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Unpasteurized Milk Consumption and Subsequent Risk of Cancer

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Abstract

Concerns have been raised regarding the possible adverse health effects of consumption of unpasteurized milk and risk of cancer. We examined the association of self-reported intake of unpasteurized milk with subsequent risk of cancer in a large population-based cohort study. The Iowa Women's Health Study is a prospective cohort study of 55-69 year old women at baseline in 1986. Of the 41,836 women in the cohort at baseline, 22,808 cancer-free women completed the fourth follow-up questionnaire in 1997. Risk ratios (RR) and 95% confidence intervals (CI) were calculated using Cox proportional hazards regression analysis. Reported intake of unpasteurized milk was high: 59.2% consumed only as a child, 2.5% consumed only as an adult, and 16.5% consumed as a child and an adult. A total of 2,379 cancers were identified in the cohort at risk. Overall, the age-adjusted risk of cancer was lower among women who reported consumption of unpasteurized milk only as a child (RR = 0.90, 95% CI: 0.82-0.99) or as a child and an adult (RR = 0.85; 95% CI: 0.75-0.97). Adjustment for confounding factors attenuated these associations (RR = 0.92, 95% CI: 0.83-1.02 for consumption only as a child, and RR = 0.91; 95% CI: 0.79-1.04 for consumption as a child and an adult). These data suggest that consumption of unpasteurized milk does not increase risk of cancer.

Keywords

cohort; risk; virus; diet; adolescence

Introduction

There is a significant need to identify avoidable causes of cancer. Extensive research has been conducted on various aspects of diet, such as intakes of fat, meat, fruits and vegetables, and micronutrients. Dairy products in general and milk in particular, have also been examined in relation to cancer risk. Among women, consumption of milk may decrease risk of colorectal cancer (1) and cervical cancer (2), but have no effect on breast cancer e.g., (3)-4) or endometrial cancer (4). Results for lung cancer are quite mixed, with some studies suggesting risk reduction e.g., (5) or risk enhancement e.g., (6) that may vary by gender (7) or the histology of the tumor (8). A recent review on ovarian cancer concluded that consumption of low-fat milk is protective (9), but a pooled analysis of 12 cohort studies observed an elevated risk associated with increased lactose intake (10). An aspect of all these previous studies that does not appear to have been considered is whether or not the milk was pasteurized.

Milk from healthy cows contains relatively few bacteria (11), but contamination can occur when it is separated from the cow (12). Furthermore, according to the US Food and Drug

Administration (<http://www.fda.gov>) unhealthy cows can transmit a variety of bacterial and viral organisms, such as *Enterotoxigenic Staphylococcus aureus*, *Campylobacter jejuni*, *Salmonella*, *E. coli*, *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Brucella* species, and others. The Bovine leukemia virus (BLV) is a retrovirus similar to the human T-cell leukemia virus (HTLV) that commonly infects cattle. Most BLV infected animals develop a B-cell lymphoproliferative syndrome and 1 to 5% die with lymphosarcomas (13). One study found that 74% of humans tested had antibodies to BLV present in sera (14). Thus, there are concerns about the potential for unpasteurized milk to increase risk of cancer in humans, especially BLV.

Pasteurization is a thermal process widely used in the food and dairy industry to minimize health hazards from pathogenic microorganisms and to prolong product shelf life. Introduced commercially in the early 1900s, most milk is now pasteurized. Federal law prohibits transport of raw milk across state lines, but each state has their own regulations and many allow it to be sold. Raw milk sold through commercial channels for human consumption is currently illegal in all or part of 42 states. There is a consumer movement that seeks increased access to raw milk because of perceived health benefits of raw milk compared to pasteurized milk. It is believed that pasteurization destroys nutrients and enzymes and potentially destroys the protective bacteria along with the harmful pathogens and is associated with allergies, arthritis, and other diseases. In addition, research has demonstrated an increase in the levels of bioactive insulin-like growth factor (IGF-1) in the milk of cows hyperstimulated with the biosynthetic bovine growth hormone (rBGH) and further increased by pasteurization (15). Thus, although exposure to unpasteurized milk is less common today than it was at the midpoint of the last century, there are still many humans who were exposed earlier in their lives, especially if they resided on farms or rural areas. The current report sought to examine potential cancer risks associated with consumption of unpasteurized milk in the Iowa Women's Health Study.

