Diet and cancer

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Abstract. The aim of our study is to evaluate the relationship between diet and cancer development. It has been estimated that 30-40% of all kinds of cancer can be prevented with a healthy lifestyle and dietary measures. A low use of fibres, the intake of red meat and an imbalance of Omega-3 and Omega-6 fats may contribute to increase the risk of cancer. On the other hand, the assumption of lots of fruit and vegetables may lower the risk of cancer. Protective elements in a cancer-preventive diet include selenium, folic acid, vitamin B_{12}, vitamin D, chlorophyll and antioxidants such as carotenoids (α-carotene, β-carotene, lycopene, lutein, cryptoxanthin). Ascorbic acid has limited benefits if taken orally, but it effective through intravenous injection. A supplementary use of oral digestive enzymes and probiotics is also an anticancer dietary measure. A diet drawn up according to the proposed guidelines could decrease the incidence of breast, colon-rectal, prostate and bronchogenic cancer. (www.actabiomedica.it)

Key words: Westerndiet, vegeterian diet, japanese diet, vitamins, soya, fibres

Introduction

The struggle against cancer is one of the greatest challenges of mankind. In industrialized countries lung carcinoma is the main cause of cancer in men and, in recent years, it has exceeded breast carcinoma which is the most frequent cause of cancer death in women. Iconsequently, while its incidence appears stabilized in men it continues to increase in women. In 1980 122,884 lung cancer deaths in 5,648,000 inhabitants were reported while in 1994, 155,879 deaths in 5,687,300 inhabitants were reported.

Some dietetic factors are considerer to have a protective role against the development of lung neoplasm, such as fish and fruit.

It has been estimated that 30-40% of all tumours can be forestalled with a correct lifestyle and diet.

Cancerogenesis, which is the loss of cellular differentiation that causes cancer, is inhibited by factors such as retinoids, vitamins E, D_3, C, poliphenols, fibres, calcium, soya, selenium and polyunsaturated fat acids such as Omega-3. Other factors such as proteins, lipids, sodium chloride, aphlatossin, nitrite and nitrates and some processes such as salting, smoking and broiling tend to favour it.

The Role of Nutrition in Cancer Prevention

A diet rich in selenium and Omega-3 has a preventive role in prostate carcinoma, while a diet rich in animal fats is responsible for increase of incidence in breast cancer among Chinese women living in the USA (1). An excessive intake of food is one of the main factors of neoplastic risk and it is proved that obesity is a condition that predisposes the development of malignant neoplasm. Overweight is responsible for 14% of cancer deaths in men and 20% in women.

Retinoids and vitamins reduce the risk of breast cancer in women with a body mass index (BMI) > 25 Kg/mq; they have a preventive action on both gastric cancer caused by Helicobacter Pilory and hepatocarcinoma caused by hepatitis B and C.

Soya

The scientific association between soya protein consumption and the reduction of risk of some kinds of tumours is clearly increasing. An epidemiological study (2) put into evidence the reduced number of prostate tumour-cases in severe-combined immunodeficient (SCID) mice. The soya rich diet of these mice supported these results. The plant, of Asiatic origin, represented the staple food in that area for 5000 years. Soya is rich in proteins (42%), lipids, glucides, vitamins, minerals, fibres, saponins and isoflavones. These last components, including phitoestrogens, guarantee a protective action. In fact, isoflavones have an empirical formula similar to estrogens and can bind to the same receptors, blocking their action. On the other hand, some studies have shown a non-estrogenic mechanism of the phitoestrogens of soya. One of them, Genistein, does not influence the enzymes involved in signal transduction that regulates cellular growth and multiplication and has antioxidant properties. Its mechanism consists in anti-oxidation, inhibition of arachidonic acid metabolism, modulation of the cellular integration signals, inhibition of hormone activity, of neoplastic cell growth and of oncogenesis. An American study (3) conducted in 59 countries shows the importance of some substances in the reduction of the incidence of prostate cancer; soya is one of these substances. A Japanese study (4) has puts into evidence that in food-restricted mice, plasma levels of anticancer substances such as IFN-gamma, TNF-alfa and cytokines are higher than in the control group. A recent study of Billings et al (5) shows that the consumption of soya beans reduces the risk of colon-cancer up to 50%. Men that ate at least 39 g of soya proteins per day for a year showed a lower cellular division of their cancerous cells than men whose diet did not include soya. An American study (6) demonstrated that a regular diet based on soya, protects from lung metastases of melanoma, showing the important action of isoflavones.

