

Does milk with IGF-1 lead to an increased incidence of breast cancer in women?

A Research Study Proposal

April 18, 2008

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Abstract

Breast Cancer is the most common cancer among women in the United States. In the Western world there is an increased incidence often attributed to lifestyle. Researchers have begun to consider dietary factors and their contribution to increased incidence of breast cancer. This is because many foods today are treated to allow for mass production and economic benefit to the manufacturers. Dairy producers have been injecting growth hormones into cows resulting in increased production of insulin like growth factor 1 (IGF-1) in the milk. IGF-1 is responsible for increased cell proliferation and inhibition of apoptosis, thus has been linked to cancer. We believe that the IGF-1 in milk will result in an increased incidence of breast cancer in women. The study proposed includes 300 women aged 40-50 years old with no history of cancer. The women will belong to one of three groups based on their diet: regular dairy consumers, organic dairy consumers, and non-dairy consumers. Their IGF-1 levels will be measured and diets followed for one year. To determine cancer incidence mammograms and tumor markers will be measured at the beginning and end of the study. Logistic regression analysis will then be utilized to determine the correlation between cancer incidence and their IGF levels and milk diet. We expect to see a strong correlation between the incidence of breast cancer and IGF-1 among the women drinking milk from cows given growth hormone. This will provide further evidence of the dietary factors contributing to cancer incidence.

Introduction

Breast cancer is the most prevalent cancer among women. In the 1980's there was a dramatic increase in the incidence of breast cancer among women. Now close to 1 in 8 women will develop breast cancer at some point in their lives. Therefore, it is speculated that close to 40,000 women will die from breast cancer in 2008 alone.¹ Research suggests that 1 in 35 women will die from breast cancer. Age has shown to be a predominant factor considering the occurrence of breast cancer is eight times higher for women over 50 years old.² However, there is a significant variation in the prevalence of breast cancer based on geographic location. Evidence suggests that this disparity is not solely due to genetic differences and therefore dietary factors have become a rising concern.³

Our assertion is that the consumption of dairy products from cows treated with growth hormone is contributing to the increase in the incidence of breast cancer. There is a great deal of controversy over the administration of bovine growth hormone (bGH) to dairy cows and the subsequent consequences of consuming the products produced from these hormonally altered animals.³ Dairy cows are often given bovine growth hormone to stimulate milk production which invariably results in increased insulin-like growth factor I (IGF-I) levels in cow milk.³ Studies have shown that IGF-I is not destroyed by pasteurization or during digestion.³ Bovine IGF-I is naturally occurring in cow milk and is identical to human IGF-I, however it is substantially increased in hormonally treated cow milk.⁴

High plasma levels of IGF-I have been linked to an increased risk of tumor development. This is because IGF-I is responsible for cell proliferation and inhibition of apoptosis.³ IGF-I is a ligand for type I IGF receptor (IGF-IR) which is extensively expressed in human tissue. Animal studies have revealed that increased levels of IGF-I cause an over expression of IGF-IR.⁵ Binding of IGF-I to IGF-IR induces conformational changes which activate signal transduction cascades that promote cell proliferation, angiogenesis and increased cell motility.⁶

Premenopausal women with high IGF-I levels have been shown to have a two to three times higher risk of breast cancer than postmenopausal women.⁷ Therefore, our proposed study will attempt to correlate the dietary intake of dairy products and breast cancer occurrence in premenopausal women.

Hypotheses

Consumption of dairy products from cows given growth hormone will result in an increase incidence of breast cancer.

Study Design

Our study design follows the dietary intake of milk and breast cancer occurrence in premenopausal women. Following a preliminary evaluation, suitable candidates will participate in a one year study designed to correlate growth hormone consumption and breast cancer incidence. There will be three distinct groups: regular dairy consumers, organic dairy consumers and non-dairy consumers (vegans). The distinction is made based on the type of milk they consume.

