

Modifiable risk factors in the development of cancer

INTRODUCTION

The formation of a cancer is a complex process in which tumor cells must overcome and evade multiple genetic mechanisms of control. During carcinogenesis cells acquire:



- Chronic proliferation
- Evade the action of suppressor genes
- Resist apoptosis
- Promote angiogenesis
- Reprogram metabolism
- Avoid the immune system

Therefore, cancer is, in part, a genetic disease; But the main causal factors to which an average etiological fraction of 90% is attributed are **lifestyle, diet, consumption of tobacco and alcohol, obesity and infectious agents**.

Cancer is therefore **largely preventable**, because most of its main risk factors are modifiable.

Currently, it is one of the biggest public health problems worldwide, occupying the second cause of mortality behind cardiovascular diseases.

In Spain, it is the leading cause of death in men and the second in women and the main cause of death in both sexes among people aged 35 to 74 years.



OBJETIVES

The objectives of this review were the study of diet, obesity and alcohol consumption as modifiable risk factors in the development of cancer.

- ❖ The importance of diet
- ❖ Different food components behavior in the carcinogenic process
- ❖ Overall magnitude of obesity and global statistics of alcohol consumption
- ❖ Molecular bases behind obesity and alcohol related carcinogenesis
- ❖ Types of cancer associated with obesity and alcohol

METHODOLOGY

Scientific databases were used, where the selection of articles was made based on the following criteria → Priority was given to English articles with a publication date of less than 5 years and that had been published in high impact journals such as Lancet.

In addition, websites, articles, documents and guides published by institutions dedicated to cancer research, such as the International Agency for Research on Cancer (AIRC), were visited and reviewed.

Likewise, reference books in the area of medical oncology, such as: "Cancer: Principles and practice of oncology" and pharmacognosy, among others, were consulted.

NUTRITION

Nutrition plays a particularly important role in the clinical appearance of a carcinogenic process; being colorectal cancer the strongest associated with diet. However, because food is a multidimensional variable

→ It is NOT possible to attribute a causal effect to an specific food, therefore we have to focus on:
cancer-food pattern relationship

Food components with **POSITIVE ASSOCIATION**

- ❑ **ACRYLAMIDS** produced during processing of potatoes and cereals at temperatures above 120 °, as in frying, baking and roasting → weak association: kidney and endometrium
- ❑ Some components formed during the preparation and preservation, such as: **NITROSAMIDES, HETEROCYCLIC AMINES, AROMATIC HYDROCARBONS**.
- ❑ **HEMOGLOBIN**, present especially in meats, can catalyze the formation of free radicals, which if not well balanced (homeostasis) can contribute to oxidative damage of cellular components such as DNA, proteins and membranes.
- ❑ **HEM IRON**, on the other hand, is the most important source for endogenous formation of nitrosamides.

Components with **PROTECTIVE EFFECT**

- ❑ Omega-3 **POLYUNSATURATED FATTY ACIDS**, from marine sources and nuts → colorectal, esophageal and hepatocarcinoma tumors.
- ❑ Fruits, vegetables, spices and herbs contain a wide variety of **FITOCHEMICALS** (carotenoids, polyphenols, organosulfur compounds, terpenes, asócianos ...) with the ability to prevent, reduce or delay the onset of a carcinogenic process → 400g / day of fruits and vegetables and not through food supplements> taking advantage of the synergies of these components → colon and rectum
- ❑ **ISOFLAVONS** of soybean [100mg / day] → against lung, prostate, breast and colon cancer,
- ❑ Plant-based foods, in addition to their own characteristics, are rich in **FIBER** → reduces the risk of colorectal cancer> 10% reduction for every 10 g intake.