Materials and Methods

Study population

The IWS is a prospective cohort study designed to identify risk factors for cancer and other chronic diseases in postmenopausal women (16). In January 1986, a questionnaire was mailed to 99,826 women who had been selected at random from a list of women ages 55-69 years holding a valid Iowa driver's license in 1985. The 41,836 respondents (42.7% response rate) form the cohort under study. Self-reported items included education, smoking habits, alcohol use, reproductive factors, medication use, anthropometric factors, and family history of cancer. Follow-up questionnaires were mailed in 1987, 1989, 1992, 1997 and 2005 to update vital status and current address and obtain selected exposure data. On the 4th follow-up (79% response rate for women alive at the time of the 1997 mailing), respondents were asked "How would you describe your lifetime consumption of unpasteurized milk?" with four options provided: never drank unpasteurized milk, drank it only as a child, drank it only as an adult, drank it as a child and as an adult. Deaths were ascertained by annual linkage to the Iowa death certificate database, supplemented by linkage to the National Death Index. The University of Minnesota human subjects review board approved this study.

Exclusions and cancer incidence

Prior to conducting analyses a set of exclusion criteria were applied. Women reporting at baseline previous cancers other than skin cancer or prior chemotherapy (n=3881), cancer between baseline and 1994 (n=4795), did not respond to the 4th follow-up survey due to death or non-response (n=16,563), or did not answer the question about unpasteurized milk consumption (n=466) were excluded from all analyses. The total cohort at risk for incident cancer in this analysis was 22,808 women (exclusions were not mutually exclusive). The following site-specific exclusions were also made, in addition to those described above: 164

women with mastectomies were excluded from the breast cancer analyses, 8191 women with hysterectomies were excluded from the uterine cancer analyses, and 6413 women with oophorectomies were excluded from the ovarian cancer analyses.

Incident cancer cases occurring from 1997 through 2003 were identified through the State Health Registry of Iowa, part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program (17). A match was performed annually between the list of cohort members and the records of Iowans with incident cancer in the registry. The match involves multiple stages of computer matching using Social Security numbers, drivers' license numbers, combinations of first, last, and maiden name; zip code; and birth date. Each possible match is confirmed visually.

Analyses

The length of follow-up for each individual in the study was calculated as the time from return of the 4th follow-up questionnaire until the date of first cancer diagnosis, date of move from Iowa, or date of death. If none of these events applied, the woman was assumed to be cancer-free and living in Iowa through December 31, 2003.

Data were descriptively summarized using frequencies and percents. Associations of unpasteurized consumption with demographic and clinical variables were assessed using chi-square tests of significances. We used Cox proportional hazards regression analysis to estimate relative risks (RRs) and 95% confidence intervals (CIs) for associations between unpasteurized milk consumption and cancer incidence. Survival was modeled as a function of age, since age is a better predictor of cancer risk in this cohort than length of follow-up time (18). Given the few women who reported consuming unpasteurized milk only as an adult, they were combined with women who reported consumption as a child and as adult, leaving three categories of our primary exposure variable: never consumed, consumed only as a child, and consumed as an adult with or without consumption as a child. Initial analyses accounted only for age, but subsequent models adjusted for potential confounding variables found to be associated with cancer risk in previous studies. The model to predict risk of all cancers combined adjusted for age, calories, physical activity, body mass index (BMI, weight in kilograms/height in meters, squared), smoking status (never, former, current), hormone replacement therapy (HRT), family history of breast cancer, residence on a farm, education, and history of diabetes. Separate models were then fit for specific cancers; breast, hematopoietic, lymphoma, uterine, ovarian, bronchus or lung, pancreatic, colon, rectum, upper digestive, proximal colon, distal colon, other cancers. To be consistent with the all cancer analyses, site-specific analyses were based only on cancer site at the first primary tumor. The variables that were adjusted for in each of those multivariate models were specific to that cancer, and may have included any of the following additional factors: education, height, parity/age at first birth, marital status, history of blood transfusions, age at menopause, family history of ovarian cancer, and screening mammography. The exact adjustment factors for each model are given as a footnote to table 2. All statistical tests were two-sided, and all analyses were carried out using the SAS (SAS Institute, Inc., Cary, NC) and Splus (Insightful, Inc., Seattle, WA) software systems.

