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EDITORIAL

Colorectal cancer and pollution

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Abstract

The incidence of colorectal carcinoma is increasing in young patients, in contrast to the well established wisdom that it is exclusively diagnosed in patients older than 40 years. In this survey, we examined all possible risk factors, and we recommend a number of measures for early detection in young patients who are at risk of developing this malignant tumor.

Key words: Colorectal adenocarcinoma; Food contamination; Pesticides; Young patients; Free radicals

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INTRODUCTION

Colorectal cancer continues to be one of the most common human malignancies, afflicting nearly one million individuals worldwide every year. The disease can be considered endemic in all western and industrialized countries, but there are indications that, in the near future, colorectal neoplasms will become frequent also in populations that at present show a low incidence of the disease[1]. Reports from Asian and African countries have demonstrated that annual diagnosis of colorectal cancer is increasing[2-5] and cases have been identified in those aged < 40 years old[6]. However, hereditary factors could not be recognized as risk factors in these cases[6] and high dietary intake of meats and fats could not be blamed as risk factors in these developing countries because of a lack of supply of either to the majority of the population[6-8]. Therefore, this phenomenon requires further investigation. It is likely to be due to chemical contamination of food and drink.

CHLORINATION OF DRINKING WATER AND DEVELOPMENT OF BOWEL CANCER

It is likely that chlorination of drinking water plays a role in the above phenomenon. During the chlorination process, chlorine reacts with organic materials in the water to produce a complex mixture of halogenated and non-halogenated by-products, the concentration and distribution of which vary with characteristics of the raw water and the treatment process[9]. A large number of halogenated chemical species have been identified, including trihalomethanes, halogenated acetonitriles, halogenated acids, haloketones, and haloaldehydes[10]. Trihalomethanes are the most frequently occurring by-products[11,12] and are routinely measured in public water supplies, thus making them a useful marker for the level of chlorination by-products in treated water. Chronic exposure to disinfected surface waters is considered one of the contributing factors to the development of urinary bladder and colon cancer[13-15]. Mutagenic activity of chlorinated water may be due to the presence of chemicals produced from reactions of chlorine with natural substances released by the breakdown of vegetation in the source water[16]. The chlorinated hydroxyfuranone [e.g. 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-

furanone], for example, has been shown to be responsible for a majority of this mutagenic activity[5,12]. 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone has been reported to occur at much lower concentrations in drinking water than other disinfection by-products, yet it might be a significant public health concern because it is the most potent mutagen currently identified in drinking water[17]. Two years of treatment with this compound in drinking water resulted in a multi-organ carcinogenic response in male and female Wistar rats[18]. Moreover, reliable evidence from epidemiological studies has suggested an increase in the risk of urinary bladder, colon, and rectal cancer among people using disinfected drinking water that contains high levels of trihalomethanes[15,19]. King *et al*[20] have reported that increasing exposure to different drinking water constituents is associated with increasing risk of colon cancer in men. In this population, several halogenated chemical species have shown a tendency for increasing colon cancer risk across different exposure categories due to increasing exposure, which reached at least a 53% elevation in risk for the highest exposure categories. Long-term (approximate 35 years) exposure to trihalomethanes at a level of approximate 75 mg/L was associated with a doubled colon cancer risk among men (OR: 2.10, 95% CI: 1.21-3.66). The highest quartile of cumulative trihalomethanes-years exposure was associated with an OR of 1.74 (95% CI: 1.25-2.43)[20]. The continuous representation of cumulative trihalomethanes exposure was associated with a 17% increase in risk for each 1000 mg/L-years (95% CI: 6-29)[20].

FOOD CONTAMINATION AND DEVELOPMENT OF BOWEL TUMORS

Polychlorinated biphenyls are possible sources of food contamination. They are synthetic organochlorine compounds that are used in industrial and commercial processes[19,21]. However, dioxins, commonly referred to as dibenzodioxins and dibenzofurans, are organochlorine by-products of waste burning, paper lightening, pesticide production, and production of polyvinyl chloride plastics[21,22]. In the United States, major dietary sources of polychlorinated biphenyls and dioxins are beef, chicken, and pork, dairy products, vegetables, fish and shellfish, and eggs[23]. Animal experiments and some evidence in humans have indicated that polychlorinated biphenyls and dioxins are carcinogenic. This is likely to be related to effects on the aryl hydrocarbon receptor, a transcription factor that affects gene expression[24,25].

Food contamination with pesticides is another example. High levels of different types of pesticides in the collected serum samples from patients with colorectal carcinoma and their relatives have been reported[26-29]. However, no significant correlation between these chemicals and development of this neoplasm has been recognized. Also, higher concentrations of these chemicals in the samples from the healthy relatives[29] might have precluded any possibility of any significant link. Nevertheless, there is increasing evidence that systemic oxidative stress plays an important role in the development and progression of cardiovascular disease and cancer[30].

Oxidative stress is defined as a state in which the level of toxic reactive oxygen intermediates (free radicals) overcomes the endogenous antioxidant defenses of the host, such as the lipid-soluble antioxidants. Oxidative stress can result, therefore, from either an excess of free radical production or depletion of antioxidant defenses. For example, in the absence of adequate levels of lipid-soluble antioxidants, increased free radical production may cause functional and structural damage by reacting with lipoproteins, thus resulting in lipid peroxidation with the formation of degradation products, such as malondialdehyde, which are themselves carcinogenic. The mechanism by which overproduction of free radicals can lead to development of a chronic non-infectious disease has been fully described previously[31].

Recent studies have reported that various pesticides can induce oxidative stress in different tissues[32-35]. The significantly reported positive correlation between different tumor stages, concentrations of lipid peroxidation products, and lack of antioxidants in the serum of patients with colorectal cancer[36-38] gives hope for screening those patients who are at risk for development of these tumors, and for detecting these malignancies at an early stage.

The failure to link measurements of pesticides in the serum of patients with diagnosed colorectal adenocarcinoma to other measurements of lipid peroxidation products, (e.g. malondialdehyde) antioxidants, (e.g. vitamin C, zinc) and copper/zinc ratio in the blood likely explains the confusing outcome of the published reports.

IMPLICATIONS IN CLINICAL PRACTICE AND IN RESEARCH

Well-structured studies need to be designed to assess a possible link between levels of pesticides in those at risk of developing bowel tumors with the levels of lipid peroxidation products for early tumor detection.

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