Cow milk protein allergy and lactose intolerance

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Cow (also buffalo) milk protein allergy (CMPA) and Lactose Intolerance (LI) due to ingestion of milk are global issues. CMPA could be either immunoglobulin E (IgE)-mediated or non-IgE-mediated, while LI is a non-allergic response. CMPA affected infants immediately after milk ingestion, express the symptoms which include urticaria, angio-oedema, vomiting or an acute flare of atopic dermatitis. If such symptoms are observed, parents should always consult a pediatrician/nutritionist/physician. The IgE-mediated CMPA can be detected by skin prick test. Boiling the milk can partly overcome CMPA. The other option is an alternate diet, such as, soya milk and rice water. LI is not an allergy. The major symptoms of LI are abdominal bloating and cramps, borborygmus (gurgling noise in the intestine), diarrhoea, nausea and vomiting. LI is a major problem in Southeast Asia and responsible for low milk consumption in countries in this region. To overcome LI, milk can be consumed as curd or yogurt or other milk products or by taking proper dose of lactase along with milk.

Keywords: Borborygmus, bloating, cow's milk protein allergy, diarrhoea, lactase, lactose intolerance, nausea, rash, vomiting.

SKIN and gut problems due to milk consumption, especially cow milk consumption in infants and toddlers bother most parents worldwide. This is due to cow milk protein allergy (CMPA), which could be IgE-mediated or non-IgE-mediated. Symptoms are similar, but are acute and seen immediately after the consumption in the case of IgE-mediated CMPA[1]. Children above three years of age have gut disturbances due to indigestion of lactose (milk sugar) due to Lactose Intolerance (LI)[2] which is non-allergic. This paper intends to review the symptoms of IgE-mediated and non-IgE-mediated CMPA and LI, their spread and ways to overcome these problems associated with the consumption of milk.

Composition of milk

Milk is considered to be a complete food as it contains all four macro nutrients essential for human beings, namely, proteins, carbohydrates, fat and water. In general, milk contains 13–14% solids (proteins, carbohydrates, fats and minerals) and 86–87% water. Worldwide the most common milk is that of cows; however, in India buffalo, milk is produced and consumed in larger amounts. Buffalo milk is richer in fat and protein than cow milk[3,4]. Despite higher fat content, cholesterol in buffalo milk (~275 mg 100 g^{-1} fat) is lesser than that in cow milk (~330 mg 100 g^{-1} fat). Human milk is the sweetest of all the three milks. With regards to energy, cow milk gives ~66 kcal 100 g^{-1} and milk of buffalo gives ~110 kcal 100 g^{-1}. Milk is also a good source of minerals, which are essential for human beings, viz. calcium (Ca), phosphorus (P), sodium (Na), potassium (K), magnesium (Mg) and zinc (Zn). It is not a rich source of, but rather deficient in iron (Fe). Milk is not a major source of vitamins and in general, contains about 14 μg of vitamin A, 0.044 mg of thiamine (vitamin B1), 0.183 mg of riboflavin (vitamin B2), 0.45 mg vitamin B12 and traces of vitamin D and K 100 g^{-1} milk. Infants and children should therefore be supplied additional vitamins.

Milk proteins

Casein (~80%) and whey proteins (~20%) are the major proteins in milk. Casein is phosphate-conjugated and mainly consists of calcium phosphate-micelle complexes[5]. Casein is of four types: alpha- (α_{s1}- and α_{s2}-casein), beta-, gamma- and kappa-casein[6]. Whey protein is a collection of globular proteins wherein acidic, basic, hydrophobic and hydrophilic amino acids are distributed in a fairly balanced form[7]. Alpha-lactalbumin (α-LA) and beta-lactoglobulin (β-LG) are prominent whey proteins, which make up about 70–80% of total whey proteins. The other whey proteins that include immunoglobulins (IgE), serum albumin, lactoferrin (LF), lactoperoxidase (LP), and protease–peptones must be mentioned[8].

Cow and buffalo milk proteins are high-quality complete proteins containing all the nine essential amino acids, namely, histidine, lysine, leucine, isoleucine, methionine, phenylalanine, threonine, tryptophan and valine[9]. Milk proteins have several health benefits, because of their anticarcinogenic, immunomodulatory, antimicrobial, antihypertensive and hypocholesterolemic properties[10]. As compared to cow and buffalo milk, human milk is low in protein and fat, making it easily digestible to infants; it is also sweeter than bovine milk.

