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Impact of Human Colostrum Associated Microbial Population on Neonatal Health

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Abstract

The first thick milk formed immediately after the delivery of newborns by memory glands of female mammals (including humans) is called colostrum. It is the basic primary requirement for the nourishment of newborns. It is a rich source of proteins, lipids, carbohydrate, vitamins and minerals which helps in developing immunity of infants. Traditionally, human colostrum was considered to be a sterile fluid. But, recent researches have shown that it contains high supply of mutualistic and commensal source of bacteria which act as a probiotic to the infant gut. Bacteria in the colostrum can stimulate anti-inflammatory response by producing specific cytokines which can reduce the risk of forming large range of inflammatory infections and can also prevent the expression of immune - mediated pathologies, such as atopic dermatis and asthma. The aim of our present review is to elucidate the role of microbiota of colostrum in infant nourishment.

Keywords - Human colostrum, Microbiota, Infant immune system.

Introduction

Breastfeeding is the initial form of neonatal feeding which assimilate all the basic requirements of nutrients for the first six months of life (Fernandez, et al, 2013). Human colostrum influences the growth of immune system and help to establish the microbial population in gut by its components, such as oligosaccharides which act as probiotics (Fernandez, et al, 2013).

The contents of human milk varies with timing of lactation. The milk formed immediately after delivery till the 5th day is very rich in nutrients and bioactive factors, such as mineral salts, antibodies, cytokines, lysozymes, oligosaccharides, proteins and compliment factors. This milk produced is called colostrum (Ballard & Morrow, 2013). The transitional milk occurs from 5th day to 2nd week of postpartum (Ballard & Morrow, 2013). It is very rich in lactose, calcium and lipids because its role is to fulfill the developmental and nutritional requirements of growing neonates. The human milk achieves standard composition after one month of childbirth which is called "mature milk". The mature milk has high concentration of

lipids and carbohydrates and lower proportion of proteins and minerals compared to colostrum (Drago L, et. al, 2017).

Since last few years, there has been advance researches of microbiota in human. According to the studies, 50 different genera having more than 200 different species are described in human milk sample (Hunt, et. al, 2011). Bacteria such as *Streptococci, Lactobacilli* and *Bifidobacterium* are recognized as potential source of bacteria (Martin, et. al, 2010). These bacteria have important role in 1st stage of initial colonization on infant gut(Fernandez, et. al, 2013). Through studies, it has been proven that infant ingest between 10^5 to 10^7 bacteria daily through their diet of approximately 800ml of milk (Drago L, et. al, 2017).

The mature milk after 1 month of delivery is totally based on lifestyle, diet and hormonal signaling from lactating mothers. The gut microbiota of lactating woman is also different according to different geographical locations (Nommsen-River, 2012). The present review is to focus on colostrum associated microbiome and its role on infants immune system.

Role of Human Colostrum Bacteria on Infant Gut

Recent studies of last few years have suggested that human colostrum bacteria play a very crucial role in infants gut. But competitive exclusion, they contribute in reducing the incidence and severity of infections in breastfed infants and also produce antimicrobial compounds (Olivares, et. al, 2006). The administration of colostrum *Lactobacillus* strain to infants during first six months of life led to reductions in causing gastrointestinal infections, respiratory tract infections and other total numbers of infections respectively (Maldonado, et. al, 2012). *Staphylococcus* and *Streptococcus* in colostrum may particularly be useful for reduction of acquisition of undesired pathogens exposed on infants by environment. It has also been showed that *Streptococci* inhibit oral colonization by MRSA in high risk to new born when exposed to open environment (Uehara Y, 2001).

The strains of *Lactobacillus gasseri* CECT 5714 has also been identified in the reduction of incidence of allergic response in animal model of Cow's milk protein allergy (Olivares, et. al, 2006). The researchers also concluded that viridian *Streptococci* has the feature on health of infant gut in contrast to atopy-suffering infants (Kirjavainen, et. al, 2001).

Human Colostrum Bacteria as Biotherapeutic Agents

Through recent studies, problems of antibiotic resistance pathogenic bacteria giving rise to inflammatory diseases and infections in developed countries have brought a new interest to the world of probiotics. Probiotics can be defined as live microorganisms that benefits the health of host when administered in adequate amounts (Guarner, 1998).