Results

Among the cohort of 22,808 Iowa women included in this analysis, there were 2379 cases of cancer during the 138,800 person-years of follow-up. Most of the respondents reported having consumed unpasteurized milk at some point in their life; only 21.8% reported never use. The majority of those who did report consumption noted that it was only as a child (59.2%). Few (n=565, 2.5%) drank only as an adult and 16.5% drank as a child and adult.

Table 1 provides the distribution of cancer risk factors by self-reported intake of unpasteurized milk as a child and adult. Women who reported consumption of raw milk tended to be less educated, reside on a farm, less likely to smoke, have higher caloric intake, to be heavier, and be less likely to get a regular mammogram. For the remaining risk factors, there were either no differences or very small differences. There was no association with family history of breast cancer or age at menopause.

We also examined the association with several variables that are crude measures of immune status. Women who reported never consuming unpasteurized milk had a slightly lower prevalence of asthma and eczema, but a slightly higher prevalence of hay fever compared to groups that had exposure to raw milk in their lifetime.

Table 2 presents the overall associations between unpasteurized milk intake and risk of cancer overall and by site. When all cancers were considered together and after adjustment for age, the relative risk was decreased for women who consumed unpasteurized milk as a child (RR = 0.90; 95% CI: 0.82-0.99) or as an adult (RR = 0.85; 95% CI: 0.75-0.97). Adjustment for other cancer risk factors attenuated the association, and the results were no longer statistically significant. Further adjustment for asthma, hay fever, eczema and other allergies, in addition to the covariates listed in Table 2, had no appreciable effect on the point estimates (data not shown).

Given the etiologic heterogeneity of cancer, we were concerned that an analysis of all cancers combined may mask important findings. Therefore, we undertook additional analyses of 13 site-specific cancers with adjustment for risk factors more particular to that particular cancer (or group of cancers). As shown in Table 2, there was a strong inverse association of raw milk consumption as an adult with risk of rectal cancer. This finding remained after multivariate adjustment, but was based on only 5 cases. There were no other statistically significant global p-values. Inspection of the direction of the point estimates of effect reveals that 6 were inverse, 5 were null, and 2 were increased.

Discussion

We examined the hypothesis that risk of cancer was increased among women who reported a history of consumption of unpasteurized milk. This hypothesis was based upon the published evidence that certain oncogenic viruses can be transmitted from cows to human through milk. Our data provide no evidence to support this as a potential risk factor for cancer. If anything, women who report consumption of raw milk have decreased risk of cancer, although residual confounding or chance, are equally likely explanations.

To the best of our knowledge, no studies have previously investigated the risk of cancer associated with intake of unpasteurized milk. However, two studies have explored cancer risks of cancer among workers in abattoirs and meatpacking plants, given their potential exposure to BLV, human papilloma viruses, and certain chemical carcinogens. One study observed significantly increased risks of soft tissue sarcoma, malignant lymphoma, and acute myeloid leukemia in abattoir workers (19). An early mortality study of nearly 10,000 abattoir or meatpackers found excess risk of all cancer combined, particularly of the lung, buccal cavity and pharynx, esophagus, colon, bladder, kidney and bone (20). The absence of adjustment for critical confounders such as tobacco and alcohol makes interpretation difficult. Investigators in Korea sought to detect evidence for BLV infection in human cancer cells in 517 cases of leukemia and 162 cases of lung cancer; no tissues tested positive (21).

