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CLINICAL ASPECTS OF ARTIFICIAL HUMAN COLOSTRUM

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ABSTRACT

Synthetic human colostrum is can produce synthetically by using natural ingredients. There are so many cases of malnutrition in all over India. The mothers are not able to feed their baby because lack of nutrition in their body and certain medication. The one and only main reason of all this is poverty in India. The main purpose of this article is to produce synthetic human colostrum in cheapest cost. The human colostrum is a source of best nutrition for the new born, millions of years of evolution says that, finely to be harmony with it is the requirements of the infant. Colostrum is the first milk and is present in a breast from 12 to 16 week of pregnancy. Human colostrum or breast milk compose of many complex proteins, lipids and carbohydrates, the concentrations of which alter dramatically over a single feed, as well as over lactation, to reflect the infant's needs. In addition to supplying a source of nutrition for infants or new born, breast milk compose of a infinite of biologically active components. These molecules plays distinct roles, both guiding the development of the new born immune system and intestinal microbiota. Corporal growth, human colostrum as a bodily fluid has a various other advantages, including modulation postnatal intestinal function, immune ontogeny, and build out of brain. Although nursing is highly recommended, breastfeeding may not always be possible, suitable or lactation insufficiently because serious illness, hypoplasia, insufficient glandular tissue, breast surgery, postpartum depression. Infant formula is an industrially produced substitute for neonate consumption. In this review, we discuss the composition of breast milk, natural sources of composition of breast milk and the factors that affect it during the course of breast feeding. To know the components of human colostrum and their functions will allow for the improvement of clinical practices, neonate nursing and our understanding of immune responses to infection and immunize to or vaccination new born.

KEYWORDS: Human colostrum, Natural ingredients, biologically active components, immune ontogeny, hypoplasia, glandular tissue, postpartum, neonate, immunize.

INTRODUCTION

The production and secretion of natural human colostrum is based on a neuroharmonal mechanism. Mothers' own milk or colostrum is considered to be the best source of new born nursing.[1] The colostrum is the first milk and present in the breast from 12 to 16 week of pregnancy.[2] The breast milk plays an important role in the brain development of an infants. Breast milk composed of a various of bioactive agents that improve function of the gastrointestinal tract (from mouth to anus) and the immune system. The breast milk is widely known as a biological fluid which required for optimal infants growth and the development.[3] Recently, studies have further suggested that breast milk make less severe infant programming of late metabolic diseases, particularly protecting against obesity or fattyness and type 2 diabetes.[4]

The World Health Organization(WHO) recommends that new born must be entirely nursed by mother colostrum for the first six month of life.[5] The American Academy of Paediatrics also recommends breastfeeding of mother colostrum for at least 12 months.[6] The best or ideal pattern for new born is entirely breastfeeding that provide a optimal nutrition and health protection for the six months of the life of the infants and that nursing with the complementary food from the six months until at least 12 month of the age is recently updated and reaffirms by the Academy of Nutrition and Dietetics.[1] The decision to nursing or breastfeeding is highly personal and is often influenced by many factors.[7] Under certain situations, breastfeeding might not be possible, unsuitable or inadequate, which warrants an interruption or discontinuation in breastfeeding or nursing.

According to the analysis of EBF trend that, over the last decade the percentage of infants (under 6 th months of age) who were exclusively breastfed in India increased from 46.4 % to 54.9 %. But till 45.1 % of infants are away from the breastfeeding because of some reasons.[8] Briefly review the nutritional composition of human milk and provide an overview of its varied bioactive factors, which include cells, anti-infectious and anti-inflammatory agents, growth factors, and prebiotics.[9] The purpose of this article is to review nutritional information on breast milk and infant formulas to reinforce the importance of breastfeeding, while also understanding the uses of infant formula.

Human colostrum

Human colostrum has higher and more concentrations of secretory Ig A, growth factors, lactoferrin, Anti-inflammatory, cytokines, oligosaccharides, anti oxidants, and other protective components than mature human milk.[10] Colostrum is deep lemon colour liquid secreted by the breast for the first several postpartum days.[11,13] Antibodies are demonstrable in colostrum immunoglobin A may protect the new born against enteric pathogen.[12] Compared with mature milk, colostrum contains more mineral and protein but less sugar and fats. The human colostrum is more thicker than the mature human colostrum. This colostrum has a viscosity greater than the mature human milk.[13] The yellow colour of colostrum is because of the beta-carotene which transformed in vitamin A into body of infants.

