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The dietary risk factors for colorectal cancer related to meat consumption*

OS FATORES DE RISCOS ALIMENTARES PARA CÂNCER COLORRETAL RELACIONADO AO CONSUMO DE CARNES

FACTORES DE RIESGO ALIMENTARIO PARA CÁNCER COLORRECTAL RELACIONADO AL CONSUMO DE CARNES

Alexandra Paola Zandonai[1], Helena Megumi Sonobe[2], Namie Okino Sawada[3]

ABSTRACT

The integrative review is one of the methodologies used for evidence-based practice which, in this study, had the objective of surveying and synthesizing the evidence available in the literature regarding the dietary risks for colorectal cancer related to the consumption of meat. The search was made using the LILACS, MEDLINE, CINAHL, and COCHRANE Library databases, and six studies considered pertinent to the consumption of meat were found. Meta-analyses showed that there is an association between the consumption of red meat and an increased risk for colorectal cancer from 28% to 35%, whereas processed meats are associated with a rise in risk from 20% to 49%. Evidence shows that the consumption of red meat, processed meat, and total meat consumption are risk factors for developing polyps and colorectal cancer. The search did not yield any studies referring to the consumption of chicken or fish as risk factors.

DESCRIPTORS

Colorectal neoplasms
Risk factors
Meat
Oncologic nursing

RESUMO

Uma das estratégias metodológicas para realizar a prática baseada em evidências é a revisão integrativa, que neste estudo teve como objetivo buscar e sintetizar as evidências disponíveis na literatura científica sobre os fatores de riscos alimentares para o câncer colorretal relacionado ao consumo de carnes. As bases de dados LILACS, MEDLINE, CINAHL e COCHRANE Library foram consultadas e os estudos pertinentes ao consumo de carnes somaram-se seis. As metanálises demonstraram que a ingestão de carne vermelha está relacionada com o aumento do risco para câncer colorretal em 28% a 35%, enquanto que a carne processada está associada ao risco elevado de 20% a 49%. As evidências apontam a carne vermelha, a carne processada e o total de carne consumida como fatores de risco para o desenvolvimento de pólipos e câncer colorretal. Não foi identificado estudo que indicasse a ingestão de frango e peixe como fatores de risco.

DESCRITORES

Neoplasias colorretais
Fatores de risco
Carne
Enfermagem oncológica

RESUMEN

Una de las estrategias metodológicas para realizar la práctica basada en evidencias es la revisión integradora, que en este estudio objetivó buscar y sintetizar las evidencias disponibles en literatura científica sobre factores de riesgo alimentario para desarrollar cáncer colorrectal en relación al consumo de carne. Se consultaron las bases de datos LILACS, MEDLINE, CINAHL y COCHRANE Library, y los estudios pertinentes al consumo de carnes sumaron seis. Los metanálisis demostraron que la ingestión de carne roja está relacionada con el aumento de riesgo de cáncer colorrectal en 28% a 35%, mientras que la carne procesada se relaciona con un riesgo aumentado entre 20% y 49%. Las evidencias exponen a la carne roja, la carne procesada y al total de carne consumida como factores de riesgo para desarrollo de pólipos y cáncer colorrectal. No existió evidencia que relacionara la ingesta de pollo y pescado como factores de riesgo.

DESCRIPTORES

Neoplasias colorrectales
Factores de riesgo
Carne
Enfermería oncológica

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INTRODUCTION

In Brazil, cancer in general represents a national public health problem. As a result of the Brazilian people's increased life expectancy and progressive industrialization and globalization, tumors have gained increasing importance in the country's mortality profile, ranking second among causes of death. Colorectal cancer figures among the first five most frequent cancer types and its incidence is not homogenous across the country, with higher prevalence levels in the South and Southeast, particularly in the States of São Paulo, Rio Grande do Sul and Rio de Janeiro[1].

In 2010, for Brazil, 13,310 new colorectal cancer cases were estimated in men and 14,800 in women. This corresponds to an estimated risk of 14 new cases for every 100,000 men and 15 new cases for every 100,000 women[2].

