Milk Fat and Gastrointestinal Illness

JAMES S. KOOPMAN, MD, MPH, VERNA JEAN TURKISK, DO, MPH, ARNOLD S. MONTO, MD, FRANCES E. THOMPSON, MPH, AND RICHARD E. ISAACSON, PHD

Abstract: The population of a pediatric practice was followed prospectively and determinants of acute gastrointestinal illness were evaluated in a nested age-matched case-control study. Children over age one taking low fat milk as their only milk source in the three weeks prior to illness had five times the risk of a doctor's visit for acute gastrointestinal illness as did children taking only whole milk during the same time period. This increased risk could not be explained by numerous potentially confounding variables or potential biases. There was no indication that the increased risk differed for rotavirus positive or rotavirus negative illness, or that it varied by children's age. (*Am J Public Health* 1984; 74:1371–1373.)

Introduction

One proposed means of reducing cardiovascular disease risk is to reduce the consumption of milk fat beginning very early in childhood.[1] The American Academy of Pediatrics has not agreed to such a strategy for children below the age of two years.[2] The potential of benefits, it was felt, did not outweigh the potential risk. Neither risks nor benefits have yet been quantified.

One potential risk of low fat milk consumption is that it contributes to a low fat diet, and associated chronic nonspecific diarrhea of childhood.[3,4] Another potential risk is the loss of antiviral properties in the lipid fraction of milk. Antiviral properties have been found in human milk lipid fractions[5] and presumably could be present in cow milk lipid fractions. Additionally, cow milk processing into formulas, which largely involves fat exchange, has been shown to result in the loss of an aqueous phase non-antibody related antiviral activity.[6] It is a reasonable hypothesis that defatting milk could do the same.

As part of a general study of risk factors for acute gastrointestinal illness, we assessed the relative risk of low fat milk consumption for acute gastrointestinal illness in children over age one in a private pediatric practice.

Materials and Methods

Study Design and Population

The private practice of one of the authors (VJT) provided the population base. The practice sees mostly lower and lower middle class patients from Ypsilanti, Michigan. A prospective, population-based, case control study was conducted from January 1980 to April 1981 with a vacation in May and June of 1980 due to personnel problems. Cases and matched controls came from cohort lists established in July 1979. Patients were placed on separate lists by birth month and by residence inside or outside of Ypsilanti. For birth months more than two years but less than four years previous to any specific time during the study, monthly lists were aggregated into quarterly lists. For birth months over four years prior to the study date, monthly lists were aggregated into yearly cohort lists. The lists were updated as patients came into or left the practice.

The cases in this study are all patients on the cohort list whose guardian telephoned or visited the practice regarding a gastrointestinal illness in the patient. Cases were not included in this study if the clinician found that there was no gastrointestinal illness, if the illness had begun more than 10 days before the office visit, if the illness was only vomiting explained by another condition, or if the patient was less than one year of age. The cases were seen free of charge and there were no refusals to participate in the study. Controls were matched to cases by birth date and geographic area through random number selection from the same cohort list containing the case. Controls were interviewed within a week of the case. Any patient who had had a gastrointestinal illness within the past two weeks was not accepted as a control. Controls included patients who at other times were cases. Less than 5 per cent of selected controls could not be contacted or refused to participate. When this occurred, a second control was drawn.

Both cases and controls were interviewed to ascertain: exposure to other cases inside or outside of the household, race, income, medical payment plan, pet exposures, number and ages of siblings, day care or school attendance by the patient or siblings, baby sitting arrangements, church attendance, breast-feeding and/or type of milk or formula feedings* in the three weeks before the onset of illness or interview. Cases were interviewed in the office and were contacted weekly by telephone to obtain further illness history. Controls were interviewed over the telephone.

Population denominators were determined in June 1980 as follows: stratified random sample of the parents of children over one year of age was selected in June 1980. The proportion of all illness care that the child received from the practice was determined by ascertaining the number of illness episodes attended in the practice or elsewhere. The number of patients multiplied by the percentage of acute illness care attended to by the practice gave the following effective population sizes: 149 children age one, 307 children age two through four, and 741 children age five to 16. Annual population rates of illness were determined from January 1979 to April 1980 with proportionate weighting so that each month contributes evenly to the annual rate.

Laboratory Methods

Stool or rectal swabs were collected in the office and transported to the University of Michigan daily. Rotavirus was detected by an indirect enzyme linked immunosorbant assay using goat antirotavirus serum as the capture antibody.[7] Results were confirmed by comparisons to controls

Address reprint requests to James S. Koopman, MD, MPH, Department of Epidemiology, School of Public Health, University of Michigan, 109 Observatory Street, Ann Arbor, MI 48109. This paper, submitted to the Journal February 13, 1984, was revised and accepted for publication June 28, 1984.

