



Calcium and/or vitamin D supplementation: could they affect your risks of colorectal cancer development or progression?

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Introduction

Colorectal cancer (CRC) is one of the most common cancers, and also one of the most common causes of cancer deaths worldwide. For example, an extensive and well-cited review by Ferlay and co-workers considered cancer rates and incidences in 40 different European countries, revealing that CRC was the second most common cancer and also second most common cause of cancer deaths in these countries in 2012 (1). While there is genetic susceptibility to this disease, the risk seems to be modifiable by environmental factors, especially high intake of dietary items such as well-cooked red meat, containing heterocyclic amines (2). The risk of CRC is not only adversely affected by environmental factors, but may be positively affected by dietary modulation to ensure a well-balanced or prudent diet (3). While this will require reduction of high saturated fats and excess calories, it will also entail attention to ensure an adequate intake of various key nutrients, including micronutrients (3). It is important, however, to recognise that recommended daily intakes (RDIs) of these nutritional factors has been conventionally based on adequacy for bone health (4). It is increasingly being recognised that other health or disease endpoints such as CRC may require different, possibly higher, intakes of some nutrients (5,6).

Why might increasing vitamin D and/or calcium intake be potentially beneficial to human health?

Both calcium and vitamin D have been considered as

micronutrients that may have an inadequate intake, because of changing environmental conditions (5,6). Milk and dairy products are good sources of calcium, but these are often used as additions to a diet rather than a major food item. Concerns have been raised over high intakes of these foods having a negative effect on the carbon food print (7). These products often contain vitamin D also, although one of the major sources of vitamin D is sunlight exposure. However, because sun exposure is being significantly curtailed because of public awareness of skin cancer dangers, increased attention is turning to dietary sources. A range of evidence has implicated vitamin D deficiency in increasing susceptibility to various gastrointestinal disorders, including CRC. On this basis, there is justification to consider increasing vitamin D intake overall, although optimal intakes are likely to vary among individuals (6).

Some calcium and/or vitamin D dietary intervention studies

In 1999, Baron and co-workers, began their “Polyp prevention study” which considered effects of daily supplementation with calcium carbonate (as supplement) or placebo on just over 900 subjects who had experienced an adenoma (5). Although there was a minor benefit (in terms of adenoma recurrence) for the supplemented group, the effect seen was very modest and unlikely to extrapolate to effects on CRC risk in the long term (8). In the follow-up Vitamin D/

Calcium Polyp Prevention Study, Baron and co-workers (9) considered the effects of daily supplementation with vitamin D₃ (1,000 IU), calcium (1,200 mg), or both after removal of colorectal adenomas. This was a randomised, multi-centre, double-blind, placebo-controlled trial, involving 2,259 participants, that took place at 11 genetically diverse centres in the USA. None of these treatments significantly reduced (or increased) the risk of recurrent colorectal adenomas over a period of 3 to 5 years (9). At the time, while the result did not appear to justify supplementation, neither did they argue against it.

The importance of different endpoints in CRC prevention studies

Adenomas are early pre-cancer lesions of CRC which can be readily removed, and controlled by regular colonoscopies. However, later stages of the disease are not so readily controlled. Sessile serrated polyps are well established pre-cancer lesions for CRC, and are considered to give rise to 20–30% of sporadic CRC cases (10). Thus, some concerns have been raised by the recent re-evaluation of the Vitamin D/Calcium Polyp Prevention study (11). The subjects in this original group had continued to be observed for several more years. The study endpoint was the serrated polyp. This new analysis showed neither vitamin D nor calcium supplementation alone reduced the risk of subjects carrying serrated polyps. In contrast, both calcium supplementation alone and calcium with added vitamin showed a significantly enhanced risk of the development of serrated polyps (11).

Implications for dietary supplementation for high risk populations

I believe that it is important to stress that, while the title of this paper might imply that either vitamin D and/or calcium supplementation could be harmful, a careful examination of the data do not show this. They emphasise that calcium supplementation, with or without added vitamin D could be harmful. While they do not show a beneficial effect of vitamin D supplementation *per se* on the formation of serrated polyps, neither do they show a harmful effect. It is very important to stress this latter point, especially as some other recent studies strongly suggest that overall, vitamin D supplementation may be beneficial (12). It stresses that there is a large jump in what is sufficient for bone health is a much lower level than that which protects against CRC. An

excellent example of this is the international pooling study of 17 cohorts, which also cites a number of other studies (12). It is noteworthy that this is especially true for individuals with certain genotypes. Having spent time reading this considerable literature, I have now requested that my own doctor provides me with a vitamin D supplement. This he was very willing to supply, commenting that others may be wise to follow suit...

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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