One unfavorable aspect of colorectal cancer is its silent development and late diagnosis, due to the long period during which lesions and the tumor remain asymptomatic. In general, when the tumor is located in the right colon, the first symptoms will be diagnosed later[3].

The risk of cancer can be reduced by eliminating carcinogen agents, or at least by minimizing exposure, but without the full identification of the corresponding risk factors, it is difficult to put in practice these actions in primary prevention. It is estimated that more than two-thirds of cancer cases could be prevented through appropriate lifestyle modifications[4].

Experimental and epidemiological studies have demonstrated an association between nutrition and foods in colorectal cancer risk. Scientific evidence has been assessed and summarized in different expert groups recommendations, in which it was concluded that red meat consumption is related with increased colorectal risk.

Scientific evidence has been assessed and summarized in different expert groups recommendations, in which it was concluded that red meat consumption is related with increased colorectal risk.

The finding that high levels of red meat consumption, but not of chicken or fish, may be associated with increased risk of colon cancer was first reported in prospective studies in 1990[5].

Thus, this study reflects expectations to contribute to and summarize evidence found in scientific literature about dietary risk factors for colorectal cancer related to meat consumption, so that this information can guide practice and scientific research.

METHOD

Evidence-based practice is an approach that encourages nurses to seek scientific knowledge through research development or application of the results found in literature in their professional practice[6].

Cancer nursing can improve the results of patient care by applying evidence-based practice. Identifying and selecting the appropriate intervention, serving patients and organizational demands can be a great challenge[7].

Evidence-based practice entailed the need to produce various types of literature reviews (integrative review, systematic review, meta-analysis and qualitative review). In the past decade, the proliferation of these review research modes contributed to stricter and more systematic methods[8].

Integrative reviews are a broad category of research reviews that can comprise empirical research, theoretical literature studies or both, depending on the study aim. Besides, they can focus on methods, theories or results of different empirical studies, with a wide range of implications[9]. As opposed to systematic reviews, integrative reviews incorporate findings from different types of research designs. And, as its focus is restricted to multiple methodological perspectives, the review process becomes even more complex[10].

To develop this integrative review, a study was proposed[11] with the following phases: 1) identification of the hypothesis or guiding question – consists in the researcher's clear and objective elaboration of a problem, followed by the search for descriptors or key words; 2) sampling selection – determination of inclusion or exclusion criteria, when transparency is established to achieve selection depth, quality and reliability; 3) study categorization – definition of information extraction from review articles with a view to summarizing and organizing this information; 4) study assessment – the extracted data should be subject to critical analysis; 5) discussion and interpretation of results – when the main results are compared, against the background of theoretical knowledge, and their applicability is assessed; 6) presentation of integrative review and knowledge synthesis – the information from each review article should be addressed in a succinct and systemized way, demonstrating the evidence found.

Evidence level analysis was classified in seven levels. At level 1, evidence results from systematic reviews or meta-analysis of all relevant randomized controlled clinical trials or from clinical guidelines based on systematic review of randomized controlled clinical trials; level 2, evidence deriving from at least one well-designed randomized controlled clinical trial; level 3, evidence obtained from well-designed clinical trials without randomization; level 4, evidence from well-designed cohort and case-control studies; level 5, evidence from systematic review of descriptive and qualitative studies; level 6, evidence deriving from a single descriptive or qualitative study and level 7, evidence from expert opinion and/or expert committee reports[12].

Thus, the following research question was defined: What scientific evidence exists about dietary habits as risk factors for colorectal cancer?

The following inclusion criteria were adopted: papers about dietary risk factors for colorectal cancer; indexed in MEDLINE, CINAHL, LILACS and COCHRANE Library; published in English, Spanish and Portuguese; published in the last 10 years (from January 1998 till May 2009) and studies involving adult human beings (≥19 years).

In each database, the search was accomplished by crossing controlled descriptors. The process started with pairs, after which the third controlled descriptor was added to specify and refine the research.

