis and vitiligo.³ Psoralens bind to DNA when exposed to ultraviolet light, inhibiting DNA synthesis and causing a decrease in cell proliferation. Methoxsalen- and psoralen-containing herbs have been reported to cause liver injuries.^{3,4} The listed herbal

TABLE. Clinical information of the four cases

Patient sex, age	Duration of HemoHIM use	Other regular drugs or health supplement used	Presenting symptom(s)	Relevant investigation results	RUCAM score (causality likelihood)
Female, 72 years	1.5 Months	Atorvastatin, amlodipine, perindopril Vitamin C, vitamin B1, pantothenic acid, biotin, omega-3 oils, vitamin E	Tea-coloured urine for 2 days	Peak ALT 530 U/L, ALP 105 U/L, total bilirubin 25 µmol/L Viral hepatitis screening (A, B, C, E) negative. Autoimmune markers not checked No imaging performed	6 (probable)
Female, 52 years	4 Months	Vitamin C, probiotics (lactobacilli), menopause formula (Dong Quai extract, chasteberry extract, black cohosh extract)	Jaundice, poor appetite, malaise, nausea and vomiting for 1 week	Peak ALT 1264 U/L, ALP 163 U/L, total bilirubin 70 µmol/L Viral hepatitis screening (A, B, C, E) negative. ANA positive (1:80, speckled pattern), other autoimmune markers (AMA, SMA, anti-LKM) negative Ultrasound hepatobiliary system: small right hepatic cyst	6 (probable)
Female, 42 years	2 Weeks	Quetiapine, sertraline	Low-grade fever, epigastric pain, vomiting for 1 day	Peak ALT 1771 U/L, ALP 177 U/L, total bilirubin 14 µmol/L Viral hepatitis screening (A, B, C) negative. SMA weakly positive. Other autoimmune markers (ANA, AMA, anti-LKM) negative Ultrasound hepatobiliary system: no focal abnormality	6 (probable)
Female, 66 years	5 Months	Calcium supplement	Jaundice and tea-coloured urine	Peak ALT 681 U/L, ALP 131 U/L, bilirubin 309 µmol/L Viral hepatitis screening (A, B, C, E) and autoimmune markers (ANA, AMA, SMA) negative Ultrasound hepatobiliary system: a 1-cm hepatic cyst	6 (probable)

Abbreviations: ALP = alkaline phosphatase; ALT = alanine transaminase; AMA = antimitochondrial antibody; ANA = antinuclear antibody; anti-LKM = anti-liver-kidney microsomal antibody; SMA = anti-smooth muscle antibody; RUCAM = Roussel Uclaf Causality Assessment Method (RUCAM) in drug-induced liver injury²

ingredients of HemoHIM should not contain psoralen or methoxsalen. Further investigations are needed to explain the occurrence of these chemical compounds in the product. Several plant species used in traditional Chinese medicine have been reported to contain psoralens,⁵ including *Fructus Psoraleae* (補骨脂, the dried seeds of *Psoralea corylifolia*), which contains a relatively high concentration of psoralens.^{2,3} Frontline doctors should be vigilant to patients presenting with symptoms of liver injury after consumption of HemoHIM or other supplements containing *Fructus Psoraleae*.

Author contributions

CK Chan drafted the letter and all authors contributed to the critical revision of the letter for important intellectual content. All authors approved the final version for publication and take responsibility for its accuracy and integrity.

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¹ CK Chan *, FHKAM (Emergency Medicine), Dip Clin Tox (HKPIC & HKCEM)

² Raymond SM Wong, FHKCP, FHKAM (Medicine)

² Jones CM Chan, FHKCP, FHKAM (Medicine)

³ YK Chong, FHKAM (Pathology)

⁴ Jamie Au Yeung, MCLinPharm, BPharm (Hons)

⁴ TH Yung, MSc (Clinical Pharmacy), B Pharm in Chinese Medicine

¹ Hong Kong Poison Information Centre, United Christian Hospital, Hong Kong

² Prince of Wales Hospital Poison Treatment Centre, Hong Kong

³ Hospital Authority Toxicology Reference Laboratory, Hong Kong

⁴ Hospital Authority Chief Pharmacist's Office, Hong Kong

* Corresponding author: chanck3@ha.org.hk

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