The introduction of multi-strain probiotics to preterm infants in a regional hospital: an observational study

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Declaration

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Acknowledgements and contributions

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Abbreviations

LOS: Late onset sepsis

NEC: Necrotising enterocolitis

LMIC's: Low- and middle-income countries

ELBW: Extreme low birth weight

GH: George hospital

AMR: Antimicrobial resistance

QIR: Interquartile range

FDA: Food and drug administration

EBM: Exclusive breastmilk

DEBM: Donor breastmilk

CRP: C-reactive protein

PCR: Polymerase chain reaction

HIV: Human immunodeficiency virus

NICU: Neonatal intensive care unit

GSH: Groote Schuur hospital

The introduction of multi-strain probiotics to preterm infants in a regional hospital: an observational study

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Abstract

Background: Worldwide 1 in 10 of all infants are born preterm. Late onset sepsis (LOS) (> 72hours of life) and necrotising enterocolitis (NEC) are important causes of morbidity and mortality in this vulnerable group. Probiotics may help to decrease the incidence of these conditions, although controversies remain.

Objectives: To describe the implementation of multi-strain probiotics in George Hospital (GH) and determine the incidence of NEC, LOS and mortality in this group. Also, to compare with previous years where there were either no probiotics or only single strain probiotics.

Methods: A retrospective observational study was conducted between February 2019 to July 2020 at George Hospital, Western-Cape, South-Africa. Data were collected from infants who weighed between 800g to 1200g to observe the occurrence of LOS and NEC.

Results: Seventy-seven inborn infants were included. They had a median weight of 1000g, IQR [900-1120g] and a median gestation of 30weeks, IQR [28-31weeks]. The ratio of male to female was 51:49. All of them received breastmilk. A total of eleven (14.3%) infants had positive cultures. These were predominantly gram-negative organisms and there were no positive cultures of probiotic organisms. Seventy five percent of the infections occurred in ELBW infants and their risk for mortality is higher overall. There was a total of seven deaths (9%) of which 3 were before 72hours of

life. Out of all the 77 infants 4 died of LOS. None of the infants in the group had clinical or radiological NEC. Compared with the previous time periods, there was a similar rate of LOS, but a reduction of NEC and death.

Conclusion: The introduction of probiotics to a regional hospital is possible. Less NEC were observed during the administration of multi-strain probiotics

Introduction

Worldwide, approximately 1 in 10 infants are born preterm (<37 completed weeks of gestation). The burden of preterm birth is highest in low- and middle-income countries (LMICs) with neonatal sepsis and necrotising enterocolitis (NEC) being two of the largest contributors to preterm neonatal mortality and morbidity.(1)

Growing evidence supports the key role of a healthy gut microbiota in promoting and maintaining a balance response and in the establishment of the gut barrier in the immediate postnatal life. However, in preterm infants, the development of the microbial community is disrupted by events related to prematurity including mode of delivery, antenatal and postnatal use of antibiotics, minimal exposure to maternal flora, and low intake of breast milk. Such disruption, called dysbiosis, results in an altered barrier and immune function and imbalance between pro- and anti-inflammatory responses, and has been associated with NEC and late onset sepsis (LOS).(2)

Neonatal sepsis is ranked as the third highest cause of neonatal deaths and has a high mortality in the newborn population, especially for preterm infants. Neonatal sepsis is a clinical syndrome consisting of nonspecific signs accompanied by bacteraemia.(3) LOS (after 72hours of life) is more common than early onset sepsis.(4) LOS are typically nosocomial infections with nonspecific features which include, lethargy, feeding intolerance, glucose instability, irritability, temperature instability, bradycardia or tachycardia, poor perfusion and apnoea.(3) Antimicrobial resistance (AMR) has emerged as a global threat to healthcare resulting in an increase in morbidity and mortality. An estimated 31% of deaths from neonatal sepsis are attributed to AMR. (5)

Measures focused on preventing sepsis of the newborn include the important pillars of hand hygiene, the reduction of invasive procedures and early enteral feeding. Breastfeeding is the ideal natural way to help impart anti-infective, anti-inflammatory and immunomodulatory properties to the newborn. (6)

Necrotizing Enterocolitis

NEC is a disease seen primarily in preterm infants. It is a serious condition and results in significant morbidity and mortality. Approximately 5% (1.9-12.9%) of infants less than 33 weeks develop NEC and mortality rates of 30% occur even in the most well-resourced units.(7) The exact cause is not understood, however, mucosal injury, destruction of bowel wall integrity, bacterial translocation and overgrowth triggers a severe and unregulated inflammatory immune response. These infants present with signs such as feeding intolerance, abdominal distention, and blood in the stools. They may have haemodynamic instability and may progress to bowel perforation and peritonitis. NEC can lead to fulminant sepsis and death (8). It is staged by the modified Bell's staging system (Appendix B). (8) NEC rates vary between units and countries with higher rates reported in LMICs. (9)

