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Vitamin D and Covid-19: A Note of Caution

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In Response to Article Entitled 'Optimisation of Vitamin D Status for Enhanced Immuno-Protection against Covid-19' by D.M McCartney et al - Ir Med J; Vol 113; No. 4; P58

Dear Sir,

We read with interest the data reported by McCartney that Vitamin D deficiency is associated with a higher incidence of respiratory tract infections.[1] We would however like to raise a word of caution in the conclusions raised by McCartney in recommending urgent widespread vitamin D supplementation for older adults to enhance resistance to COVID-19. Indeed one of the published studies referenced to support this assertion noted only a 2% absolute risk reduction in "acute respiratory infection"; with the accompanying editorial suggesting that this should "probably not" change practice.[2]

Immunonutrition is not a new phenomenon; and is a term used to describe nutritional supplementation in some combination of vitamins, amino acids, omega-3 fats, and anti-oxidants in the belief that these compounds may have a beneficial impact upon immune function. Unfortunately, the evidence to date is conflicting and littered with failures based on similar observational data e.g. Glutamine, Arginine, Selenium, Vitamin E, C and of course Vitamin D.

Supplementation with micronutrients can potentially be seen as a 'harmless' intervention but prescribers and patients should retain a healthy scepticism of such supplementation without evidence of benefit for a given indication or where there may be in fact evidence of harm. For instance; the SELECT trial investigated the role of Selenium and Vitamin E supplementation in prostate cancer risk. The original trial recruited 35,533 participants across 427 sites and was discontinued because of lack of efficacy for risk reduction and because futility analysis demonstrated no possibility of benefit for the supplements. However, concerned by a small, statistically insignificant, trend towards higher prostate cancer risk in the population taking Vitamin E alone, the authors carried out an extended follow-up period of the cohort and found a 17% increase in prostate cancer incidence in those who took Vitamin E supplementation alone compared with those who took selenium alone, selenium with Vitamin E, or placebo only.[3] We acknowledge that Vitamin D supplementation is safe but beware the law of unintended consequences.

The role of Vitamin D in critical illness is perhaps more relevant to COVID-related illness than acute respiratory infection as described which included things as diverse as otitis media and self-reported colds in the referenced studies.[1,2] Vitamin D deficiency is widely recognised in the critical care literature but to date the only robust randomised phase II trial performed has shown no statistically significant benefit with respect to mortality or length of stay to routine supplementation.[4] A phase 3 trial is currently recruiting.

In conclusion, while the data presented to date are interesting and certainly warrant further investigation in appropriately powered randomised control trials with clear research questions and end-points, to recommend urgent supplementation of a population as a strategy against COVID-19 is imprudent and not supported by any clear evidence. While it is understandable to search for strategies against this unprecedented healthcare challenge, it would be folly to abandon the principle of evidence-based care for our most vulnerable patients lest we all descend in to "Donald Trumpisms".

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