Probiotics

Bacteria located in the intestine generally have a symbiotic relationship with their host. These beneficial bacteria produce natural antibiotics and prevent diarrhoea and infection; they produce some vitamins that can be utilized by the organism. Moreover, they help the digestion of food through auxiliary enzymes such as lactate. They enhance the absorption of minerals and can prevent the development of allergies and food intolerances. An increase in the use of fibres develops the growth of intestinal bacterial flora. The Lactobacillus species that produce lactic acid are associated with subjects that have the lowest risk of colon-cancer. There are some solid theoretic bases according to which probiotics can prevent cancer and even make it regress: they may produce fatty acids with a short chain in the colon that reduce the level of procarcinogenic enzymes such as beta-glucuronidase, nitroreductase and azoreductase (7).

The Metabolism of Glucose

The glycemic index indicates the quantity of sugar that is adsorbed by an organism through the assumption of food. Recent studies are evaluating the association between a high glycidic diet and the risk of gastric (8), digestive (9), endometric (10), ovarian (11) and colon-rectal (12, 13) cancers. Glycate Haemoglobin (HbA_1C) is a control index of the quantity of glucose and, indirectly, of the insulin level. Patients suffering from diabetes have a three time higher risk of colon-rectal cancer. Therefore it is evident that an glucose induced alteration the metabolism is a condition that predisposes the development of cancer.

Red Meat

Bingham et al (14), have shown the important relationship between red meat and colon-rectal cancer; the heterocyclic amines produced in cooked meat are related to breast-cancer. Nitrites and nitrates are used because they bind to myoglobin in meat inhibiting botulinic exotoxin production. On the contrary, they are powerful cancerous agents and their action can be in contrast with compounds derived from ascorbic acid. Charcoal cooking and/or smoke-curing of food produce harmful carbon compounds such as pyrolysates and amino acids have a strong cancerous effect, even if

Table 1

Substances	Salmon	Red peppers	Tomatoes	Turnip-greens	Asparagus
Eicosapentanoic Acid	+				
Docosaesanoic Acid	+				
Omega-3	+				
Vit. B$_{12}$	+				
β-carotene		+	+		
Vit. C		+	+		
Lipoxene			+		
Sulphide G, S				+	
Folic acid					+
Carotenoids					+
Saponins					+

Table 2

Substances	Cabbage	Carrots	Onions	Melon	Strawberries	Green tea
β-carotene	+	+		+		
Vit. C	+				+	
Fibres	+					
Calcium	+					
Lutein	+					
Zeaxantin	+					
Quercetin			+			
Antocianin					+	
Poliphenols						+

appropriate precautionary measures can limit negative consequences.

Food Physio-Pathological Evaluation

Different studies have revaluated some foods pointing out their beneficial effects on our health (15, 16).

The National Cancer Institute (NCI) has set a dietetic guideline for cancer prevention (16).

1. Keep a correct body weight. An incorrect caloric assumption has been placed in relationship with an increased mortality rate for some neoplasms, such as breast, uterus, colon, gall bladder and prostate tumours.

2. Vary your diet. It is difficult to isolate the factors that may cause or prevent cancer due to the large number of components in each food and the complex interactions among them. A varied diet with moderate quantities of food offers the best hope for lowering the risk of cancer.

3. Include fruit and vegetables in your daily diet. The consumption of vegetables and fruit is associated with a lower risk of lung, prostate, bladder, esophagus and stomach cancers. These foods contain vitamins, minerals, fibres and non-nutritional components that may reduce the risk of cancer. They can be used together or on their own. Fruit and vegetables are a good source of vitamins and minerals. They are a source of phytochemical substances (chemical substances derived from vegetables) that although lacking in nutritive value are however biologically active compounds. Phytochemical substances protects plants in the same way as antibodies defend the body from infections. Indols in cabbages, sulphar compounds in garlic and leeks, isoflavones (estrogens of plants) in soya and carotenoids in many vegetables are included in this category. Phytochemical substances produce physiologic effects with many different mechanisms. They may incite the immune system, contribute to reduce the toxicity of adverse chemical products, influence hormonal levels, and control cellular growth. The antioxidant action of some phytochemical substances has a particular importance:

living cells require oxygen since the enzymes that produce energy depend on it. In cells, anomalous results of oxidation may happen during the chemical reactions that utilize O_2. Some of these reactive products are potentially dangerous and can be involved in the origin of cardiopathies or give rise to tumour processes.

