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Clinical Case Reports and Trails
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ISSN: 2836-2217 RESEARCH ARTICLE

Correlation of Bovine Dairy Igf-1 and the Neoplasia Development

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Received: 18 August 2022; **Accepted:** 31 August 2022; **Published:** 31 October 2022.

Citation: Jesus, V. A., Destefani, A. C., (2022). Correlation Of Bovine Dairy Igf-1 And the Neoplasia Development. Clinical Case Reports and Trails.1(1). DOI: 10.58489/2836-2217/004

Abstract

Cow's milk and its derivatives are among the most consumed foods in the world being part of the daily diet of several people. However, its consumption is linked to factors that were associated with neoplastic development, such as IGF-1. IGF-1 acts by stimulating growth effects on most cells of the body via the IGF1R receptor. In this context, this work aimed to investigate studies that correlate these variables: IGF-1, cow's milk, and neoplasias. The results showed that IGF-1 in cow's milk may increase serum IGF-1 levels in humans from milk consumption. Also, we have shown it that some supplements such as choline and casein do not alter the amount of IGF-1, but when the cow undergoes recombinant bovine somatotropin treatment, there is a significant increase in circulating IGF-1. However, further studies are needed to explain the cause-and-effect relationship noted in this study.

Keywords: IGF-1; milk; neoplasia; cancer

Introduction

Cow's milk and dairy products are of great nutritional importance as we consider them a biological source of protein, vitamins, and minerals. It is daily consumed by many people, but although milk and dairy products are common in most of the world, few studies assess the disadvantage of its use (MUNIZ; MADRUGA; ARAÚJO, 2013).

Much has been discussed the increase in type 1 insulin-like growth factor (IGF-1) through the consume of cow's milk since IGF-1 is considered one of the main factors in the increase of cell proliferation in carcinogenesis (FRYSTYK, 2004; IBRAHIM; YEE, 2004).

Cancer accounts for over 12% of the world's causes of death. A worldwide estimate for 2012 showed about 14.1 million new cancer cases and 8.2 million deaths. In Brazil, there are projections of occur 600 thousand cases for the period 2018-2019. This estimate includes the most common cancers in the country: prostate, lung, female breast, colon and rectum, and high rates for cervical, stomach and esophageal cancers (BORGES et al., 2017; (MENDONÇA; NORONHA; ALMEIDA, 2006).

The mechanism of lactation in dairy cows is identical to that of humans because it is a mammalian being. Breast development and growth are the main determinants of milk capacity and production in cattle, and the number of mammary alveolar cells influences milk production (MORAES, 2018).

Metabolic hormones, such as growth factors, and prolactin (PRL) are needed for normal mammary gland development with some special importance for mammalian sex steroid hormones. Besides, throughout pregnancy, the proliferate the mammary epithelium depends on estrogens and progesterone (SOUSA, 2015). Other hormones include growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The major hormones involved in the growth process are PRL and GH, classified in the somatotropin family. The GH is very important in the postnatal period and lipid, protein and mineral metabolism. All effects are mediated by IGF-1 and IGF-2. The GH increases the transport of amino acids in muscle cells, stimulated protein synthesis, induces RNA/DNA synthesis in tissues. Dairy cattle have more GH and less insulin than beef cattle, but the prolactin level is similar (GAONA, 2001).

The IGF system is of paramount importance in milk production. It binds to somatotropin receptors in the liver stimulating nutrient transport for milk synthesis. The IGF system includes IGF-I and IGF-II ligands, and their receptors (IGF Type 1 and 2, IGF-IR and IGF-IIR) (MARTINELLI JR; CUSTÓDIO; AGUIAR-OLIVEIRA, 2008)

IGF-1 circulates to major target organs such as cartilage and bones and thus acts endocrinology. Circulating IGF-1 also provides a feedback effect within the somatotropic axis through its suppression of pituitary GH release (LE ROITH et al., 2001). IGFs have immediate and long-term effects on various cellular activities, and cell proliferation, differentiation, migration and cell survival in the body. (MARSHMAN; STREULI, 2002).

