

Effect of cow milk on pulmonary function in atopic asthmatic patients

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Background: There is a perception by some asthmatic patients that stimulation of respiratory mucous production by cow milk may worsen airway obstruction.

Objective: To determine whether cow milk ingestion reduces bronchial airflow in asthmatic patients as measured by standard spirometry.

Methods: Twenty-five atopic adults with mild asthma but no history of cow milk allergy or lactose intolerance participated in a prospective, randomized, double-blind, placebo-controlled crossover study. Subjects were randomly assigned to ingest either a solution containing cow milk powder or a placebo solution, received neither during a 14-day washout period, then ingested the alternate solution. Forced vital capacity (FVC), forced expiratory volume in 1 second (s) (FEV₁), and FEV₁/FVC were measured at 30 minutes, 1 hour (h), and 7 hours after challenge. A $\geq 20\%$ decrease in FEV₁ or FEV₁/FVC was considered clinically significant.

Results: FEV₁ was slightly lower at 30 minutes than the baseline value (mean change, .6% to 3.3%) for both challenges. None of the subjects experienced any adverse symptoms, acute or delayed, after cow milk or placebo challenges. Statistically significant changes in FEV₁ were reached 30 minutes after cow milk challenge ($P = .0007$) and at one hour after placebo ($P = .0027$). These changes are not clinically significant.

Conclusion: Although this study disclosed no acute or delayed asthmatic symptoms or deterioration of pulmonary function detected by using conventional spirometry, methacholine inhalation before and after cow milk challenge may be more sensitive for evaluation of cow milk-induced bronchial hyperreactivity.

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INTRODUCTION

Many members of the lay public perceive that the ingestion of cow milk stimulates the production of respiratory mucus and therefore could worsen asthma symptoms. No data, however, support this concept.

Several investigators have evaluated the effect of cow milk ingestion on bronchial airflow and respiratory mucus production. Haas et al¹ showed that the forced expiratory volume in 1 second (s) (FEV₁) and forced expiratory

flow at 50% of vital capacity (V₅₀) did not change when ten healthy or 11 asthmatic subjects were openly challenged with whole cow milk, skim cow milk, or water. The pulmonary diffusion capacity (DLCO) progressively decreased in the three hours after patients were challenged with whole cow milk but not after challenge with skim cow milk or water. Pinnock et al² showed no statistically significant association between cow milk intake and symptoms of mucous production in healthy adults with rhinovirus infection. Pinnock and Arney³ surveyed 169 healthy adults who were given either cow milk or soymilk placebo; 70% of these adults believed that cow milk produced mucus. They³ concluded that no statistically significant difference existed in the perception of mucous production whether the subjects were given cow milk or a soymilk placebo.

We report a prospective, randomized, double-blind, placebo-controlled crossover study of 25 adult atopic patients with mild asthma but no history of cow milk allergy or lactose intolerance who received whole cow milk powder or a placebo mixed in a strawberry-flavored solvent (Mocha Mix).

This study examined whether the ingestion of cow milk would exacerbate airway obstruction in a group of adult patients with mild asthma but no history of cow milk allergy as measured by standard spirometry.

METHODS

The 25 adult patients with mild asthma who were recruited voluntarily in 1992 with a flier posted in the allergy department consisted of 18 women and 7 men ranging in age from 23 to 64 years (median age, 36 years). All subjects met the American Thoracic Society (ATS) criteria for asthma and had documented immunoglobulin E-mediated allergy to environmental inhalant allergens (positive skin-prick test results to mite, pollen, or both, with wheals 5 mm or more greater than those for the saline controls). They had no history of cow milk allergy or lactose intolerance, and their skin (1:20 prick and 500 PNU/mL intradermal) tests to cow milk were negative. All asthmatic patients were receiving inhaled beta agonists, or theophylline, or both. Spirometrically measured baseline FEV₁ was $\geq 80\%$ of that predicted before the study. Patients did not use inhaled steroids for at least 1 month before the study. The study protocol was approved by the Kaiser Permanente Medical Care Program, Northern California Region, Institutional Review Board, and informed consent was obtained from all subjects.

