EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY LOW BIRTH WEIGHT NEONATES AT KENYATTA NATIONAL HOSPITAL: A PILOT RANDOMIZED CONTROLLED TRIAL.

A DISSERTATION IN PART FULFILLMENT OF THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH OF THE UNIVERSITY OF NAIROBI.

BY

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

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DEDICATION

This book is dedicated to my wife Dorcas, and our children Kipkoech and Tala, for their patience and unwavering support throughout the period of my postgraduate programme. I cannot forget to dedicate this to my mother Esther Rob and my late father James Rob for their constant encouragement all through my academic career thus far.

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6. All parents and neonates who participated in the study.

May God richly bless you all.

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DEFINITIONS

Early enteral feeds - enteral feeds given within 24 - 48 hours of birth.

Average daily weight gain - the weight gained in grams per kilogram per day. Calculated by subtracting the birth weight from the day 28 weight, then dividing the difference by 28.

Major congenital malformations - include severe gastrointestinal structural anomalies and abdominal wall defects, congenital heart disease, severe respiratory defects, severe neural tube defects, and severe renal anomalies.

Full enteral feeds - enteral feeds providing ≥ 100kcal/kg /day which on average are provided by about 150ml/kg day of expressed breast milk.

HIV exposed neonates - infants born to HIV positive mothers.

LIST OF ABBREVIATIONS

KNH	Kenyatta National Hospital
UN	United Nations
WHO	World Health Organization
NEC	Necrotizing enterocolitis
LBW	Low birth weight
VLBW	Very low birth weight
IUGR	Intrauterine Growth Restriction
g	grams
Kg	kilograms
IT ratio	immature neutrophil to mature neutrophil ratio
CSF	Cerebrospinal fluid
HIV	Human immunodeficiency virus
AIDS	Acquired Immunodeficiency Syndrome
SPSS	Statistical Package for Social Sciences
Epi info	Epidemiological Information
RR	Respiratory rate
NICU	Neonatal Intensive Care Unit
KEMRI	Kenya Medical Research Institute
KMC	Kangaroo Mother Care
bpm	breathes per minute

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ABSTRACT

Background: Introduction of standardized feeding regimens for neonates has been associated with better weight gain, earlier attainment of full enteral feeds and reduced risk of necrotizing enterocolitis (NEC) in high income countries. Better weight gain is in turn associated with better short and long-term physical and neurological outcomes for low birth weight neonates.
This pilot study was aiming to assess the effect of a standardized feeding regimen on early neonatal growth.

Objectives: The primary objective was to determine the effect of a standardized feeding regimen (SFR) on neonatal growth, measured at twenty eight days of age, and obtain preliminary data on safety and feasibility. The specific objectives were to describe and compare the average daily weight gain between the two feeding groups, that is, the standardized feeding regime (SFR) group and the current feeding regime (CFR) group at 28 days of age; to describe and compare the proportion of neonates in the two feeding groups who had attained or surpassed their birth weight by 21 days of age and to describe the proportion of neonates that attained full enteral feeds at or before 7 days of age.

Design: Open randomized control trial.

Methods: Seventy two neonates with birth weights between 1000g and 1999g were randomly assigned into two feeding arms, one(CFR) with 37 and the SFR group with 35 babies. Initial measures taken included birth weights taken using a digital weighing scale able to measure up to 10 grams. Those in the intervention arm received enteral feeds according to a standardized feeding regimen beginning within 4 hours of age for the 1500g - 1999g subgroup and at 24 hours for the 1000g - 1499g neonates. The SFR consisted of early introduction of feeds and rapid increment in volume of feeds .The control group's feeding was the current feeding regime (CFR) in the newborn unit in Kenyatta National Hospital which mainly consisted of slow introduction of, and low volume increment of enteral feeds.

Main outcome measure: Average daily weight gain calculated at 28 days of age. Secondary outcomes were; time (in days) till regaining of birth weight, time to attaining full enteral feeds and frequency of feed intolerance or NEC.

Data Analysis: Analysis was by intention to treat. Descriptive statistical and analytical methods were used for data evaluation and results presentation.

Results: Seventy two neonates were recruited and randomly assigned to the two feeding groups with thirty seven in the CFR group and thirty five in the SFR

group. Thirteen patients (18.05%) died, six (8.33%) developed feed intolerance and one was lost to follow-up.

The baseline characteristics, including the number of males and females, numbers in the weight subgroups and mean birth weight, between the two groups were the same.

The neonates on the SFR had a mean weight gain of 14.1 g/kg/day compared to a mean weight gain of 9.8 g/kg/ day in the CFR group and this was a statistically significant difference (p= <0.001).Those on the SFR also attained full feeds earlier at a mean of 5.6 days compared to a mean of 7.0 days in the CFR group and this was a statistically significant difference (p=0.002). Those babies fed by the SFR regained their birth weight by a mean of 7.2 days compared to a mean of 9.9 days in the CFR group and this too was statistically significantly different(p=0.001).

The episodes of significant feed intolerance did not differ between the two feeding regimes.There was no difference in mortality between the two feeding regimes though the study was not powered to detect a difference between the two groups.

Conclusions: There was a statistically significant weight gain advantage and earlier attainment of full feeds and regaining of birth weight in the neonates fed using the standardized feeding regime. The study did not find any difference in the episodes of feed intolerance between the two feeding regimes. Mortality between the two groups did not differ though the study was not powered to detect a difference.

INTRODUCTION

The reduction of the under five mortality rate by two thirds between the years 1990 and 2015 is the fourth of the UN Millennium Development Goals [1]. In Kenya the under five mortality in 2003 was 114 deaths per 1000 births, with an infant mortality rate of 78 per 1000 live births [2]. Prematurity, together with birth asphyxia, was found to account for sixty two percent of early neonatal deaths (those occurring before the end of the first week of life) in Kenya [3].

Provision of appropriate nutrition for growth and development is a cornerstone in the care of low birth weight and preterm infants. Early and adequate nutrition during this critical period of extra uterine growth has a substantial impact on clinically important short and long term outcomes, both physical and neuro-developmental [4,5].

For low birth weight neonates less than 1.75 kilograms, early introduction of enteral feeds and rapid daily increments in feed volumes are associated with better weight gain, earlier attainment of full enteral feeds and thus earlier discharge from hospital in developed country settings [6]. A systematic review of two studies with a total of seventy two patients concluded that such early feeding (< 4 days) had no significant adverse effects particularly on incidence of necrotizing enterocolitis (NEC) in these settings [6].

In contrast to variable clinician-directed approaches to initiating and increasing feeding, introduction of standardized feeding regimens has also been associated with better weight gain and earlier attainment of full enteral feeds that may result in better short-term and long-term physical and neurodevelopmental outcomes for low and very-low birth weight neonates [7]. Introduction of standardized feeding regimens has also been shown to reduce the risk of NEC, the benefit being related to minimization of variations in enteral feeding practices as well as increased awareness leading to early detection of signs of feed intolerance [8]. However, such standardized feeding regimens had not been evaluated in settings (like Kenyatta National Hospital) that are unable to provide total parenteral (intravenous) nutrition.

This pilot study aimed to assess the effect of introducing a standardized feeding regimen on neonatal growth ,measured by average daily weight gain and early clinical outcomes including; time till regaining birth weight and time to attainment of full enteral feeds. These measures represent important clinical parameters that may provide an indication of the possible direction of effects on mortality as well as providing important baseline data for possible, future studies. These endpoints were compared between two groups randomly assigned to either follow a standardized feeding regimen or the current feeding

regimen in the Kenyatta National Hospital newborn unit. The current feeding regimens reflect different consultants' preferences but in general comprised low volume increment of feeds and late starting of enteral feeds especially for sick neonates.

