

COVID-19: the case for supporting the human immune system with vitamin D

Here we are again: another winter of COVID, with increasing restrictions and the threat of cancellation of Christmas. This is all down to the fear of the Omicron variant, despite Dr Angelique Coetzee, chair of the South African Medical Association, reassuring us that Omicron's symptoms are "extremely mild" [1].

We will probably never be without COVID-19; indeed we are still living with respiratory viruses from the three pandemics of this century (SARS, MERS and swine flu) [2]. The fact that these and other viruses have not wiped out the human race is down to the human immune system, which is a nothing short of miraculous in its abilities. As a species, humans have overcome every single microbial infection since we evolved into *homo sapiens*; if we had not, the human race would be extinct by now. Yes, there have been some deaths along the way, but the human immune system, when properly supported, can overcome any challenge.

Sadly, the human immune system is a resource which has not yet been utilised by the government or public health authorities. Their messaging on supporting the immune system is non-existent. This is needlessly jeopardising lives and health, particularly among those most at risk of severe COVID. Yet, the single greatest difference that we could all make to our immune health is to raise our vitamin D levels, something that could be accomplished very simply and cheaply.

So let's take a look at the abundance of evidence that vitamin D can support the immune system.

Vitamin D can improve immunity and suppress the inflammatory cytokine response, particularly important for COVID-19, while low vitamin D levels predispose us to increased risk of respiratory tract infections and pneumonia [3-11]. Systematic reviews and meta-analyses (both looking at the totality of the evidence) show that vitamin D supplementation reduced the risk of acute respiratory infection [8,12].

How does this translate to COVID-19? At the time of writing, although a small number of studies found no difference, no fewer than 20 studies showed that adults and children with low vitamin D levels were more likely to test positive for COVID-19 [13-32] and several studies showed that they had more severe symptoms [16,24,33-39], a longer hospital stay [31,40,41], admission to intensive care or the high dependency unit [30,35,42,43] and increased inflammation [31,34,37,40,44], blood clotting [37,43,40] and acute respiratory distress syndrome (ARDS) with need for mechanical ventilation [45-47]; a Spanish study found that over 82% of hospitalised COVID-19 patients had vitamin D deficiency [38]. A meta-analysis of 23 studies containing 11,901 participants found that in patients with vitamin D deficiency, the risk of being infected with COVID was 3.3 times higher and the risk of developing severe COVID was around 5 times higher compared to those with more healthy vitamin D levels [48]. A further 17 studies confirmed that in vitamin D-deficient individuals the risk of death was higher [19,29,34,35,37,44,46,47,49-57]; a meta-analysis found that death could theoretically be avoided at vitamin D levels of 125 nmol/l [58]. This is hardly surprising as we know that patients with severe COVID-19 have depleted numbers of critical immune cells and their function is exhausted [59].

So what about vitamin D for COVID prevention and treatment? Two large UK studies found that use of vitamin D supplements was associated with a significantly lower risk of COVID-19 infection [60,61], while a Spanish study found that achieving blood levels of 75 nmol/l reduced infection incidence, severity and death [62]. A meta-analysis found a consistently lower mortality rate among those given oral vitamin D [63]. COVID patients given vitamin D to bring blood levels up to 75 nmol/l had a more than 50% decreased rate of death and a shortened hospital stay [64]. Vitamin D-deficient patients given 280,000 IUs vitamin D over 7 weeks suffered significantly fewer deaths [65], while 200,000 IUs administered over two consecutive days significantly reduced transfer to intensive care and/or death [66]. Vitamin D is now included in several successful COVID-19 treatment protocols [67-72].

With this number of studies clearly demonstrating the importance of adequate vitamin D levels, it is astonishing that the government has not seized on vitamin D as the answer to their COVID prayers. Imagine if this was a drug deficiency - wouldn't the drug be handed out like smarties?

So what should our vitamin D levels be? It appears from these COVID studies that a minimum level should be 75 nmol/l, with a meta-analysis showing that death could theoretically be avoided at vitamin D levels of 125 nmol/l [58,73]. Yet some doctors still believe that 50 nmol/l is sufficient, since this level is necessary to prevent certain bone and muscle conditions, but it is inadequate for immune support. Many experts agree that for immunity, and particularly for severe COVID prevention, a level of 100-150 nmol/l is necessary.

Unfortunately, many of us don't even achieve 50 nmol/l. A study showed that in the UK over 61% had vitamin D levels below 50 nmol/l [74], i.e. an inadequate level even for prevention of those bone and muscle conditions, never mind the immune system. A large study showed that the UK had among the lowest mean vitamin D levels in Europe [19].

So how much vitamin D should we take? Government guidance for the autumn and winter months is to take a vitamin D supplement to 'support general health and in particular for bone and muscle health' [75]. Indeed it helpfully offered free supplements containing 400 International Units (IUs) to the 'clinically extremely vulnerable', although applications closed in February 2021 and have not reopened. There is not a single word about vitamin D for immune support and in any case 400 IU/day is a woefully low dose for the vulnerable. The UK recommended level does not even compare well with the US, where the National Institutes of Health recommend 600 IU/day, with 800 IU/day for those aged >70 years [76].