Composition of human colostrum

Nutritional factors

Human breast milk is a complex matrix with a generly contain 87% water, 3.8% fat, 1.0% protein, and 7% lactose or milk sugar.[14] The total energy of milk or human colostrum is provided by fat and lactose with proportion of 50% and 40% , respectively.[15] However, the composition of human colostrum or human mature milk is dynamic and frequently changes over time of period, adapting a changes in itself according to needs of the growing child. content in human milk varies from 1.4–1.6 g/100 mL, to 0.8–1.0 g/100 mL after three to four months of lactation, to 0.7–0.8 g/100 mL after six months.[7,15] It has been observed that a mother's colostrum and breast milk always satisfactory of essential nutrients for her term infant's growth and development, even when her own nutrition is inadequate, Although the mean concentrations.

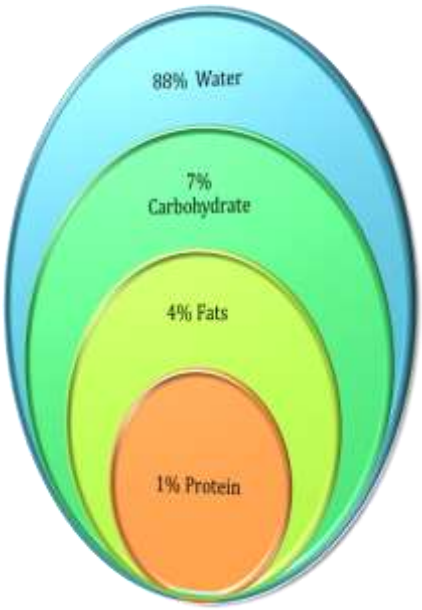

Fig. 1: Basic Component of Human Colostrum.

Protein in human colostrum

There are two classes of protein in breast milk: Casein and whey.[16] Casein protein convert into clots or curds in the stomach; while whey protein remains a same as a liquid and is easier to digest. Depending on the stage of milk secretion or lactation, it contains 80% to 50% of protein in breast milk is whey.[15] The whey/casein proportion human milk changes between 70/30 and 80/20 in early human milk secretion and decreases to 50/50 in late lactation or milk secretion.[17] Traditionally, infant formulas are contains more casein, making them difficult digest as compared to human breast milk. Because the amino acid profiles of casein and whey proteins are different, the overall amino acid profile of human milk varies depending on the stage of secretion of human colostrum. Glutamine, the most abundant free amino acid, is nearly 20 times more than in mature milk than its lowest value in colostrum.[18] Glutamine is important for supplying ketoglutaric acid for the tricarboxylic acid cycle, possibly plays and role of a neurotransmitter in the brain, and act as a major energy substrate for intestinal cells.[19] The main whey proteins are alpha-lactalbumin, lactaferrin and secretory IgA and serum albumin. Other proteins contain lysozyme, folate-binding protein, bifidus factor, casein, lipase and amylase, alpha1-antitrypsin and antichymotrypsin, and haptocorrin.[15] After ingestion, these proteins are broken down rapidly to separate amino acids for assimilation and utilization. Most of these proteins also plays a role in bioactive functions and non-nutritive functions.[20] For instance, alpha-lactalbumin is must for lactose preperation binding of Ca and Zn ions. Casein facilitate to form masses with calcium and phosphorus.

Fats in human colostrum

Fats are the most important composition of breast milk, providing energy and helping the development of the central nervous system. Milk fat is a carry of taste and aroma in milk.[15] In general, human breast milk concentrations of fat ranges from 3.5% to 4.5% during lactation. The main lipid fraction is triglycerides, which account for about 95% of total lipids. Near half of milk fatty acids are saturated fatty acids, with 23% palmitic acid (C16:0) in total fatty acids.[15] The monounsaturated fatty acid, oleic acid (18:1w9), is in the highest percentage (36%) in milk. Human breast milk also contains two essential fatty acids, linoleic acid (C18:2w6) at 15% and alpha-linolenic acid (C18:3w3) at 0.35%.[15] These two essential fatty acids are, respectively, converted to arachidonic acid (AA, C20:4w6) and eicosapentaenoic acid (EPA, C20:5w3), the latter of which is further converted to docosahexaenoic acid (DHA, 22:6w3). AA, EPA and DHA are important for regulating growth, inflammatory responses, immune function, vision, cognitive development and motor systems in newborns. Cell differentiation and development of active synapses in the brain need specific requirements of DHA and AA.