Similar to the studies reporting the poor biological activity of other hormones and pathogens in milk, it is possible that these oncogenic viruses, although can be transmitted from cows to human through milk, are not biologically active in humans. Additionally, the bovine

vaccination programs specifically targeting BLV and similar strains may offer protection to the bovine population from transmitting biologically significant amounts of intact pathogens to humans. The primary exposure of interest was correlated with a large number of cancer risk factors, some of which were correlated with increased risk of cancer (e.g., smoking and BMI), but others were correlated with decreased risk of cancer (e.g., high parity, residence on a farm). This makes it particularly difficult to tease out the effect of unpasteurized milk, if any, on the risk of cancer. We adjusted for many of these potential confounding variables in multivariate models, but it is possible that residual confounding remains.

Strengths of the current study include the prospective cohort design and collection of exposure information prior to diagnoses of cancer. Therefore, although we did rely on recall of unpasteurized milk intake that occurred fifty years or more in the past, there is no opportunity for differential recall by case status. The sample size is large and the number of cancer cases overall affords good statistical power. The availability of data on other cancer risk factors permitted adjustment for a large number of potential confounders.

Despite these strengths, there are limitations that should be considered in the interpretation of these findings. The assessment of exposure to unpasteurized milk did not discriminate between cows and goats, sheep or other mammals and ignored other dairy products made from milk, such as cheeses. We also did not have any direct measurement of contamination of milk or meat with bacterial and viral species that may be transmitted to humans. Thus, there may have been some misclassification of exposure. Finally, since the question on unpasteurized milk was not asked until the 1997 survey, there is some potential for a survivor or non-response bias. To address this possibility we compared the incidence of cancer among women who did (versus did not) answer the question on unpasteurized milk. Of the fourteen cancer outcomes listed in Table 2, there were no sites in which cancer risk was lower among responders (and therefore indicative of a healthy participant bias). There was evidence that women who responded to the question were significantly more likely to develop lymphoma (RR = 1.81; CI: 1.1 – 2.9), but this is consistent with the expected number of associations based on the number of comparisons performed. We conclude that there is no strong evidence for non-response bias.

In conclusion, our study found no compelling evidence that cancer risk is adversely affected by consumption of unpasteurized milk.

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Table 1
Relation between self-reported consumption of unpasteurized milk and selected cancer risk factors at the fourth follow-up survey of the Iowa Women's Health Study

