Basic study

Implication of milk and dairy products consumption through insulin-like growth factor-I in induction of breast cancer risk factors in women

Implication de la consommation de lait et des produits laitiers à travers le facteur de croissance analogue à l'insuline dans l'induction des facteurs de risque du cancer du sein chez les femmes

Djamil Maliou , Arezki Bitam *

Department of human nutrition, National High School of Agronomy, Belfort, El-Harrach, Algiers, Algeria

Abstract

Several studies have evaluated the link between diet and breast cancer in women. This link receives increasing attention from scientists, and many reports have examined the implication of milk and dairy products in the development this disease. Indeed, the available evidence shows that milk increases circulating levels of a mitogenic hormone: insulin-like growth factor-I (IGF-I), and this may affect breast cancer risk. However, epidemiological studies were unsuccessful to establish a strong relationship between this food and the disease. Many other studies measured the role of dairy products in the development of breast cancer risk factors, and our review tried to examine these associations. Our investigation suggests that milk increases appearance of greater adult-attained height, early menarche, delayed menopause and higher birth weight which are all considered as breast cancer risk factors and associated to higher levels of IGF-I. The relationship with adult weight and breast density is still not clear and inconsistent. Our hypothesis suggests that milk intake may influence breast cancer, through some breast cancer risk factors, and IGF-I has an important role in this relationship, but the association with other dairy products is less certain. That is why we suggest that women should consume dairy products other than milk to prevent breast cancer risk.
© 2015 Elsevier Masson SAS. All rights reserved.

Keywords: Breast cancer; Risk factor; Growth factor; Milk; Dairy product

Résumé

Plusieurs études ont évalué le lien entre l'alimentation et le cancer du sein chez la femme. Dans ce sens, de nombreux rapports ont évalué l'implication du lait et des produits laitiers dans le développement de cette maladie. Les preuves disponibles montrent que la consommation de lait augmente la concentration sérique d'une hormone mitogénique, le facteur de croissance analogue à l'insuline-I (IGF-I), qui peut affecter le risque de cancer du sein. Cependant, les études épidémiologiques n'ont pas réussi à établir une relation forte entre cette catégorie d'aliments et la maladie. Beaucoup d'autres études ont mesuré le rôle des produits laitiers dans le développement des facteurs de risque du cancer du sein, et nous avons tenté d'examiner cette association. Notre enquête suggère que le lait favorise l'apparition d'une plus grande taille chez l'adulte, rend l'apparition des règles plus précoce, favorise une ménopause tardive et un plus grand poids à la naissance, qui sont tous considérés comme des facteurs de risque du cancer du sein et associés à des niveaux plus élevés d'IGF-I. La relation avec le poids à l'âge adulte et la densité mammaire n'est pas claire. Notre hypothèse suggère que la consommation de lait peut influencer le cancer du sein, à travers certains de ses facteurs de risque, et l'IGF-I semble avoir un rôle important dans cette relation, mais l'association avec les autres produits laitiers est moins certaine. Nous suggérons que les femmes devraient consommer des produits laitiers autres que le lait pour éviter les facteurs de risque du cancer du sein.
© 2015 Elsevier Masson SAS. Tous droits réservés.

Mots clés : Cancer du sein ; Facteur de risque ; Facteur de croissance ; Lait ; Produit laitier

* Corresponding author.
E-mail address: a.bitam@ensa.dz (A. Bitam).

1. Introduction

Breast cancer is the second most commonly diagnosed cancer around the world with 1.67 million new cases in 2012, and represents the first diagnosed cancer in women [1]. The incidence of breast cancer has doubled between 1975 and 2000, and this may be attributable to increasing life expectancy and westernized lifestyle which includes several risk factors [2]. Cancer is considered to be highly affected by environmental factors [3], and the available evidence confirms that there is a direct relationship between unhealthy diet and lifestyle with the increase of cancer risk. It is estimated that 35% of risk factors are associated to diet and therefore cancer risk can be modified [4]. Concerning breast cancer, it was estimated that diet accounts for 50% of deaths from this disease [5].