1. **Initial Survey and Testing:** Each participant will be required to complete a general health survey and testing. The survey (Appendix A) includes preliminary information to assess patient risk factors for cancer as well as general medical history. Upon approval of the survey results the participant will then have initial testing to include: IGF-1 levels, Breast Cancer tumor markers, and a mammogram. The tumor markers and mammogram will be performed again in the 12th month. The tumor markers to be tested for are CA15-3 and CA 27.29. The selected tumor markers were chosen because of their specificity for breast cancer and they can be measured in the blood and do not require more invasive procedures such as biopsy. All sample collection and testing will occur at the Cancer Therapy and Research Center at the University of Texas Health Science Center at San Antonio (CTRC). This is so the mammogram and all other tests can be performed on site.

Significance: This survey will provide information and allow us to identify any factors that may affect our later statistical analysis as well identify any reasons to exclude a participant.

Monthly Testing: Participants will be required to come in and have blood drawn to measure their IGF levels. They must also complete a monthly Self Breast Examination and reports those results to us. At their initial meeting they will be showed how to properly perform this examination and provided written instructions to take home with them (Appendix B). If a participant reports atypical results of their self breast examination they will be referred to a doctor and tumor marker tests performed. They will then be given the option to continue in the study or stop their participation.

Significance: The measurement of the IGF-1 on a monthly basis will aid in the identification of trends as well as correlation with the participants dairy consumption. The self breast examination serves as an early indicator for breast cancer.

2. Dairy Products/Food Diary: Each participant at their monthly visit will receive a voucher to purchase the dairy products of their respective group. Their purchases will be limited to the brands and products readily available at their local grocery store and pre-approved by this research group. They will also be required to submit a monthly food diary. This will be available to submit online or when they return for their monthly visit.

Significance: The vouchers will decrease any cost to participants as well as control what products are being consumed and that they do coincide with the participants group. The food diary will allow us to determine any outlying factors in the participant diet that may contribute to our results as well as examine factors such as serving size for each product.

3. Statistical Analysis: In order to determine if there is any correlation between IGF-1 consumption and the occurrence of breast cancer, logistic regression analysis will be utilized. This will allow us to characterize the relationship of the incidence of breast cancer to each group and their IGF-1 levels. This analysis will be further explained in the results and interpretation section of this proposal.

Test groups/participants

1. Population: 300 women will be selected from the random population of the Bexar county area. To be included in the study the women must meet the following criteria: be between 40 to 50 years of age, and have no personal or family history of cancer. Another criterion will be their dairy consumption. Of the 300 participants, 100 will belong to one of three groups: regular dairy consumers, organic dairy consumers, and non-dairy consumers. This will be monitored by submission of the monthly food diaries and voucher distribution. The participants must also not be diabetics.
2. Risks: During their initial screen and visit patients will have no more than 20 mL of blood drawn. At the subsequent monthly visits no more than 10 mL of blood will be drawn. Blood will be collected through routine venipuncture. There is low risk to the patient.
3. Consent and Confidentiality Procedures: The purpose, risks, and procedures involved in participation in the study will be explained in detail to those who decide to enter the study. Informed consent will be obtained by the principal investigators and kept in a confidential place. All medical records and results will remain in secure computer files and file cabinets. Participant identity will remain anonymous by identifying them by numerical code.
4. Potential Benefits: The study provides testing that could be an early identifier for breast cancer for those who do not normally receive annual exams or testing.
5. Protection of Participants: Any woman with positive tumor markers or mammogram in the initial testing will be referred to an oncologist to perform any further testing and will be eliminated from the study so she can receive proper treatment if necessary. The same referral will be made for those who receive positive results in the final testing.

Expected Results & Interpretation

The values obtained from the monthly IGF will be utilized to visualize any trends in the patient IGF levels that may be attributed to their intake and will be associated with the food diary accordingly. We expect increased IGF-1 levels in the regular dairy consumers, normal levels in the organic dairy consumers, and normal to decreased levels of IGF-1 in the non-dairy consumers. To determine the correlation between milk consumption and breast cancer incidence logistic regression analysis will be performed. Logistic regression is a statistical analysis model used to predict the probability of an event occurring based on several variables of prediction.⁸ In the case of our study, the event would be the development of breast cancer as shown by a positive mammogram and tumor marker result. The predictor variables would be the woman's dairy consumption group and her IGF-1 levels.