The papers were pre-selected when in line with the study proposal; then, the pertinence of the title and abstract were verified with a view to further analysis of the full version.

This research had to be limited to evidence level 1, 2 and 3 studies, with strict methodological designs. Besides, the Jadad Scale[13] was applied to each study in order to measure methodological quality, as this is a reliable indicator of essay quality and based on the quality of randomization, blinding and losses during follow-up. The maximum research quality score is 5[14].

The information was extracted and summarized with the help of the instrument Ursi[15] elaborated and validated. This tool addresses the following aspects: identification of the publication (title, authors, place, publication type, language); methodological design of the study (aim, sample, inclusion and exclusion criteria, data treatment, results and conclusions); and assessment of methodological rigor (clarity during methodological trajectory, limitations and bias).

RESULTS

In this integrative review, 26 full articles were analyzed, 21 of which were selected from MEDLINE and 5 from the COCHRANE Library. Some studies were indexed in both CINAHL and MEDLINE. No study was obtained from LILACS.

Six papers were related to meat consumption. Concerning the research design, three meta-analyses were found, two systematic reviews with meta-analyses and one randomized controlled clinical trial. Five studies were classified with evidence level 1 and one with evidence level 2. Only the randomized controlled clinical trial was assessed according to the Jadad scale[13] and obtained score 3. Table 1 shows the studies selected in this integrative review.

Table 1 - Studies on dietary risk factor for colorectal cancer according to title, authors, journal and publication year - Ribeirão Preto - 2010

Category	No.	Title	Author(s)	Journal	Year
Meat consumption and risk factors for colorectal cancer	1	Systematic review of the prospective cohort studies on meat consumption and colorectal cancer risk: a meta-analytical approach	SANDHU, MS; WHITE, IR; MCPHERSON, K	Cancer Epidemiology, Biomarkers & Prevention	2001
	2	Meat consumption and risk of colorectal cancer: a meta-analysis of prospective studies	LARSSON, SC; WOLK, A	Int. J. Cancer	2006
	3	Meat consumption and colorectal cancer risk: dose-response meta-analysis of epidemiological studies	NORAT, T; et al	Int. J. Cancer	2002
	4	Systematic review of epidemiological studies on meat, dairy products and egg consumption and risk of colorectal adenomas	YOON, H; et al.	European Journal of Cancer Prevention	2000
	5	Fish consumption and markers of colorectal cancer risk: a multicenter randomized controlled trial	POT, GK; et al	Am J Clin Nutr	2009
	6	Fish consumption, n-3 fatty acids, and colorectal cancer: a meta-analysis of prospective cohort studies	GEELEN, A. et al	Am J Epidemiol	2007

Study 1 is a systematic review with meta-analysis, in which prospective cohort studies were assessed, containing information about the relative risk for colorectal cancer associated with meat consumption. The results of this study evidenced a strong association between the consumption of all meats and red meat with the risk for the development of colorectal cancer. When grouping the results, the authors concluded that a daily 100-gram increase in all meat and red meat is associated with a significant increase by 12% to 17% in the risk of colorectal cancer. Also, a significant 49% increase is highlighted as a result of a daily 25-gram increase in processed meat.

In *study 2*, a meta-analysis was developed to assess the association between red meat and processed meat consumption and mortality incidence levels related to colon, rectal and colorectal cancer. The findings in this meta-analysis, involving approximately 8000 cases from 19 prospective studies, demonstrated consistent associations between high red meat and processed meat consumption levels and elevated risk for colorectal cancer. In this study, risks were calculated according to the anatomic regions, including the colon, rectum and colorectal junction. A stronger positive association was found with processed meat consumption for distal colon cancer than from proximal colon cancer. In addition, a dose-response meta-analysis was developed, in which it was estimated that the relative risk for colorectal cancer when red meat consumption increased by 120 grams/day corresponded

to 1.28 (95% CI: 1.18-1.39), without heterogeneity among the studies. The synthesis of the estimated relative risk for colorectal cancer when processed meat consumption increased by 30 grams/day corresponded to 1.09 (95% CI: 1.05-1.13), without heterogeneity among the studies.