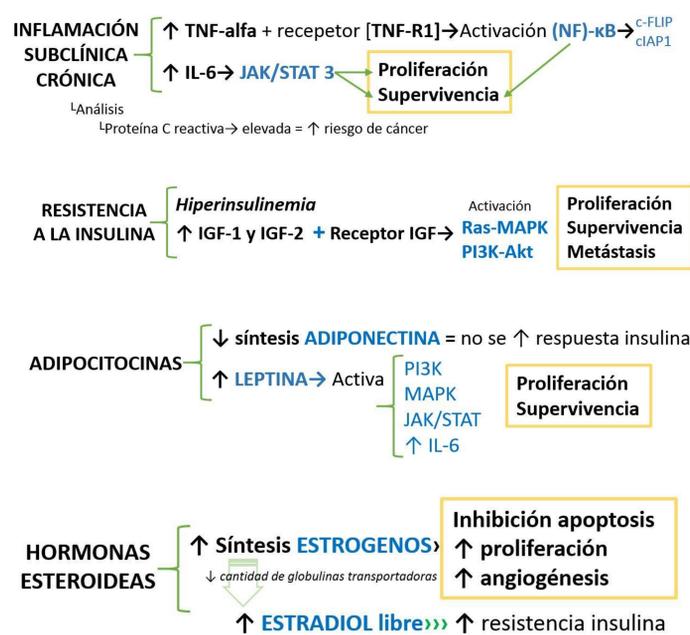
OBESITY

Obesity is a chronic and multifactorial disease, which affects approximately 38% of the population.

In Spain, in recent years its prevalence has doubled in both men and women and it is currently estimated that 22.9% of the population suffers from it.

Theoretically, it is a modifiable risk factor, which is why it is potentially one of the most effective strategies to tackle in order to avoid or reduce the risk of cancer.

The **MECHANISMS** through which obesity produces a cell environment suitable for the initiation and progression of cancer are multiple and are related to metabolic processes. They are detailed in the following figure:



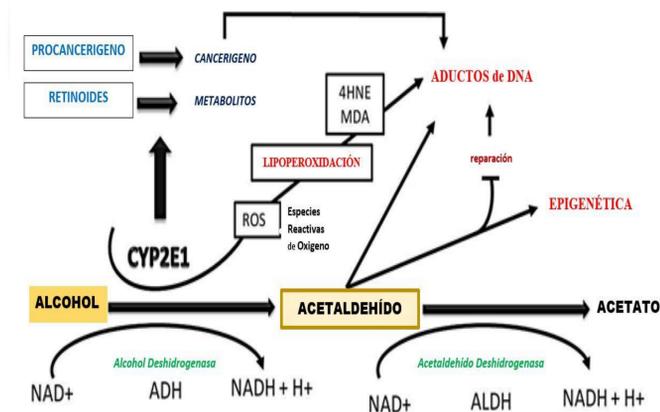
There is sufficient evidence for a positive association of obesity with pancreas, liver, esophagus, breast (in postmenopausal women), colon, rectum, non-hodgkin's lymphoma, kidney and endometrium cancer.

ALCOHOL

The common active ingredient in all alcoholic beverages, although in different concentrations, is ethanol (CH₃-CH₂-OH), which is obtained through fermentation of sugars with yeasts and whose energy content is 7 kcal / g.

During metabolism, alcohol is oxidized to acetaldehyde mainly through the action of ADH and to a lesser extent (10-15%) by cytochrome P4502E1, present in the liver. Acetaldehyde is then oxidized by ALDH to produce acetate.

The **MECHANISMS** responsible for the carcinogenesis produced by alcohol intake are not known in depth → elucidating them is crucial for the development of future antitumor therapeutic strategies.



Although not known in depth, these mechanisms include:

- 1). The genotoxic effects of acetaldehyde
- 2). The reactive oxygen species (ROS) produced when cytochrome P450 2E1 mediates
- 3). Interferences in the metabolism of retinoic acid and folate, the increase in the concentration of estrogens
- 4). Genetic polymorphism in ADH and ALDH enzymes.
- 5). The suppressive effect of alcohol on the immune system, directly responsible for the progression and metastasis of cancer.