Subjects were reminded to refrain from consuming all dairy products five

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days before the study and discontinue use of inhaled bronchodilators or caffeine 4 h and theophylline 24 h before challenge. Each was asked to keep a diary of food and medication consumption which was checked on challenge days. They were randomly assigned to ingest solution A (10 g of whole cow-milk powder dissolved in 60 mL of strawberry-flavored Mocha Mix) or solution B, the placebo (60 mL of strawberry-flavored Mocha Mix). Mocha Mix ingredients were hydrogenated soybean oil, corn syrup, mono/diglyceride soy protein, β -carotene, polysorbate sodium, stearoyl lactylate (not a cow-milk derivative), and artificial strawberry flavor. The solutions were freshly prepared in the pharmacy. The code was not revealed to patient or physician until after the study. A 14-day washout period separated the challenges to prevent a crossover effect. Milk products again were discontinued 5 days before challenge.

On each challenge day, spirometry was done at baseline, 30 min, 1 h, and 7 h after challenge. Forced vital capacity (FVC), FEV₁, and FEV₁/FVC were measured using ATS criteria. A decrease in FEV₁ or FEV₁/FVC $\geq 20\%$ would be considered clinically significant.

The data were analyzed by using the repeated-measures linear regression method and the SAS procedure PROC MIXED (SAS Institute Inc, Cary, NC).⁴ In determining the statistical significance of comparisons, this technique accounts for correlation between measurements for the same person at different points in time. Outcome variables analyzed were FEV₁ and FEV₁/

Table 2. Mean Change in FEV₁ and FEV₁/FVC

Challenge Type	30 min		1 h		7 h	
	Change	%	Change	%	Change	%
Mean change in FEV ₁ , L						
Cow milk (challenge A)	-.09	3.3*	-.05	1.8	.04	1.8
Placebo (challenge B)	-.02	0.8	-.07	2.8*	-.01	0.6
Mean change in FEV ₁ /FVC, %						
Cow milk (challenge A)	-2.32	2.7*	-0.68	0.7	0.12	0.3
Placebo (challenge B)	-1.44	1.7	-1.44	1.7	-0.68	0.7

* Statistically significant change from baseline value.

FVC, and changes from baseline values after the two challenges were compared.

RESULTS

The baseline FEV₁ values (mean, standard deviation) were similar on cow milk and placebo challenge days (Table 1). None of the patients experienced any adverse symptoms, acute or delayed ($\geq 20\%$ decrease in FEV₁), to cow milk or placebo challenge.

No clinically significant (20%) decrease in FEV₁ or FEV₁/FVC occurred 30 minutes, 60 minutes, or seven hours after cow milk challenge (Table 2).

After both challenges, FEV₁ was slightly lower than the baseline value after 30 minutes, one hour, and seven hours. Mean change ranged from .6% to 3.3%. Statistical significance was reached at 30 minutes for cow milk challenge ($P = .0007$) and at one hour for placebo ($P = .0027$); no change was clinically significant. After cow milk challenge, FEV₁/FVC decreased by 2.7% after 30 minutes ($P = .0337$, not clinically significant) and gradually increased to the baseline value at seven hours. No associated clinical symptoms, that is, no rhinorrhea, no cough, and no bronchospasm were noted.

No evidence of acute or delayed reaction was found after cow milk challenge done as described.

DISCUSSION

Some asthmatic patients eliminate certain foods, especially cow milk, from the diet because they suspect that these foods intensify asthma symptoms. Whether immunologic or nonimmuno-

logic, wheezing as a reaction to food has been confirmed by double-blind, placebo-controlled food challenge in only 0% to 5.2%⁵ of patients with a history of food-induced respiratory symptoms.

