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ASSOCIATION OF CARCINOGENIC ACTIVITY AND OXIDATIVE STRESS: LITERATURE REVIEW

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Abstract: Introduction: Cancer is considered the main cause of a public health problem, evidenced by the high associated mortality, composed of somatic and genetic factors, associated with several mechanisms of action. It is essential to study the association of carcinogenic activity and oxidative stress through biochemical, immuno-genetic bases. **Objectives:** To carry out a literature review on the association of carcinogenic activity, oxidative stress, taking into account the activity of free radicals and antioxidant defense, associated literary review topics. **Conclusion:** This literature review positively impacts the elucidation of the topic addressed, through the dissemination of theoretical-scientific, medical oncology content.
Keywords: Cancer, Oxidative Stress, Free Radicals.

INTRODUCTION

Cancer disease is considered the main cause of public health problem, evidenced by the high associated mortality, which in this scenario surpassed cardiovascular diseases in Brazil and in the world. According to data from the National Cancer Institute (INCA) 7.6 million people on the planet die as a result of cancer, whose disease is composed of somatic (80%-90%) and genetic factors (10%-20%), associated with various mechanisms of action, proliferation, cell evasion, lymphatic invasion, angiogenesis, metastatic activity, among others (BRAY et al., 2018). Thus, it is essential to study this disease, as well as the association with reactive oxygen species, oxidative stress, corroborating biochemical and immunogenetic bases, fundamental data in the development and perpetuation of carcinogenic activity, as well as for greater dissemination of medical content. / specific oncology.

GOALS

The present work, in essence, aims to carry out a literature review about the association of carcinogenic activity, oxidative stress, taking into account the activity of free radicals and antioxidant defense, topics of associated literature review. In the course of this work, the authors present the main considerations on the presented theme, relating it to the current literary data.

LITERATURE REVIEW

FREE RADICALS

Organic and inorganic atoms or molecules that contain one or more unpaired electrons in the last valence shell are called free radicals (Halliwell, 1994). Highly unstable chemical species, with a short half-life and very reactive, act as mediators for the transfer of electrons in various biochemical reactions (BARBOSA et al., 2010).

Free radicals are classified as Reactive Oxygen Species (ROS) or Reactive Nitrogen Species (RNS) (BARBOSA et al, 2010). Intrinsically, associated with intercellular signaling, cell growth, energy synthesis and fundamental biological substances in our body. However, their excess is associated with several pathologies, thus also considered harmful to our health, and those responsible for combating their activity are designated as antioxidant agents, which can be produced by our body or absorbed through the diet (BARREIROS, DAVID and DAVID, 2006).

The generation of free radicals comes from oxygen metabolism. Since the mitochondrial activity performed in the electron transport chain is fundamental as it helps as a mediator in the transfer of electrons. Therefore, it is considered the main source that generates ROS, in addition, mitochondrial activity in correct functioning helps in the production of ATP energy, however, when there is an imbalance of such activity, the action of cytochrome oxidase is of great relevance since it helps in the control of ATP energy. generation of ROS through mitochondrial activity (BARBOSA et al., 2010).

Regarding free radicals, the superoxide, hydroxyl and peroxynitrite radicals stand out. The agent, hydrogen peroxide, even though it is not classified as a free radical, has significant importance since it is an oxygen metabolite, which has a reactive potential with the erythrocyte membrane, in addition to being active in the reaction, in the synthesis of hydroxyl radical (SCOTT et al., 1991; HEBBEL, 1986).

Superoxide radical, a radical classified as little reactive taking into account aqueous solutions. This radical originates after the first reduction in O2 and is produced during the maximum activation of neutrophils, phagocytes, monocytes, macrophages and eosinophils (HALLIWELL and GUTTERIDGE, 1990; BARBOSA et al., 2010). Hydroxyl radical, classified as the most reactive of the ROS. Such information is corroborated by the rapid binding between this radical and the other radicals or metals at the binding site itself. Since the hydroxyl has potential associated with the process of activation and inactivation of proteins, oxidation of fatty acids associated with lipoperoxidation (HALLIWELL and GUTTERIDGE, 1986). The peroxynitrite radical, recognized for having great oxidative potential, comes from the reaction between the superoxide radical and nitric oxide, acting mainly from the peroxidation of lipids (FERREIRA and MATSUBARA, 1997).