Several risk factors for NEC have been identified including maternal, perinatal and infant factors. Maternal factors include gestational diabetes, isoimmunization, chorioamnionitis, gestational hypertension and fetal growth restriction. Perinatal factors include fetal distress and fetal hypoxia. Infant factors contribute the greatest risk for NEC. The incidence of NEC is inversely proportional to the gestational age and birth weight. Intra uterine growth restriction, congenital heart disease, umbilical vascular access lines, polycythaemia, sepsis and exchange transfusion all pose risks. (10) Human breast milk is well known to be protective against NEC as compared to formula. (6)

Most theories about the pathogenesis of NEC have focused on the most important risk factors, such as immaturity, formula feeding and the presence of bacteria. Most recently, gut dysbiosis has been proposed as the main risk factor for development of NEC. Based on this theory several clinical strategies are being recommended. These include breast milk feeding, restrictive use of antibiotics, supplementation with probiotics and standardized feeding protocols. (11)

Probiotics

Probiotics are known to improve gut maturity and function in preterm infants. (12) Probiotics are defined as "live microorganisms" which confer health benefits to the host. They are classified as a food supplement, rather than medication, that beneficially affects the host by improving the intestinal microbial balance. At present, several well characterized strains of *Lactobacilli* and *Bifidobacteria* are available to reduce the risk of gastrointestinal infections or to treat such infections. (13)

Probiotics administered at adequate doses, have been proposed as potential tools to prevent NEC and LOS. Updated meta-analyses confirm the benefits of probiotics in reducing the risk of NEC, the time to achieve full enteral feeding, and the risk of LOS in preterm infants. (6) However, most of these meta-analyses fail to explore the role of probiotics in deeper detail, and do not provide specific

recommendations regarding which probiotic strain or mixture of strains should be used, and which population would benefit most from the use of probiotics. (6) The studies however agree that the use of multi-strain probiotics especially Lactobacillus and Bifidobacterium proved to be more effective than single strains. (14)

A recent Cochrane 2020 meta-analysis showed there was benefit in using probiotics to help reduce the risk of necrotizing enterocolitis, sepsis and mortality. However, when only studies with a low risk of bias were included, there was only a benefit for preventing necrotizing enterocolitis. The benefit for ELBW infants was not significant. (15)

A potential disadvantage for probiotic usage is the cost. Expense is an extremely important factor in routine probiotic use and represents a large financial commitment in a resource limiting setting. Although multi-strain is considered better than single strain, the exact strains are still not agreed upon. There is also limited research published on ELBW neonates.

The neonatal unit at George hospital (GH) is the secondary level hospital for the Eden and Central Karoo districts. GH is the referral point for 9 level one hospitals and performs some tertiary level functions such as ventilation and therapeutic hypothermia due to distance from tertiary centre in Cape Town. It has a milk bank and a policy of using only exclusive breastmilk (EBM) from the mother or donor EBM (DEBM) for all infants with a birth weight less than 1500g until their weight exceeds 1500g. All medical NEC cases are managed in GH with surgical referrals transferred to Red Cross War Memorial Children's Hospital in Cape Town.

George Hospital adopted single strain probiotics *Lactobacillus reuteri* in June 2017 and collected data to see if there was any decline in sepsis in their unit. This was presented at a national neonatal conference in Port Elizabeth, South Africa, where they showed that there was a decline in their sepsis rate since the introduction of single strain probiotics (*Lactobacillus reuteri*). (Appendix C) In February 2019 the decision was made to rather introduce multi-strain probiotics (Labinic®) in the unit.

Labinic® drops are a probiotic solution introduced into South Africa in 2018. The 3 strains present equal quantities in Labinic® Drops, *Daniso Howaru Dophilus – Lactobillus Acidophilus* (NCFM), *Daniso Florafit Bididobacterium bifidum* (Bb-01) and *Daniso Florafit Bifidobacterium infantis* (Bi-26). Each Labinic vial cost R842 ($52) in 2020.

All infants 800-1200g that were born in GH from February 2019 were eligible for Labinic drops. The probiotics were given (2drops per day) from the first day of life, once a day, and continued until they reached a weight of 1200g.

Importance of study

This study was important to determine if the introduction of probiotics was possible in a level two hospital in LMIC's. It would also be important to measure if there was any associated decrease in NEC, LOS or mortality.

Objectives

Primary: To describe the implementation of multi-strain probiotics in GH and determine the incidence of NEC, late onset sepsis and mortality in this group.

Secondary: To compare with previous years where there were either no probiotics or single strain probiotics.