In *study 3*, the authors developed a meta-analysis to verify meat consumption and risk for the development of colorectal cancer. The estimated risk associated with the consumption of 120 grams/day of red meat in comparison with no consumption corresponded to 1.24 (95% CI: 1.08 – 1.41). The results do not mean that red meat should be totally avoided, as part of a balanced diet. They do support existing recommendations to adopt a diet characterized by low levels of red and processed meat intake.

In *study 4*, a systematic review with meta-analysis was developed, focusing on epidemiological studies that related foods of animal origin with colorectal cancer risks. The results showed that the combined probability indices indicated a positive association between meat consumption and the risk of developing colorectal polyps, against a negative association with fish or chicken consumption.

Study 5 presents a randomized, multicenter controlled intervention research. The population was randomly selected and allocated to dietary counseling and received 300 grams/week of fatty fish (salmon in this case) and 300 grams/week of non-fatty fish (codfish). No support was found for the hypothesis that additional fish consumption for more than six months alters the number of mitoses and apoptosis of colon cells or the distribution of mitotic cells in the crypts. Besides, no clear difference was found between fatty and non-fatty fish.

In *study 6*, the authors conducted a meta-analysis of prospective cohort studies that assessed the association between fish or n-3 fatty acid consumption and colorectal cancer incidence or mortality. For the meta-analysis of the estimated risk of colorectal cancer, which compared the highest and lowest fish consumption category, 14 cohort studies were used. The analysis resulted in a relative risk of 0.88 (95% CI: 0.78-1.00) for the highest when compared with the lowest fish consumption category. For fish consumption and colorectal cancer mortality, the relative risk corresponded to 1.02 (95% CI: 0.90-1.16) when comparing the highest and lowest fish consumption category. The relative risk amounted to 0.91 (95% CI: 0.70-1.19) for the highest category when compared with the lowest n-3 fatty acid intake category. These study results indicate that fish consumption and possibly n-3 fatty acid intake inhibit colorectal carcinogenesis.

DISCUSSION

Meat consumption has been associated with colorectal cancer in epidemiological literature. The strength of this association and the type of meats involved are not consistent though. Few studies have assessed meat consumption or the relation between meat consumption and colorectal cancer risk in the long term[16].

In countless studies, the biochemical mechanisms and genetic models in which high red and processed meat consumption can enhance the risk of colorectal cancer have been discussed. These include the formation of carcinogenic agents from meat products, such as nitric components, heterocyclic amines and aromatic polycyclic hydrocarbons. This same effect was not observed in white meats like poultry and fish[17].

Red meat and heme iron supplement intake have demonstrated an increase in the fecal concentration of nitric compounds, many of which are powerful carcinogen agents. The positive association with processed meat consumption can be partially due to the nitric compounds already present in the meat. The nitric compounds are alkaline agents capable of reacting with the DNA of target tissues to alter their bases and, thus, can start carcinogenesis[18].

Nitric compounds are powerful carcinogen agents and also include nitrosamines, which need metabolic activation to be converted into a carcinogen form. Similarly, heterocyclic amines are classified as mutagenic and carcinogen. These and other compounds present in meat (salts, nitrates, iron, saturated fat, estradiol) indicate an increase in DNA synthesis and cell proliferation, similar to insulin growth factors, a hormone that affects the metabolism and causes damage to free radicals, besides producing heterocyclic amines that can enhance cancer development[19].

Meat cooked at high temperature also contains other powerful mutagenic and carcinogen agents, in the form of heterocyclic amines and aromatic polycyclic hydrocarbons. The cancer risk these substances impose on humans depends on the extent to which metabolic enzymes activate these components[18].

In this sense, heterocyclic amines demonstrated high mutagenic capacity and are developed on the surface of meat that is directly cooked in flames or at high temperatures. Heterocyclic amines require metabolic activation for the mutagenic function and genetic polymorphism for these enzymes shows interaction with meat consumption and modifies the risk of colorectal cancer[20].