IGF-1 is a straight-chain peptide containing 70 amino acids. For growth to be adequate, both circulating IGF, hepatic, and tissue-produced IGFs are critical. They produced in most organs and tissues of the body and secreted as it produces them and there is no storage organ. It stimulates them in response to GH with an important role in muscle growth and development and immune system function (MARTINELLI JR; CUSTÓDIO; AGUIAR-OLIVEIRA, 2008).

IGF-1 acts on the cell by binding to IGF1R. Its action mediated by the primary receptor within the cell because it is a transmembrane structure present in various cell types in different tissues. Connecting to IGF1R from within the cell, a receptor tyrosine kinase starts the intracellular signal. IGF-1 is one of the most potent endogenous activators of protein kinase B - a stimulant of cell growth and proliferation, and a potent inhibitor of programmed cell death (MAGALHÃES et al., 2012).

The structural similarity between IGF-IR and IGF-IIR allows hybrid receptors formed in cells expressing both receptors. These hybrid receptors have IGF affinity comparable to IGF-IR. The presence of IGF receptors in various cell types, associated with an expression of IGF genes in various tissues, allows IGF's endocrine actions (MARTINELLI JR; CUSTÓDIO; AGUIAR-OLIVEIRA, 2008).

In human fetal serum IGF-1 levels are low. There is a gradual slow rise in serum concentrations during childhood. During sexual maturation IGF-1 concentrations increase. Girls with gonadal dysgenesis do not show any increase in serum IGF-1 in adolescence, establishing an association of pubertal IGF-1 increase with sex steroid production (SPERLING, 2016).

IGF-1 acts by stimulating growth effects on most cells in the body, muscle cells, cartilage, bones, kidney, liver, skin, and lung, and regulating nerve cell growth and development and synthesis of cellular DNA. Thus, if we look at the concept of neoplasia, we can relate the increase in IGF-1 associated with its onset. There is strong evidence of an association between the progression of the neoplasm and increased expression of IGF-IR, in prostate cancer (CASTRO; GUERRA-JÚNIOR, 2005).

In this context, the present work addressed the concepts about IGF-1 and its increase through consuming cow's milk, aiming to test the data about its effects on the organism.

Material and Methods

Data collected by researching content that addressed dairy-associated cancer from 1999 to 2018, available in books, dissertations, theses and articles published in PubMed, Scielo, and Lilacs databases. We used the following descriptors: IGF-1, neoplasia, cancer, and milk. Inclusion criteria comprised books, original works, case reports, and bibliographic reviews and research without a basis on the proposed theme excluded.

Results and Discussion

After the bibliographic survey, all material read, and we selected the main information. They followed their descriptive analysis seeking to establish a better understanding and broaden the knowledge about the researched theme.

For this review, 42 articles found, we excluded of which 4 because they were duplicates and we excluded 28 because they had no alignment with the theme, leaving 5 articles. The following result from this research, by presenting the selection table of articles for the study.

The present work aimed, through literature review, to verify if there was a relationship between the consumer of cow's milk and cancer development, by a quantitative relation of IGF-1 in milk. Thus, several journal articles consulted to support this study for its development.

IGF-1 acts on the cell by binding to the IGFIR receptor. This receptor is a transmembrane structure present in various cell types in different tissues (MAGALHÃES et al., 2012).

According to Parodi (2005), justifying absorb IGF-1 from the intestine using breastfed rat models, there is a discussion about the increased amount of IGF-1 present in cow's milk or dairy products, and if when consumed, the intestinal absorption of IGF -1 occurs (PARODI, 2005). The Quin studies (2009) confirmed that in adult rats IGF-1 absorb by the gastrointestinal tract which may influence different tissue types (QIN; HE; XU, 2009). This finding corroborates the work conducted by Quin and colleagues (2008) who showed that cow's milk consumption induces a breast tumor process (related to the effect on IGF-1 triggered tissue) (QIN et al., 2008).