Methods

This is a retrospective observational study. Inclusion criteria were all infants born at GH from February 2019 till July 2020 with birth weights 800-1200g. Exclusion criteria were infants with missing or incomplete records. Infants were identified from a probiotic register book where all those who received probiotics were recorded. Folders of these infants were reviewed (all infant records in the neonatal unit are stored electronically). Case report forms were completed on Microsoft Forms. Late onset sepsis was defined as infants (> 72hours of life) with a positive blood culture and NEC was defined as Bells criteria of Stage 2 and above at any period of the admission in the unit. Mortality was documented as any deaths till discharge home or transfer. Late onset sepsis and NEC outcomes in this cohort were compared with the pre- probiotic and single strain eras.

Results from this cohort of infants were then compared with the two time periods when there was no probiotics (January 2016-May 2017) and single-strain probiotics (June 2017-January 2020). This information was extracted from a study done by Myberg et al which was presented at a national neonatal conference in Port Elizabeth, South Africa, (Appendix C)

Statistics

Descriptive statistics were performed with numerical variables expressed as means and standard deviations (parametic) or median and IQR (non-parametic). Chi-squared tests were used to determine if there is a difference between categorical variables.

Ethics

Institutional permission: Ethical clearance was obtained from Health Research and Ethics Committee of the University of Cape Town (HREC nr 537/2022) and permission was obtained from GH.

Results

Seventy-nine infants received probiotics. Two infants were excluded on weight criteria (720g and 780g) which left a total of 77 infants. All folders were retrieved. All 77 infants received probiotics.

Maternal Characteristics (75 mothers)

There were 75 mothers whose infants were included in the study. There were 3 sets of twins, but one twin weighed more than 1200g.

All the mothers received antenatal care prior to their deliveries. Fifty-nine (78.6%) mothers had caesarean sections. Sixty-five (86.6%) of the mothers received antenatal steroids. Two of the mothers tested positive for syphilis in pregnancy but were fully treated and their infants were asymptomatic. Thirteen of the mothers were HIV+, but only one did not have anti-retroviral drugs prior to delivery as she was diagnosed during labour. There were five mothers who were treated for chorioamnionitis in the group.

Infant characteristics (77 infants)

All infants were inborn. They had a median weight of 1000g (IQR 900-1120g) and a median gestation of 30weeks (IQR 28-31weeks). The ratio of male to female was 51:49. One infant was transferred to a tertiary institution due to suspected ileal atresia and he returned after surgery. All infants received exclusive EBM and/or DEBM until they were 1500g. They all received probiotics within 24hours, and it was stopped when the infants reached 1200g or soon afterwards.

All of the 13 HIV-exposed infants birth polymerase chain reaction (PCR)’s were negative. The ten-week PCR results were negative in 11 (84.6%) infants and not done in 2 (15.4%).

Outcomes

A total of eleven (14.3%) infants had positive cultures. One of the infants had 2 positive cultures on separate days and one infant grew 2 different organisms on the same culture. (Table 1). There were no positive cultures of probiotic organisms. Nine (81.8%) of the infants who had positive cultures were ELBW infants.

There was a total of seven (9%) deaths with 3 of these being within the first 72hours of life. The other four (5%) all died of LOS. Two of these cultured *Enterobacter cloacae* and one cultured both *E. cloacae* and *Serratia marcescens.* One baby cultured *Klebsiella Pneumoniae* and died on the same day as the positive culture. The rest of the infants died 1-2 weeks after their positive cultures. (Table 1)

Table 1: Details of infants with confirmed sepsis

Infant	Birth Weight (grams)	Gestation	Day of life	Sepsis 1	Sepsis 2	Outcome (and day of death)
1	980	28	10	*Klebsiella Pneumonia Enterobacter Cloacae*		Alive
2	920	28	25	*Klebsiella Pneumonia*		Died (25)
3	1140	28+3	11	*Klebsiella Pneumonia*		Alive
4	980	28+6	4	*Klebsiella Pneumonia*		Alive
5	840	32	13	*Serratia Marcescens*		Alive
6	880	28	12/21	*Serratia Marcescens*	*Enterobacter Cloacae*	Died (29)
7	1160	31	4	*Enterobacter Cloacae*		Died (19)
8	810	28	7	*Enterobacter Cloacae*		Died (19)
9	840	31	32	*Enterobacter Cloacae*		Alive
10	820	31	8	*ESBL Klebsiella*		Alive
11	920	28	5	*Enterococcus Faecalis*		Alive

NEC was also an important factor to measure due to its potential devasting effects. No NEC was observed or diagnosed amongst this group of infants during the study period.

Comparison with previous time periods:

From January 2016 to May 2017 there were no probiotics in use. Single-strain probiotics were used from June 2017 to January 2019 and multi-strain probiotics from February 2019 to July 2020.