© 1984 American Journal of Public Health 0090-0036/84 $1.50

*Skimmed (0.5 per cent) or 2 per cent fat milks were recorded.

using pre-immune goat sera from the same animal. Beginning in January 1980, specimens were examined for a full range of bacterial pathogens including enterotoxigenic *E. coli* and colonization factor positive *E. coli*. The laboratory methods used are described in more detail elsewhere.[8]

Statistical Analyses

Associations of feeding type with gastrointestinal illness were assessed with matched pair odds ratios. Confidence intervals were calculated with reference to tables of the exact confidence limits of the binomial distribution as outlined by Fleiss.[9] Attributable risks were estimated as outlined by Schlesselman.[10] Confounding of the associations by all measured third variables together or separately was controlled by logistic regression of the discordant pairs.[11]

Results

Disease Frequency and Etiology

The estimated incidence in one year old children was 0.39 episodes of acute gastrointestinal illness per child-year. In two- to four-year old children, it was 0.17. In children over age five, it was 0.02. There were 131 case-control pairs over the age of one year who had the type of milk they were consuming specified. Fifty-seven were age one, 54 were two through four years of age, and 20 were five years or older. There were no bacterial pathogens isolated among cases in this study. Seventeen per cent of the one-year old cases had rotavirus identified in their stool; 15 per cent of the two- through four-year old cases were rotavirus positive; there were no rotavirus positive cases over the age of four.

Whole versus Low Fat Milk Analyses

Skimmed milk was distinguished from 2 per cent and 0.5 per cent fat milk. Only six cases and one control had skimmed or 0.5 per cent milk so these were combined with the 2 per cent milk under the heading of low fat milk. The detailed distribution of the 131 case-control pairs with regard to type of milk consumed is presented in Table 1. Twenty-six cases and six controls consumed low fat milk. The matched pairs odds ratio (which approximates the increase in gastrointestinal disease risk in low fat milk consumers over consumers of other milks) is 4.3 (26/6; 95 per cent CI = 1.7−12.3). Restricting the study to subjects exclusively on whole or low fat milk, the odds ratio is 5 (25/5; 95 per cent CI = 1.9−15.7).

The risk of low fat milk consumption was not confined to any age group. There were 14 discordant pairs in one-year olds (odds ratio of seven); 12 discordant pairs among two- to four-year olds (odds ratio of six); five discordant pairs among children age five and older (odds ratio of four).

The risk did not differ for rotaviral or non-rotaviral illness. All four rotavirus positive discordant pairs had the case on low fat milk. There were 27 discordant pairs where the case was rotavirus positive; in five of these, the case was on whole milk, and in 22, the case was on low fat milk. This gave an odds ratio of 4.4.

TABLE 1—Case-Control Pairs in Children Age One or Older by Type of Milk Consumption

	Cases				
Controls	Total	Whole Milk	Low fat Milk	Breast or Formula	Breast and Lowfat Milk
Total	131	89	26	15	1
Whole Milk	121	83	25	12	1
Low fat Milk	6	5	0	1	0
Formula	4	1	1	2	0

TABLE 2—Symptom Frequencies in Acute Gastrointestinal Illness Cases in Children over Age One by Type of Milk Consumed

Symptom	Exclusively Whole Milk	Exclusively Low Fat Milk
Total Number	89	26
	%	%
Diarrhea	93	93
Vomiting	58	61
Fever	52	61
Abdominal Pain	42	44
Mucus in Stool	35	30
Anorexia	58	68
More Than 5 Stools per Day	44	39
More Than 10 Stools per Day	14	13
Cough	51	43
Rhinorrhea	63	54
Average Duration	10 days	6 days

The symptoms of cases consuming whole or low fat milk are presented in Table 2. These data bear on possible case selection bias: if parents who give their children low fat milk contact the pediatrician for illnesses of less severity than the parents of children receiving whole milk, a case selection bias might be creating the association of illness with low fat milk consumption. There is no evidence to support this interpretation.

Because low fat milk consumption has been associated with chronic diarrhea, we evaluated the possibility that chronic, or recurrent cases account for the increased risk of low fat milk consumption. The average duration seen in Table 2 is not consistent with this possibility.

We had been recording cases in a prospective fashion for one year before the case-control study, and therefore could evaluate illness recurrence by milk consumption type. Sixty-three per cent of the low fat milk consuming cases and 44 per cent of the whole milk consuming cases were seen more than once during the course of the study. The average number of visits during the entire study for those cases consuming low fat milk was 2.0 and for those consuming whole milk was 1.8.

The risk factors for acute gastrointestinal illness identified in this study were used to control for confounding of the relation between low fat milk consumption and illness. The distribution of these factors in cases and in controls on whole or low fat milk is presented in Table 3; the lack of potential for confounding can be appreciated. In general, the children on low fat milk have fewer other risk factors. When the discordant pairs were controlled for the influence of these other factors, separately or together, the estimated odds ratios increased considerably over those presented earlier.

Attributable Risks

Using a relative risk estimate of five, we estimate that 14 per cent of the cases seen in the practice population over age one are attributable to low fat milk consumption. The rate of illness attributable to low fat milk consumption in low fat milk consumers is 1.2 episodes per year for one-year olds, 0.5 episodes per year for children ages two through four, and 0.06 episodes per year for children over the age of five.