ANTIOXIDATIVE DEFENSE

Regarding antioxidant defense, the balance between oxide-reducing agents and the antioxidant defense mechanism in aerobic environments is fundamental. Since Glutathione is considered one of the agents with the greatest impact on defense activity, this agent is found in the cytosol and in the mitochondrial matrix region, it presents itself in two forms, reduced and oxidized (BARBOSA et al., 2010).

Regarding the cellular protective system, this can act in two ways, one front related to defense, the repair of injured damage represented by Glutathione reductase and ascorbic acid, among others and the other front related to detoxifying activity, represented mainly by Glutathione reduced, among others (BELLÓ and MARRONI, 2002).

OXIDATIVE STRESS

Oxidative stress comes from the imbalance between synthesis, production of oxidative compounds and the action of antioxidant defense agents. Since when the oxidizing agents are over expressed, that is, there will be a significant presence of Glutathione disulfide, evidenced by its production, for that there will be reduced Glutathione consumption, evidencing the failure of the protective system (HEBBEL, 1986; EATON, 1991).

Oxidative stress can be the cause of several diseases in the most varied human systems. In the central nervous system it helps in the development of Parkinson's disease and dementia, in the joints it helps in the process of arthritis, in the lung asthma, in the gastro-intestinal treatment, pancreatitis and hepatotoxicity, it acts by helping the atherosclerotic activity affecting vessels, in the enterocytes anemia and malaria. In addition, it acts in various activities such as inflammation, intoxication, aging, ischemia, radiation and in the development of cancerous disease (BARBOSA et al., 2010).

CARCINOGENIC ACTIVITY, ROS AND OXIDATIVE STRESS

ROS are associated with multiple genetic pathways, transduction, cell division, cell evasion, erroneous anti-proliferative signals, angiogenesis, among others, thus assisting in the initiation, propagation and progression of tumor activity, metastatic activity (HABAHAN et al., 2011).

Among the most varied oncological tumor subtypes, the most associated with the activity of reactive oxygen species, due to their levels of presentation, are melanoma skin cancer, breast, gastric, prostate and colon cancer. leukemias (REUTER et al., 2010).

The main pathways related to carcinogenic activity related to ROS are the protein kinase (PTKs), which has the potential to activate transcription factors, helping in processes related to cell proliferation, mitotic activity (DHILLON et al., 2007). Another associated pathway is phosphoinositide-3-kinase (PI3K), intrinsically related to the RAS gene, also associated with mutated ataxia-telangiectasia kinase, which proves to be vulnerable by the oxidative stress reaction, with the potential to activate p53, helping in the development of several tumor subtypes (TAKASHIMA and FALLER, 2013; MENENDEZ et al., 2011).

Epigenetic processes, such as DNA methylation intrinsically associated with a decrease in carcinogenic activity, are affected by ROS activity, since it has reduced activity, and certain sites, promoter areas affected by carcinogenic activity will tend to demethylation, altering gene transcription (JONES and LIANG, 2009).

Furthermore, there is evidence of association between environmental factors, such as infections by external pathogens, and carcinogenic activity. In relation to this process, human papilloma virus (HPV) and Hepatitis C (HCV) infections are very frequent and associated with the alteration of ROS processes (De Marco, 2013).

CONCLUSION

Therefore, the present literature review about the association of carcinogenic activity and oxidative stress has a positive impact on the dissemination of theoretical-scientific, medical/oncological content. Through elucidation of the topic addressed, helping to confirm the association between oxidative stress and carcinogenic activity, mainly evidenced by the activity associated with reactive oxygen species reported.