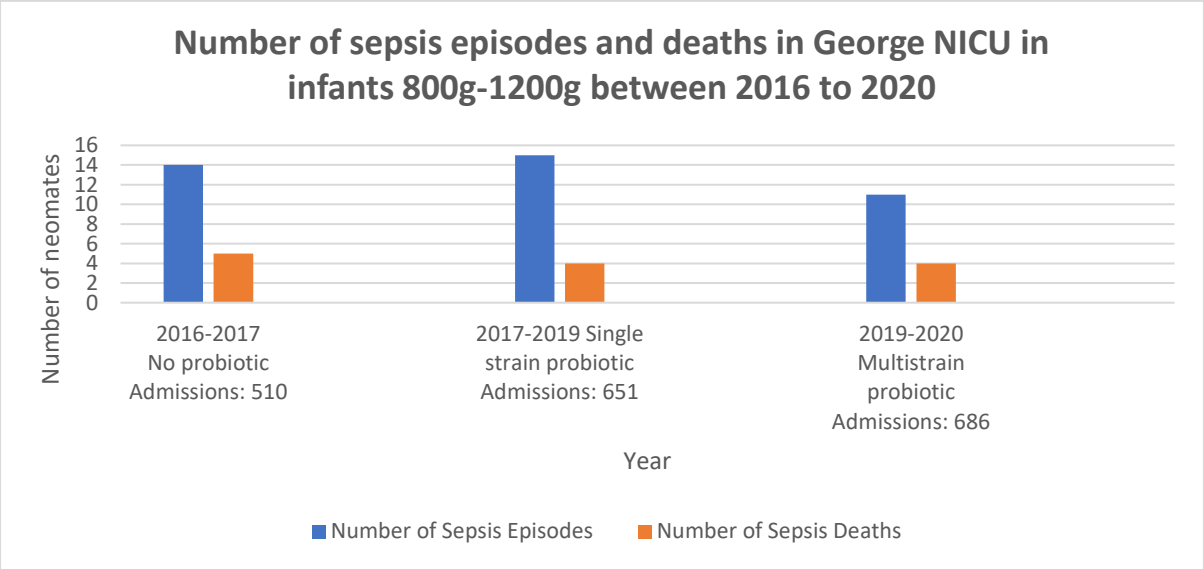

Figure 1: Sepsis episodes and deaths during the three time periods.

Admissions are the total number of all infants admitted to the unit during the time periods. The differences in sepsis rates (2.7%, 2.3% and 1.6%) were not statistically significant (p=0.39)

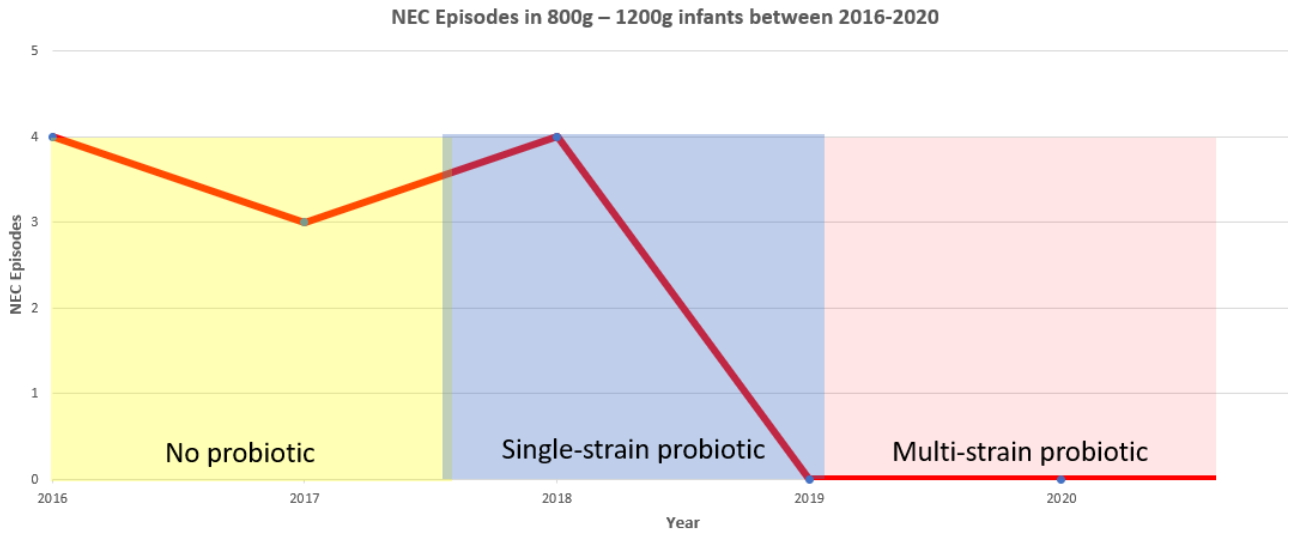

Figure 2: NEC episodes in the 800-1200g infants during the no probiotic, single strain and multi-strain probiotic time periods.