LITERATURE REVIEW

Standardized feeding regimens

The introduction of standardized feeding regimens has been shown to reduce the risk of necrotizing enterocolitis (NEC). Patole et al in a systematic review and meta-analysis of six studies (carried out over a 25 year period) concluded that introduction of a standardized feeding regimen reduced the incidence of NEC by 87 percent [8].

The introduction of a standardized feeding regimen that includes rapid advancement of feed volumes is also associated with better weight gain and earlier attainment of full enteral feeds. A meta-analysis of 3 randomized controlled trials showed an overall reduction in mean days to full enteral feeds and days to regain birth weight among infants in the rapid rate of feed advancement group. There was no significant effect on NEC [6].

Street et al in an observational study also concluded that implementing feeding guidelines in NICU patients <2000g birth weight was associated with significantly less variability in feeding-related outcomes which include; day of life when first enteral feed given, number of days during entire hospitalization when no feeds given, and number of days when feeds of 80ml/kg/day and 100kcal/kg/day of enteral feeds were achieved [9].

These studies were carried out in centres with the capability of administering parenteral nutrition. The impact of these standard feeding protocols in settings without parenteral nutrition needed to be studied.

Early growth of low and very-low birth weight neonates

Premature infants weighing less than 1500g who have a weight appropriate for gestational age (AGA) normally regain their birth weight by two to three weeks and by 40 weeks post-conceptual age (term) should be within two standard deviations (SD) of the expected mean birth weight [10]. After regaining birth weight subsequent weight increment is expected to be on average ≥ 15g/kg/day till the age of their expected time of delivery [10]. Head growth also continues at a rate similar to intrauterine expectations but linear growth stagnates at 34 weeks gestation after which it accelerates to attain the expected level at term. Earlier regaining of birth weight is associated with better growth velocity [10].
Inadequate nutrition and illness during the neonatal period are potent inhibitors of growth and conversely the presence of failed growth indicates the presence of one or both factors [11].

Other factors also influence early neonatal growth. Were in a cross-sectional survey of 175 very low birth weight infants at the Kenyatta National Hospital newborn unit showed that factors associated with better growth at term included feeding on preterm formula ($p < 0.001$) and absence of neonatal morbidity ($p < 0.001$). Infants who were appropriate for gestational age at birth also had better catch up growth at term compared to those born small for gestation ($p < 0.001$) but their neonatal growth itself was not significantly better [11].

In a randomized controlled trial of 161 infants at the KNH newborn unit, Mwendwa, found that neonates on partial kangaroo mother care (KMC) had a significantly higher growth rate compared to a control group. The infants in the KMC group had statistically significant higher weight gain of 22.5g/kg/day compared to 16.7 g/kg/day in the control group and higher mean head circumference of 0.91cm/week compared to 0.54cm/week in the control group. Kangaroo mother care was found to the strongest predictor of mean weight and head circumference [12].

Muhudhia , in a prospective cohort study of 61 preterm infants weighing between 1001- 1750g at the KNH newborn unit found that the rates of weight gain, after regaining birth weight, were 12.7g/kg/day,10.4g/kg/day and 8.7g/kg/day for those with birth weights of 1001-1250g,1251-1500g and 1501-1750g respectively. In this cohort, the quality and quantity of breast milk fed to the babies (low protein in preterm breast milk), unrecognized subtle illness (like mild anemia, electrolyte imbalance, mild acidosis and low grade infection) and inadequate temperature control (due to faulty incubators, babies being kept out of incubators for long periods during feeding) were thought to be the main contributing factors to the observed lower rate in weight gain [13].

Early growth is an important determinant of later development. Lucas established that infants who were inadequately fed and failed to grow normally during the first month of life had lower neuro-developmental scores when assessed in later childhood [14]. In a two year longitudinal descriptive survey of 120 infants with birth weights between 1000g and 1500g,Were et al concluded that slower growth, choice of early nutrition and post discharge morbidity were associated with subsequent neurological dysfunction which included cerebral palsy and delayed cognitive function [7, 5].

Benefits of early feeding

Enteral feeding of preterm infants with milk in the first five days of life promotes maturation of intestinal motility patterns and endocrine adaptation. It also provides luminal nutrients and may also benefit immune function [15]. These result

in clinical benefits including earlier tolerance of enteral feeds, reduced risk of infection and thus earlier discharge from hospital[15].

Rapid advancement of enteral feeds in low birth weight infants has been shown to reduce the days to regaining birth weight and days to attaining full enteral feeds [6].A longitudinal cohort study on 117 VLBW infants concluded that early and aggressive introduction of feeds (both parenteral and enteral) resulted in better growth in weight, length and head circumference, and a reduction of nutritional deficits at 40 weeks of postmenstrual age [16]. Though the study included parenteral nutrition it signified the importance of early introduction of enteral feeds.

A retrospective study on 385 infants evaluated the effect of age at introduction of enteral feeding on the incidence of neonatal sepsis and NEC in VLBW infants. The conclusion was that early enteral feeding (2.8 days vs. 4.8 days p=0.001) was associated with a reduced risk of neonatal sepsis but no change in the risk of NEC. Possible mechanisms explaining the reduced rate of infection with early enteral feeding included: prevention of gastrointestinal atrophy, reduced intestinal bacterial contamination in presence of enteral feeds, decreased use of total parenteral nutrition and likely improved mucosal immunity due to possible development of gut associated lymphoid tissue [17].

Conclusions from studies on rapid advancement of feeds remain uncertain about the effect of different rates of feeding on NEC. For the three studies and 371 infants evaluated by Kennedy et al, the confidence intervals for this outcome were broad because of the low rate of occurrence [6]. Thus rapid advancement could be associated with either a beneficial or deleterious effect on NEC with insufficient data to draw firm conclusions.

Conclusions

Standardized feeding regimens that included rapid feed volume advancement were associated with earlier attainment of full enteral feeds and earlier regaining of birth weights at no obvious increased risk of NEC in high income settings where co-administration of parenteral nutrition was also used. Earlier regaining of birth weights was associated with better neonatal growth velocity. Attainment of early normal neonatal weight gain in very low birth weight infants was shown to be associated with better long term neuro-developmental outcomes, both physical and cognitive, in these children. It was therefore possible that a standardized feeding regimen could improve weight gain and be associated with other benefits at no excess risk if introduced in lower income settings such as KNH.

STUDY JUSTIFICATION

Studies have shown that early and rapid enteral feed volume increments result in better neonatal growth. Feeding on preterm formula and absence of neonatal morbidity have been associated with better neonatal growth. In KNH breast milk is the predominant milk used in feeding of neonates. But the effect of early and aggressive feeding on growth in low and very-low birth weight neonates in low income settings represented by the Kenyatta National Hospital newborn unit had not been studied.

KNH had not yet implemented a standardized feeding regimen that comprised rapid feed volume increments, thus an assessment of its impact and likely benefit needed to be documented. This is in keeping with the hospital's goals to introduce best practice.

Proper administration of total parenteral nutrition to neonates admitted at KNH was not yet possible, thus early attainment of adequate enteral feeds was thought to be important even in sick neonates although the feasibility, safety and preliminary evidence of effectiveness of standardized, aggressive enteral feeding of the sick babies needed to be established.