Risk factor	Level	Unpasteurized milk consumption		p-value [/]
		Never drank	Drank as a child only	Drank as an adult
Level of Education	< high school	263 (5.3%)	972 (7.2%)	548 (12.7%)
	high school	2592 (52.1%)	6738 (50.6%)	2319 (53.7%)
Marital status	> high school	2118 (42.6%)	5764 (42.8%)	1451 (33.6%)
	Never	138 (2.8%)	297 (2.2%)	71 (1.6%)
	Current	3498 (70.3%)	9583 (71.1%)	3059 (70.8%)
	Sep/divorced	228 (4.6%)	492 (3.6%)	148 (3.4%)
Residence on a farm	Widow	1114 (22.4%)	3123 (23.1%)	1040 (24.1%)
	Yes	118 (2.4%)	518 (3.8%)	457 (10.6%)
	Never	2993 (60.4%)	9432 (70.1%)	3448 (80%)
Smoking status	Former	1570 (31.7%)	3213 (23.9%)	662 (15.4%)
	Current	396 (8%)	806 (6%)	201 (4.7%)
	Low	2181 (45.7%)	5907 (45.5%)	1913 (46.5%)
Physical activity	Moderate	1275 (26.7%)	3689 (28.4%)	1175 (28.6%)
	High	1316 (27.6%)	3393 (26.1%)	1026 (24.9%)
	Mean (S.D.)	1718.2 (650.1)	1789.9 (647.0)	1920.1 (848.6)
Total Calories	Mean (S.D.)	64.1 (2.41)	64.2 (2.46)	64.1 (2.51)
Height (inches)	Mean (S.D.)	26.8 (5.11)	27 (5.35)	27.8 (5.63)
BMI	Nulliparous	483 (10.1%)	1120 (8.6%)	268 (6.4%)
Parity/Age at first birth	1-2, <=20 yrs	317 (6.6%)	888 (6.8%)	300 (7.2%)
	1-2, >20 yrs	1299 (27.1%)	3258 (25%)	764 (18.2%)
	3+, <=20 yrs	882 (18.4%)	2703 (20.7%)	1170 (27.9%)
	3+, >20 yrs	1821 (37.9%)	5081 (38.9%)	1685 (40.2%)
Menopause age (years)	Quartile1	1454 (30.5%)	3796 (29.4%)	1221 (29.5%)
	Quartile2	1627 (34.2%)	4308 (33.3%)	1346 (32.5%)
	Quartile3	689 (14.5%)	2025 (15.7%)	654 (15.8%)
	Quartile4	992 (20.8%)	2804 (21.7%)	917 (22.2%)
Regular screening mammograms	Yes	3118 (67.7%)	8474 (67.4%)	2427 (61%)
	Family history of breast cancer	700 (14.8%)	2056 (15.9%)	610 (14.8%)
	Hormone therapy	2546 (51.1%)	6853 (50.8%)	2364 (54.7%)
	Never	1294 (26%)	3583 (26.5%)	1114 (25.8%)
History of blood transfusions	Former	1141 (22.9%)	3066 (22.7%)	847 (19.6%)
	Current	1473 (29.6%)	3900 (28.9%)	1316 (30.4%)
	Yes	502 (10.1%)	1242 (9.2%)	519 (12%)
	Diabetes mellitus	327 (6.6%)	947 (7.1%)	325 (7.6%)
Asthma	Yes	434 (8.8%)	971 (7.3%)	311 (7.3%)
	Hayfever	539 (10.9%)	1566 (11.7%)	469 (11%)
Eczema	Yes			
Values report as number (percent).				

[/] Chi-square test of significance

Table 2
Association of self-reported intake of unpasteurized milk with incidence of cancer among postmenopausal Iowa women, overall and by cancer site

