



Research on A1 and A2 milk: A1 milk is not a matter of health concern

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ABSTRACT

Milk has special significance in Indian mythology, culture and diet. While milk has been considered as a complete food since ages, there are many lobbies, who have been discouraging consumption of milk citing health or cruelty reasons. This review article discusses about the latest controversy about the quality of milk produced by certain exotic breeds of cattle.

Key words: A1 milk, A2 milk, Cattle, Health

Distribution of cows producing A1 and A2 types of milk

Extensive worldwide surveys have revealed that A1 type beta-casein was found in milk of breeds of North European origin such as Friesian, Ayrshire, British Shorthorn and Holstein. A2 type milk was found in cows of Guernsey, Jersey and Channel Islands and Southern French breeds. Charolais and Limousin breeds in Europe and Zebu cattle in Africa and Asia were also producing A2 type milk (Ng-Kwi-Hang and Grosclaude 1992). Cows of Holstein Friesian and Jersey breeds had both A1 and A2 types all over the world, but a majority of the Jersey produced A2 type milk, while A2 type producing cows in Holstein were in lower proportion. The frequency of A1 and A2 type of cows were more area specific than breed-specific. While 50–65% HF cows in North America produce A1 type of milk, over 90% of HF cows in Germany produce A2 type of milk.

A1 type milk linked with diabetes Type 1 (DM-1)

In the 1990s, Elliott and McLachlan in New Zealand developed a hypothesis that the protein in the milk of some cows has a compound which is likely to cause diseases like Type 1 diabetes (DM-1) and coronary heart disease (CHD). Elliott (1992) observed that there was over a 10 fold difference in the incidence of Type 1 diabetes in Samoan children living in New Zealand and those living in Samoa, which was linked to the quantity of milk consumed by them. Samoan children who drank more milk, had higher incidences of DM type 1. He also observed that Masai children in Kenya rarely had Type 1 diabetes, although they consumed a large quantity of milk.

As is already known, cow milk contains around 3.4% protein, of which 30–35% is β -casein. There are 13 different allelic variants of B-casein (Farrell *et al.* 2004) and most A1 and A2 types are common genetic variants,

with a chain of 209 amino acids. A1 beta-casein contains histidine molecule in 67th position while A2 milk contains proline in that position. At the time of digestion in the smaller intestine, A1 type of milk releases a bioactive peptide known as beta-casomorphin-7 or BCM-7. This is an opioid, having an inhibitory effect on immune function and suspected to induce DM-1, CHD, infant death and autism (Elliott 1992). Several other research groups have also suggested that BCM-7 may be harmful. In series of experiments, 47% mice fed with A1 beta-casein suffered from diabetes. In 2003, Laugesen and Elliott reported a strong relationship between A1 beta-casein and DM-1 in 19 developed countries during the period 1990 and 1994. However, almost all the human feeding studies have reported that there was no trace of BCM-7 in adults, but a few studies reported the presence in the blood of infants (Wasilewska *et al.* 2011). These studies could not prove that BCM-7 was the cause of disease but observed aggravation in health status of the patients who were already suffering from diabetes. However, no clinical trials on human beings were carried out to study the effect of A1 beta-casein on patients of DM-1.

A1 milk and coronary Heart disease (CHD): McLachlan (1996) reported a correlation between national A1 β -casein consumption and mortality caused by CHD in 16 countries. Tailford *et al.* (2003) reported a rabbit experiment, where rabbits fed with 10% A1 β -casein for 6 weeks, showed larger areas of aortic fatty streaks than those which received A2 β -casein. Results of extensive studies on A1 β -casein and other dietary variables against DM-I and CHD were reported by Laugesen and Elliott (2003), where they concluded that A1 β -casein per capita supply in cow milk and cream was significantly and positively correlated with ischaemic heart disease (IHD), over a 20 year period in 20 affluent countries. However, Chin-Dusting *et al.* (2006) did not find any difference in mice fed with A1 or A2 β -casein.

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Venn *et al.* (2006) also did not find any significant difference on plasma cholesterol concentrations in human beings after consuming A1 or A2 type of dairy products.

Other effects of A1 Type beta-casein: Sun *et al.* (2003) reviewed the possibility of A1 type milk causing sudden infant death syndrome (SIDS), which is the most common cause of death in infants. They suspected that circulation of beta-CM in the infant's immature central nervous system might inhibit the respiratory centre in the brainstem leading to apnoea and death. Lucareli *et al.* (1995) indicated that drinking of cow's milk might worsen behavioural symptoms of autistic children. Reichelt and Knivsberg (2003) reported the presence of opioid peptides derived from food proteins in the urine of autistic patients. However, Hunter *et al.* (2003) and Cass *et al.* (2008) did not find any opioid peptides in the urine of children with autism.