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It is recommended that children are breast fed for 4 months and preferably for 6 months after birth[11].

Allergy to milk proteins

Infants of age up to 2 years are more susceptible to milk protein allergy. The global estimate of the prevalence of cow milk protein allergy (CMPA) varies from 2% to 7.5%[12,13]. CMPA is also reported from India[14,15] and about 3% kids are estimated to be affected in India[16]. CMPA is the result of immunological reaction to one or more milk proteins[17]. The reason that distinguishes CMPA from other adverse reactions to cow milk, such as lactose intolerance is immunological[18]. CMPA may be immunoglobulin E (IgE)-mediated or non-IgE-mediated[19]. These early reactions usually manifest as urticaria, angio-oedema, vomiting or an acute flare of atopic dermatitis. Infants with early reaction will more likely test positive when subjected to skin prick test[20,21]. Major allergenic proteins in cow's milk are: α_{s1}-, α_{s2}-, β-, and κ-casein from casein and α-lactalbumin and β-lactoglobulin in whey. The incidence of CMPA decreases as the age advances; only 0.4% of the adults in USA showed allergy to milk proteins. Symptoms of IgE and non-IgE have many similarities, however, Wlash[22] have separated the two as follows:

(1) IgE-mediated CMPA: Skin: pruritis, erythema, acute utricaria, acute angioedema of lips and around the nose; Gastrointestinal: angioderma of the lips tongue and palate, oral puritis, nausea, colicky abdominal pain, vomiting, diarrhea; Respiratory symptoms: upper respiratory tract symptoms (nasal itching, sneezing, rhinorrhoea, or congestion, with or without conjunctivitis), Lower respiratory tract symptoms (cough, chest tightness, wheezing, or shortness of breath).

(2) Non-IgE-mediated CMPA: Skin: pruritis, erythema, atopic eczema; Gastro-oesophageal reflux disease: loose or frequent stools, blood and/or mucus in the stools, abdominal pain, infantile colic food refusal or aversion, constipation perianal redness, pallor and tiredness.

Since, there are quite a lot of overlapping symptoms in IgE-mediated and non-IgE, it is also a challenge to sort out between the two; skin prick test is the most common way to differentiate between the two.

Milk protein allergy could have rapid-onset (ranging from a few minutes to 2 h after intake) or delayed-onset (ranging up to 48 h or even 1 week after intake) depending on the mechanisms involved. Rapid allergy onset reactions are described as IgE-mediated, in which B cells, a subset of white blood cells, rapidly synthesize and secrete immunoglobulin E (IgE), a class of antibody which bind to antigens, i.e. the foreign proteins and negates their harmful effects.

Ways to overcome CMPA

(1) There is some evidence that if a nursing mother avoids allergens, it may reduce CMAP risk of the children born to her, but definite confirmation of this is lacking[23].
(2) Avoid milk and milk products.
(3) Soy formula is a common substitution to cow milk, but some of the infants with milk allergy may also have an allergic response to soy formula[24].
(4) Hydrolysed rice formula is another option, as are the amino acid–based formulas, which are more[25]. Rice water, obtained by boiling rice with water is used widely in several Southeast Asian countries, which do not have adequate milk supply, such as, Vietnam, Philippines, etc.
(5) Heating or boiling changes the protein structure[26] and it may reduce CMPA.

Lactose intolerance

A reduced capacity to digest lactose, the milk sugar, results in lactose intolerance. It is a major problem that keeps milk consumption by some people, as those in East Asia, very low. As a contrast to milk protein allergy (CMAP), LI starts after the weaning–off in infants and continues until adulthood[27,28]. CMPA is, sometimes, confused with lactose intolerance, but the two are very different. LI does not involve body's immune system. Although, the two exhibit similar signs and symptoms, such as stomach and gut problems, CMPA usually occurs in babies younger than one year but lactose intolerance is very rare in children below five years of age. LI causes symptoms only in the bowel, for example, abdominal pain, bloating, flatus and diarrhoea.

