Scientific Advisory Committee on Nutrition

Nutrition and immune function in relation to COVID-19 – a rapid scoping exercise

June 2020

Introduction

1. This paper provides an overview of a rapid scoping exercise considered by the Scientific Advisory Committee on Nutrition (SACN) at its meeting on 11 June 2020 and the subsequent discussion and interim conclusions agreed by SACN.

Background

2. Since the COVID-19 outbreak, a number of academic papers and media articles have hypothesised that:
   - poor nutritional status could compromise immune function and increase the risk of adverse COVID-19 outcomes
   - supplementation with some micronutrients could improve immune function in relation to COVID-19.

Objective

3. In this context, SACN agreed to conduct a rapid, member-led scoping exercise on nutrition and COVID-19.

4. The purpose was
   - to provide SACN with an overview of the available evidence on nutrition, SARS-CoV-2 virus/COVID-19 disease and general immunity, with particular reference to acute respiratory tract infections (ARTI) and vaccine response
   - for SACN to consider whether this issue should be reviewed in more detail.

5. The aim was to survey the available evidence from high-quality systematic reviews, randomised controlled trials (RCTs) and other clinical trials in humans. As this was a scoping exercise, identification and consideration of relevant evidence was rapid; it only reported on author conclusions of cited papers, did not consider the quality or limitations of the evidence identified or adhere to SACN's usual process for risk assessment. Vitamin D and obesity were not considered as primary topics though there was some reference to these in the context of other findings.

6. A separate SACN rapid review has been published on vitamin D and ARTI. In addition, the National Institute for Health and Care Excellence (NICE) has published an evidence review on Vitamin D for COVID-19. Emerging evidence on COVID-19 and obesity is being considered by PHE separately.

7. The scoping exercise also included background information on the SARS-Cov-2 virus and COVID-19 disease, and potential mechanisms of action of specific

nutrients on immune function, neither of which have been covered in detail in this summary.

Overview of identified evidence

8. Four scoping searches were conducted in PubMed between 21 and 25 May 2020: “nutrition and immune” identified 14962 citations; “nutrient and immune” identified 4692 citations; “COVID-19 and nutrition” identified 34 citations; and “COVID-19 and nutrient” identified 8 citations. A full systematic search was not undertaken. The identified citations on nutrition/nutrient and COVID-19 were mostly narrative, non-systematic reviews focusing on micronutrients. One new observational study specific to vitamin D and COVID-19 was identified (D'Avolio et al, 2020).Two additional observational studies, 1 on vitamin D and 1 on selenium and COVID-19, were identified at a later date (Hastie et al, 2020; Zhang et al, 2020). No RCTs were identified.

9. Members also provided additional evidence after the SACN meeting on 11 June 2020 (Calder, 2020; Gibson et al, 2012; Ivory et al, 2017; Lee et al, 2018; Prendergast, 2015; Zimmermann & Curtis, 2019). These papers are also considered briefly.

Respiratory tract infections

10. One narrative review, which used a systematic search strategy, evaluated evidence from 43 clinical trials of nutrition-based interventions (including vitamins, minerals, nutraceuticals and probiotics) on viral and respiratory infections in humans (Jayawardena et al, 2020). The review included previous meta-analyses but Jayawardena et al (2020) did not carry out a meta-analysis themselves due to the heterogeneity of studies, especially in relation to reported outcomes. The authors concluded that vitamins A and D showed a potential benefit especially in deficient populations and reported that selenium and zinc had favourable immune-modulatory effects in viral respiratory infections. The authors noted that high dose vitamin C and E supplementation was generally inefficient in enhancing immunity and that most included studies reported adverse effects of vitamin E supplementation on immune response.

11. One systematic review and meta-analysis concluded that vitamin D supplementation protected against ARTI, particularly in participants with low vitamin D status (Martineau et al, 2017). This paper is reviewed in the SACN rapid review on vitamin D and ARTI. Two observational studies on vitamin D and COVID-19 were identified (D'Avolio et al, 2020; Hastie et al, 2020). These papers are reviewed in the NICE evidence review of vitamin D for COVID-19.

12. Zinc status was reported to influence immune function and related health outcomes, including respiratory morbidity (Bonaventura et al, 2015; Maares & Haase, 2016; Roth et al, 2010). A number of studies noted that the zinc metallopeptidase angiotensin-converting enzyme 2 (ACE2) provides the cellular entry point for SARS-CoV-2 (Brielle et al, 2020; Guy et al, 2005; Oudit et al, 2009; Turner et al, 2004).