HYPOTHESIS

The standardized feeding regimen was going to lead to improved weight gain and earlier regaining of birth weight in the low and very-low birth weight neonates.

Null Hypothesis: There would be no difference in neonatal weight gain between those receiving feeds according to current practice and those whose feeding was guided by a standardized regimen aiming at early introduction and reasonably rapid increases in feeds.

OBJECTIVES

Broad objective

To determine the effect of a standardized feeding regimen on neonatal growth, measured at twenty eight days of age, and obtain preliminary data on safety.

Specific objectives

1. To describe and compare the average daily weight gain between the two feeding groups at 28 days of age

2. To describe and compare the proportion of neonates in the two feeding groups who had attained or surpassed their birth weight by 21 days of age.

3. To describe the proportion of neonates that attained full enteral feeds at or before 7 days of age.

METHODOLOGY

Study design: Open randomized controlled trial

Study Location: Kenyatta National Hospital Newborn Unit.

Study population:

Neonates with a birth weight between 1000g and 2000g who met the inclusion criteria.

Inclusion Criteria:

Preterm neonates (AGA) admitted with a birth weight of between 1000g and 1999g who would normally be started on intravenous fluids in the first 4 -24 hours

Informed consent given by the parent

Exclusion Criteria:

Major congenital malformations including those that were likely to interfere with possible early enteral feeding and growth including; severe gastrointestinal structural anomalies and abdominal wall defects, congenital heart disease, severe respiratory defects, severe neural tube defects, and severe renal anomalies.

Preterm neonates with IUGR, due to likely difference in growth velocity.

Term infants (>36 weeks gestation) with severe IUGR, resulting in a weight less than 1999g.

Severe birth asphyxia - neonates with clinical features of hypoxic ischemic encephalopathy stage 2 or 3.

Severe respiratory distress - infants with a respiratory rate of ≥ 60 breaths per minute, sternal recession and who remained cyanosed on oxygen at birth and continuing beyond 72 hours of age

Infants of mothers known to have HIV infection or AIDS since such infants, if infected, are known to be independently predisposed to abnormal growth

Neonates who were under the private care of consultants.

Sampling and sample size

The sample size was estimated using the formula given below:

$$n = \frac{7.85\,[(R+1) - p2\,(R^2+1)\,]}{p2\,(1-R)^2}$$ [18]

n = sample size in each group
7.85 derived from power (1 – ß) of 0.8 and type 1 error (α) of 0.05.
p1= event rate in treatment group (estimated reduction in growth faltering to 30% of neonates)
p2 = event rate in control group (60% of neonates gained weight at <15g/kg/day in the study) [11]
R = risk ratio (p1/p2)

R = 0.5

n = 40 children in each arm,

An additional 32% and 22% will be added to cater for mortality during the neonatal period for the birth weight categories 1000-1499grams and 1500-1999grams respectively [19].
This means an additional 16 babies in each arm.
Total babies in each arm will be 56.

Total number to be recruited 112.

Stratification
Distribution of the numbers between the two strata will be as follows:

1000g – 1499g =55% = 58 pts

1500g – 1999g = 45% = 54 pts

This is based on the number of admissions between April and July 2007.

Screening and Recruitment

Enrolment
The neonates were enrolled during working hours between Monday and Friday. Neonates with birth weights 1500-1999g were enrolled within 4 hours of birth while for those with weights of 1000-1499g enrolment was within 24 hours.

Consent
Consent was sought from the parent as soon as possible, preferably within 4 hours of birth but not later than 24 hours.

Assignment and Randomization
The neonates were stratified into two weight groups; those of birth weight between 1000g and 1499g, and those between birth weights 1500g and 1999g.

Randomization was carried out using a table of random numbers thus enabling neonates within each weight group to be randomly assigned to either feeding arm.

Neonates meeting the inclusion criteria were allocated sequential study numbers within the weight groups using two different sets of opaque envelopes, one for each weight stratum, pre-labeled with the study number. Inside the envelope, opened after consent had been gained, were instructions on the feeding regimen to be used.

Clinical Methods
The principal investigator collected sociodemographic data and filled out a standard form that was provided for each neonate in the study. A full history was taken and a physical examination carried out on all the eligible neonates. The Modified Ballard's score (see Appendix 11) was used to estimate gestational age. Once the gestational age was confirmed using the Ballard's Score the weight was checked against standard curves to confirm if the neonate was AGA by virtue of being above the 10^{th} percentile for gestation and sex. All this was done by the principal investigator.

The feeding regimen assigned was prescribed, according to a feeding chart provided in each opaque envelope, in addition to the routine care of neonates admitted at KNH including; vitamin K, thermoneutral environment, regular monitoring of vital signs and specific treatment as indicated. Feeds given were entered in a standard feeding chart. Daily review of the feeding charts was carried out by the principal investigator to ensure conformity with the feeding regimens.

Measurements

The birth weight was taken at admission and subsequently measured every two days. The weights taken were those of unclothed neonates. The weighing scale was zeroed and calibrated every fortnight using standard 500g and 1kg weights that were used throughout the time of the study. The scale used was a digital scale (ADE/Germany Model M10612) with a maximum of 20kg and providing weight measures in increments of ten- grams.

Investigations

Any neonate with suspected neonatal sepsis had relevant investigations done, at the discretion of the attending clinician, including; full blood count and IT ratios, blood cultures, urine cultures and lumbar puncture for cerebrospinal fluid microbiology and biochemistry(if indicated).

Any neonate who developed signs and symptoms of necrotizing enterocolitis (see Appendix 10) had a plain abdominal radiograph done and the films examined by a radiologist who remained blinded to the feeding regimen allocation.