All infants produce lactase in amounts sufficient to digest lactose in mother's milk, but this capacity to produce disappears after they are weaned-off. Some human populations develop lactase persistence. In such individuals lactase production continues into adulthood. Most probably it is the natural response of the body to long-term association with farm animals. High rates of lactase persistence have been observed in the populations in Europe, India, Arabia and Africa. Bayless *et al.*[29] estimated that about 65% of the global population suffers from LI. Rates of lactose intolerance vary between regions, from less than 10% in Northern Europe to as high as 95% in parts of Asia and Africa. In India, a 1981 study showed that LI incidence was 66.6% in the subjects from two South Indian centres at Trivandrum and Pondicherry, whereas it was only 27.4% in the subjects from a North Indian centre at New Delhi[30]. However, in a recent study during 2015 at Sanjay Gandhi Post Graduate Institute of Medical Sciences at different centres in south and north India including Lucknow and Bengaluru it was discovered that over 74% people were lactose mal-absorbers[31]. Keeping in view the fact that most of such studies are conducted by health professionals who most of the times encounter those people who are at disease visiting health

centres, the likelihood of skewed samples cannot be ruled out and the estimate may not be a true reflection of the entire population.

But, one important thing that the above study confirmed and which cannot be ruled out is that the capacity to absorb milk decreases naturally with the advancement of age and in most people the problem shows up when they are in mid-30s. LI manifests in functional gastrointestinal problems like irritable bowel syndrome (IBS) and gastro-oesophagal reflux disease (GERD). While IBS is known to affect about 5% Indians, an estimated 8–20% people suffer from GERD. There is some relief from LI, because consumption of dairy foods containing lactose can promote a colonic bacteria adaptation, enhancing a favourable microbiome, which allows people with primary lactase deficiency to diminish their intolerance and to consume more dairy foods[32].

In the absence of lactase, lactose is not broken down and ingested. It passes on intact into the colon and there it ferments and produces copious amounts of gas. The gas, a mixture of hydrogen, carbon dioxide and methane causes various abdominal symptoms. The major symptom of lactose intolerance are abdominal bloating and cramps, borborygams (gurgling noise in the intestine), diarrhoea, nausea and vomiting. These symptoms appear within half an hour to two hours after consumption. Lactose mal absorption (LM) is currently diagnosed using lactose hydrogen breath and tolerance tests (LHBT, LTT). Ghoshal *et al.*[33] have suggested a 25 g dose of lactase for these tests in LM areas. Recommendation for avoiding LI has to be obtained from a pediatrician/nutritionist/physician.

Ways to overcome LI

(1) Avoiding milk and milk-products. (2) Taking milk and milk-products in smaller amounts and at wider spacing of time. (3) Taking milk and milk products with meals. (4) Curdling: While curdling the milk, lactose is changed to lactic acid by *Lactobacilli*[34] and LI is easily overcome. Curds and yogurts are therefore easily digestible and their use is one way of overcoming the reduction in milk consumption. (5) Use of enzyme lactase.

Conclusion

CMPA and LI occur widely in India, but people who suffer are not properly diagnosed. Parents with infants and toddlers showing CMPA symptoms, such as, skin rash, diarrhoea or vomiting must consult a pediatrician/nutritionist/physician and if possible shift to alternatives to cow milk, such as, rice water or soya products during the weaning phase. Women working as Aanganwadi sevikas should be educated about CMPA. As regards LI, the symptoms are bloating, barborygums, diarrhea, nausea, etc. Children, adolescents and adults should call for the use of curds, yogurts and lactase tablets as per the advice of a dietician/nutritionist.

Recommendation: There is an urgent need for creating awareness among people about cow/buffalo milk protein allergy and lactose intolerance. For CMPA, use of foods alternative to cow/buffalo milk, such as, rice water and soya products are suggested and parents are advised to consult a pediatrician/nutritionist/physician. For LI, use of curd/yogurt and lactase is suggested. It is also suggested that small amounts of milk and milk products be consumed at wider time intervals and if possible, with regular meals.

Relevance: The reluctance on the part of toddlers, children and adolescents is well known to parents, but they are unaware of CMPA and LI. This awareness has to be created both in rural and urban areas. Larger milk consumption is in the interest of a stronger body and good health.

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