Probiotic bacteria originally were isolated from human colostrum are the most useful organisms as they fulfill all the necessary criteria's that are recommended for human probiotics. Bacteria such as *L.fermentus, L.salvarius, L.bifidobacterium* are those with high probiotic potentials and successfully cleared the Qualified Presumption of Safety (QPS) status conceded by European Food Safety Authority (EFSA). These bacteria seems to be uniquely adapted to reside in human digestive system to maintain a symbiotic relation from the time of our birth. Some of these strains have been shown to play anti-inflammatory, anti-infectious immunomodulatory and metabolic roles in both vitro and vivo (Jimennez, 2010).

Exclusive breastfeeding during first month of life is strongly recommended to mothers with family of atopy as it reduces the risk of asthma and atopic dermatitis rates during childhood (Gdalevich, et. al, 2001). Gut bacteria are considered as the most earliest and stimulus for

development of gut associated lymphoid tissue and they promote antiallergenic process (Kalliomaki, 2001). Therefore, colostrum of healthy female can be considered as potential source of probiotics or therapeutic bacteria with a role of protection of neonatals against various kind of inflammatory or infectious diseases.

Neonatal's Immune System and the Milk Microbiota

The formation of microbiota in human milk is yet not known; but there are different hypothesis from various researchers explaining the origin of milk-associated bacteria. Microorganisms from infant's oral cavity and maternal skin may become integral component of milk microbiota by milk flow back during lactation into mammary glands (Rodriguez, 2014). Rather than this, human milk also contain large number of intestinal bacteria; which may spread from maternal intestine by involving $CD18^{+}$ and dendritic cells, these cells would take intestinal microorganisms from gut lumen and transfer them to mammary glands of lactating mothers by the means of translocation. This results to be increased during late pregnancy and lactation (Rodriguez, 2014). Milk produced by lactating mothers has the efficiency to stimulate the proliferation of large number of *Lactobacillus* and *Bifidobacterium*, which are the main probiotic microorganisms present in gut, forming rich acidic environment (Walker and Jyengar, 2015).

The continuous supply of bacteria through colostrum highly impacts on newborn's development, mainly acting on maturating the immune system (Houghteling and Walker, 2015). Several researches showed the strict link between gut microbiota signals, maturation of immune system and the mucosal host defense. Infants depending on breast feed are shown to possess more stable intestinal bacterial population and a well balanced immune system in comparison to infants depending on formula-fed (Kalliomaki, 2001).

Intestinal bacterial is also to have role in stimulation of lymphoid elements and positively have influence of maturation of adaptive and innate immunity, as demonstrated by (Cash & Hooper, 2005). It was shown that in germ free mice villus capillaries poorly develops during weaning and remains the same during adulthood. It suggest us that intestinal microbiota has fundamental role for intestinal blood vessel to completely get developed (Martin, et.al, 2010). Microbiota of intestine can also promote B cell development in Peyers Patches and increase the proportion of mucosal IgA, which is the main antibody class in secretion that act as first tool of defense (Martin, et.al, 2010).

Microbial Network in Human Milk

The study of microbial interaction with population of bacteria is highly important to understand the role of microbiome. Microorganisms compete for exchange of genetic material and metabolities, nutrients and many other factors. Microbiota of milk can be considered as a complex and variable ecosystem which is often understood well due to its dynamic nature (Layeghifard et.al, 2017). Bacterial networks has become highly essential for studying microbial relationships and also clarifying the impact of various interaction on host by identifying the main "hub" member in bacterial community (Layeghifard, et.al, 2017).

Numerous techniques have been used to identify network hub. But in past few years, Auto-contractive map (Auto CM) has been used very interestingly. It is the 4th generation unsupervised Artificial Neutral Network (ANN) that can perform unsupervised algorithms in very large numbers (Buscema and Sacco, 2016). This system uses minimum spanning tree (MST) theory for understanding the natural connections among variables (Buscema and Grossi, 2008). Auto CM is already being used in the field of microbiology to study the networks of

human colostrum and mature milk in Burundian and Italian populations which highlights the main microbial hubs for the representation of biological leading structure of entire network (Drago, et.al, 2017). In future, it may be possible to understand the direct involvement of microbe in stimulation and manipulation of newborns immune system.

Conclusion

Microbiota of human colostrum seems to have a key role in stimulation of infant's immune system and having great contribution in creating first transitional microbiota with strong immunomodulatory activities. However, still further studies are required to highlight the direct and strong connection between microbiota of human colostrum and stimulation of infants immune system. Benefits of network biology will improve our knowledge of bacterial interactions among the milk microbiota, with more applications for eventually targeted modifications of bacterial composition, targeted to enhance the abundance of those microbiota that may be beneficial not only for modulation of infant's immune system but also improving the whole host's health.

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