

Probiotics / Prebiotics and Preterm Baby: A Literature Review

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Abstract

Improvement of obstetric services has led to smaller preterm babies presenting in the NICU (Neonatal Intensive Care Unit). There are many problems faced by preterm babies and the severity increases with less weight and gestational age. Prebiotics, Probiotics and also postbiotics appear to present a new hope for these babies. Many studies and trials have shown benefits in conditions like Necrotizing enterocolitis, Feeding intolerance, Neonatal sepsis and in overall morbidity and mortality. The benefits in these areas leads to better neuro-developmental outcome in later life. Present article presents the review of literature about status of probiotics, prebiotics and post biotics use in preterm babies.

Keywords: Prebiotics; Probiotics; Postbiotics; Preterm Babies.

A preterm baby specially below 34 weeks is a real challenge for a neonatologist, and the challenge increases with reduction in gestational age. These babies face multiple problems starting from inability to suck, swallow, tolerate the given feed and more serious and life threatening problems like necrotizing entero-colitis (NEC), sepsis respiratory distress syndrome (RDS) etc. Once survival is looked after poor weight gain may be the result. Effect on late neurodevelopmental status is also common.

Neonatologists are always in search of something which can look after these problems resulting due to immaturity of organs and systems. The organ system immaturity again may come in the way of using any such agents.

Recently a lot of trials studies and metanalysis [1,2,3,4] have shown benefits of using Probiotics in preterm babies. The result seems to be encouraging. Prebiotics, Postbiotics and Synbiotics are other terminologies which have been defined as follows.

Definitions

Probiotics

WHO defines probiotic as live microorganism when administered in adequate amounts confers health benefit to the host [5].

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Prebiotics

A selectively fermented ingredient allowing specific changes both in composition and/or activity of intestinal flora, that is beneficial to the host [6]. Lactobacilli and bifido-bacterium are usual target. Breastmilk has oligosaccharide as probiotic.

Synbiotics

A product that contains probiotics and prebiotics both.

Postbiotics

These are metabolic byproducts of probiotic microorganisms which confer similar health benefits. They have been found to be useful as these exert similar effects as probiotics.

Mechanism of Action

Prebiotics support growth of probiotic organisms. Which acts by promoting intestinal barrier function, reducing inflammation and cellular apoptosis. The metabolic products (postbiotics) also exhibit activity similar to probiotics [7,8].

A newborn baby's gut transits from no organism to normal commensals, starting from maternal

passage during birth to initiation of breast milk. In preterm baby these opportunities are lost due to frequent Cesarean section births and delayed initiation of feeding due to other health problems. At the same time due to poor immunity and multiple interventions needed for management, colonization with pathological organism is always a possibility. This is a usual reason for feeding intolerance, NEC or sepsis.

Many countries like Finland, Columbia have included probiotics in their neonatal intensive care unit protocols since long time. In this article we will discuss different aspects of probiotic use in preterm babies.

The Organisms

Bifidobacterium and Lactobacilli are the organisms preferred. Bifidobacterium is the main organism in the infancy and along with lactobacilli produces short chain fatty acids by fermentation process which promotes growth of indigenous lactic acid bacteria popularly known as bifidogenic effect [8]. Other organisms are enterococcus, streptococcus, Escherichia, Saccharomyces Bolardi which is a fungus has also been used. The special advantage of this organism is, it grows at normal body temperature and is resistant to antibiotics which preterm receives very frequently [9].

As far as source of organism is concerned, both human and bovine can be used but human strains are preferred due to their natural occurrence and safety in babies [10].

Effects of probiotics are described to be strain specific but in preterm specially in NEC it may not matter as NEC has many pathogenetic mechanisms so different strains can also act in different ways [11]. As far today a preparation of different strains and species is preferred specially in preterms so that organisms can act in multiple ways and high dose of single strain is more likely to cause bacteremia and infection [12]. Multi strain product is more functionally effective than single strain. Lactobacillus GG when tried as single strain did not show any role in NEC prevention [13]. It is safe to use previously tested combinations.

Dosage and Duration of Probiotics in Preterms

It is essential that probiotic should be given in optimal dosage. Dosage in different trials ranged from 35×10^9 to 6×10^9 CFU /day. The dosage suggested for preterms below 32 weeks is 1.5×10^9 CFU/day to start with then can be increased to $3.5 \times$

10^9 when 50-60ml/day oral feeds are reached [14].

Different trials have started prebiotics at different age starting from birth onwards but majority started with first week of life. It is important for preterm to have normal commensals in the gut as early as possible so it needs to be started as early as possible as soon as medically baby is stable [14]. This is especially important for prevention of NEC. Toxic dose has not been identified in preterms. Probiotics should be stopped during acute illness.

The micro-organisms are excreted for at least 3 weeks after stopping the preparation. Hence it is suggested that preparations should be given till 36 to 37 weeks of corrected gestational age [15]. The osmolarity of feeds also is an important factor in NEC, the suggested osmolarity is below 600 mosmol/lit. Dilution can be done in breastmilk. Better benefit is seen if a standard feeding regimen is followed [16]. Volume can be 1-1.5ml/dose [14]. Single or divided doses can be given.

Problems During Use

Intolerance, abdominal distention, Flatulence may occur and usually die to prebiotics or other additives [17]. Usually needs stopping the preparation temporarily. Occasionally nosocomial infections to other babies by probiotic strain may occur. Microbiologists need to be trained to identify organism in gram stain or culture.

Production and Packaging

Changes in methods of manufacturing can affect the properties of probiotics. Hence a standard procedure is warranted. Packaging should be water and air proof otherwise moisture and oxygen can denature the product. Refrigeration may be required. The product form whether powder, liquid or tablets may affect the stability [18].

Prebiotics in Preterms

Prebiotics in newborns have not been much studied. Breast milk contains prebiotics in the form of Oligosaccharides and probiotics as lactobacilli also hence it appears that synbiotics may have beneficial role in neonates [15,17]. It is also shown to improve gut motility and gastric emptying thereby reducing intolerance of feeds.

Postbiotics

These are inert metabolic byproducts of organisms

and have been shown to retain the same function as probiotics. As these are inert products they will not be affected by antibiotics as probiotics do hence may be more useful. Further studies are required to study postbiotics in preterm babies.

Conclusion

Based on evidences available today probiotics can be used in NICU with proper selection and monitoring of the baby for adverse effects. It can help in reducing feed intolerance, NEC, may be sepsis and ensure better weight gain. Indirectly probiotics can reduce NICU stay, improve survival and as morbidity is reduced it may have effect on long term neurodevelopment of baby. More trials and studies are required to prove this.

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