POTENTIAL INTEREST OF VITAMIN D SUPPLEMENTATION TO PATIENTS WITH RESPIRATORY TRACT INFECTIONS (RTIs).

Roland Amir, Centre de Santé des Fagnes, Nuclear Medicine Department,
Boulevard Louise, 18 – 6460 Chimay, Belgium.

Background – Aims

Previous observational studies report independent associations between low serum concentration of 25-hydroxy-vitamin D (25OH vitamin D) and susceptibility to acute respiratory tract infections [(1)]. In a systematic review and meta-analysis of 25 randomised controlled studies, Martineau et al has described that vitamin D protected against acute respiratory tract infection overall [(2)].

Vitamin D is considered to be important for a healthy immune system, by inducing expression of antimicrobial peptides in immune-cells and at epithelial surfaces [(3)]. In addition, vitamin D has broad anti-inflammatory effects on the adaptive immune system and can down-regulate pro-inflammatory cytokines and increase immuno-regulatory T-cells [(4,5)].

Methods

Available data suggest that the beneficial effect of vitamin D supplementation appeared after approximately 3 months. This finding is correlated with significantly increased serum levels of 25OH vitamin D in the supplemented individuals as described in the original publication [(6)].

The data presented in several studies provide additional evidence for a beneficial role of vitamin D in preventing RTIs. Although many pieces of key information are still lacking, including the dose, target vitamin D serum levels and populations in need of supplementation, we believe that vitamin D should be a parameter to be taken into account when meeting patients with frequent RTIs. It is also important to say that we did not record, in these presentations, any related adverse events. Thus vitamin D represents a safe, cheap and potentially important factor to correct among vitamin D deficient patients with frequent RTIs.

Results

Several reviews consider the ways in which vitamin D reduces the risk of viral infections [(7,8)].

Vitamin D has many mechanisms by which it reduces the risk of microbial infection and death. A recent review regarding the role of vitamin D in reducing the risk of the common cold grouped those mechanisms into three categories: physical barrier, cellular natural immunity, and adaptive immunity [(9)]. Vitamin D helps maintain tight junctions, gap junctions, and adherens junctions (e.g. by E-cadherin [(10)]. Several articles discussed how viruses disturb junction Integrity, increasing infection by the virus and other microorganisms [(11,12)].

Vitamin D enhances cellular innate immunity partly through the induction of antimicrobial peptides, including human cathelicidin, LL-37, by 25OH vitamin D [(13,14)], and defensins [(15)].

Cathelicidins exhibit direct antimicrobial activities against a spectrum of microbes, including gram-positive and gram-negative bacteria, enveloped and nonenveloped viruses, and fungi [(16)]. Those host-derived peptides kill the invading pathogens by perturbing their cell membranes and can neutralize the biological activities of endotoxins [(17)]. They have many more important functions, as described therein. In a mouse model, LL-37 reduced influenza A virus replication [(18)]. In another laboratory study,25(OH)2 vitamin D reduced the replication of rotavirus both in vitro and in vivo by another process [(19)]. A clinical trial reported that supplementation with 4000 IU/d of vitamin D decreased dengue virus infection [(20)].

Vitamin D also enhances cellular immunity, in part by reducing the cytokine storm induced by the innate immune system. The innate immune system generates both pro-inflammatory and

anti-inflammatory cytokines in response to viral and bacterial infections, as observed in Covid-19 in patients [21].

Conclusion

The vitamin D supplementation increase the probability to stay free of RTIs.

In many studies, the findings support the notion that vitamin D status should be monitored in adult patients with RTIs and suggest that an adapted supplementation of vitamin D deficiency could be a safe and cheap way to reduce RTIs and improve health in this vulnerable patient population.

To reduce the risk of infection, it is recommended that people at risk of RTIs consider taking for adult patient about 2000 UI/d of vitamin D_3 to raise 25(OH) D concentration above 40-50ng/ml.

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