Carbohydrates in human colostrum

When glucose and galactose join together they create lactose. Lactose is main carbohydrate present in human milk.[21]

Vitamins in human colostrum

The bioavailability of ingested vitamins in the organism is affected by several aspects, including physiological factors, such as nutritional status, amount of fat in the diet, food matrix, and interactions with other nutrients .Colostrum appears enriched in vitamin A, C, and K as compared to maternal serum, possibly indicative of active mammary gland transport mechanisms. Inter-individual and inter-study high variability in colostrum's vitamin content endorses its sensitivity to external factors.[22]

Enzymes in human colostrum

γ-Glutamyl transferase activity is high in human colostrum, and although activity decreases thereafter, considerable amounts of enzyme are present in transitional and mature milk.[23]

Minerals in human colostrum

The principal mineral constituents of human milk are Na, K, Ca, Mg, P, and Cl. Calcium concentrations reported in various studies vary from 25 to 35 mg/100 ml. Phosphorus at 13 to

16 mg/100 ml is much more constant but is lower in proportion to casein and calcium than in milks of most other species. Iron, copper, and zinc contents of human milk vary consider.[24]

Immune factors

IgA: The presence of IgA in milk has been known for a long time; however, less information is available about the presence of other Igs such as IgM, IgG, and their subtypes (IgG1, IgG2, IgG3, and IgG4) or even IgE or IgD. The total Ig concentration and profile will change during the course of lactation. It is act as a important first line defence. IgA also an important serum immunoglobin.[25]

IgG: Immunoglobin g neutralizes pathogen Such as virus and bacteria binding to key pathogen surface protein and preventing interactions of pathogen with host cell.[25]

IgM: Immunoglobin m not only serve first line of host defence agents infection but also plays an important role in immune regulation and immunological tolerance.[25]

IgD: The function of immunoglobin d is single the B cell to be activated. The active B cell take a part in defence mechanism in immune system.[25]

IgE: The role of immunoglobin E is central in allergy sensitization and atopic disorder such as allergic rhinitis, asthma and atopic dermatitis.[25]

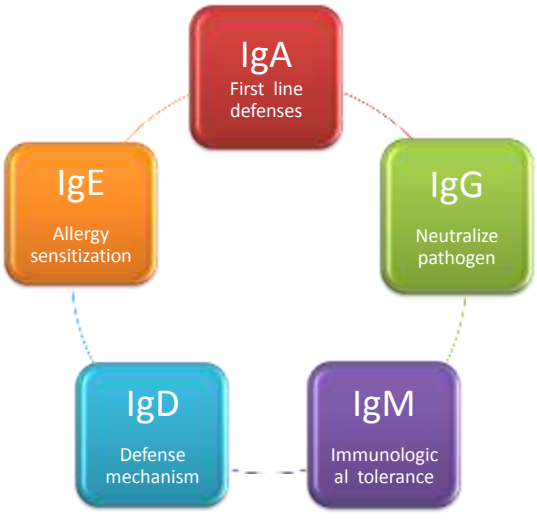

Fig. 02: Immunoglobin.

Lactoferrin

Lactoferrin (Lf) is a multifunctional protein and one of the most abundant proteins in human milk. The Lactoferrin concentration in milk from women delivering at term was 3.16 g/L, 1.73 g/L and 0.90 g/L for colostrum, transitional milk, and mature milk, respectively. Lactoferrin concentrations changed significantly between stages of lactation (colostrum vs. transitional milk, colostrum vs. mature milk, transitional milk vs. mature milk, all $p < 0.001$). The immunologically important bioactive factors present in human milk or human colostrum, lactoferrin (Lf) has emerged as a key player with wide-ranging features that directly and indirectly protect the infant against infection caused by a variety of pathogens and bacteria. The concentration of Lactoferrin (Lf) in human milk is lactation-stage related; colostrum contains more than 5 g/L, which then significantly decreases to 2–3 g/L in mature milk. Lactoferrin (or lactotransferrin, Lf) is an approximately 78 kDa glycoprotein from the transferrin family of proteins.[26]