Feeding procedures

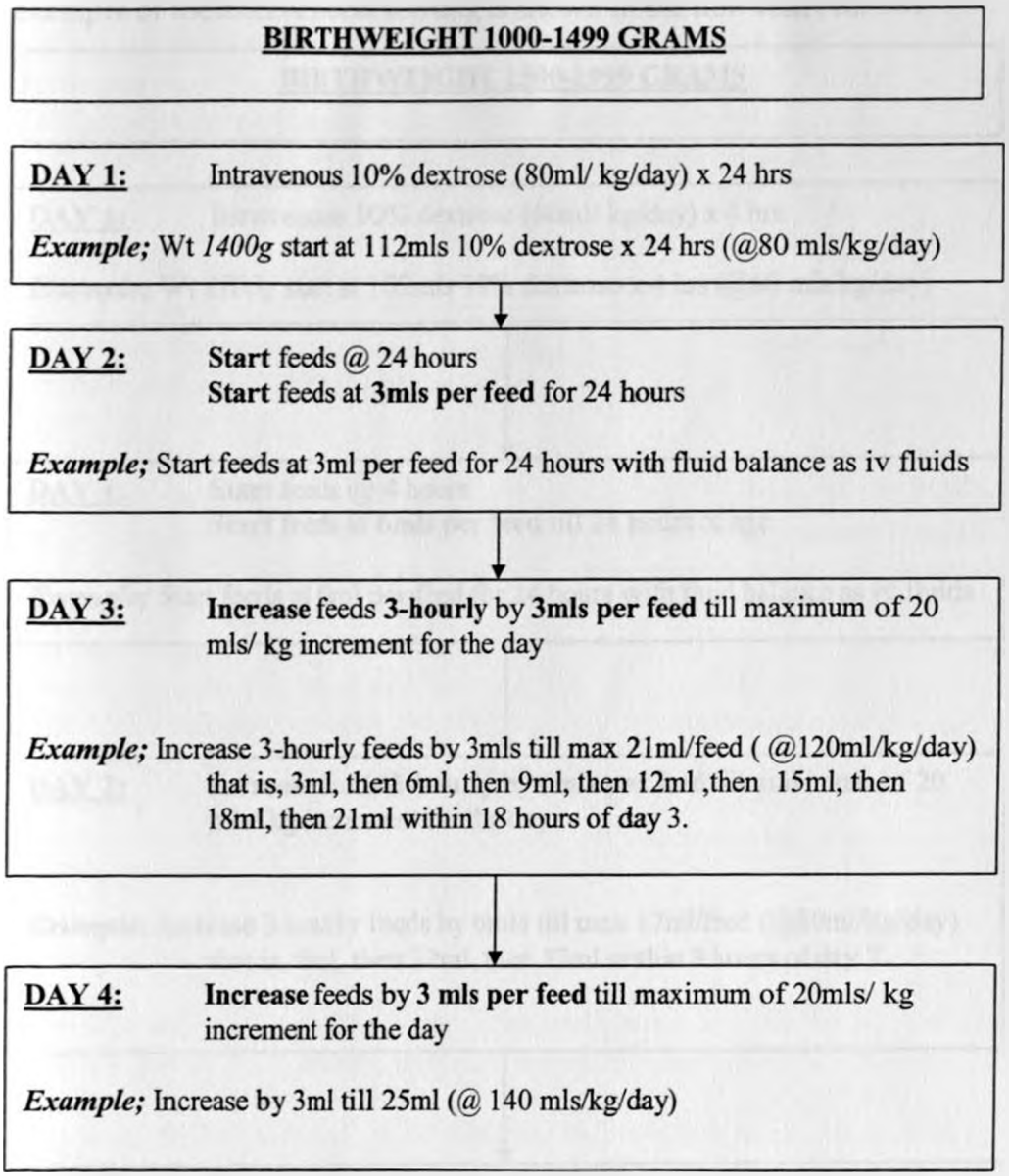
For the intervention arm, feeding was as follows

Babies < 1500g

For those < 1500g, enteral feeding was started at 24 hours. The neonates had been on intravenous 10% dextrose in the first 24 hours. Feeding was by intermittent bolus gavage through a nasogastric tube for those weighing less than 1500g with progression to intermittent cup feeds as soon as possible while maintaining the prescribed feed volumes. The milk given was expressed mother's breast milk (preferred) unless this was unavailable due to the mother's inability to provide breast milk. Breast milk fortifiers were added to milk for those children < 36 weeks corrected gestational age. Fortifiers are started once the baby was on full enteral feeds and at two weeks of age or older. Breast milk fortifiers are nutritional supplements, available as additives in powder or liquid form, to be mixed with human milk. These are commercially available (we used FM85 from Nestle) with added protein, carbohydrate, fat and various minerals (see Appendix for composition of FM85).

For these babies the starting feeding volume was 3mls every 3 hours for 24 hours then incremental volumes of 3mls per 3 hourly feed were given but not exceeding a total increment of 20mls/kg/day(see Appendix 9 for feed tables for 3-hourly feed volumes).

An example of the intervention feeding is shown in the flow chart below:



Babies 1500g - 1999g

For babies 1500-1999g enteral feeds were started at 4 hours of age. Feeds were given by cup.

For these babies the starting feeding volume was 6mls 3-hourly for 24 hours then incremental volumes of 6mls per 3-hourly feed but not exceeding a total increment of 20mls/kg/day (see Appendix 8 for feed tables for 3-hourly feed volumes). The neonates were on supplemental intravenous fluids until the total calculated fluid requirement were able to be given orally. The total maximum volume of feeds was to be 180mls/kg/day.

An example of the intervention feeding is shown in the flow chart below:

BIRTHWEIGHT 1500-1999 GRAMS

DAY 1: Intravenous 10% dextrose (60ml/ kg/day) x 4 hrs

Example; Wt *1700g* start at 102mls 10% dextrose x 4 hrs (@60 mls/kg/day)

↓

DAY 1: **Start** feeds @ 4 hours
Start feeds at **6mls per feed** till 24 hours of age

Example; Start feeds at 6ml per feed for 24 hours with fluid balance as iv fluids

↓

DAY 2: **Increase** feeds **3-hourly** by **6mls per feed** till maximum of 20 mls/ kg increment for the day

Example; Increase 3-hourly feeds by 6mls till max 17ml/feed (@80ml/kg/day) that is, 6ml, then 12ml, then 17ml within 9 hours of day 2.

↓

DAY 3: **Increase** feeds by **6 mls per feed** till maximum of 20mls/ kg increment for the day

Example; Increase by 6ml till 22ml (@ 100 mls/kg/day)

Significant feed intolerance was gastric aspirates ≥ one half of previous feed when enteral feeds were providing more than half of total fluid intake and only if this aspirate was persistent, that is two consecutive large aspirates of at least half of previous feeds. Feeds were stopped if there was blood stained or persistent bile stained gastric aspirates. Investigation for possible NEC was started.

Enteral feeds were stopped for all babies who developed suspected or confirmed NEC defined by Bell's staging[24] (see Appendix 10). Development of NEC (constituted an end point in the study.

Current feeding regime

For the other feeding arm, the feeding regimen was that practiced at the Kenyatta National Hospital newborn unit. In this regime feeds were only started when the baby was assessed to be stable, that is, severe respiratory distress had settled (RR < 60 bpm), no evidence of severe neonatal sepsis with haemodynamic compromise. The starting feed volumes ranged from 1-3 mls of milk and the incremental volumes were very low at 1-2 mls per three-hour feed until maximum incremental volumes of 20ml/kg/day were attained. There was also routine pre-feed aspiration of gastric contents in babies with nasogastric tubes. The aspirates that were clean were fed back to the baby while pre-feed aspirates that were dirty, blood-stained or bile stained were discarded and the decision on continuation of feeds made by the doctor.

Follow up

The neonates and their feeding charts were reviewed every day by the principal investigator to check on compliance of the feeding regimens and to look at the record keeping. Weights were taken every two days until 28 days of age. Those discharged before 28 days of age were reviewed in the follow up clinic at 28 days of age.

Data Management
Analysis of data was by intention to treat.

Data collected was entered into a computer, cleaned, verified and analyzed using the SPSS version 16.0 software.

Means, ranges and standard deviation were calculated for the continuous variables.

Categorical variables were compared using appropriate non parametric measures. Means were compared with independent t tests.

The level of significance was a p value less than or equal to 0.05.

The summarized data was presented in the form of tables, pie charts and graphs as shown below.

RESULTS

The study was conducted in the period between April 2008 and December 2008.

The total number of neonates in the weight group of 1000g to 1999g was three hundred and ninety two (392). Those in the weight group below 1500g were two hundred and four (204) while those between 1500g and 1999g were one hundred and eighty eight (188).

Those neonates excluded were the small for gestational age babies who were one hundred and thirty seven (137), the HIV exposed neonates who were twenty six (26) and others meeting the other exclusion criteria who numbered fifty two (52).

Six mothers were either unavailable to give consent or refused to give consent for participation in the study.

Seventeen of the neonates were also excluded due to severe illness.

One hundred and twenty nine neonates were not recruited due to the unavailability of the principal investigator.