CONCLUSIONS

1. Cancer is a complex, multifactorial and largely preventable disease. Preventable, since the influence of genetic heritage is minimal and it is mainly caused due to lifestyle and environmental factors.
2. Diet related cancer understanding is complex, since it is difficult to attribute a direct causal effect to an specific food.
3. The components of foods associated with cancer are: hemoglobin, acrylamide and nitrites, nitrites, HPA, HCA. While the consumption of ω -3 from marine sources, fruits, vegetables, species and natural fiber, could decrease the risk of developing rectal and colon cancer.
4. Obesity abridge is potentially one of the most effective strategies to reduce the risk of liver cancer, pancreas, esophagus, breast, colon, rectum, non-Hodgkin's lymphoma, kidney and endometrium.
5. The mechanisms by which obesity produces cancer are multiple and they are related to metabolic processes.
6. Alcoholic beverages can cause cancer in the oral cavity, pharynx, larynx, esophagus and male breast. The molecular bases responsible for the carcinogenesis of ethanol result mainly in the genotoxic effect of AC.

BIBLIOGRAPHY

1. Hanahan D, Weinberg RA. Hallmarks of Cancer: The Next Generation. Cell [Internet]. 4 March 2011 [cited 25 January 2018];144(5):646–74. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21376230>
2. Anand P, Kunnumakara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, et al. Cancer is a Preventable Disease that Requires Major Lifestyle Changes. Pharm Res [Internet]. 15 September 2008 [cited 25 January 2018];25(9):2097–116. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18626751>
3. Vincent, Lawrence TS, Rosenberg SA. Cancer : principles and practice of oncology. Wolters Kluwer/Lippincott Williams Wilkins Health; 2015.
4. Stepien M, Chajes V, Romieu I. The role of diet in cancer: the epidemiologic link. Salud Publica Mex [Internet]. April 2016 [cited 21 March 2018];58(2):261–73. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/27557384>
5. Herrera-Covarrubias D, Coria-Avila GA, Fernández-Pomares C, Aranda-Abreu GE, Manzo Denes J, Hernández ME. Obesity as a risk factor in the development of cancer. Rev Peru Med Exp Salud Publica [Internet]. October 2015 [cited 15 January 2018];32(4):766–76. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26732928>
6. Van Krujsdijk RCM, van der Wall E, Visseren FJL. Obesity and Cancer: The Role of Dysfunctional Adipose Tissue. Cancer Epidemiol Biomarkers Prev [Internet]. 1 October 2009 [cited 23 February 2018];18(10):2569–78. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19755644>
7. Arnold M, Pandeya N, Byrnes G, Renehan PAG, Stevens GA, Ezzati PM, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol [Internet]. January 2015 [cited 26 January 2018];16(1):36–46. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S1470204514711234>
8. Kanker W, Fonds O. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. [cited 8 January 2018]; Available at: http://www.aicr.org/assets/docs/pdf/reports/Second_Expert_Report.pdf
9. Roswall N, Weiderpass E. Alcohol as a Risk Factor for Cancer: Existing Evidence in a Global Perspective. J Prev Med Public Health [Internet]. 27 January 2015 [cited 21 January 2018];48(1):1–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25652705>
10. Ratna A, Mandrekar P. Alcohol and Cancer: Mechanisms and Therapies. Biomolecules [Internet]. 14 August 2017 [cited 3 February 2018];7(4):61. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/28805741>
11. Leon ME, Peruga A, McNeill A, Kralkova E, Guha N, Minozzi S, et al. European Code against Cancer, 4th Edition: Tobacco and cancer. Cancer Epidemiol [Internet]. 1 December 2015 [cited 10 March 2018];39:S20–33. Available at: <https://www.sciencedirect.com/science/article/pii/S187782115001290>
12. Praud D, Rota M, Rehm J, Shield K, Zatořski W, Hashibe M, et al. Cancer incidence and mortality attributable to alcohol consumption. Int J Cancer [Internet]. 15 March 2016 [cited 21 March 2018];138(6):1380–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26455822>