Debate on A1 and A2 milk

In 2005, Prof. Truswell, reviewed the research on A1 type milk and reported that for both DM-1 and CHD, the correlation between different countries and consumers of different types of milk was unreliable and was negated when data from more countries were included. In Switzerland, DM-1 had increased three times since 1990 without any increase in milk consumption, as observed by Crawford *et al.* (2003). The animal experiments with diabetes prone mice, which supported this hypothesis, were not confirmed by multicentre experiments, and single animal experiment supporting A1 beta-casein and CHD was very small with faulty design. He further stressed that release of BCM-7 has not been demonstrated in human beings. Hence, he reported that there was no convincing evidence to link A1 beta-casein consumption with DM-1. Mortality caused by CHD had significantly decreased in USA, Australia and Switzerland without any reduction in milk and cheese consumption. Hence, the available evidence was not convincing to prove that A1 type milk consumption was the cause of CHD. This was also supported by the study conducted by Elwood and others (2004).

In 2007, the book, 'Devil in the Milk', linking A1 β -casein intake with Type 1 diabetes, frightened milk consumers and gave a boost to the sale of A2 milk in New Zealand and Australia. The book had referred to over 100 scientific papers on the adverse effects of A1 milk and elaborated on how BCM-7 gets into the blood stream, when released in the gut, particularly of those who suffer from leaky gut syndrome. It further argued that in a similar way, BCM-7 can enter the blood stream of infants. BCM-7 was also linked with symptoms of autism and schizophrenia (Woodford 2007).

Scientific review of research on A1 milk by the European Food Safety Authorities

In 2008, the New Zealand Food Safety Authority engaged the European Food Safety Authority (EFSA) to conduct a scientific review and address consumer concerns on A1 milk. The EFSA's report in 2009 declared that no

cause and effect relationship could be established between the dietary intake of BCM-7 and various diseases.

According to the report, very little was known about the mechanisms of transfer of intact peptides longer than 3 amino acids across the intestinal barrier. Even if this happened, the transfer was very low, through passive diffusion. The presence of intact β -casomorphin molecules in blood after intake of milk or casein was not established in any of the *in vivo* studies conducted so far. Asopioid peptides, including β -casomorphin 4, -5 and -7 are highly sensitive to hydrolysis by dipeptidyl peptidase IV, transfer of these peptides in an intact form across the intestinal mucosa and the blood-brain barrier was not likely. Although the food-derived peptides pass through human intestinal mucosa, no quantitative data was available for proving it except in the case of di- and tri-peptides with reported antihypertensive properties. Food-derived peptides, including casomorphins can have different effects on the intestinal lumen and the intestinal mucosa, such as regulatory effects on gastro-intestinal motility and on gastric and pancreatic secretions. Although many studies suggested the effects of β -casomorphins on the central nervous system (CNS) following i.p. or i.c.v. administration in animals, and a possible link between BCM-7 intake and sudden infant death syndrome (SIDS), no clear evidence for such a relationship was found by the reviewing team. The data did not support the link between casein-derived peptides and autism in subjects with increased intestinal permeability.

Although some studies, particularly in rabbits had suggested that BCM-7 might be atherogenic, the validity of the model for human beings was not convincing. Subsequently, many *in vitro* studies indicated that many food derived peptides/hydrolysates display antioxidant activity. The speculations of BCM-7 intake to cause cardiovascular disease (CVD) was based on ecological studies, which did not account for several confounding factors. Subsequent large cohort studies led to opposite conclusions. Human intervention studies comparing diets containing β -casein A1 and A2, did not show any correlation between the estimated β -casein A1 consumption and development of certain biomarkers for CVD. Thus the review team did not find strong evidence for a link between the consumption of β -casein A1 and increased risk for CVD in human beings. There were no clear evidence to link BCM-7 intake with SIDS and casein-derived peptides with autism. Although some ecological studies have linked the intake of BCM-7 with IDDM, these studies were unable to establish a cause-effect relationship. Thus the report concluded that oral intake of BCM-7 or related peptides will not cause any non-communicable diseases contrary to that reported by earlier studies. Accordingly, no formal EFSA risk assessment of food-derived peptides was recommended (EFSA 2009).

This report was accepted by the Food Safety Authorities in New Zealand, Australia and other countries, and brought relief to the consumers of regular milk at large. The report

also nullified most of the fear created by the book 'Devil in the Milk' and other reports.

Studies on A1 milk after 2009

After the Report of EFSA in 2009, the researchers who had all along warned about the health hazards of consuming A1 type milk, accepted the fact that there was no threat of DM-1, coronary heart diseases, autism and schizophrenia. However, as the report had accepted that some gastronomical changes could take place in certain people, the focus was shifted to the studies related to digestive disorders caused by A1 milk, particularly among those who were intolerant to milk.

Beta-casomorphine-7 association with gastrointestinal discomforts: Ho *et al.* (2014), reported that A1 milk had led to significantly higher stool consistency compared to A2 milk and a positive association existed between abdominal pain and stool consistency. According to them, after consuming milk or milk products, the digestive enzymes in the gut react with A1 beta-casein to release bioactive opioid peptide BCM-7, while A2 beta-casein releases much less BCM-7, under normal gut conditions. They observed that although these preliminary results suggested differences in gastrointestinal responses in some adult persons consuming milk containing either A1 or A2 beta-casein type, further confirmation was needed through a larger study of participants with perceived intolerance to ordinary A1 beta-casein-containing milk. In another study restricted to persons who had discomfort after milk consumption, sponsored by A2 Corporation, Deth *et al* (2016) reported that consumption of A2 milk was associated with a greater increase in plasma glutathione concentrations compared to the consumption of milk containing both β -casein types, and it did not increase plasma BCM-7 concentrations. They claimed that milk containing A2 β -casein has the potential to promote production of antioxidant glutathione in human beings.