Discussion

In this observational study, the introduction of multi-strain probiotics was a success. The procedure for giving the probiotics was done correctly for all except two infants who received probiotics outside of the weight criteria and were not included in the study. The staff, especially the nurses, were well informed about the probiotic procedures and were vigilant about starting, daily administration and stopping the probiotics. Frequent assessment on ward rounds by the doctors ensured compliance.

As this was a small observational study with historical controls only, therefore no conclusions can be made from the findings. However, it was interesting to note the differences between time periods in a real world (not part of a clinical trial) secondary level setting.

In this group of infants 11 out of 77 (14.3%) had sepsis of which four infants died. This rate is higher than a study done in Cape Town but falls within the interquartile range of units in a large international database. (16) It is important to note that these comparative studies were for VLBW infants and not only the 800-1200g infants in this study. The cultures were predominately gram-negative organisms with only one-gram positive culture (*Enterococcus Faecalis*). This correlates with a study by Dramowski et al which found that sepsis is a leading neonatal cause of death in sub-Saharan Africa and is mainly cause by Gram-negative pathogens with substantial antimicrobial resistance. (17) Four of the infants with positive cultures died. Although three of these died more than a week after the positive culture, it is assumed that the death was still related to the sepsis or a complication thereof.

When comparing the three time periods at GH there was not a significant change in the incidence of sepsis in the 800-1200g infants, nor in deaths related to sepsis. A review by Neu et al, evaluated the effect of probiotics for LOS prevention in preterm infants according to type of feeding (EBM vs exclusive formula or mixed feeding). Overall, probiotic supplementation resulted in a significantly lower incidence of LOS only in human milk-fed preterm infants (RR 0.75 (95% CI 0.65-0.86).(7)

However, this study at GH did illustrate a decrease in the incidence of NEC, as there were no cases during the study period. Comparing with previous time periods, the rate of NEC at GH was less when single strain probiotics were administrated compared to when no probiotics were used. There is stronger evidence that probiotics decrease NEC rates in VLBW infants. A meta-analysis by Deshpande et al results confirmed the significant benefits of probiotic supplements in reducing death and the risk of NEC in preterm neonates (18). However, many questions remain. Robertson et al showed that although probiotics may reduce the incidence of NEC in preterm infants less than 28 weeks gestational age, the evidence was still low for extreme low birth weight (ELBW)(<1000g) neonates (12).

Although invasive sepsis from probiotic organisms is very rare, it can be devasting, as seen recently in the United States, where in October 2023 the Food and Drug Administration released a new warning raising concerns about the use of probiotics following the death of an ELBW infant.

If the controversies around probiotics are resolved for example the cost, strain preferences and more research about ELBW infants, they would be a welcome addition to the management of small infants. NEC has a high mortality and morbidity in South Africa and often requires the use of TPN and prolonged antibiotic use.(19)

Other factors which may have contributed to the decrease in NEC included that GH has a strict breast milk policy for all infants <1500g, standardized feeding protocols and a strict hygiene policy.

The cost-effectiveness of probiotics, especially in low-income countries with their resource limitations has been investigated. In 2020 Atoosa et al examined the cost-effectiveness of prophylactic probiotics on NEC prevention in VLBW infants and concluded that prophylactic probiotics were a cost-effective strategy in NEC reduction. (20) GH used two vials of probiotics per month (R842 per vial in 2020) so the cost was not prohibitive.

Limitations

This was a small retrospective sample of infants with only a historical control group and no placebo arm and thus is purely observational. We were also unable to ascertain the exact number of admissions in each time period in the 800-1200g category and therefore used the total admissions of

all infants during those periods to calculate sepsis rates. Although this is not ideal, the ratio of 800-1200g infants is likely to be relatively similar between time periods

Conclusion

It is possible to effectively introduce probiotics into a secondary level hospital neonatal nursery. This observational study showed a similar rate of LOS to other time periods and no cases of NEC.

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Appendix A

Ethics approval letter

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☐ Approved	Annual progress report	Approved until/next renewal date	30.03.2025
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee	Signed by candidate	Date Signed	17/3/2024

Note: Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf file to hrec-enquiries@uct.ac.za.

HUMAN RESEARCH ETHICS COMMITTEE
12 MAR 2024
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

Please clarify your plan for research-related activities during COVID-19 lockdown

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	12 March 2024		
HREC REF Number	537/2022	Current Ethics Approval was granted until	30/9/2023
Protocol title	The introduction of multi-strain probiotics to preterm infants in a regional hospital: an observational study		
Principal Investigator	Lloyd Tooke		
Department / Office Internal Mail Address	Neonatal Department, Old Main building		
1.1 Does this protocol receive US Federal funding?		☐ Yes	✓ No

2. Protocol status (tick ✓)

☐	Research-related activities are ongoing
✓	Data collection is complete, data analysis only
Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.	