There has been widespread concern about both the target vitamin D level of 50 nmol/l and the suggested dosage. The Royal Society recommended that since vitamin D has an important regulatory role in the human immune system, the government should provide a stronger public message about the importance of preventing Vitamin D deficiency and should suggest supplementation at 800-1000 IU/day for all, making it clear that this intake is to help optimise immune health; they also suggest that adults likely to be deficient should consider taking 4000 IU/day for the first four weeks [77]. The French National Academy of Medicine recommend rapid vitamin D testing for all COVID patients aged over 60, with immediate administration of high dose intravenous vitamin D as necessary and advice for daily supplementation with 800-1000 IU for everyone else [78]. A report from the Joint Committee for Health in Ireland concluded that it is essential for the entire Irish population to take

vitamin D supplements daily and recommends that anyone attending a COVID-19 test centre should be offered vitamin D supplements [79]. There is even a resolution before the US congress that would require that the House of Representatives to recognise the correlation between vitamin D deficiencies and poor COVID-19 outcomes [80]. This concern culminated in more than 220 scientists, doctors and leading authorities (including this author) signing an open letter to world governments, calling for immediate widespread action to increase vitamin D use to combat COVID-19. The vast majority recommend 4,000 IU (10 times the level recommended in the UK), but many take amounts in excess of this, of up to 10,000 IU. [81]

Studies show that poor vitamin D status is regularly observed in the elderly [82] and in members of the black, African and minority ethnic (BAME) community; two UK Biobank studies found that the prevalence of vitamin D deficiency (<25 nmol/l) was highest among those of Asian and African ancestry [83], with 92% of Asians having vitamin D levels of less than 50 nmol/l and 55% having levels less than 25 nmol/l [84]. One Biobank study commented that the prevalence of vitamin D deficiency in the UK was alarming [83]; a low vitamin D level is also a risk factor for several conditions which are in turn risk factors for COVID-19, particularly obesity and type 2 diabetes [85].

The BAME community are particularly at risk of low vitamin D levels because the melanin pigment in darker skin reduces sun effects and vitamin D production [86,87,88]. It is possibly no coincidence, then, that the BAME community suffer disproportionately from COVID-19 infection, complications and mortality [89,90]; this is also the group that tends to have lower vaccine uptake [91]. UK NHS healthcare workers from the BAME community were nearly nine times more likely to have vitamin D deficiency; while only 21% of NHS healthcare workers come from the BAME community, they accounted for 63% of COVID-19 deaths [92].

Although Public Health England reviewed the reasons why the BAME community are disproportionately affected by COVID, they did not specifically investigate the role of vitamin D and it was not mentioned in their report. However, in 2020 the National Institute for Health and Care Excellence (NICE) has published a review of vitamin D and COVID-19 and concluded that there was no evidence to support taking vitamin D supplements specifically to prevent or treat COVID-19 [93]; they might care to take another look at the evidence, now that so many new studies have reported.

If you want to increase your levels, unfortunately very little vitamin D is found in food. The principal source is sunshine during the summer months, however you can supplement with Vitamin D3 very easily and cheaply [94]. Many experts recommend supplementing 4,000 IU/day (10,000 IU/day for the first two weeks to bring blood levels up quickly). These levels are safe and effective [95-97]. The elderly, those with COVID-19 risk factors or members of the BAME community are recommended to take 8,000 IU/day (15,000 IU/day for the first two weeks to bring blood levels up quickly).

The NHS states that not more than 4000 IU/day should be taken [98]. That is because they are advised by the 2016 SACN (Scientific Advisory Committee on Nutrition) report [99]. SACN claim that vitamin D produces toxic effects above 2000 IU/day but they came up with their claim through misreading or misinterpreting an important paper. What this paper actually states is that toxicity may occur at blood levels beyond 500 nmol/L [100], which could not be achieved unless an individual was taking extremely high doses (>30,000 IU/day) for a prolonged period of time. This warning has been misunderstood and misquoted and has given rise to a lot of pointless restriction of vitamin D intake in the UK. Daily doses of

10,000 IU and even 30,000 IU have in fact been demonstrated to be perfectly safe by the European Food Safety Authority Panel [101].

As it is now scientifically established that the virus is becoming more resistant to neutralisation by antibodies or vaccines [102], we propose the following:

- The immediate recommendation that the public take high dose vitamin D (i.e. at least 4,000 IU/day, not 400 IUs) for COVID prevention.
- That free high dose vitamin D (i.e. at least 4000 IUs,) is provided to the BAME community and all healthcare workers.

Vitamin D is very cheap. The cost of supplying it would be significantly lower than the cost of hospitalisation of further COVID-19 cases, particularly in intensive care. And it is impossible to put a price on the value of lives saved. The University of Birmingham estimated that offering free vitamin D supplements of 800 IU/day to the elderly and the BAME community, plus fortifying flour with vitamin D, would save the economy £65 million by reducing demand for healthcare [102]. A further study estimated that treating the UK elderly with 800 IU/day would prevent falls, long term care and death by a net saving of £420 million [103]. Similarly in Germany, reports showed that vitamin D supplementation in the elderly was estimated to prevent almost 30,000 cancer deaths per year at net savings of €254 million (around £217 million) [104].

Much of the UK population is still living in a state of fear and helplessness. These measures would foster a greater sense of safety and personal control among many, reducing mental health issues and giving people the confidence to venture out to resume normal life with the sense of optimism and positivity which is so badly needed to rebuild our lives and our economy. We understand that as Omicron sweeps the globe, our leaders have to be seen to be doing something, but rather than further curtailing liberties, why not just prescribe vitamin D?

Endnotes

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