Polypeptide

Bioactive peptides are short fragments of proteins that influence biological processes. Peptide abundance (sum of ion intensities) and count (number of unique peptide sequences) in each milk sample were determined from this analysis. Our recent work confirmed that native proteases exist in milk, including (from highest to lowest concentration) carboxypeptidase B2, plasmin, kallikrein, elastase, thrombin, cathepsin D, and cytosol aminopeptidase. Besides cathepsin D, which is inactive at milk pH, all of these milk proteases are in active forms within milk.[27]

Oligosaccharides

Milk oligosaccharides (OSs) confer unique health benefits to the neonate. Although human digestive enzymes cannot degrade these sugars, they support specific commensal microbes and act as decoys to prevent the adhesion of pathogenic micro-organisms to gastrointestinal cells Twenty-one oligosaccharides of human milk were quantified by high performance anion-exchange chromatography. Oligosaccharides are the third largest solid component in human milk. These diverse compounds are thought to have numerous beneficial functions in infants, including protection against infectious diseases. The structures of more than 100 oligosaccharides in human milk have been elucidated so far.[28]

Cytokines

The frequently studied cytokine in breast milk include interleukin (IL)-1beta , IL-6, IL-8, IL-10, and IL-12 and tumor necrosis factor (TNF) alpha which are found in the colostrum and mature milk secretion. the presence of cytokines in colostrum was unsuspected but it has been now clarified that normally there are at least four cytokines, namely interleukin 1 and 6, tumor necrosis factor and interferon gamma, that may exert an important immunostimulatory role particularly on the oropharyngeal-associated lymphoid tissue. As a corollary, physiological concentration of cytokines administered per os may exert a useful adjuvant activity in aged or immunodeficient people.[29]

Lactalbumin

Alpha -lactalbumin is the major protein in breast milk (20 to 25 % of protein) and has been described to several physiological function in the neonatal period.[30]

α-Lactalbumin, a major component of human milk, is important both from a nutritional point of view, and as a component of the enzyme system biosynthesizing lactose. It is structurally homologous to lysozyme of both human milk and hen's egg white. The most abundant component of the casein fraction of human milk is *β*-casein, which exists in the form of genetically-determined polymorphs. The polymorphs apparently differ in their phosphate content only. The amino acid sequence of the N-terminal region of human milk *β*-casein bears a strong structural homology to that of bovine milk *β*-casein. Human *α*-casein is also in the form of genetically-determined polymorphs; however, it has not been purified and characterized.[31] Human *κ*-casein is a glycoprotein which releases a glycomacropeptide when acted upon by rennin. Though it has not been characterized to any great extent, there is evidence that there may be several forms of *κ*-casein in human milk. Also the nature of the glycomacropeptide varies depending on whether purified *κ*-casein or whole casein fractions are subjected to the action of rennin. The amino acid sequence of a glycomacropeptide produced from *κ*-casein-enriched fraction of human milk casein was structurally homologous to the glycomacropeptides from other. α-Lactalbumin contributes to infant growth, and the commercial availability of α-lactalbumin allows infant formulas to be reformulated to have a reduced or less protein content. α-lactalbumin has the potential to be added to food products as a supplemental protein. It also has potential as a nutritional supplement to support neurological function and sleep in adults and treat insomnia, owing to its unique tryptophan content. Other components of α-lactalbumin that may have usefulness in nutritional

supplements include the branched-chain amino acid leucine, which promotes protein accretion in skeletal muscle, and bioactive peptides, which possess prebiotic and antibacterial properties. It has an amino acid composition that is high in essential amino acids and comparatively rich in tryptophan, lysine, cysteine, and the branched-chain amino acids (BCAAs) leucine, isoleucine, and valine. work as a therapeutic agent with applications in conditions or diseases such as sarcopenia, mood disorders, seizures, and cancer.[30]

Lysosomes

The innate immune system is the first line of defence against infection and is activated within minutes, reacting in a nonspecific, preprogramed, and patterned manner to various infectious or foreign (non-self) stimuli.[32] The infant's immune system is immature at birth, and this immaturity is pronounced for the premature infant placing the infant at increased risk of infection.[33] Important developmental immune deficiencies at birth include incomplete physical and chemical barriers, poor innate effector cell function, limited and delayed secretory immunoglobulin A (IgA) production, incomplete complement cascade function, and insufficient anti-inflammatory mechanisms of the respiratory and gastrointestinal (GI) tracts.