The number eligible for the study and those finally recruited into the study are summarized in the flowchart below:

FLOWCHART

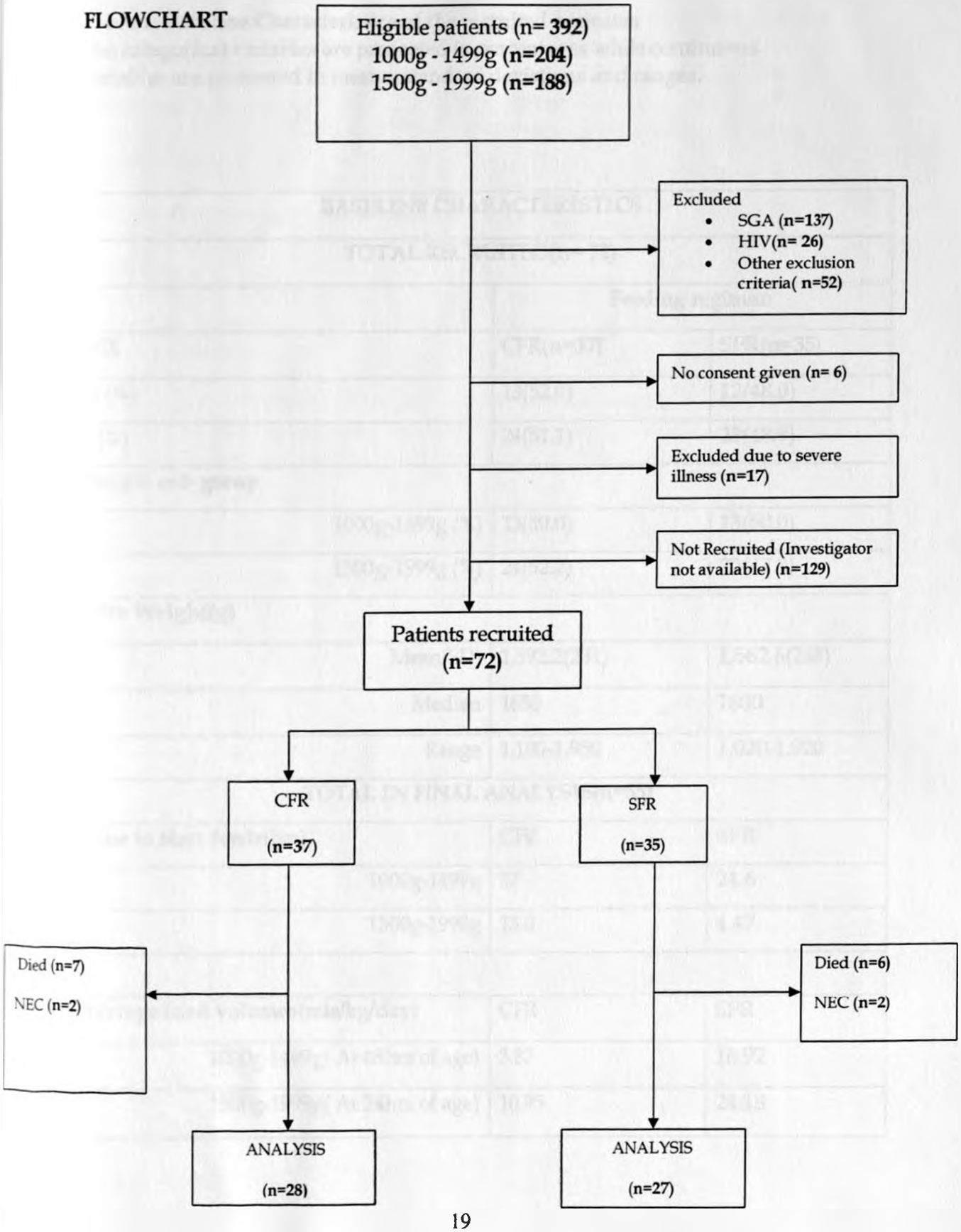

Eligible patients (n= 392)
1000g - 1499g (n=204)
1500g - 1999g (n=188)
Excluded
SGA (n=137)
HIV(n= 26)
Other exclusion criteria(n=52)
No consent given (n= 6)
Excluded due to severe illness (n=17)
Not Recruited (Investigator not available) (n=129)
Patients recruited (n=72)
CFR (n=37)
SFR (n=35)
Died (n=7)
NEC (n=2)
Died (n=6)
NEC (n=2)
ANALYSIS (n=28)
ANALYSIS (n=27)

Table 1: Baseline Characteristics of the recruited neonates
The categorical variables are presented in percentages while continuous variables are presented in means, standard deviations and ranges.

BASELINE CHARACTERISTICS		
TOTAL RECRUITED(n= 72)		
	Feeding regimen	
SEX	CFR(n=37)	SFR(n=35)
M (%)	13(52.0)	12(48.0)
F (%)	24(51.1)	23(48.9)
Weight sub group		
1000g-1499g (%)	13(50.0)	13(50.0)
1500g-1999g (%)	24(52.2)	22(47.8)
Birth Weight(g)		
Mean(SD)	1,592.2(231)	1,562.6(248)
Median	1650	1600
Range	1,100-1,950	1,020-1,920
TOTAL IN FINAL ANALYSIS(n=55)		
Time to start feeds(hrs)	CFR	SFR
1000g-1499g	37	24.6
1500g-1999g	13.0	4.47
Average feed volumes(mls/kg/day)	CFR	SFR
1000g-1499g(At 48hrs of age)	3.87	16.92
1500g-1999g(At 24hrs of age)	10.95	24.18

The number of males in the two feeding regimes was 13 for the CFR and 12 for the SFR and this was statistically similar (p=0.94). The number of females in the CFR and SFR groups were 24 and 23 respectively and there was no statistically significant difference (p= 0.940). The number of neonates in the two weight subgroups of 1500g - 1999g and 1000g - 1499g was not significantly different statistically (p= 0.589).

The mean birth weight between the current feeding regime which was 1,592.2g and the standard feeding regime(1,526.6g) were not significantly different (p= 0.602).

The enteral feeds were started earlier in the standardized feeding regime in both weight categories.

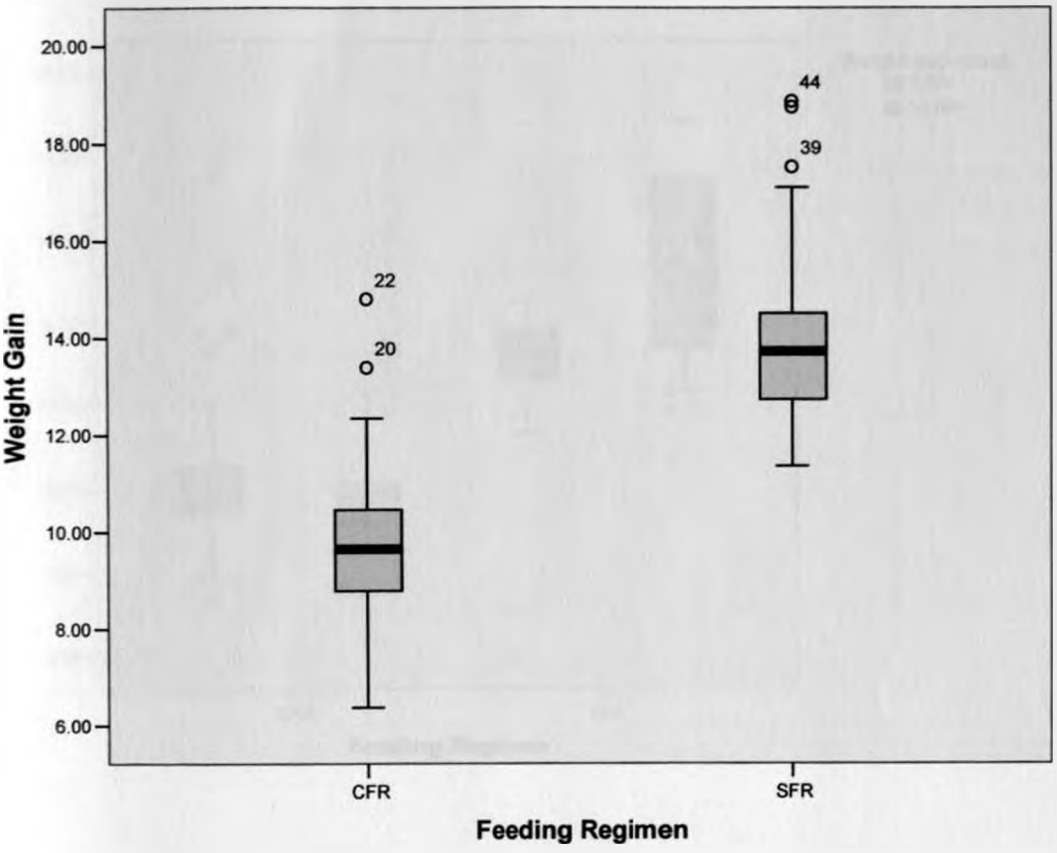
The average feed volumes at the start of oral feeds were higher in the standardized feeding regime in both weight categories. These findings and those on earlier start on feeds signify good compliance with the feeding regimes.

