Cancer Chemo-prevention - Pragmatic or Over-optimistic

Itrat Mehdi (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Pages with reference to book, From 53 To 53

Cancer prevention can be primary prevention (avoding known carcinogens like tobacco, alcohol, ultraviolet light exposure, high fat diet, chemicals and prevention and prompt treatment of viral infections or using protective dietary supplements like fruits and vegetables) or secondary prevention (early detection and intervention). Chemoprevention of cancer, using naturally occurring substances, specific nutrients, or pharmaceutical agents which interfere with initiation, promotion, or progression of cancer or reversing the process to prevent development of invasive cancer[1,2]. Chemo-prevention is not a recent concept[1]. The concept of field carcinogenesis of epithelial cancer, well established in head and neck cancer, that in higher risk of individuals there is wide surface area of carcinogenic change which can be detected at gross appearance (leukoplakia, polyps), microscopic picture (metaplasia, dysplasia) or genetic level (gene deletion, amplification, etc.[2]

Chemo-preventive agents used so far in clinical trials are antioxidants (tocopherols, ascorbic acid, selenium, carotene), N SAID's, indoles, flavones, isothiocynates, vitamin D, retinoids, calcium, terpenes, anti-estrogens (tamoxifen), methylorn ith i ne and dehydroopiandrosterone[3]. Their putative mechanism of actions is a reduced oxidative DNA damage, altered enzyme detoxification, glucoronidase inhibition, induction of cell differentiation, reduce hormone or oncogene dependent proliferation and reduced G-6-PD activity[3]. Chemo-preventive agents used for site specific chemo-prevention are vitamin A in lung, oral cavity and skin tumors, retinoids in cervix, head and neck, breast and lung tumors, vitamin C in colon and stomach cancer, carotenes in breast, colon, cervix, lung and stomach cancer, selenium in liver cancer, calcium in esophagus and bladder cancer, vaccination in liver cancer, aspirin and NSAIDs in breast, lung and colon cancer, vitamin E in breast, esophagus and prostate cancer, antibiotics in stomach cancer and tamoxifen in breast cancer[2,4-6].

There has been some optimistic and quite a few disappointing resu Its of large-scale chemoprevention trials carried out as seen in literature[7-9]. Some of these trials have even shown a potentiating effect on carcinogenesis[2]. The most extensively chemopreventive drug studied so far is tamoxifen in breast cancer prevention; which also has not been able to give clear cut, universally acceptable and statistically significant, incidence benefit in many studies despite very optimistic claims by many investigators[10-12]. The patient population, tumor site, histopathology, chemopreventive agent, duration of treatment, dose of the agent used and time of intervention are key determining factors of ultimate outcome[2].

Chemo-prevention strategy for cancer is definitely a very reasonable and valid option like ones seen in many other sub-specialties of medicine (e.g., in cardiology) and probably will be a modality in cancer management of preventable cancers in times to come. It, however, is in early infancy with a lot of optimism seen initially not replaced by disappointments as yet. The pragmatic approach will be not to get disappointed by reported under expectations from clinical trials at one hand and not be over-optimistic about the validity of chemoprevention approach on the other. The future for sure holds promise from ongoing trials in chemopreventive approach. Presently it is believed that about 1/3 of all cancers can be prevented by different strategies but in future cancer might turn out to be a major preventable disease.

References

1. Osborne M, Boyle P, Lipkin N. Cancer prevention. Lancet, 1 997;349:Sll 26-30.
2. Mayne ST, Lippman SM. Cancer prevention: chemopreventive agents, In “Cancer principles and practice of oncology”, fifth edition, eds. De Vita, Jr., VT, Hel lman S. Rosenberg SA. I ippincott-Raven publishers, Philadelphia, USA., 1997, pp. 585-99.
3. Lipkin N. Strategies for colon cancer prevention. Annals NY Acad. Sci., 1995; 768:129-40.
4. Kelloff 0, Boone C. Cancer chemopreventive agents: Drug development status and future prospects. J. Cell Biocheni., 1994;S20:1-303.
5. Kelloff 0, Johnson J, Crowell J, et al. Approaches to the development and marketing approval of drugs that prevent cancer, Cancer Epidemiol. Biomark., 1995 ;4: 1-10.
6. Keloff G, Crowell J, Boone C, et at. Strategy and planning for chemopreventi ye drug development: clinical development plans. J Cell Biochem., 1 994;S20:55-299.
7. Blot WJ, Li JY, Taylor P, et al. Nutrition intervention trials in Linian, China: Supplementation with specific vitamin/mineral combinations, cancer incidence and disease-specific mortality in the general population. J.Natl.Cancer lnst.,1933:85:1483-92.
8. Omenn GS, Goodman GE, Thornquist MD, et al. Effecls of combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. N. Engl.J. Med., 1 996;334: 1150-55.
9. Hennekens CH, Buring JE, Manson JE, et al. Lack of effect of long term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. N.Engl .J.Med., 1 996;334: 1145-49.
10. Margolese RG. I-low do we interpret the results of the breast cancer prevention trial? CMAJ., 1998;158:1613-14.
11. Goel, V. Tamoxifen and breast cancer prevention: what should you tell your patients? CMAJ., 1998;158:1615-l 7.
12. Early breast cancer Collaborative group. Tamoxifen for early breast cancer: an overview of the randomised trials. Lancet. 1998:351:1451-67.