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		65
Total number of records or specimens collected, reviewed or stored since last progress report		
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	✓ No

4. Signature

Signature of PI	Signed by candidate	Date	12 March 2024

Appendix B

Modified Bell's Criteria for NEC

NEC stage	Findings		
	Clinical	**Gastrointestinal**	**Radiographic**
I	Apnoea, bradycardia	Gastric residuals	Mild intestinal dilatation
		Mild abdominal distension	
IIa	Apnoea, bradycardia	Grossly bloody stools	Marked intestinal dilatation
	Mild inflammation	Marked abdominal distension	Ileus
		Absent bowel sounds	
IIb	Thrombocytopenia	Abdominal tenderness	Pneumatosis intestinalis
	Mild acidosis		Portal venous gas
	Inflammation		
IIIa	Moderate acidosis	Abdominal discolouration	Pneumatosis intestinalis
	Coagulopathy		Portal venous gas
	Hypotension		
	Oliguria		
IIIb	Shock	Perforated bowel	Free abdominal air

Source document Necrotising enterocolitis (NEC) staging (adapted from Walsh and Kliegman 1)

Appendix C (Study at GH)

Background for the sepsis survey and enteral probiotic use in preterm infants conducted by Dr Myburgh in 2016

Background:

George Regional Hospital is the only level 2 hospital for the 2 Geographical Service Areas of Eden and Central Karoo. It provides care and service the town of George and to 6 level one hospitals in Eden Subdistrict and 3 level 1 hospitals of Central Karoo. A yearly average is showing around 10 000 deliveries in comparison to the yearly average of around 100 000 deliveries in the Western Cape, according to yearly PPIP data. The distance to our tertiary referral hospital forced the George Hospital unit to provide tertiary care to improve outcome and provide equal and safe neonatal care.

The Neonatal unit statistics shows average of 600 admission per year of which on average 7/month admissions come from level one hospitals.

Intensive training and outreach and support program is running to all the level one hospital's in the 2 GSA's. MSSN and HBB training was completed at all the hospitals and CPAP with surfactant treatment was standard care at 5 of the level 1 hospitals. Daily discussion with all level one units to address any neonatal questions happen to help decrease need for transfers to the busy George unit.

The Neonatal service at George Regional Hospital, comprise of 8 bed Neonatal unit (classified as high-Care, but functioning as NICU), 13 high-care beds and 6 KMC beds. The Neonatal ICU provide level 3 care, inclusive of BiPAP, SIMV, HFOV, total parenteral nutrition (TPN) and inotropic support via central lines would be standard care. Nursing allocation is a challenge with the unit not accredited as a neonatal ICU, but most of our sisters have completed the Advanced Midwifery and Neonatal diploma course. The allocation of staffing at the time of the survey in 2016, the unit at daytime were staffed with 2 PNB1/2 and at nighttime 1 PNB 1 sister with an ENA Nurse. The high care unit is staffing is at a ratio of 2-3 staff to 13 high babies and 7 KMC babies and mothers. The biggest challenge of the Neonatal Unit is floor space and bed occupancy rate. The bed occupancy rate for high care are showed a median of 114,8% and for NICU 100%. The recommended space between incubators cannot be met with current available floor space.

Klebsiella sepsis, the most common organism cultured, posed a crisis with a 2.7/1000 death rate. The challenges required an action plan based on a literature and clinical practice reviews to help us improve our sepsis. We discussed our crisis with the hospital management, but no plan regarding floor space could be made.

The standard interventions were re-enforced:

- Hand washing techniques to all staff and visitors
- Alcohol based hand rub at each bedside
- Insertion of all peripheral and central lines with prepared sterile packs and with use of chlorhexidine antiseptic and using strict aseptic technique when inserting central lines
- Ward protocols were revised on washing incubators, changing suction bottles and using suction catheters only and cleaning protocols applied
- Visiting policy – maximum of 2 people at the bedside, only parents and grandparents allowed to visit.

In addition to the above-mentioned interventions, the literature search supports the use of probiotic preparations in neonates. This was a viable and only new intervention we identified to implement in our resource limited level 2 hospital.

Study:

The aim of the study was to target the highest risk group for late onset sepsis, the babies with a birth weight less than 1.2kg. On 22nd of June 2017 the standard use of a single strain Lactobacillus species probiotic was introduced from admission to the unit, to all babies with a birth weight of less than 1.2kg, as a daily dose of 2 drops daily orally, the supplementation was continued until the baby reached 1.2kg.