Aromatic polycyclic hydrocarbons are formed when the incomplete combustion of organic material occurs (pyrolysis). The act of grilling meat directly in flames results in fatty juices and blood dripping into this hot fire, which in turn produces smoke that contains a large number of aromatic polycyclic hydrocarbons, such as benzopyrene, which will adhere to the food surface. Aromatic polycyclic hydrocarbons are mainly found in grilled, carbon grilled and smoked meats[18]. Depending on individual factors, total aromatic polycyclic hydrocarbon consumption can vary between 25 and 300 µg/day[21].

Exposure to aromatic polycyclic hydrocarbons and the metabolism of these compounds and their carcinogenicity have demonstrated that their reactive metabolites can also be formed in the colon. These compounds' enterohepatic circulation has been reported in various animal studies, but has not been informed in human studies. Benzopyrene exposure was found in the induction of various genotoxic effects in colon cells[21]. To be excreted, aromatic polycyclic hydrocarbons need to be metabolized and it is during this detoxification process that reactive metabolites are formed, which are capable of causing DNA damage[18].

In studies on the interaction between fish consumption (rich or poor in n-3 fatty acids) and colorectal carcinogenesis, a protective effect was evidenced, synthesized in the meta-analysis.

N-3 fatty acids display mechanisms that can modify the carcinogenesis process, which are: suppression of the biosynthesis of eicosanoids deriving from arachidonic acid, which results in alteration of the immunological response to the carcinogen cells and modulation of the inflammation; impact on cell proliferation, apoptosis, dissemination of metastases and angiogenesis; influence on the activity of the nuclear transition factor, on genic expression and signal transduction routes, leading to changes in cell metabolism, growth and differentiation; modification in estrogen metabolism, which causes less stimuli to hormone-dependent cell growth; increase or decrease in free radical production; and involvement in mechanisms directly related to insulin sensitivity and membrane fluidity[22].

The role of nursing in primary colorectal cancer prevention is characterized by actions that stimulate the adoption of healthy dietary habits and orientations, together with other team professionals, in a way that respects the individual's dietary culture. It should be highlighted that nurses, like other health professionals, become a behavioral model for the patients they attend. Therefore, they need to attempt to give an example and adopt the same habits they recommend[23].

The need and importance of setting up a nutritional surveillance program is appointed, directing health services towards active research on the dietary quality and nutritional status of their populations, without remaining restricted to service users only[24].

CONCLUSION

In sum, meta-analyses **1**, **2**, **3** and **4** found strong evidence when relating total red and processed meat consumption with increased risk for the development of polyps and colorectal tumors. **Studies 5** and **6** appointed a possible protective effect, instead of a risk factor, of fish and n-3 fatty acid consumption to inhibit colorectal carcinogenesis.

It should be emphasized that, in their recent meta-analyses, the researchers of **studies 1** and **2** found associations that indicate that red meat intake is associated with a 28 to 35% higher risk of colorectal cancer, while processed meat is associated with a 20 to 49% risk increase.

In line with the previous studies discussed in this integrative review, the authors found that red meat, processed meat and total meat consumption are risk factors for the development of polyps and colorectal cancer. No study was found that indicated chicken and fish intake as risk factors and the authors recommend replacing red by white meat.

Disagreement was found among the studies analyzed in these meta-analyses, as they did not address the definitions of meat, consumption and exposure time in a standardized way, thus limiting data collection and understanding when applying statistical methods.

As for the studies that assessed the consumption of fish rich in n-3 fatty acids and its influence on colorectal carcinogenesis, it is confirmed that n-3 fatty acids are important components present in cell membranes, with possible inflammatory effects, and inhibit the growth of multiple tumor cell types.

Nursing stands out as a primary colorectal cancer prevention agents, as nurses are capable of stimulating actions to adopt healthy dietary habits and promote nutritional orientations together with other health team professionals, through respect for each population's dietary beliefs and health education. To exert this responsibility, nursing is responsible for seeking greater support to found its interventions.

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