TABLE 3—Selected Exposure Frequencies in Cases and Controls on Low Fat or Whole Milk

Exposure	Cases		Controls	
	Low Fat	Whole	Low Fat	Whole
Total Number	26	89	6	121
	%	%	%	%
Black Race	4	11	0	14
Medicare	13	32	0	20
<$10,000 income	15	42	0	24
Day Care Nursery	8	19	33	7
Baby Sitter	31	40	17	50

Discussion

There are no comparable data to ours that we could locate assessing the association between the consumption of low fat milk and acute gastrointestinal illness. There were data available for analyses, however, in the First National Health and Nutrition Examination Survey (NHANES) conducted from 1970 to 1974. A detailed description of the specific content and plan of operations of this study has been published.[12] This survey collected data only on children over age one. There were 2,652 children in the NHANES survey between the ages of one and six who drank some milk. The usual consumption of skimmed and whole milk in the past three months was ascertained in these children. Two per cent milk was used relatively infrequently at that time and was not ascertained. There were only 185 children in these ages who consumed predominantly skimmed milk. Only six of these had diarrhea at the time of the interview; five of the six were age one. The diarrhea prevalence in children age one who drank predominantly skimmed milk was 3.4 times the prevalence in those drinking predominantly whole milk. Thus the NHANES data demonstrate an association between low fat milk consumption and gastrointestinal illness similar to the association we observed.

We do not feel that the association we observed is artifactual. Confounding seems very unlikely to explain the association we observed because we controlled many potential confounders in our analysis. The symptom picture we observe is not consistent with a case selection bias. Recall bias seems quite unlikely for so easily obtained a datum as the type of milk a child is consuming in the past few weeks. The direction of a causal relation is not well established by this study as it is possible that children with a predisposition to acute gastrointestinal illness are put on low fat milk. This seems unlikely, however, because cases on low fat milk did not have more frequent prior illness than cases on whole milk.

Causal inferences about the associations we have observed should await demonstration of causal mechanisms or replication of the study findings in other populations. The estimation of a rate of disease of 1.2 episodes per year in one-year old children potentially attributable to the consumption of low fat milk demonstrates the importance of eventually making a judgment about causation. If the mechanism of this association is the lack of some anti-infective factor in low fat milk, then we might expect to see an even higher rate of illness attributable to low fat milk consumption in developing countries. The findings in this study should thus raise concern about the common practice of sending defatted milk from developed countries to developing countries where diarrhea is a severe problem.

REFERENCES

1. Mitchell S, Blount GS, Blumenthal S, Jesse MJ, Weidman WH: The pediatrician and atherosclerosis. Pediatrics 1972; 49:165–168.
2. Committee on Nutrition, American Academy of Pediatrics: Childhood diet and coronary heart disease. Pediatrics 1972; 49:305–307.
3. Cohen SA, Hendricks KM, Mathis RK, Laramee S, Walker WA: Chronic nonspecific diarrhea: dietary relationships. Pediatrics 1979; 64:402–407.
4. Cohen SA, Hendricks KM, Eastham EJ, Mathis RK, Walker A: Chronic nonspecific diarrhea. Am J Dis Child 1979; 133:490–492.
5. Falker WA, Diwan AR, Halstead SB: A lipid inhibitor of dengue virus in human colostrum and milk; with a note on the absence of dengue secretory antibody. Arch Virol 1975; 47:3–10.
6. Mathews TJH, Nair CDG, Lawrence MK, Tyrrell DAV: Antiviral activity in milk of possible chemical importance. Lancet 1976; 2:1387.
7. Kapikian AZ, Yolken RH, Greenberg HB, Wyatt RG, Kalica AR, Chanock RM, Hyan NK: Gastroenteritis viruses. *In:* Lennette EH, Schmidt NJ (eds): Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections. Washington, DC, American Public Health Association, 1979.
8. Monto AS, Koopman JS, Longini IM, Isaacson RE: The Tecumseh Study: XII. Enteric Agents in the Community, 1976–1981. J Infect Dis 1983; 148:284–291.
9. Fleiss JL: Statistical Methods for Rates and Proportions, 2nd Ed. New York: Wiley, 1982.
10. Schesselman JJ: Case Control studies: Design, Conduct, Analysis. New York: Oxford University Press, 1982.
11. Rosner B, Hennekens CH: Analytic methods in matched pair studies. Int J Epidemiol 1978; 7:367–372.
12. National Center for Health Statistics: Plan and Operation of the Health and Nutrition Examination Survey, United States 1971–1973. Vital and Health Statistics, Series 1, Numbers 10a and 10b, DHEW Pub. No. (HSM) 73-1310. Washington, DC: Health Services and Mental Health Administration, Govt Printing Office, 1973.

ACKNOWLEDGMENTS

The assistance of Kathy Hall in data collection and coding, Sujan Srivastava in data handling and analysis, and David Havorka in laboratory analysis is gratefully acknowledged. This work was supported in part by NIAID contract N01AI72536 and in part by a grant from the Thrasher Research Fund.