Outcome: we looked at 3 outcomes to measure the effect of probiotic use in our unit

1) Number of positive blood cultures represented in figure 1
2) The sensitivity of klebsiella isolates to Piperacillin and Tazobactam since starting probiotics, figure 2
3) Mortality risk measured from PPIP data, figure 3

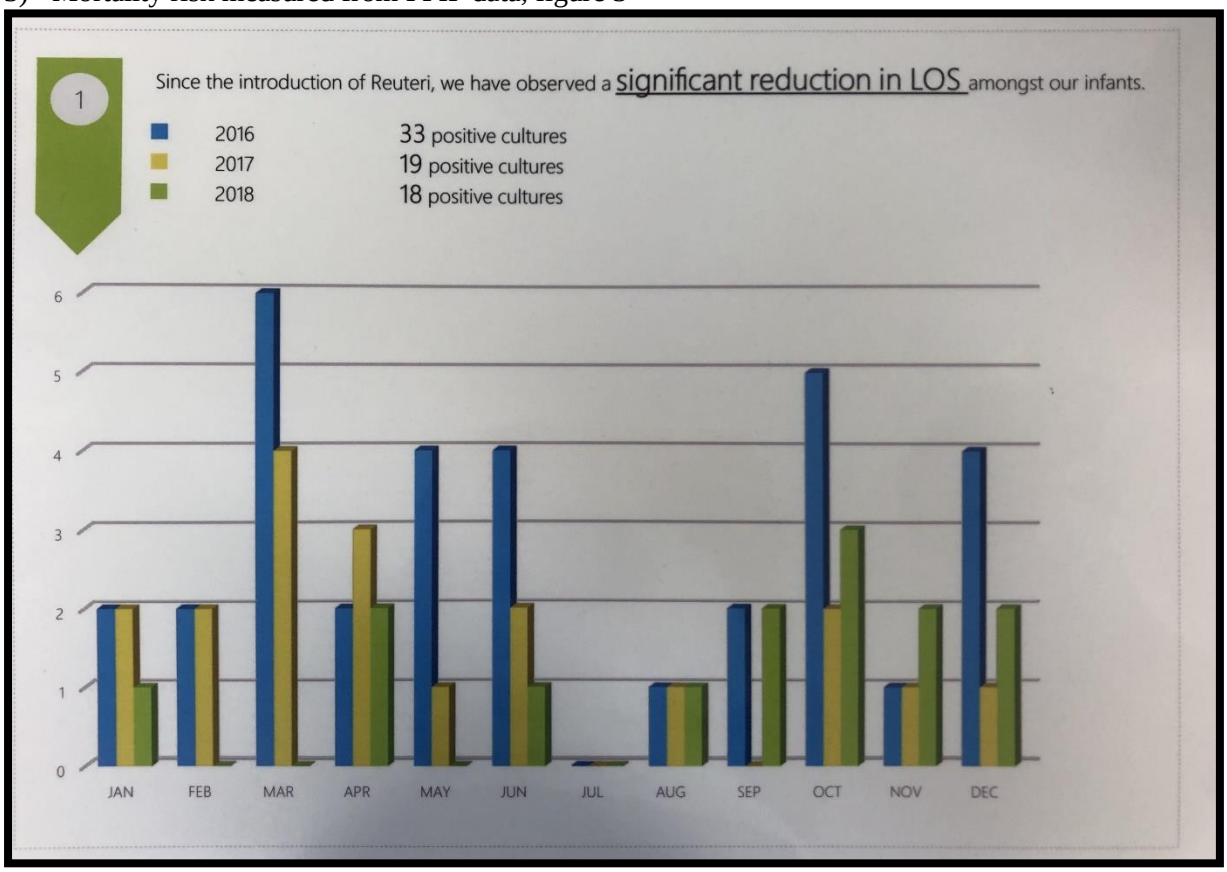

Fig 1. Reduction in culture positive sepsis following the introduction of Probiotics