$$f(z) = \frac{1}{1 + e^{-z}}$$

z represents the risk of the event occurrence based on the exposure to a set of risk factors.⁹

z is calculated by:

$$z = \beta_0 + \beta_1 x_1 + \beta_2 x_2$$

β_0 is the intercept...i.e. where the risk factor is zero

β_1 and β_2 are the regression coefficients of the x_1, x_2, x_3 , each standing for a risk factor¹⁰

Upon completion of data collection the analysis will be performed utilizing patient final mammogram and tumor marker results and mean IGF-1 level for the 12 months. Each group will be assessed independently of each other and the final results should reveal the correlation. From the analysis we expect the group of regular dairy consumers to show the highest incidence of breast cancer. We would also expect the organic dairy and non-dairy consumers to have decreased or no incidence. These results would then validate our hypothesis.

If the study is successful, the implications about the effects of milk on breast cancer incidence would be shown conclusively. This would open the door to future more extensive studies on this issue. A larger population of women in the Western world could be examined. It could also bring more attention to what is being done to food and where research may need to go in order to continue the fight against cancer.

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Appendix A

General Health Survey

Directions: Please fill out this form and answer all questions completely and as truthfully as possible.

General Information

Last Name _____ First Name _____ MI _____

Social Security # _____ Date of Birth (mm/dd/yyyy) _____

Marital Status Married Single Divorced # of Pregnancies _____ # of Children _____

Height _____ Weight _____

Ethnic Background Caucasian Hispanic African-American Asian/Pacific Islander Other Mixed

Residential Address _____

Name of Family Physician _____

Physician's Phone # (_____) _____

Physician's Address _____

In the event of an emergency, we may need to contact a family member or friend. Please provide the contact information we may need if such an event should occur.

Primary Contact

Name _____ Day Phone # (_____) _____
 Evening Phone # (_____) _____
 Cell Phone # (_____) _____

Secondary Contact

Name _____ Day Phone # (_____) _____
 Evening Phone # (_____) _____
 Cell Phone # (_____) _____

Appendix A cont'd

Questionnaire

Please answer these questions to the best of your ability. Place a in the appropriate box to answer the following questions:

- | | | Yes | No |
|-----|---|--------------------------|--------------------------|
| 1. | Are you a smoker? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, for how long? _____ | | |
| 2. | Do you chew tobacco? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, for how long? _____ | | |
| 3. | Do you drink alcohol? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, how much and how often per week? _____ | | |
| 4. | Have you started menopause? | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. | Are you pregnant? | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. | Are you trying to get pregnant? | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. | Are you on birth control pills? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, for how long? _____ | | |
| 8. | Are you on hormone replacement therapy? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, for how long? _____ | | |
| 9. | Are you on growth hormones? | <input type="checkbox"/> | <input type="checkbox"/> |
| 10. | Have you ever undergone radiation therapy? | <input type="checkbox"/> | <input type="checkbox"/> |
| 11. | Do you ingest dairy products? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, for how long? _____ | | |
| | b. If so, are they organic? | <input type="checkbox"/> | <input type="checkbox"/> |
| 12. | Do you exercise? | <input type="checkbox"/> | <input type="checkbox"/> |
| | a. If so, how often? (hrs/wk)_____ | | |
| 13. | Have you ever had a mammogram performed on you? | <input type="checkbox"/> | <input type="checkbox"/> |
| 14. | Have you ever had an abnormal mammogram result? | <input type="checkbox"/> | <input type="checkbox"/> |

Appendix A cont'd

15. Are you taking any antioxidant supplements? Yes No
16. Do you consider yourself a vegan (a person who does not eat any meat nor any food products that has come from an animal e.g. dairy milk)
17. Have you ever been diagnosed or suffered from any of the following: Yes No Don't know
- a. Cancer
 - i. If so, what type? _____
 - b. Type II Diabetes
 - c. Obesity
 - d. Dwarfism
 - e. Acromegaly
 - f. HIV/ AIDS
 - g. Hepatitis B or C
 - h. Active TB
 - i. Li-Fraumeni Syndrome
 - j. Cowden Syndrome
 - k. Bannayan-Riley-Ruvalcaba Syndrome
18. Do you have any family medical history of cancer? This includes immediate family and other relatives such as aunts, uncles, cousins, grandparents, etc. Yes No Don't know
19. Do you live near:
- a. chemical plant
 - b. nuclear plant
 - c. industrial waste dumping ground
 - d. an area that is known or rumored to cause cancer
20. Are you routinely exposed to UV light/radiation? (e.g. tanning booths, x-rays)