4. Eat a larger quantity of foods rich in fibres, such as cereals, whole wheat flour and legumes. Fibres contribute to reduce colon cancer in two ways. Bran and whole wheat bread that have a high content of fibres containing insoluble fibres that soak up liquids, causing them to swell and increasing the fecal mass. This contributes to a reduction in the concentration of harmful biliary acids and other potential cancerous agents in excrements. Oats, bran and many vegetables contain soluble fibres. This kind of fibre does not increase the fecal mass but forms a gelatinous matrix promoting the elimination of biliary acids and other compounds that are potentially harmful for the colon. Therefore, it is important to consume a diet rich in cereals, whole wheat bread, fruits and vegetables.

5. Reduce total consumption of fats. Since 1940, some wise pioneers suggest that fat in the diet has an important role in the risk of cancer. The American Health Foundation (AHF) of New York showed a dramatic difference in the incidence of cancer breast between American and Japanese women (17). American women have an average consumption of fats of about 40% of the total daily calories while Japanese women have a consumption of fats of about 10-20%. Italian women also have a low incidence of cancer notwithstanding a diet that is comparatively rich in fat. This has raised other questions on the kinds of fats that are present in a diet in addition to their quantities. Further studies have indicated that a large use of animal fat and of polyunsaturated oils, such as safflower or corn oil, may increase the onset of colon and breast tumours when compared with a reduced use of fats. For example, a large quantity of corn oil, may cause an increase in biliar acid synthesis that in turn may increase the risk of the colon cancer. Yet, other kinds of fats, may have different effects. Omega-3 fat acids that are present in fish oils and in some vegetables may reduce the incidence of breast and colon cancer. It seems that monounsaturated oils such as olive oil, behave in a neutral manner. Even if it has not been examined, canola oil probably has a low risk if compared with other vegetable oils. It is rich in monounsaturated fatty acids and also contains some kinds of Omega-3 fatty acids. A similar consideration can be made for linseed oil that is rich in Omega-3 fatty acids. Both monounsaturated fatty acids and Omega-3 fatty acids can protect from cardiopathies. This may contribute to explain the lower risk incidence of cancer and of cardiopathies in Southern Italy and in Greece. Even if these diets are relatively rich in fats, a large part of the fats used for cooking in these countries belong the family of monounsaturated or the Omega-3 fatty acids family.

6. Limit the consumption of alcohol. Hard drinkers have a higher risk of developing several tumours: oral, laryngeal and oesophagus cancers. Smoking is also a risk factor for these neoplasms.

7. Limit the consumption of salt or foods preserved with nitrite. They can increase the risk of oesophagus and stomach cancers in countries where the use of them is large.

Diet and custom

The vegetarian diet is very popular today. It is a cultural, ethical, economic, ecological behaviour that respects life, the life of others and the environment. Its supporters do not drink alcohol, do not smoke, do not take drugs and have a life style that aims at the preservation of an ideal well body weight and daily physical activity. Meat and fish are excluded from the diet while there is room for fruit, vegetables, cereals, legumes, seeds and nuts. Some vegetarians also include milk, dairy products and eggs in their diet.

Some studies (15, 18) have shown that a greater use of fibres, fruit and vegetables and a lower use of total fats, cholesterol and caffeine reduce the incidence of colon cancer and heart attack.

How vegetarian diets protect from cancer

Vegetarians become ill less frequently than meat eaters. Cancer study is complicated since it is a condition that may develop over the course of time. Since

many factors based on life style have an influence on the risk of cancer, it is always difficult to establish the real effect of only one of these factors. We suppose that vegetarians may have a reduced mortality because they are less obese, practice physical activities, smoke less and frequently submit to medical controls. A lower incidence of smoking is one of the reasons why vegetarians develop lung cancer less frequently. In vegetarian diets, the factors that seem protective against cancer are:

1. A wider use of fibres. Vegetarians eat an amount of fibres that is two or three times higher than in non-vegetarians. Some studies (18, 19) exhort the use 20-40 g of fibres a day. Vegetarians have 30-45 g of fibres a day, while in the Western culture consumption is only 15 g (20, 21).

2. A reduced use of fats. Milk-egg-vegetarians have a diet containing about 10% less of fats than a meat eater and a "vegana diet" is about 20% poorer in fats. Diets with a high percentage of fats may increase the risk of colon, breast and prostate tumours. Moreover, many vegetarians follow a diet exceeding the 30% limit of fats fixed by the National Cancer Institute.

3. No use of meat. Beef in particular may originate cancerous compounds when cooked at a high temperature. The metabolism of these compounds is a risk factor for the development of cancer.

4. More limited Fe reserve. A high degree of Iron may increase the risk of cancer, but this is still a supposition. Excessive Iron may promote reactive species of free radicals that can damage the cells.

5. A larger use of anti-oxidants. These compounds contribute to neutralize the effects of free radicals. Some of them are vitamins, such as Beta-carotene, vitamin C and vitamin E. Vegetarians consume 50% more vitamin C than non-vegetarians and they also consume twice as much vitamin E and Beta-carotene (20).