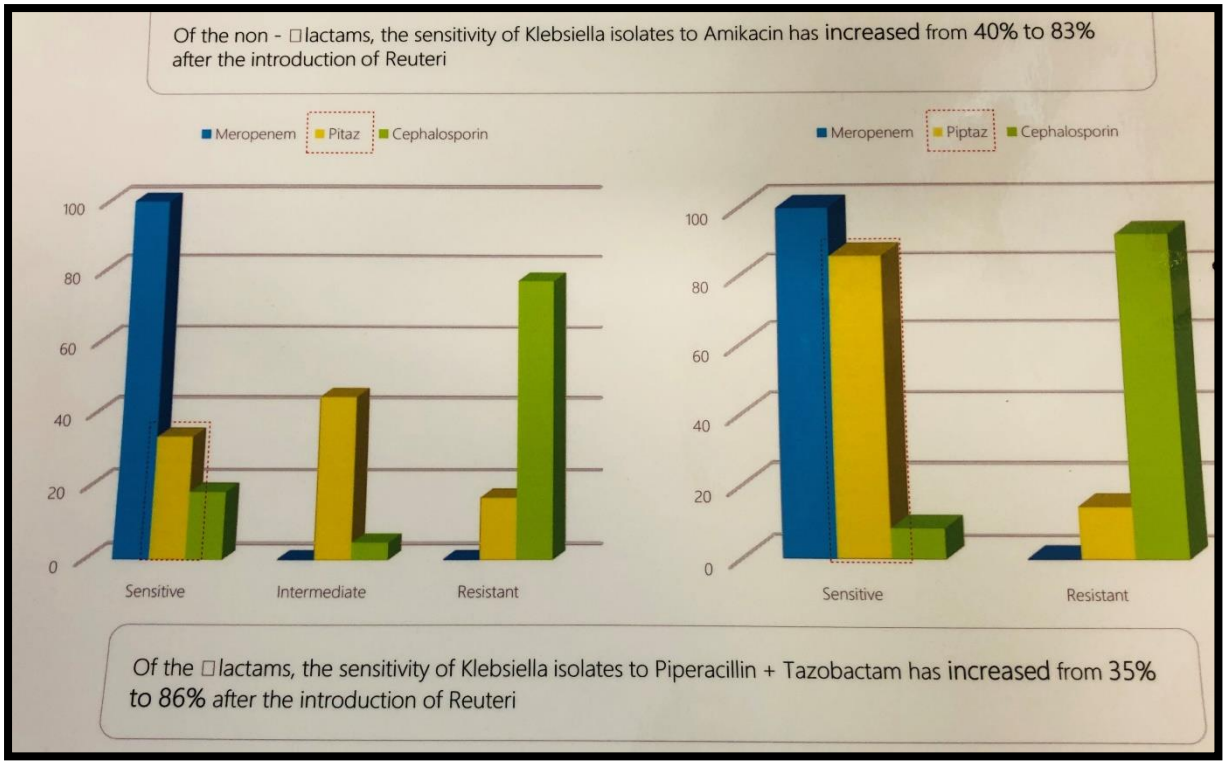

Figure 2. Increased sensitivity of the Klebsiella isolates to second line antibiotics

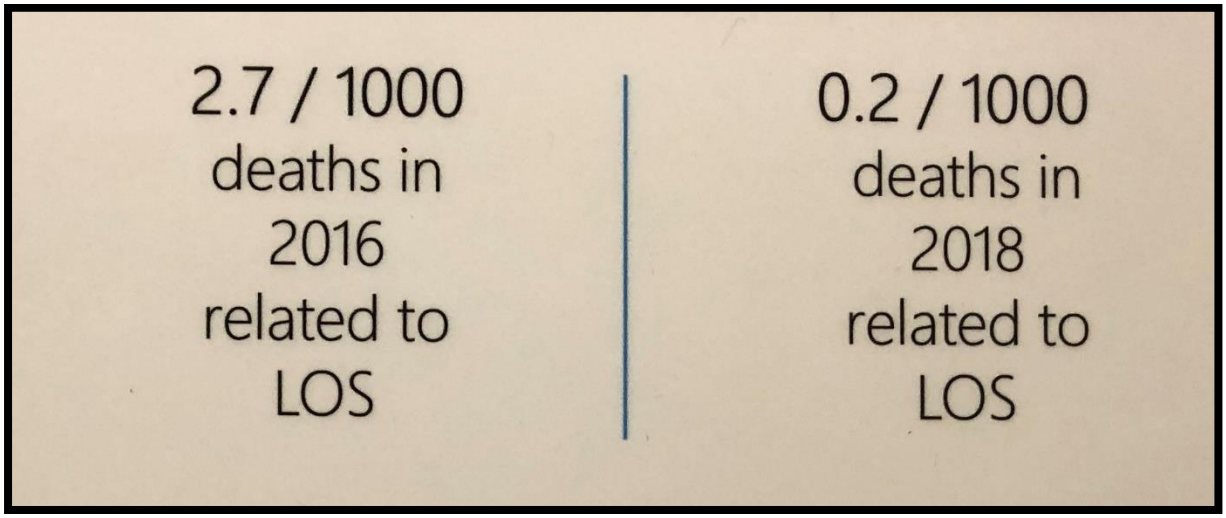

Figure 3. PPIP data analysis, showing statistically significant risk for death since introduction of probiotics

Conclusion:

The routine use of a single-strain Lactobacillus species probiotic was safe and effective in reducing LOS in our high-risk population. It showed increased susceptibility of Klebsiella species to our second-line antimicrobials. Realizing the short coming of needing a bigger sample size and to compare the efficacy of different probiotic strains.