Table 2: Association between feeding regimen and weight gain, days to full feeds and days to regaining birth weight(n=55)

Factors	Mean (SE)	SD	Range	p-value (*Independent t-test for difference between means*)
Regained Birth Weight (days)				
• CFR (n=28)	9.9 (0.6)	3.4	6-20	0.001
• SFR (n=27)	7.2 (0.5)	2.5	4-15	
Full Feed (days)				
• CFR (n=28)	7.0 (0.4)	1.9	5-13	0.002
• SFR (n=27)	5.6 (0.3)	1.6	3-11	
Weight gained (g/kg/day)				
• CFR (n=26)	9.8 (0.4)	1.9	6.4-14.8	<0.001
• SFR (n=26)	14.1 (0.4	2.0	11.4-18.9	

The neonates on the SFR had a mean weight gain of 14.1 g/kg/day compared to a mean weight gain of 9.8 g/kg/ day in the CFR group and this was a statistically significant difference (p= <0.001).Those on the SFR also attained full feeds earlier at a mean of 5.6 days compared to a mean of 7.0 days in the CFR group and this was a statistically significant difference (p=0.002). Those babies fed by the SFR regained their birth weight by a mean of 7.2 days compared to a mean of 9.9 days in the CFR group and this too was significantly different(p=0.001).

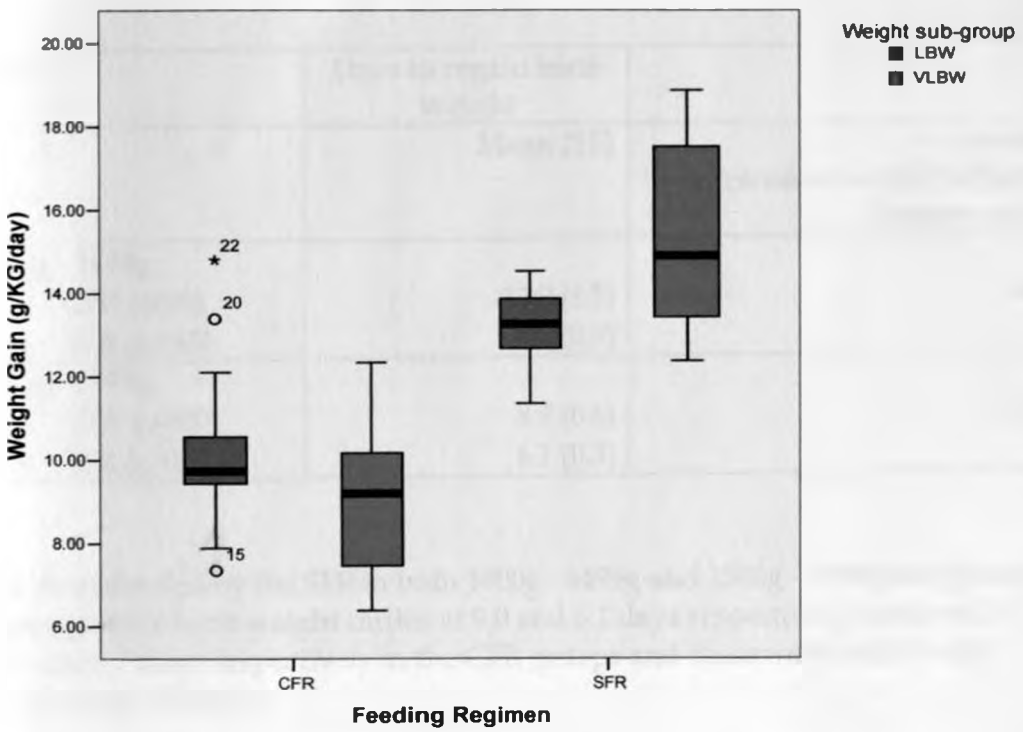
Figure 1: Comparison of overall mean weight gain between the two feeding regimens (n=55)



Explanation of Box plot used in Figure 1: The box contains the middle 50 percent of the data. The upper and lower margins of the box indicate the 75th and 25th percentiles of this data set. The line in the box indicates the median weight gain. The whiskers indicate minimum and maximum data values. Points on the ends of the whiskers indicate outliers.

The mean weight gain for neonates on CFR was 9.8 while for those on SFR was 14.1 ($p<0.001$).

Figure 2: Association between the feeding regimen and the weight gains in the weight sub groups (n=55)



VLBW (1000g -1499g) p-value, comparing means, <o.oo1

LBW (1500g-1999g) p-value, comparing means, <0.001

In the 1000g - 1499g subgroup there was a statistically significant difference in weight gain in the SFR group who had a mean weight gain of 15.4g/kg/day compared to a mean of 9.0g/kg/day in the CFR group (p=<0.001). The SFR group in the 1500g - 1999g neonates also gained weight significantly better at 13.2g/kg/day compared to 10.2g/kg/day in the CFR group(p=<0.001)

Table 3: Association between the days to regain birth weight and feeding regimen stratified by weight group at study entry (n=55)

The association between the days to regaining birth weight and the feeding regime in each weight subgroup is summarized in table 5 below:

Factors	Days to regain birth weight	
	Mean (SE)	p-value (*Independent t-test for difference between means*)
1000g - 1499g		
• CFR (n=8)	13.0 (1.1)	**0.010**
• SFR (n=10)	9.0 (0.9)	
1500g - 1999g		
• CFR (n=20)	8.7 (0.6)	**0.001**
• SFR (n=17)	6.1 (0.3)	

The neonates fed by the SFR in both 1000g - 1499g and 1500g - 1999g subgroups regained their birth weight earlier at 9.0 and 6.1 days respectively compared to 13.0 and 8.7 days respectively in the CFR groups and these were statistically significantly different.