Norat et al. (2007) suggested that there is a direct association between cow's milk consumption and increased IGF-1 concentration and that when consumed increases the amount of serum IGF-1 in man. The same was a case-control study in a population of 2109 people. Comparison criteria were the age at enrolment, follow-up time, daytime of blood collection, and study center. It measured diet using validated questionnaires. Immunoenzymatically assays measured serum hormone concentrations. Linear regression explored the relationship between serum IGF-1, IGFBP-3 and nutrient, and in models adjusted for energy intake, age, body mass index, smoking, physical activity, center and laboratory lot. However, these authors also mention that the mechanisms of action of IGF-1 in cancer development are not explained, but associate IGF-1 with increased cell proliferation, inhibition of apoptosis in normal and neoplastic cells, and induction of tumor growth (NORAT et al., 2007).

Drug or supplement treatment that cows receive to stimulate increased milk production matters in understanding the increase in IGF-1. It may relate some supplements to altering the amount of circulating IGF-1 in cow's milk. A study by Pauletti et al. (2005) of 42 pregnant Dutch cows, assigned to two groups, compared the pre-partum serum fluctuation of IGF-1 against colostrum immunoglobulin G (IgG) (a first ejected milk) and milk secretions which quantified by the immunodiffusion method from treatment with 500g of recombinant bovine somatotropin. The findings of this study showed an increase in IGF-1 colostrum in cows submitted to somatotropin treatment. A post-extraction immunoradiometric assay quantified IGF-1 concentrations in serum, colostrum, and milk using the DSL-5600 kit. The authors suggested that the use of recombinant bovine somatotropin (used as a cow's milk production stimulant) increases circulating IGF-1 (PAULETTI et al., 2005). This finding corroborates the results of the study conducted by Um et al. (2017), which also showed that dairy product consumption can increase circulating IGF-1 levels. It measured this hormone using the solid phase sandwich enzyme immunoassay. Serum samples and recombinant human standards added to wells pre-coated with the human IGF-1 monoclonal antibody and incubated (UM et al., 2017).

Marín-Quiroga et al. (2015) reported positive associations of milk consumption with IGF-1 concentrations and related to the development of colorectal cancer. Also, the amount of IGF-1 concentration in 3 milk brands marketed in Durango, Mexico, was tested over 18 months. The analysis results revealed a positive exponential association of IGF-1 concentration (MARÍN-QUIROGA et al., 2015)

In contrast to previous findings, Aires et al. (2016) showed that dairy cows under choline supplementation did not increase circulating serum IGF-1 concentrations nor did they influence milk production. Pre and postpartum choline supplementation did not change the biochemical parameters of dairy cows. However, it observed a reduction in the number of cases of endometritis (AIRES et al., 2016). Also, Park and colleagues (2014), using casein as a supplement, showed a relationship between casein and prostate cancer, but the effect of supplementation did not alter circulating IGF-1 levels (PARK et al., 2014). However, the supplementation fed to dairy cows may be related to circulating IGF-1 concentrations in milk, as shown by the research by Pauletti et al. (2005) showing a significant increase in IGF-1 concentration from the administration of recombinant bovine somatotropin. However, the findings by Park et al. (2014) and Aires et al. (2016) found different results regarding casein and choline supplementation which did not affect the amount of circulating IGF-1

Conclusion

In this context, this work aims to contribute to a better understanding of IGF-1 found in cow's milk. Results showed that increased circulating IGF-1 in cow's milk may increase the serum IGF-1 level in humans from milk consumption. Besides, some types of supplementations such as choline and casein do not alter the amount of IGF-1, but when the cow undergoes treatment with recombinant bovine somatotropin, there is an increase in IGF-1 circulating in the cow’s colostrum. However, the relationship of IGF-1 with the development of neoplasms is not yet explained, so further work needed to explain the mechanisms between IGF-1 and neoplasms development

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