Vaccine response

13. Only a small number of non-COVID-19 specific studies on vaccine response were identified.

14. One RCT of vitamin D supplementation in deficient older adults reported altered markers of immune function in response to influenza vaccination but without improving antibody production (Goncalves-Mendes et al, 2019); while a systematic review and meta-analysis reported that vitamin D status did not affect the immunological response to influenza vaccination (Lee et al, 2018). A RCT of selenium supplementation reported beneficial and detrimental effects on immunity to influenza vaccination (Ivory et al, 2017).

15. One RCT reported that increased fruit and vegetable intake improved response to the pneumovax II vaccination in older adults (Gibson et al, 2012).

16. A non-systematic review discussed the relationship between infection, immunity and malnutrition with a focus on children in developing countries. It noted that most studies suggested that malnourished children can mount an adequate response to vaccines, whilst noting major knowledge gaps in this area (Prendergast, 2015).

17. Other studies suggested that vaccinated adults living with obesity have twice the risk of influenza or influenza-like illness compared with vaccinated adults living with a healthy weight, despite equal serological response to vaccination. It was also suggested that obesity increased the risk of morbidity and mortality following infection with influenza A (H1N1) virus (Green & Beck, 2017; Milner & Beck, 2012). One non-systematic review reported that higher body mass index (BMI) is associated with a lower immune response to several vaccines (Painter et al, 2015).

Nutrition and immune function / response

18. One non-systematic review considered the literature on nutrition and immune function in the context of COVID-19. The authors concluded that there was evidence for a range of nutrients influencing one or more aspects of immune function. The nutrients included vitamins A, B6, B12, C, D, E and folate; trace elements, including zinc, iron, selenium, magnesium, and copper; and the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid (Calder et al, 2020). An additional

non-systematic narrative review on the same topic suggested that that zinc and selenium may be particularly important for antiviral defence (Calder, 2020).

19. Other reviews focused on specific nutrients or nutrient groups and their effect on immune function relevant to COVID-19. These included consideration of zinc, copper, selenium, vitamin D, antioxidants and omega-3 fatty acids (Basil & Levy, 2016; Brielle et al, 2020; Broome et al, 2004; Calder, 2013; Carr & Maggini, 2017; Guillin et al, 2019; Guy et al, 2005; Martineau et al, 2017; Oudit et al, 2009; Raha et al, 2020; Turner et al, 2004; Zdrenghea et al, 2017).

20. One recent observational study considered hair selenium concentration – previously correlated with selenium intake – and COVID-19 severity and “cure rate” (Zhang et al, 2020). However, the nature of the statistical association with selenium could not be established in this observational study.

21. Shi et al (2020) hypothesised that genetic differences could contribute to individual variations in the immune response to pathogens and some of these may be nutrient-related. Bourgonje et al (2020) explored possible polymorphisms in the pathways of zinc metabolism in relation to COVID-19 severity and progression.

Nutritional deficiencies in clinical setting

22. It was noted that viral infection, especially severe infection, may affect micronutrient status as micronutrients are used by the host to defend itself against attack and there may be a need to address specific dietary deficiencies (Guillin et al, 2019).

23. The European Society for Clinical Nutrition and Metabolism (ESPEN) has set out practical guidance for the nutritional management of COVID-19 patients in intensive care (Barazzoni et al, 2020). Risk management is outside SACN’s remit.

Discussion

24. SACN noted that there is an extensive volume of literature on nutrition and immune function and it is a challenging area of research. The complexity of this issue was clear in previous SACN risk assessments that included immune function as an outcome of interest (notably the SACN reports on vitamin D and iron and position statements on selenium and trans fats).

25. Members noted the disparities in mortality risk from COVID-19 particularly in relation to ethnicity and BMI. It was also noted that genetic differences contribute to individual variations in the immune response to pathogens and some of these may be nutrient-related.

26. Members noted that the majority of recent reviews on nutrition and COVID-19 were not systematic reviews of the evidence base. SACN agreed that, at the time the literature search was undertaken, there was a lack of robust evidence to suggest that specific nutrients or nutritional supplements can reduce the risk or severity of COVID-19.

Interim conclusions

27. SACN agreed that the scoping exercise indicates a lack of robust evidence at this current time to suggest that specific nutrients or nutritional supplements can reduce the risk or severity of COVID-19.

28. While the literature search was for nutrition, most of the evidence identified was for micronutrients.

29. SACN will keep this topic under review. This scoping exercise may be updated, or a more formal assessment undertaken, if robust evidence becomes available on nutrition and immune function specific to COVID-19, including vaccine response.

30. SACN noted that there was currently no new evidence that would change current dietary advice in relation to immune function.

UK government advice

31. There are several nutrients that are involved with the normal functioning of the immune system. Most people can get all the vitamins and minerals they need by eating a healthy, balanced diet and do not need to take supplements. The government therefore continues to advise that during this time everyone follows a healthy, balanced diet, as illustrated by the Eatwell Guide.

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