Table 4: Association between the days to full feeds and feeding regimen stratified by weight group at study entry (n=55)

The weight subgroup analysis of the association between the mean number of days to attaining full days and the feeding regimen is shown in table 6 below:

Factors	Days to Full Feed	
	Mean (SE)	p-value (*Independent t-test for difference between means*))
1000g - 1499g • CFR (n=8) • SFR (n=10)	 8.8 (0.3) 6.3 (0.6)	0.004
1500g - 1999g • CFR (n=20) • SFR (n=17)	 6.3 (0.4) 5.0 (0.3)	0.013

In the 1000g - 1499g weight subgroup the neonates on the CFR took a mean of 8.8 days to achieve full feeds compared to a mean of 6.3 days in the SFR group. The 1500g - 1999g babies on the SFR achieved full feeds by a mean of 5.0 days while those in the CFR category took longer at a mean of 6.3 days and this was a statistically significant difference in both weight subgroups (p=0.004 and p= 0.013 respectively)

Table 5: Association between the feeding regimens and the incidence of NEC and mortalities. (n=72)

	CFR	SFR
NEC(% of total recruited)	3(8.10)	3(8.57)
MORTALITY(% of total recruited)	7(18.92)	6(17.4)

The incidence of NEC did not differ between the two feeding regimes.

The mortality in the two feeding regimes was similar, though this study was not powered to detect a difference between the two groups.

DISCUSSION

In the study period between April 2008 and December 2008 there were three hundred and ninety two neonates in the weight group between 1000g and 1999g who were admitted into the KNH NBU and were thus eligible for enrolment in this study. Seventy two (18.3) % of these were finally recruited into the study.

The analysis of the baseline characteristics showed a similarity between the two groups at the start of the study. This means that the randomization and allocation was done well.

The neonates fed using the standardized feeding regimen had a significantly higher daily weight gain. This significant difference in weight gain was also seen in both weight sub groups. These findings are similar to previous studies by Kennedy et al and Dinnerstein et al that showed that feeding regimens that included rapid advancement of feed volumes were associated with better neonatal weight gain [6, 16]. Possible mechanisms for this could be that earlier attainment of full feeds due to the rapid feed volume advancements ensures adequate provision of nutrients thus better growth. This is especially so in settings where parenteral nutrition is not possible.

The hypothesis in this study was thus proved and the null hypothesis rejected as shown by the statistically significant increase in weight gain in the neonates fed using the standardized feeding regimen.

The better weight gain is important for the long term neurological development of the neonate [7, 14]. Lucas and Were in separate studies showed that neonates who had slower growth in the neonatal period had lower neuro-developmental scores and neurological dysfunction in later childhood [14, 7].

In this study the neonates in the SFR group had a statistically significant better neonatal weight gain but the average neonatal weight gain was 14.1g/kg/day. This is lower than the expected growth of ≥15g/kg/day[10]. This was likely due to other factors like unrecognized subtle illness (like electrolyte imbalance, mild anemia, and mild acidosis), neonatal infection and inadequate temperature control. These factors have been associated with lower neonatal growth [13].

The neonates on the standardized feeding regimen regained their birth weight significantly earlier than the CFR group. This has also been shown in other studies whereby there was a reduction in mean days to regaining birth weight among infants in the rapid rate of feed advancement group [6] .Earlier regaining of birth weight is associated with better growth velocity in the neonatal period [10]. This subsequently results in better neonatal weight gain with its associated better neurological outcomes at two years[7] and later childhood [14] .

The neonates in the SFR group attained full feeds statistically significantly earlier (a mean 1.6 days earlier) than the control group. These findings are similar to studies that have shown that feeding regimens comprising rapid advancement of feed volumes were associated with both earlier attainment of full feeds and better weight gain. McGuire et al in a systematic review of three studies involving a total of 396 infants found a statistically significant longer median time to full feeds in neonates in the slow advancement group [22]. Association between earlier attainment of full feeds and better weight gain also portends better neurological outcomes.

Feeding regimens that include early enteral feeding and rapid feed volume advancement are associated with earlier regaining of birth weight and higher neonatal weight gain. Possible mechanisms for this could be that earlier attainment of full feeds ensures adequate provision of adequate nutrients with subsequent better growth as shown in previous studies [6]. This is especially so in settings where parenteral nutrition is not possible.

The findings in this study are similar to other studies that showed a shorter median time to regaining birth weight in the rapid feed volume advancement group [6].

Six (8.3%) of the neonates recruited developed NEC on or before 5 days of age. Five of these had stage one NEC while one had stage two NEC. All exited the study and even if feeds were reintroduced NEC had already formed an end point in this study. Though the study was not powered to detect a difference in NEC between the two feeding regimes the figures did not show any major difference. None of the patients who developed NEC contributed to the mortalities that were computed in this study.

The one neonate who was lost to follow-up was in the CFR group and weighed 1900g which was higher than the mean weight. The baby regained birth weight at eight days which was similar to the mean of 8.6 in this group and also attained full feeds on day 6 compared to 6.3 the mean for the group. This was also similar. The patient did not return for follow-up thus no average daily weight gain was calculated.

The number of mortalities were thirteen (18%) of the patients recruited. 61.5% of these deaths occurred before the seventh day of life. The average mortality of neonate in the 1000g to 1999g weight group admitted in the KNH NBU during this period was about 44%.The mortality seen in this study was lower and may have been as a result of a survivor bias whereby very sick neonates were not recruited at the outset thus resulting in seemingly better survival rates. The

higher mortality is also seen in the 1000g - 1499g and fewer of these were recruited into my study.

The small for gestational age preterm babies comprised 35% of those admitted and these were excluded from the study. These numbers are similar to those found in the study by Were et al who were 36.6%[11]. The SGAs were excluded due to their different pattern of growth compared to AGA preterm babies.

For six of the neonates that met the inclusion criteria consent was denied. Parents declined to give consent mainly out of fear of a possible different feeding regime. This was despite adequate information given to the mother on procedures and possible outcomes.

In one hundred and twenty nine (32.9%) of the cases the principal investigator was unavailable to assess and possibly recruit the patients. The main reason for this is that this was a lone investigator with no funding to get research assistants to help in recruitment. This also meant that the investigator was unavailable at all times even when neonates meeting the inclusion criteria were admitted. This number which was not recruited was a significant (32.9%) percentage. Including these cases would have added more data that would have been useful in improving the internal validity of the study.

The sample size calculated in order to detect a possible 30% difference between the two groups was 40 for each arm with an addition of 16 per arm to cater for mortalities giving a total 116. The sample size accumulated in this study was seventy two. With this sample size we were able to show a significant difference in the main outcome measure of weight gain and also in the secondary outcomes of days to regaining birth weight and days to full feeds. This shows that that the difference between the two groups was larger than anticipated in the sample size calculations (or the standard errors were smaller) and thus the sample size actually achieved was still able to detect a significant difference (using a standard p value of < 0.05 as indicative of significance). The larger than anticipated differences between groups therefore meant the study was adequately powered to detect a difference of the actual magnitude observed despite recruitment of a smaller number of cases than sample size calculations suggested would be necessary.

Data on possible confounding factors especially neonatal illnesses and temperature regulation was not available for comparison between the two feeding groups. The allocation of the feeding regimes was not blinded to the

investigator, NBU clinicians and parents and this may have made contamination possible.

This study was done in the setting of Kenyatta National Hospital, a tertiary referral hospital with a level two newborn unit. Of all the possible neonates to be recruited, only 18.3% were recruited. These two factors plus the relatively low mortality in the study group make it difficult to generalize the findings of the study to provincial and district hospitals which do not have facilities and staffing similar to that found in KNH. The data on NEC and mortalities was also not conclusive. Even so this pilot study helped to show the feasibility and outcomes of introducing the standardized feeding regimen in settings where close monitoring for any complications especially NEC could be done.