Appendix A cont'd

21. How many servings does your diet include of:
- | | 0 servings/day | 1-2 | 3-5 | >5 |
|------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| a. Fruits | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| b. Vegetables | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| c. Whole grains | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| d. Milk | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| e. Other Dairy | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| f. Processed Meats | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| g. Red Meat | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
-
22. Of the food categories listed in Question 21, do you always buy any of these as organic? . . .
- | | Yes | No |
|---|--------------------------|--------------------------|
| | <input type="checkbox"/> | <input type="checkbox"/> |
| a. If so, list the food category(s) from Question 21 that you buy as organic. _____ | | |
-
23. Do you consider yourself lactose-intolerant?
- | | Yes | No | Don't know |
|--|--------------------------|--------------------------|--------------------------|
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Appendix B

How to Examine Your Breasts for the Monthly Self-Breast Examinations*

This procedure for doing breast self-exam is different than previous procedure recommendations. These changes represent an extensive review of the medical literature and input from an expert advisory group. There is evidence that the woman's position (lying down), area felt, pattern of coverage of the breast, and use of different amounts of pressure increase the sensitivity of BSE as measured with silicone models.

>>For this study, perform this procedure monthly before coming in for your monthly general health screen/IGF-1 measurement. Please report your results during this general health screen or AS SOON AS POSSIBLE if you find anything abnormal. If you have any questions on how to perform this procedure, ask us and we will demonstrate the procedure for you.

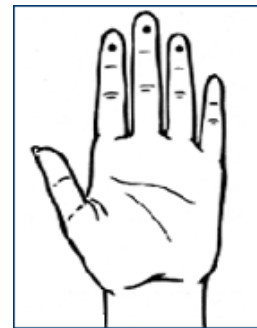
1. Lie down and place your right arm behind your head. The exam is done while down, and not standing up. This is when lying down the breast tissue evenly over the chest wall and it is as possible, making it much easier to all the breast tissue.



behind lying because spreads as thin feel

2. Use the finger pads of the three middle fingers on your left hand to feel for lumps in the right breast. Use overlapping dime-sized circular motions of the finger pads to feel the breast tissue.

3. Use 3 different levels of pressure to feel all the breast tissue. Light pressure is needed to feel the tissue closest to the skin; medium pressure to feel a little deeper; and firm pressure to feel the tissue closest to the chest and ribs. A firm ridge in the lower curve of each breast is normal. If you're not sure how hard to press, talk with your doctor or nurse. Use each pressure level to feel the breast tissue before moving on to the next spot.



middle

Appendix B cont'd

4. Move around the breast in an up and down pattern starting at an imaginary line drawn straight down your side from the underarm and moving across the breast to the middle of the chest bone. (sternum or breastbone). Be sure to check the entire breast area going down until you feel only ribs and up to the neck or collar bone (clavicle).

* There is some evidence to suggest that the up and down pattern (sometimes called the vertical pattern) is the most effective pattern for covering the entire breast without missing any breast tissue.

5. Repeat the exam on your left breast, using the finger pads of the right hand.

6. While standing in front of a mirror with your hands pressing firmly down on your hips, look at your breasts for any changes of size, shape, contour, dimpling, or redness or scaliness of the nipple or breast skin. (The pressing down on the hips position contracts the chest wall muscles and enhances any breast changes.)

7. Examine each underarm while sitting up or standing and with your arm only slightly raised so you can easily feel in this area. Raising your arm straight up tightens the tissue in this area and makes it difficult to examine

*This procedure was taken directly from the American Cancer Society website. All credit goes to them for providing this information, which was reproduced for the convenience of the patients in this study.

"How to Perform a Breast Self-Exam." Cancer Reference Information. 13 Sept. 2007. Online. Internet. American Cancer Society. 6 Apr. 2008 <http://www.cancer.org/docroot/CRI/content/CRI_2_6x_How_to_perform_a_breast_self_exam_5.asp>