Ul Haq *et al.* (2014) reported that mice fed on A1 milk had increased inflammatory responses as compared to A2 milk fed mice. Another study, sponsored by A2 Corporation, was conducted by Jianqin *et al.* (2016) on human beings, covering both males and females in the age group of 25 to 68 years, as being irregular milk consumers and who had reported intolerance to regular milk, now experiencing mild to moderate digestive discomfort after milk consumption. The study indicated that consumption of milk containing A1 β -casein, worsened gastrointestinal symptoms, increased gastrointestinal transit time, increased serum inflammation markers, lowered total fecal SCFA content, slowed cognitive processing speed and decreased processing accuracy compared to the baseline values. Consumption of milk containing only A2 β -casein had no adverse effects. In another study supported by A2 Corporation, He *et al.* (2017) also reported that consumption of milk containing A2 β -casein reduced acute gastrointestinal symptoms, in Chinese people, who were lactose intolerant and who were consuming conventional

milk containing A1 and A2 β -casein.

A systematic review of the gastrointestinal effects of A1 and A2 milk conducted by Brooke-Taylor *et al.* (2017), reported that BCM-7 and related short BCMs are released by gastrointestinal digestion from A1-type (not A2-type) β -caseins under *in vitro* conditions and in animals, A1 slows gastrointestinal transit. A clinical study also reported the release of pharmacologic quantities of BCM-7 in human beings after the consumption of a quantity of bovine casein equivalent to 1 litre of milk. Although the gastrointestinal effects from A1 and BCM-7 in animal trials and *in vitro* studies were conclusive, the evidence from human clinical studies are still emerging. Two clinical studies in adult human beings, which investigated Bristol Stool Scale measures of faecal consistency, reported softer stools with A1 relative to A2, with one of these studies also showing softer stools associated with the A1 diet, relative to a non-dairy baseline diet. It was also evident in animals and at least in some human population groups that the A1-derivative peptide BCM-7 was pro-inflammatory. Although the current gastrointestinal evidence was strongly linked to BCM-7 and μ -opioid pathways, the possibility that some gastrointestinal effects involve non-opioid pathways was relevant. Hence, further clinical studies of A1 effects in a broad range of population groups and dietary conditions were found to be necessary.

As many of these studies were sponsored by A2 Corporation, and carried out on people intolerant to milk and some other studies were inconclusive, further validations are needed to assess the harmful effects on a larger human population. The role of A2 Corporation could be seen in creating scare about A1 type milk. However, none of the Governments have agreed to notify the difference between A1 and A2 milk and adverse impact of A1 milk on human health.

Research on A1 and A2 milk in India

The first review paper on A1 and A2 milk in India was published by Mishra *et al.* (2009), which highlighted the hazards of consuming A1 type milk, based on the papers published by Elliott *et al.* but missed out on the reports of Truswell (2005) and EFSA (2009). They screened 618 cattle belonging to 15 breeds and reported that 98% cattle were of A2 type. Only two breeds namely Malnad Gidda and Kherigarh had 20% animals with A1A2 genotypes. All 8 breeds of buffaloes were of A2A2 genotypes. Sodhi and others (2012) screened 180 bulls at random from different regions and reported that only 11% bulls had A1/A1 genes. Among HF bulls, 22% had A1/A1 genes, whereas 45% had A1/A2 genes and 33% had A2/A2 genes. Among Jersey breed, 60% bulls had A1/A2 genes and 37.5% had A2/A2 genes, with only 2.5% having A1/A1 genes. Among crossbred bulls, only 1% had A1/A1 genes, while 50.6% had A2/A2 genes and 39% bulls had A1/A2 genes.

Way Forward

After the release of the EFSA Report in 2009, the focus

in other countries shifted to studying the effect of A1 milk on digestive disorders, which is not a serious problem. However, in India, ignoring the EFSA Report, wider publicity was given to health hazards in consuming A1 type milk and blaming the crossbred cattle. This created a serious concern among farmers and milk consumers, while traders encashed this opportunity to sell milk of Indian breeds at an exorbitant price. It is well known that people in Europe and US have been consuming A1 milk for centuries and there have been no adverse effects of consuming this milk by the common public. People in India, have been drinking crossbred cow milk for over 50 years, without any adverse effects. Hence, it is necessary to inform the common public about the safety of crossbred cow milk. Fortunately, about 50% of the milk produced in India is contributed by buffaloes, which has higher content of fat, protein, lactose and calcium and lower cholesterol, as compared to cow's milk. By separating the surplus cream, buffalo milk can be healthier than cow's milk.

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