A healthy diet may reduce breast cancer risk, but an unbalanced diet can increase it by different ways, like by impair hormonal balance. In cross-sectional analyses, a link between the IGF (insulin-like growth factor) axis and several components of diet was observed [6–8]. IGF-I (insulin-like growth factor-I) is the most important hormone of the IGF axis, and it is a well-established mitotic and anti-apoptotic peptide, which also affects mammary epithelial cells [9,10]. Interestingly, several studies found a positive association between high IGF-I (insulin-like growth factor-I) serum levels and the risk of prostate, colorectal and even breast cancer [11,12]. For example, in one clinical study the median of total IGF-I serum concentrations was lower in healthy women (160.7 ng/mL) compared to breast cancer patients (226.9 ng/mL, $P < 0.001$), but no differences observed in free IGF-I [13]. In contrast, one case-control study found higher levels of free but not total IGF-I in women with breast carcinoma [14]. Many epidemiological studies showed a significant association between breast cancer risk and IGF-I circulating levels [15–19]. Some of them confined this association in premenopausal women [17,18], and another in women after 50 years [19], which corresponds approximately to the postmenopausal women.

As mentioned before, diet can influence the IGF axis; and changes in eating habits can make a good alternative to prevent breast cancer [4]. Cross-sectional analyses found that IGF-I serum levels in adult men and women increase particularly with dairy protein consumption [6,7]. Same results were seen for milk, but not yoghurt and cheese [8]. Moreover, high milk consumption is associated with a 10–20% increasing circulating IGF-I levels among adults, and 20–30% in children [20,21], this is why we based on dairy products. The most likely theory underlying the increase of IGF-I after dairy proteins intake is the stimulation of endogenous production by the casein fraction of milk [22,23].

Paradoxically, the nutritional richness of milk is unquestionable, which contains high biological value proteins [24], and it is considered the only food that contains approximately all different substances known to be essential for human nutrition [25]. In addition, many reviews have investigated the link between milk, dairy products intake and breast cancer risk [26–28], but results were inconclusive and no clear association was proposed.

The aim of the present review is to summarize the link between the consumption of milk, dairy products and the breast risk factors induction through IGF-I without neglecting other components of this food, to assess the potential impact of this consumption of dairy on the risk of developing breast cancer in women.

2. Epidemiological evidence

Some cohorts did not support a relation between milk and dairy intake during childhood and adult breast cancer risk [29,30]. Increasingly, total dairy intake during adulthood and childhood was not associated with breast cancer risk in a prospective cohort study of 64,904 Norwegian women with a hazard rate ratio in the 4th quartile vs. 1st quartile of 1.10 (95% confidence interval: 0.64–1.86, $P = 0.91$) and 1.04 (95% confidence interval: 0.80–1.35, $P = 0.98$) for premenopausal and postmenopausal women, respectively [31]. But in the same cohort, white cheese has shown to be significantly protective against breast cancer risk particularly among premenopausal women with hazard rate ratio in the 4th quartile vs. 1st quartile 0.50 (95% CI: 0.29–0.87, $P = 0.02$) [31]. In the same way, one meta-analysis suggests that increased total dairy food, but not milk may be associated with reduced risk of breast cancer [32]. Furthermore, few cohorts studies found a reduction in breast cancer risk in postmenopausal and premenopausal women with a high dairy intake, and high intake of low-fat dairy products, respectively [33,34]. In addition, a Nurse Health Study (NHS) II nested case-control study found that consuming whole milk at age 3–5 y was associated with a significant decrease in adult breast cancer risk [35]. In contrast, an ecological study showed that milk was positively correlated to breast cancer incidence ($r = 0.817$, $P < 0.01$) [36], but some confounders like the predominance of risk factors in western countries may distort the correlation. A meta-analysis and a Norwegian prospective cohort supported that high fat milk had a positive association with breast cancer risk [37,38].

A recent Swedish cohort study found that high milk intake was associated with cancer mortality in women who consume ≥ 3 glasses milk/d 1.44 (95% CI: 1.23–1.69) compared to those consume < 1 glass milk/d [39]. In contrast, cheese and fermented dairy had shown an inverse relation with cancer mortality [40].

Currently, the epidemiological link between dairy intake and breast cancer risk is inconclusive and insufficient to determine a concrete association, and this was confirmed in other reviews [26–28]. However, dairy products other than milk and low in fat seem to be better to avoid breast cancer risk.

In sum, epidemiological studies provide very conflicting and inconclusive results, and it is for this reason that we tried to find the link between milk, dairy intake and breast cancer risk factors.

3. The link between dairy products intake and breast cancer risk factors

3.1. Overweight and obesity

Overweight women might be more likely to have breast cancer. Also, this association is not shown in all women. Postmenopausal women are more vulnerable, and many analyses