Prebiotics for Feeding of Preterm Infants

Thesis submitted in partial fulfillment for the Master Degree in Paediatrics

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ABSTRACT

BACKGROUND The intestinal flora of breast-fed infants is generally dominated by bifidobacteria which have beneficial properties. Their presence is due to various components of breast milk, including prebiotic substances .These prebiotics have been added to artificial milk formulae so as to mimic breast milk in its action on intestinal flora.

METHODS We here report 100 healthy preterms born in our hospital and were admitted to our NICU over a period of 7 months.They were divided into two groups (50 preterms each). Preterms in group 1 were given milk formula enriched wth prebiotics (Bebelac EC containing GOS), while preterms in group 2 were given premature formula not enriched with prebiotics. Preterms in both groups were then compared regarding their growth rate, frequency of stools, development of feeding intolerance, electrolyte disturbance and the development of sepsis during their NICU stay.

RESULTS Significant improvement in average daily weight gain and stool frequency in preterms receiving prebiotics observed during their stay ($p < 0.05$). Significantly less incidence of feeding intolerance was observed in prebiotics receiving preterms ($p < 0.05$). Sepsis screening through CRP and CBC shift showed significant less incidence of sepsis in preterms receiving prebiotics ($p < 0.05$). No disturbance in serum electrolytes was noted in either groups.

CONCLUSIONS Prebiotics have beneficial effects in feeding preterm infants**.**

Key words: Gut microflora, preterms, necrotising enterocolitis, prebiotics.

Contents

List of Tables

List of Figures

List of Abbreviations

ALP	Alkaline phosphatase
BiPAP	Bilevel positive airway pressure
BUN	Blood urea nitrogen
CFU	Colony forming unit
CPAP	Continous positive airway pressure
CSF	Cerebrospinal fluid
DGGE	Density gradient gel electrophoresis
ECG	Electrocardiogram
EGF	Epidermal growth factor
ELBW	Extremely low birth weight
eNOS	Endothelial isoform of nitric oxide synthetase
Epo	Erythropoietin
ET-1	Endothelin- 1
ETA	Endothelin A
ETB	Endothelin B
FGF-2	Fibroblast growth factor – 2
FOS	Fructooligosaccharides
GALT	Gut assoiated lymphoid tissue
GI	Gastrointestinal
GOS	Galactooligosaccharides
HCL	Hydrochloric acid
IBD	Inflammatory bowel disease
IgA	Immunoglobulin A
IL	Interleukin
INR	International normalization ratio
LBW	Low birth weight
LDL	Low density lipoproteins
MAMPs	Microbial associated molecular patterns
MMC	Migrating motor complexes
NDOs	Non-digestible oligosaccharides
NEC	Necrotising enterocolitis
NICU	Neonatal intensive care unit
NO	Nitric oxide
NPO	Nothing by mouth
NSP	Nonstarch polysaccharides
PAF	Platelet activating factor
PAF-AH	Platelet activating factor-acetyl hydroxylase
PDGF	Platelet-derived growth factor

PGE2	Prostaglandin E2
PRN	As needed
PRR	Pattern recognition receptor
PTT	Partial thromboplastin time
RS	Resistant starch
SCFA	Short chain fatty acid
SNPs	Single nucleotide polymorphisms
TGF-β	Transforming growth factor-β
TLR-4	Toll- like receptor 4
TNF-α	Tumour necrosis factor – α
TPN	Total parenteral nutrition
UC	Ulcerative colitis
VEGF	Vascular endothelial growth factor
VLBW	Very low birth weight

Interoduction

Introduction

The fully developed gastrointestinal system posses local nonspecific barrier defences and cell-specific antigen interactions that function together to protect the gut from colonization and translocation of potentially pathogenic bacteria and antigens. ***(Walker, 2002)***

The local defenses include gastric acidity and digestive enzymes to destroy ingested pathogens and associated antigens, mucus production to inhibit microbial adherence, active regular peristalsis to prevent bacterial stasis and rapidly eliminates antigen-antibody complexes, and secretory IgA to bind luminal antigens impending antigen interaction with the intestinal epithelial cell thus reducing antigen penetration ***(Winkler et al., 2007)***

In addition to the above mechanisms, the establishment of a stable and diverse intestinal flora with commensal organisms is essential for the initial priming and regulation of the gastrointestinal immune defenses and modulation of intestinal inflammation. ***(Caplan, 2000)***

Commensal organisms enhance and maintain the integrity of the mucosal barrier by reducing mucosal permeability, increasing mucus production, strengthening intestinal tight junctions, and inhibiting bacterial translocation. This is accomplished by producing toxic substances against aerobic bacteria, reducing intraluminal pH, and competing for binding sites. (***Collins et al., 1999)***

The preterm infant demonstrates colonization patterns distinctly different from that of a full term infant. These differences are largely explained by the developmental immaturity of intestinal epithelial

glycoconjugate expression and the unique environmental exposures experienced by the preterm infant. ***(Mack et al., 1999)***

Almost all preterm low birth-weight infants in the NICU experience delayed enteral feedings , exposure to early and prolonged broad-spectrum antibiotics and are introduced to the hospital environmental flora. All of these factors contribute to the delay in intestinal colonization by commensal, non-pathogenic bacteria, to the paucity and lack of diversity of bacterial species, and to the increased risk of colonization by pathogenic bacteria. ***(Fanaro et al., 2003)***

Breast-fed babies tend to have fewer incidences of infection than their bottle-fed counterparts, possibly due to the protective components of breast milk. These components include antibodies and its 'prebiotic' effect on gut flora. ***(McCartney, 2004***)

It is now possible to have commercially available non-digestible oligosaccharides and supplement formulas with these ingredients, known as prebiotics. Galactooligosaccharides (GOS) and fructooligosaccharides (FOS) have been used to stimulate Bifidobacteria, and several studies have demonstrated their prebiotic effects. (***Gibson et al., 1995)***

Aim of the work