Mini-Review

Nutrients Impact the Pathogenesis and Development of Colorectal Cancer

Wan Du Jing-Yuan Fang

Division of Gastroenterology and Hepatology, Shanghai Institute of Digestive Disease,
Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China**Key Words**

Calcium · Colorectal cancer · Dietary fiber · Selenium · Vitamins

Abstract

Background: Colorectal cancer is a commonly diagnosed cancer and the cause of many cancer deaths worldwide. Nutrients might be crucial in the pathogenesis and development of colorectal cancer. Although a number of studies have demonstrated the potential effects of nutrients, many challenges still remain. **Summary:** A tremendous amount of research has emerged concerning the roles of nutrients in colorectal cancer during the past decades. Here, we review the latest research progress on nutrients, including vitamins, folic acid, calcium, selenium and dietary fiber, involved in colorectal cancer prevention. **Key Message:** Nutrients are commonly consumed in foods or dietary supplements. It is clear that nutrients could play an important role and influence colorectal cancer outcomes. The relationship between nutrients and colorectal risk is complex. Vitamins, folic acid, calcium, selenium and dietary fiber have been proposed as potential agents to prevent colorectal cancer. However, some studies found that these nutrients did not reduce the incidence of colorectal cancer. **Practical Implications:** The supplementary dose of nutrients, the length of time required to observe the effects and confounding factors during the study might influence the role of nutrients in the prevention of colorectal cancer. Therefore, more evidence from ongoing clinical trials with different population groups and longer follow-up periods is critical to determine the relationship between nutrients and colorectal cancer.

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Jing-Yuan Fang
Division of Gastroenterology and Hepatology, Shanghai Institute of Digestive
Disease, Renji Hospital, Shanghai Jiao Tong University School of Medicine
145 Middle Shandong Road, Shanghai 200001 (China)
E-Mail fangjingyuan_new@163.com

Introduction

Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with an estimated 1.4 million cases and 693,900 deaths in 2012 [1]. The occurrence of colorectal cancer is associated with dietary factors. Some nutrients affect the pathogenesis and development of colorectal cancer. Nutrients involved in colorectal cancer prevention include vitamins, folic acid, calcium, selenium and dietary fiber.

Vitamins A, C, D, E and Folic Acid

Studies of the effectiveness of vitamins to prevent colorectal cancer are highly inconsistent and controversial (reviewed in [2]). Vitamins A, C and E are major antioxidant vitamins that have been proposed as potential agents to prevent colorectal cancer. Their beneficial effects involve inhibition of free radicals and reduction of oxidative damage to DNA [3, 4]. However, some studies found that vitamins A, C and E did not reduce the incidence of colorectal cancer [5, 6]. Therefore, the potential effects of antioxidant vitamin supplementation on colorectal cancer require further study.

Several studies suggested that vitamin D levels were inversely related to the pathogenesis and development of colorectal cancer [7–11]. Vitamin D could reduce cell proliferation, inhibit angiogenesis, promote cell differentiation and stimulate apoptosis, thus reducing the risk of colorectal cancer [6]. A few randomized controlled trials failed to find a protective role of vitamin D intervention on colorectal cancer [12, 13]. The reason may be that the low dose of vitamin D used did not increase the circulating serum levels of 25-hydroxyvitamin D₃ [25(OH)D₃]. In a meta-analysis, individuals who achieved 25(OH)D serum levels ≥ 33 ng/ml (82 nmol/l) had a 50% lower incidence of colorectal cancer [14]. Two meta-analyses showed that taking high doses of vitamin D (1,000–2,000 U/day) reduced the risk of colorectal cancer by 50% [14, 15]. Further studies of the exact doses of vitamin D required to prevent colorectal cancer are needed.

The effect of folic acid on colorectal cancer development remains controversial. Some studies reported that high levels of folic acid in the diet or blood inhibit the development of colorectal cancer [16, 17]. In contrast, recent data suggest that dietary high folic acid might enhance colorectal cancer progression [18, 19]. The underlying state of the tissue may affect the role of folic acid on colorectal cancer development. Some scholars have suggested that folic acid supplementation protection against colonic carcinogenesis might depend on the neoplastic status of the colorectal cancer. Folic acid supplementation would protect against carcinogenesis before neoplastic transformation, whereas supplementation after the formation of preneoplastic colonic lesions might increase the risk of colorectal cancer risk. The connection between folic acid and colorectal cancer carcinogenesis is possibly associated with nucleotide biosynthesis and DNA methylation [20, 21].

Calcium

Calcium intake plays a crucial role in the prevention of colorectal cancer. Large prospective studies confirmed the inverse association between high doses of dietary calcium and the risk of colon cancer development [22, 23]. Calcium reduces the risk of colorectal cancer by binding to toxic secondary bile acids and ionized fatty acids, forming insoluble soaps in the colon [6]. Calcium could also inhibit colorectal cancer development by reducing proliferation, stimulating differentiation and inducing apoptosis of the colonic mucosa [24,

25]. However, some studies revealed that calcium supplements do not reduce the risk of colorectal cancer [14, 26]. This inconsistency may reflect the doses of dietary calcium used and the length of the studies.

Selenium

Several studies have demonstrated a protective effect of selenium on colorectal carcinogenesis [27, 28]. Selenium may invoke preventive mechanisms by enhancing immune cell activity as well as anti-oxidative and anti-inflammatory properties [29]. Potential gender differences in selenium metabolism might explain the controversial effect of selenium on colorectal cancer prevention identified in several studies [29–31]. Several randomized trials and observational studies found no clear association between selenium levels and the risk of colorectal cancer [32–34]. Long-term selenium supplementation may lead to an increase in side effects, including an increased incidence of diabetes [35]. Therefore, we do not advocate selenium supplementation for people with adequate selenium levels.

Dietary Fiber

Studies identified from a search of PubMed and several other databases demonstrated an inverse association between dietary fiber intake and risk of colorectal cancer [36–39], which suggested that high dietary fiber intake could prevent colorectal cancer. However, some cohort studies and randomized trials were equivocal. Prospective cohort studies found different associations with fiber intake between men and women [40, 41]. A pooled analysis of two clinical trials indicated that men may obtain more benefits from dietary fiber than women [42]. These inconsistencies may be explained in part by lifestyle and dietary factors that are also associated with colorectal cancer.

Conclusion

Many studies have demonstrated the potential effects of nutrients in the prevention of colorectal cancer, but many challenges remain. Future studies and clinical trials must be conducted, with different population groups and longer follow-up periods, which will help determine the role of nutrients in the prevention of colorectal cancer.

Disclosure Statement

The authors declare no conflicts of interest.

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