This study examined whether cow milk ingestion may reduce bronchial airflow measured objectively by standard spirometry. Results of a prospective, randomized, double-blind, placebo-controlled crossover study of 25 adult atopic patients with mild asthma but no history of cow milk allergy (negative cow milk prick and intradermal skin test results) disclosed no correlation between cow milk intake and deterioration of pulmonary function test results (FEV₁, FEV₁/FVC).

These results are consistent with those of Bock,⁵ who studied 598 patients (including children age ≤ 19 years) and found that wheezing as the only manifestation of food reaction is rarely found in double-blind, placebo-controlled food challenge studies (5/1338 challenges, or .4%), even when food allergy is suspected on the basis of patient history. They⁵ were unable to show a delayed or late-phase asthmatic reaction or reduction in airflow after double-blind, placebo-controlled food challenge.

Novembre and his group⁶ found that asthma symptoms occurred in 8 of 140 asthmatic children (5.7% of patients) who received double-blind, placebo-controlled food challenge. The foods that most frequently produced reactions were cow milk, egg, and peanut.

In a double-blind, placebo-controlled food challenge study of 300 patients, Onorato et al⁷ found that cow

Table 1. Baseline Values for Each Challenge in a Double-Blind, Placebo-Controlled Study of Reaction to Cow Milk in NonCow-Milk-Sensitive Asthmatic Patients

	Cow milk (Challenge A)		Placebo (Challenge B)	
	Mean	SD	Mean	SD
FEV ₁ , L	2.86	(0.71)	2.85	(0.69)
FEV ₁ /FVC, %	81.4	(6.6)	81.8	(7.0)

milk was responsible for only one positive result.

Zwetchkenbaum et al⁸ investigated the role of food challenge in altering airway responsiveness by giving methacholine before and 24 hours after double-blind, placebo-controlled food challenge to 11 atopic asthmatics who had a history of food-induced asthma and had positive results of prick tests. They found no statistically significant difference between the number of patients who had changes in airway hyperresponsiveness after placebo ingestion and the number who had such change after food challenge.

In contrast, in a study of 323 children with atopic dermatitis and food allergy, James and his group⁹ provoked respiratory symptoms, including wheezing, in 17% of these patients receiving double-blind, placebo-controlled food challenge. Egg and cow milk were the main triggers; however, clinically significant bronchospasm (decrease in FEV₁ >20%) was rare, and no late phase asthmatic response was observed. In a series of 20 food-allergic subjects that included mostly older children with asthma and other allergy manifestations, asthma was reproduced by food challenge in two subjects only.¹⁰

In a more recent study, James et al¹¹ did spirometry and gave inhaled methacholine before and after double-blind, placebo-controlled food challenge of 26 asthmatic children with documented food hypersensitivity. Seven of 12 patients had chest symptoms and clinically significant increase in airway reactivity (twofold or greater decrease in the provocative dose of methacholine precipitating a 20% fall in FEV₁ during double-blind, placebo-controlled food challenge with egg (7/12), cow milk (2/12), wheat (1/12), and soy (1/12); however, none had a

clinically significant change in FEV₁ during challenge. James et al concluded that food-induced allergic reactions can increase airway hyperresponsiveness in a subset of patients with moderate to severe asthma and may do so without inducing acute asthmatic symptoms or spirometric changes.

In conclusion, this study did not show any acute or delayed asthmatic symptoms or deterioration of pulmonary function test (FEV₁, FEV₁/FVC) after cow milk intake in a group of atopic adult patients with mild asthma but no history of cow milk allergy. Conventional spirometry, however, may lack the sensitivity to detect subtle cow milk-induced pulmonary changes. Methacholine inhalation before and after double-blind, placebo-controlled cow-milk challenge may be more sensitive for evaluation of possible cow-milk-induced bronchial hyperresponsiveness.

The lack of late-phase asthmatic responses in all published studies suggests that food-induced pulmonary responses may activate mechanisms other than the classic immunoglobulin E-mediated allergic reaction.

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