

Editorial

Goat Milk Allergenicity

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Cow's milk allergy is the most common food allergy among infants; some large clinical trials (1,2) have found a prevalence among infants under the age of 2 years of approximately 2%. It is normally outgrown by 6 years of age (3), although cow's milk allergy in teenagers and adults has also been described (4).

Milk from various mammalian species is used as an alternative to cow's milk in the preparation of hypoallergenic formulas and safe foods for allergic subjects. They are normally preferred to soy milk or hydrolyzed formulas by adult consumers because they cost less and taste better. Until now, however, there has been no significant clinical study examining the safety of this dietetic approach, although other scientific papers have shown that bovine milk substitutes could present problems. For this reason, the new results presented by Lara-Villoslada et al. (5) enrich the discussion on the use of goat's milk in cow's milk allergy.

There is evidence to suggest a lower allergenic potential of goat's milk compared with cow's milk. The true prevalence of this allergy is not known, but a few cases have been reported indicating immunoglobulin E-mediated sensitization and allergic reaction to goat's milk in children and adults who were tolerant of and not significantly sensitized to cow's milk. Thus, allergic reactions after ingestion of goat's milk or derivatives have been reported in a 25-year-old patient (6), in a 2-year-old girl (7), in a young adult male (8) and in 18 children (9), all of whom tolerated cow's milk and cheese. There are two main possible explanations: 1) goat's milk allergy is independent of cow's milk allergy and the goat's milk allergy is rare; 2) the two allergies are related and, as patients becoming allergic to cow's milk normally avoid any type of milk, the clinical cross-reactivity is underestimated.

Goat's milk is usually sold in health food stores or in supermarkets as a safe cow's milk substitute for people with lactose intolerance and cow's milk allergy. Most of the evidence of its efficacy is anecdotal. It has been

shown that goat's milk, which has virtually the same lactose content as cow's milk, has no special value in cases of lactose intolerance or galactosemia. Its value in treatment of allergy to cow's milk protein, adopted because of the potential immunologic differences between beta-lactoglobulins and alpha-caseins in the two mammalian species, is controversial. Indeed, immunologic differences between goat and cow beta-lactoglobulin or caseins have not been directly proved.

Positive evidence for goat's milk tolerance is reported in very few scientific papers; a clinical trial performed at Creteil, France, in the 1990s showed that 51 of 55 children with cow's milk allergy tolerated goat's milk for feeding periods ranging from 8 days to 1 year (10). On the other hand, several articles indicate that subjects allergic to cow's milk proteins do not tolerate goat's milk or sheep's milk either. Allergenicity of infant formulas based on goat's milk was studied in 26 Italian infants and children (aged 5 months to 7 years) who were allergic to cow's milk proteins. All subjects showed positive skin test responses to both cow's milk and goat's milk; in a double-blind, placebo-controlled food challenge, 26 of 26 children reacted to cow's milk and 24 of 26 reacted to goat's milk (11). However, the amount of goat's milk required to elicit a reaction after oral challenge was significantly higher for goat's milk (mean value, 38 mL) than for cow's milk (8 mL). The same clinical cross-reactivity was observed in adult allergic patients (12). Another group of children included in a study where the skin prick test, RAST and provocation test were performed showed 22 to be allergic to both milks and six allergic to cow's milk only (13).

The clinical observations in these studies correlate well with the pattern of cross-reactivity shown in *in vitro* tests. Immunoglobulin E cross-reactivity between milk proteins from different animal species has been shown by several independent studies using immunoblotting (14) or the enzyme allergosorbent test (15) on the sera from subjects with severe cow's milk allergy.

Taking all these findings together, one must conclude that only in certain cases may goat's milk be tolerated by subjects with cow's milk allergy, with the percentage of

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tolerant patients varying widely from 92.7% (10) down to 7.7% (11), and given the severity of allergic reactions sometimes observed after oral challenge with goat's milk—urticaria, respiratory symptoms, angioedema, vomiting and rash—it must be concluded that goat's milk must not be considered an appropriate replacement for infant/children with cow's milk allergy at present. Moreover, a recommendation must be made regarding the inclusion of warnings on packaging of goat's milk, and labels suggesting the use of goat's milk for intolerant/hypersensitive subjects should be banned.

This precautionary attitude towards goat's milk should not preclude the examination of why some subjects allergic to cow's milk can tolerate goat's milk. If the reasons for a lack of clinical cross-reactivity in a proportion of patients were known, new dietetic applications that would avoid dangerous practice could be devised for this milk.

In this context, certain studies in laboratory animals support a possible "hypoallergenicity" of goat's milk. Bevilacqua et al. (16) studied systemic and intestinal sensitization in 40 guinea pigs fed for 20 days with cow's milk proteins (CM) or goat's milk containing high (GM1) or low (GM2) amounts of alpha(s1)-casein. Guinea pigs fed on CM or GM1 developed high titers of anti-beta lactoglobulin immunoglobulin G1, with significant cross-reactivity between cow's and goat's lactoglobulins, whereas in guinea pigs fed GM2, anti-goat beta-lactoglobulin immunoglobulin G1 antibodies and the intestinal anaphylaxis (measured in vitro in Ussing chambers) were significantly lower than in the GM1 group. The authors suggested that the discrepancies observed in the use of goat's milk in cow's milk allergy could be attributable, at least in part, to the high genetic polymorphism of goat's milk proteins. However, it is not known how different quantities of alpha(s1)-casein can modulate the sensitization to beta-lactoglobulin, and current scientific data supporting an enhancement (in human beings) of the digestibility of other allergens resulting from the specific composition of goat's milk are weak.

More interesting data arise from the study of Lara-Villoslada et al. (5), in which Balb/c mice were sensitized intragastrically, using cow's or goat's milk as the first protein sources after breast feeding. After 6 weeks of sensitization, animals were challenged with the corresponding allergen (cow's milk or goat's milk) and the reactions were scored. Symptoms and biochemical parameters showed a general biochemical switch from allergenic to tolerogenic profiles.

Although the results obtained in this mouse model cannot be directly extrapolated to human immunologic

pathways, they seem to indicate that goat's milk may be less immunogenic than cow's milk when fed immediately after weaning. If the results are confirmed, clinical trials could be programmed to evaluate the suitability of goat's milk in artificial feeds for infants, particularly in the weaning of children at risk of atopy. Exaggerated enthusiasm for goat's milk should be tempered if dangerous adverse reactions are to be avoided, but this new evidence should stimulate new research into the treatment and prevention of cow's milk allergy.

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