Bovine milk intolerance in celiac disease is related to IgA reactivity to \( \alpha \)- and \( \beta \)-caseins

Francisco Cabrera-Chávez, M.Sc., and Ana María Calderón de la Barca, Ph.D.*

Centro de Investigación en Alimentación y Desarrollo, A. C., Carretera a La Victoria, Hermosillo, Sonora, Mexico

Manuscript received October 16, 2008; accepted January 9, 2009.

Abstract

Celiac disease is an autoimmune disease triggered mainly by ingestion of wheat gluten proteins. However, some other dietary proteins, such as those of cow’s milk, induce celiac disease-like symptoms in some patients with celiac disease. Different approaches have been done to detect the component responsible for this problem, including the possibility of gluten peptides present in cow’s milk. © 2009 Elsevier Inc. All rights reserved.

Keywords: Bovine caseins; Immunoglobulin A reactivity; Celiac disease

In a recent issue of Nutrition [1], intolerance to bovine milk of some patients with celiac disease (CD) was reported to not be due to the presence of epitopes from wheat gluten. In the excellent work by Dekking et al. [1], the investigators did not detect gluten proteins or peptides in bovine milk from cows fed diets containing large amounts of wheat. Thus, it was demonstrated that the symptoms seen in patients with CD after cow’s milk consumption are not related to gluten proteins in bovine milk coming from wheat-containing feed. In a previous study, bovine caseins were shown to induce an inflammatory response in the mucosa of patients with CD [2] and were recognized by their immunoglobulin A (IgA) antigliadin antibodies [3]. Therefore, epitopes from bovine casein could be responsible for triggering symptoms.

Currently, we are evaluating sera from patients with CD for IgA reactivity to dietary proteins including bovine caseins. For this purpose, sodium dodecylsulfate polyacrylamide gel electrophoresis of wheat gliadins and bovine caseins was performed [4]. Gels were stained with Coomassie blue or electrophoretically transferred to nitrocellulose membranes. After transfer, immunodetection of antigens on nitrocellulose membranes was carried out [5]. Membranes were incubated overnight with a sera pool from 14 patients diagnosed with CD, followed by incubation with rabbit anti-human IgA, and an extra incubation with alkaline phosphatase–conjugated goat anti-rabbit antibodies. Alkaline phosphatase activity was developed.

Figure 1 shows the gliadins (Fig. 1A, lane 2) and bovine caseins (Fig. 1B, lane 2) electrophoretic patterns and their respective immunodetections with serum IgA from patients with CD (lane 3 for gliadins in Fig. 1A and lane 3 for caseins in Fig. 1B). As expected, there was a clearly different electrophoretic mobility for the two protein types. In Figure 1A, lane 2, gliadins had a molecular weight from 40 to 66 kDa; in Figure 1B, lane 2, there was a mixture of \( \alpha \)-casein of 39 kDa, \( \kappa \)-casein of 30 kDa, and \( \beta \)-casein of approximately 28 kDa. The estimated molecular masses of bovine caseins were apparent because they moved abnormally on sodium dodecylsulfate polyacrylamide gel electrophoresis [6]. However, separation was excellent and identification was done by comparing with patterns of purified caseins. The immunodetection showed that CD IgA strongly recognized gliadin subunits from 38 to 58 kDa (Fig. 1A, lane 3) and \( \alpha \)- and \( \beta \)-caseins of approximately 39 and 28 kDa (Fig. 1B, lane 3), but not \( \kappa \)-casein near 30 kDa. The minority fraction of caseins, \( \kappa \)-casein, has the higher antigenicity for milk-intolerant individuals [7]. Therefore, the IgA immunoreactivity found against \( \alpha \)- and \( \beta \)-caseins is not attributable to antigenicity.

Previous studies [2,3] have demonstrated a reaction to caseins, although these were mixtures of \( \alpha \)-, \( \beta \)-, and \( \kappa \)-caseins and probably other milk proteins; however, a distinctive identification had not been done. It has been published that there is a high homology of some peptides in bovine \( \beta \)-casein to the gluten peptide, mainly with the amino acid...
sequence LQLQPFPQPQLPYPQPQLPYPQPQLPYPQPQPF [8]. Thus, the serum IgA response of patients with CD to bovine milk could be related to gliadins and caseins sharing epitopes recognized by antigliadin IgA antibodies, as previously proposed [3].

References