Cancer site	Unpasteurized Milk intake	Person-years	Number of cancers	Age-adjusted Relative risk (CI)	Age-adjusted p-value	Covariate adjustment ⁴	Multivariate-adjusted Relative risk (CI)	Multivariate-adjusted p-value
All cancers	never	29996	557	1.00(Ref)	0.035	a-i, n	1.00(Ref)	0.24
	only as child	82598	1397	0.9(0.82,0.99)			0.92(0.83,1.02)	
	as adult	26207	425	0.85(0.75,0.97)			0.91(0.79,1.04)	
Breast ¹	never	29750	186	1.00(Ref)	0.075	a-k, n, q	1.00(Ref)	0.19
	only as child	82033	434	0.85(0.71,1.01)			0.86(0.71,1.03)	
	as adult	25995	128	0.79(0.63,0.99)			0.82(0.64,1.05)	
Hematopoietic	never	29996	30	1.00(Ref)	0.45	a-f, h, k	1.00(Ref)	0.35
	only as child	82598	68	0.81(0.52, 1.24)			0.79(0.51, 1.22)	
	as adult	26207	28	1.02(0.61,1.71)			1.05(0.61, 1.79)	
Lymphoma	never	29996	36	1.00(Ref)	0.18	a-f, h, l, m, n	1.00(Ref)	0.21
	only as child	82598	71	0.71(0.48,1.06)			0.73(0.49, 1.1)	
	as adult	26207	21	0.66(0.38, 1.13)			0.63(0.36,1.12)	
Uterine corpus ²	never	19687	24	1.00(Ref)	0.17	a-f, h, n	1.00(Ref)	0.43
	only as child	52929	71	1.1(0.69,1.75)			1.04(0.65,1.65)	
	as adult	16249	31	1.57(0.92,2.67)			1.36(0.78,2.36)	
Ovary ³	never	21447	17	1.00(Ref)	0.42	a-e, h, k, o, p	1.00(Ref)	0.58
	only as child	59278	33	0.7(0.39,1.25)			0.72(0.39,1.33)	
	as adult	18940	10	0.66(0.3,1.44)			0.8(0.35,1.81)	
Bronchus/lung	never	29996	56	1.00(Ref)	0.36	a-e, h, i	1.00(Ref)	0.78
	only as child	82598	137	0.89(0.65,1.21)			1.07(0.78,1.48)	
	as adult	26207	36	0.74(0.49,1.12)			1.17(0.75,1.82)	
Pancreatic	never	29996	13	1.00(Ref)	0.18	a-e, h, n	1.00(Ref)	0.10
	only as child	82598	59	1.63(0.89,2.97)			1.92(1. 3,67)	
	as adult	26207	13	1.20(0.52,2.41)			1.36(0.6,3.07)	
Colon	never	29996	65	1.00(Ref)	0.77	a-f, h, i, n	1.00(Ref)	0.68
	only as child	82598	199	1.08(0.81,1.43)			1.06(0.79,1.41)	
	as adult	26207	60	0.99(0.69,1.4)			0.93(0.64,1.34)	
Rectum	never	29996	22	1.00(Ref)	0.019	a-e, h, n	1.00(Ref)	0.02
	only as child	82598	40	0.66(0.39,1.11)			0.65(0.38,1.09)	
	as adult	26207	5	0.26(0.1,0.68)			0.26(0.1,0.69)	
Upper Digestive	never	29996	18	1.00(Ref)	0.43	a-e, h	1.00(Ref)	0.41
	only as child	82598	38	0.75(0.43,1.32)			0.82(0.46,1.45)	
	as adult	26207	10	0.61(0.28,1.33)			0.56(0.24,1.32)	
Proximal Colon	never	29996	50	1.00(Ref)	0.95	a-f, h, i, n	1.00(Ref)	0.92
	only as child	82598	146	1.02(0.74,1.41)			1(0.72,1.39)	
	as adult	26207	46	0.97(0.65,1.44)			0.93(0.61,1.41)	
Distal Colon	never	29996	15	1.00(Ref)	0.90	a-f, h, i, n	1.00(Ref)	0.73
	only as child	82598	46	1.1(0.61,1.97)			1.08(0.59,1.97)	
	as adult	26207	13	0.97(0.46,2.05)			0.83(0.37,1.83)	
Other Cancer Site	never	29996	89	1.00(Ref)	0.93	a-e, h, i	1.00(Ref)	0.86
	only as child	82598	240	0.96(0.75,1.22)			0.99(0.77,1.27)	
	as adult	26207	80	0.99(0.73,1.34)			1.06(0.77,1.46)	

Cox proportional hazards regression analysis.

¹Restricted to women who had not had a mastectomy .

²Restricted to women who had not had a hysterectomy

³ Restricted to women who had not had an oophorectomy

⁴ Results based on adjustment for these variables shown in next column.

Covariate adjustment: a, age (modeled as the time variable); b, caloric intake; c, physical activity; d, BMI; 3, smoking status; f, HRT; g, family history of breast cancer; h, farm resident status; I, educational status; j, height; k, parity/age at first birth; l, marital status; m, history of blood transfusions; n, diabetes mellitus; o, age at menopause; p, family history of ovarian cancer; q, screening mammogram.