Conclusion

In ancient times man ate food that was available in nature: wild fruit, berries, vegetables, seeds and roots. They drank animal milk, but did not eat lots of meat. In modern times, many countries have adopted the meat-and-potatoes diet with an excessive use of salt. Scientific Research has indicated some guidelines for a healthy life-style aiming at the reduction of the risk of tumours. Westerner have detrimental food habits because of the large use of fats, meat, salted food associated to an insufficient use of fibres. Better food habits should include soya, cereals, whole wheat bread, legumes, fruits and vegetables. Moreover, the use of monounsaturated fatty acids and Omega-3 fatty acids should be preferred to animal fats and other vegetable fats.

References

1. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 2003; 348: 1625-38.
2. Aronson WJ, Tymchuk CN, Elashoff RM, McBride WH, McLean C, Wang H, Heber D. Decreased growth of human prostate LNCaP tumours in SCID mice fed a low-fat, soy protein diet with isoflavones. *Nutr Cancer* 1999; 35: 130-6.
3. Hebert JR, Hurley TG, Olendzki BC, Teas J, Ma Y, Hampl JS. Nutritional and socioeconomic factors in relation to prostate cancer mortality: a cross-national study. *J Natl Cancer Inst* 1998; 90: 1637-47.
4. Matsuzaki J, Yamagji R, Kiyomiya K, Kurebe M, Inui H, Nakano Y. Implanted tumor growth is suppressed and survival is prolonged in sixty percent of food-restricted mice. *J Nutr* 2000; 130: 111-5.
5. Billings PC, Newberne PM, Kennedy AR. Protease inhibitor suppression of colon and anal gland carcinogenesis induced by dimethylhydrazine. *Carcinogenesis* 1990; 11: 1083-6.
6. Li D, Yee JA, McGuire MH, Murphy PA, Yan I. Soybean isoflavones reduce experimental metastasis in mice. *J Nutr* 1999; 129: 1075-8.
7. Goldin BR, Gorbach SL. The effect of milk and lactobacillus feeding on human intestinal bacterial enzyme activity. *Am J Clin Nutr* 1984; 39 (5): 756-61.
8. Augustin LS, Gallus S, Negri E, La Vecchia C. Glycemic index, glycemic load and risk of gastric cancer. *Ann Oncol* 2004; 15: 581-4.
9. Augustin LS, Gallus S, Franceschi S, et al. Glycemic index and load and risk of upper aero-digestive tract neoplasms. *Cancer Causes Control* 2003; 14: 657-62.
10. Augustin LS, Gallus S, Borsetti C, et al. Glycemic index and glycemic load in endometrial cancer. *Int J Cancer* 2003; 105: 404-7.
11. Augustin LS, Polese J, Borsetti C, et al. Dietary glycemic index, glycemic load and ovarian cancer risk: a case-control study in Italy. *Ann Oncol* 2003; 14: 78-84.
12. Franceschi S, Dal Maso L, Augustin L, et al. Dietary glycemic load and colorectal cancer risk. *Ann Oncol* 2001; 12: 173-8.

13. Slattery ML, Boucher KM, Caan BJ, Potter JD, Ma KN. Eating patterns and risk of colon cancer. *Ann J Epidemiol* 1998; 148: 4-16.

14. Bingham SA, Hughes R, Cross AJ. Effect of white versus red meat on endogenous N-nitrosation in the human colon and further evidence of a dose response. *J Nutr* 2002; 132: 3522-5.

15. Adams SM, Standridge JB. What should we eat? Evidence from observational studies. *South Med J* 2006; 99: 744-8.

16. Butrum RR, Clifford CK, Lanza E. NCI dietary guidelines: rationale. *Am J Clin Nutr* 1988; 48: 888-95.

17. Weisburger JH. Dietary fat and risk of chronic disease: mechanistic insights from experimental studies. *J Am Diet Assoc* 1997; 97: 16-23.

18. Trepel F. Dietary fibre: more than a matter of dietetics. II. Preventative and therapeutic uses. *Wien Klin Wochenschr* 2004; 116: 511-22.

19. Escudero Alvarez E, Gonzalez Sanchez P. Dietary fibre. *Nutr Hosp* 2006; 21: 60-71.

20. Leitzmann C. Vegetarian diets: what are the advantages? *Forum Nutr* 2005; 57: 147-56.

21. Kapiszewska M. A vegetable to meat consumption ratio as a relevant factor determining cancer preventive diet. *Forum Nutr* 2006; 59: 130-53.

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