Editorial

All quiet on the vitamin D front?

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No, not quite so quiet. Recently, vitamin D has caused some turmoil regarding its potential role to aid in the prevention and amelioration of the COVID-19 infection. This has included for example a meta-analysis showing the relation of low serum status of vitamin D and increased risk of COVID-19 infection [1], while such findings have been refuted in another meta-analysis of RCTs and cross-sectional studies, which did not find an association between vitamin D supplementation and risk of COVID-19 infection and death after adjustment for confounders, based on multivariate analyses [2].

The topic whether or not vitamin D may reduce severity of COVID-19 symptoms and complications has been discussed in this special issue by Shiravi et al. [3], focussing on the plausibility based on the underlying molecular pathways. Potential roles and pathways scrutinized in this review included the role of vitamin D in apoptosis, calcium signalling in the mitochondria and endoplasmatic reticulum, immunomodulatory effects on immune cells, involvement in anti-microbial molecules such as defensins, up-regulated expression of several antioxidant systems (e.g. glutathione and superoxide dismutase), and possible down-regulation of the renin-antiotensin system involved in blood-pressure regulation. Despite all plausible involvements, the role of vitamin D supplementation to prevent COVID-19 or reduce its related mortality is questionable.

However, the "multi-talented" vitamin D has stirred discussions and triggered studies related to many other health outcomes. Derosa et al. [4] have employed vitamin D3 in patients with type 2 diabetes and vitamin D deficiency. In their placebo-controlled trial with over 220 persons, at least 25.000 IU every 2 weeks for 6 months (weekly during the first 3 months) were administered. Compared to placebo, improvements were found in glucose markers such as HbA1c. It is apparent that low vitamin D levels can predispose to more severe diabetes consequences. Another diabetes related topic was highlighted in a Letter to the Editor by Yarahmadi et al. [5], pointing out that foot ulcers as the most severe complication of diabetes, may be a target for vitamin D supplementation. Ostentibly, patients with this condition have often low levels of this vitamin, plus elevated markers of inflammation, and vitamin D may be beneficial for wound healing.

Bariatric surgery patients are also at risk for vitamin D (in addition to other micronutrient) deficiencies. Galyean et al. [6] have studied, in a randomized clinical trial, the effect of monthly administration of 100.000 IU. Though the increases in the treated group were only marginally significantly higher than in the control group, the study showed the safe and somewhat efficient use of ergocalciferol in those patients.

From borderline to no significant effect of vitamin D supplementation takes us a study by Lee et al. [7]. Their team studied the association of vitamin D serum levels (25 OH vitamin D) and the length of the hospital stay and mortality in critically ill patients in intensive care units, and no significant relations were revealed. However, low serum vitamin D concentrations were related to sequential organ failure assessment score, C-reactive protein, selenium and triglyceride levels, proposing a connection of vitamin D levels and inflammation.

Since low levels of vitamin D may – in addition to lack of sunlight exposure – be related to dietary intakes, a look into the main sources contributing to vitamin D intake is appropriate. This was investigated in the review by Benedik et al. [8], reminding us that sufficient vitamin D intake (15 µg/day) from the diet is hard to achieve, with good sources being some types of fatty fish, mushrooms, reindeer lichens and fish liver oils.

Some food items even appear to be related to vitamin D deficiency. This was emphasized in the study by Chen et al. [9], as demonstrated with caffeine based on data from the NHANES study, perhaps due to a decreased expression of vitamin D receptor (VDR). The odds ratio for the most fully adapted model for the highest vs. lowest caffeine intake was 1.48 (95% CI: 1.16 to 1.78). Persons with a certain genetic variant of the VDR may have to take care.

Somewhat overlooked complications where vitamin D may play a role include nutritionally less studied ones such as polycystic ovary syndrome. In the review by Menchini et al. [10], it was emphasized that vitamin D may be beneficial against insulin resistance and endometrial susceptibility, while higher doses may be detrimental for oocyte development and embryonal quality. Their recommendation was a low-dose supplementation of 400–800 IU per day.

In summary, vitamin D has been related in epidemiological studies with many health complications, and due to the often low circulating levels in many persons (especially if sun exposure is low), many applications for supplementation have been reflected on. While there is much plausibility for the relation of especially low circulating levels of vitamin D and increased inflammation and repercussions on the immune system, supplementation for disease prevention or reduction, especially for only marginally deficient persons, appears to remain questionable for many complications.

References

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