REFERENCES

1. BARBOSA, Kiriaque Barra Ferreira et al. Estresse oxidaivo: conceito, implicações e fatores modulatórios. **Rev. Nutr**. v.23, n.4, 2010.

2. BARREIROS, A. L. B. S.; DAVID, J. M. e DAVID, J. P. Estresse oxidativo: relação entre geração de espécies reativas e defesa do organismo. **Quím. Nova** v.29, n.1, 2006.

3. BELLÓ, A.; MARRONI, N. P. et al. **Dano Oxidativo e Regulação Biológica pelos Radicais Livres.** Porto Alegre. Editora Ulbra, 2002.

4. BRAY, F et al., Global câncer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancer in 185 contries. **CA Cancer J Clin.** V. 68, N.394- 424, 2018.

5. De Marco, F. "Oxidative stress and HPV carcinogenesis". **Viruses**, v.5, n 2, 2013.

6. DHILLON, A.S. *et al.* «MAP kinase signalling pathways in cancer". **Oncogene,** v. 26, n.22, 2007.

7. EATON JW. Catalases and peroxidases and glutathione and hydrogen peroxide: mysteries of the bestiary (editorial; comment). **J Lab Clin Med**, v.118, p.3-4, 1991.

8. FERREIRA, A. L. A e MATSUBARA, L. S. Radicais Livres: conceitos, doenças relacionadas, sistemas de defesa e estresse oxidativo. **Rev. Assoc. Med. Bras**. v.43, n.1, 1997.

9. HALLIWELL, B; GUTTERIDGE JMC. Role of free radicals and catalytic metal ions in human disease: an overview. **Methods Enzymol**. v. 186, n 1-85, 1990.

10. HALLIWELL, B; GUTTERIDGE JMC. Oxygen free radicals and iron in relation to biology and medicine: some problems and concepts. **Arch Biochem Biophys**. V.246, n. 501-14, 1986.

11. HANAHAN, D.; WEINBERG, R.A. "Hallmarks of cancer: the next generation". **Cell,** v. 144, n. 5, 2011.

12. Hebbel, RP. Erythrocyte antioxidants and membrane vulnerability. **J Lab Clin Med. V.** 107, n. 401-4, 1986.

13. ISTITUTO NACIONAL DE CÂNCER JOSÉ DE ALENCAR GOMES DA SILVA (INCA). **Estimativa 2020 Incidência de Câncer no Brasil**.v.1, n.1-122, 2020.

14. JUNIOR, L. R.; HOEHR, N. F.; VELLASCO, A. P. e KUBOTA, L. T. Sistema antioxidante envolvendo o ciclo metábolico da glutationa associado a métodos eletroanalíticos na avaliação do estresse oxidativo. **Quím. Nova**. v.24, n.1, 2001.

15. Jones, P.A.; Liang, G.. "Rethinking how DNA methylation patterns are maintained". **Nat Rev Genet**. v. 10, n 11, 2009.

16. Menendez, J.A. *et al.* "Metformin and the ATM DNA damage response (DDR): accelerating the onset of stress-induced senescence to boost protection against cancer". **Aging** (Albany NY). v. 3, n 11, 2011.

17. Reuter, S. *et al.* «Oxidative stress, inflammation, and cancer: how are they linked?. **Free Radic Biol Med**, v. 49, n 11, 2010.

18. SANTOS, F. A. A. e MAZO, G. Z. **Ativida Física e o estresse oxidativo no processo do envelhecimento.** 2006

19. SCOTT MD, LUBIN BH, Zuo L, KUYPERS FA. Erythrocyte defense against hydrogen peroxide: preeminent importance of catalase. **J Lab Clin Med**. v.118, n. 7-16, 1991.

20. TAKASHIMA, A.; FALLER, D.V.Targeting the RAS oncogene. **Expert Opin Ther Targets.** v. 17, n 5, 2013.