Growth factors

PDGF

PDGF stands for plate derived growth factors. PDGF inhibits the differentiation of stromal cells into cells of the osteoblastic lineage (Tanaka and Liang, 1995). Platelet-derived growth factor (PDGF) constitutes a family of dimeric isoforms, acting on connective tissue cells and certain other cell types. PDGF was originally discovered as a constituent of platelets, which are released into serum in conjunction with blood coagulation. Although the α-granules of platelets are a major storage site for PDGF, PDGF is also produced by many other cell types. PDGF stimulates the growth of its target cells.[34]

EGF

The EGF stand for epidermal growth factor. It plays important role in wound healing by stimulating epidermal and dermal regeneration.[34]

IGF

IGF stands for insulin like growth factors .IGF-I and IGF-II, as well as IGF binding proteins and IGF-specific proteases, are found in human milk.[35,36] Levels are highest in colostrum,

and steadily decline over the course of lactation.[37,38] There are no significant differences between preterm and term milk, with the exception of IGF binding protein-2, which is higher in preterm milk.

Production of synthetic human colostrum

The energy content is 60 – 75 kcal / 100 ml. Protein content is considerably higher and carbohydrates content lower in colostrum than in mature milk. Lactose is main source of energy in human colostrum. The main source of lactose is cows milk, goat milk, yogurt, cheese, etc. We can extract lactose from milk by adding enzyme lactase or beta – galactosidase in the milk.[39] The lactose can be isolate as the alpha – anomer by the addition of ethanol and crystallization from resulting water ethanol mixture at room temperature.

Extraction of protein

We can extract the both protein casein and whey. The high content and natural sources of protein is cows milk and goat milk. The casein is easily separated from the milk by making the milk more acidic. Heat the milk at 40 degree Celsius. Add acetic acid or acetate buffer drop by drop in 100 ml of milk. Then stir it with the glass rod and the casein will get precipitate and isolate from the milk. This is how we extract casein from the milk.[40]

Fig. 03: Flow chart of Casein Formation.

There are so many natural sources of the whey protein like egg white, soy, veg pea protein, lactose free. We can easily separated whey protein. Heat the milk at 100 degrees Celsius. Then add citric acid in it then sieve this milk. The watery fluid and wait for 24 hours. Then extraction of whey is occure.

Fig. 04: Flow chart of Whey Extraction.

Generally all the vitamin and minerals present in egg yolk. This vitamin are easily get extract from the egg yolk by dry distillation method, baking method, reduce pressure distillation, solvent extraction method, supercritical co2 extraction method, sub-critical propane extraction method and enzymatic method.[41]

Add some essential oil like clove oil in it for fat content.

Food-specific IgG concentration for each of the 44 food antigens tested.

Clinical uses of synthetic colostrum

The human colostrum is a source of best nutrition for the new born, millions of years of evolution says that, finely to be harmony with it is the requirements of the infant.[42] There are so many cases of malnutrition In all over the India. The main reason of the malnutrition is the poverty in the country. Hence the mothers are not able to feed their babies. The main purpose of this article is the production and supply of human colostrum in cheapest cost. The malnutrition is because of lack of nutrition. It is mostly found in children and new born. There are two types of malnutrition. First is kwashiorkor and another is marasmus. The kwashiorkor is the protein malnutrition and marasmus is lack of all nutrients.[43] Mother are not able to feed their neonate because of some serious diseases, hypoplasia, insufficient glandular tissue, breast surgery, postpartum depression and unfortunately the death of mother or the breastfeeding is highly personal decision of mother.[44,45] So the main purpose of this formulation is provide a human colostrum to all the infants in cheapest.

CONCLUSION

There are so many cases of malnutrition in all over India. The main reason of malnutrition is poverty in the country. There are so many causes for the mother is unable to feed the child, feed or nursing the child is highly personal decision of the mother, There is another cause like mother having breast cancer and breast was remove by surgically, many mother is die due to

parturition labour. So there is so many causes for neonates are away from breast feeding. The main purpose of this project is aware people about Artificial human Colostrum in Cheapest Cost.

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