The findings of this pilot study though done on a small number helped to show the potential importance of standardized feeding regimens that comprise early onset of enteral feeds and rapid advancement of enteral feeds on early neonatal growth. Further studies on extremely low birth weight neonates may be useful. The study also provided some estimates for future sample size calculations for NEC and mortalities that could be useful in large trials. Studies looking at differences in necrotizing enterocolitis and mortalities in the two feeding regimes could further help in providing data on this important management intervention.

Future studies should also consider relaxing entry criteria to include babies born small for gestational age and those with moderate illness as in a many real-life settings where there are few clinicians and feeding guidelines will be applied to all babies admitted to newborn units.

CONCLUSION

There was a significant improvement in weight gain and earlier attainment of full feeds and regaining of birth weight in the neonates fed using the standardized feeding regimen, compared to those fed using the regime that comprised slow introduction of, and low volume increment of enteral feeds. The study did not find any difference in the episodes of feed intolerance between the two feeding regimes.

Mortality between the two groups did not differ though the study was not powered to detect a difference.

RECOMMENDATIONS

The findings of this pilot study show a benefit in the introduction of a standardized feeding regime in the KNH newborn unit in babies with birth weight 1000-1999g who are AGA and not seriously ill at birth. A larger study recruiting more babies and potentially relaxing inclusion criteria especially for the 1000g - 1499g neonates will be of benefit to try and compare the primary and secondary outcomes and also try and find out if there will be significant differences in the outcomes of NEC and mortalities between the two feeding regimens.

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APPENDIX 1 Client No---------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH.

PARENT INFORMATION SHEET

English version

Dear Sir/Madam/Master/Ms

I am conducting a study on a standardized feeding regimen in low birth weight neonates. This letter is to inform you about the study and to seek your support. Your baby is admitted at the newborn unit in Kenyatta National Hospital due to prematurity and/or their birth weight being lower than the normal. In addition to other standard care your newborn baby will be started on feeds which will entail intravenous fluids if they are < 2000g. The baby may be started on milk feeds from four hours of age and this will be increased while checking that your baby tolerates the feeds until the required volume to help your baby grow is reached over the next few days. The study aims to compare a standardized feeding regimen to the current practice. The feeds will be advanced at a faster rate. In other countries this approach seems to be safe and may help the baby to grow faster but we want to look at the approach in Kenya . Your child is being asked to participate in this study because he/she meets the inclusion criteria.

Benefits of participation:

1. Your participation will provide us with information that may be useful in formulating better feeding practices for newborns in this hospital in the future.

Risks arising from the study: More regular weighing will mean more handling of the baby but efforts will be made to ensure that further unnecessary handling is kept to the minimum. All babies have a risk of an intestinal condition associated with poor feed tolerance, that is, necrotizing enterocolitis but we will be careful in looking for this.

Your obligations:

1. Know that your baby's participation in the study is voluntary.
2. Know that you are free to withdraw consent even after recruitment in the study.

My obligations

1. To keep all your personal information confidential.
2. To make available results of the study to you and the medical staff in the unit.

Our contacts:

UNIVERSITY OF NAIROBI,
DEPARTMENT OF PAEDIATRICS AND CHILD HEATH.
DR. E. K. NGETICH. TEL: 0722794585; 020-3595925. (Investigator)
PROF. F. N. WERE KNH EXT 43184 ;020-2714877 (Supervisor)

If you agree to participate in this study please sign the consent form attached.

APPENDIX 2 Client No---------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH.

MAELEZO YA IDHINI KWA MZAZI WA MGONJWA

Kiswahili

Maelezo haya ni ya kukufahamisha kuhusu utafiti tunayofanya wa kulisha watoto wenye uzani mdogo kuliko kawaida wakati wanapozaliwa.

Utafiti huu unahusisha watoto wenye uzani wa gramu chini ya 1999 waliolazwa katika wadi ya watoto waliozaliwa hivi karibuni. Bali na matibabu mengine ya kawaida wanaopewa hawa watoto wataanzishiwa lishe ya maziwa waakiwa na umri ya masaa manne kwenda mbele. Utafiti unatofautisha kati ya mbinu taratibu ambaye itatumika na mbinu ya kulisha ambaye hutumika kwa wakati huu kwa hii wadi.

Manufaa ya kushiriki

Tarakimu zipatikanapo zitatusaidia kupata taratibu halisi ya kuwapa hawa watoto lishe.

Madhara ya kushiriki

Mtoto atasumbuliwa zaidi kidogo kwa sababu ya kupimwa uzani kila baada ya siku mbili.

Wajibu wako

Kujiunga kwa hiyari yako na pia kujiondoa kwa hiyari yako.

Wajibu wangu

Kuweka tarakimu na mapato zako siri ila tu kwa wanaotibu mtoto na madaktari wenzangu.

Kuona kwamba hakuna madhara yoyote hayapati mtoto wako.

Anwani zetu:
UNIVERSITY OF NAIROBI
DEPARTMENT OF MEDICINE
DR. E. K. NGETICH 0722794585; 0203595925 (Mtafiti)
PROF. F. N. WERE KNH EXT 43184 ; 020-2714877 (Supervisor)

Ukikubali kushiriki kwa utafiti huu,tia sahihi kwa karatasi ya idhini ifuatayo.

APPENDIX 3 Client No---------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH.

PARENT/GUARDIAN CONSENT FORM

I,Mr/Mrs/Ms ----------, the parent/legal guardian

of----------.

I agree to the above and give consent for my child to be included in this study

as explained to me by----------

I understand the purpose of the study and conditions of his/her participation.

Sign---------- --------

Date----------

Witness

Sign----------

Date----------

APPENDIX 4 Client No---------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH.

IDHINI YA MZAZI AU MTUNZAJI WA MTOTO

Kiswahili

Mimi----------ni

mzazi/mtunzaji wa----------

Nimekubali ashiriki katika utafiti huu kama nilivioelezwa na Daktari----------

---

Sahihi----------

Tarehe----------

Shahidi ----------

Sahihi----------

APPENDIX 5 STUDY NO --------- BABY _____

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH

FEEDING AND OBSERVATIONS CHART

SEX: BIRTH WT: _____ CWT: _____ DATE: _____

INSTRUCTIONS FOR DAY: _____

TIME	INPUT		OUTPUT(GASTRIC ASPIRATE)		OBSERVATIONS		
	FEEDS(TYPE)	AMT(MLS)	AMT (MLS)	COLOUR	RR	HR	TEMP
8AM							
9AM							
10AM							
11AM							
12MD							
1PM							
2PM							
3PM							
4PM							
5PM							

TIME	INPUT		OUTPUT(GASTRIC ASPIRATE)		OBSERVATIONS		
	FEEDS(TYPE)	AMT (MLS)	AMT (MLS)	COLOUR	RR	HR	TEMP
6PM							
7PM							
8PM							
9PM							
10PM							
11PM							
12MN							
1AM							
2AM							
3AM							
4AM							
5AM							
6AM							
7AM							

APPENDIX 6 STUDY NO ---------- BABY _____

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT

DATA COLLECTION SHEET

DAY OF LIFE: _____ FEEDING REGIME: _____

SEX: _____

BIRTH WEIGHT: _____ CURRENT WT: _____

WEIGHT GAIN (g/kg/day) _____

FEED VOLUMES: Expected Total 24 hour feed volume (mls) _____ (ml/kg) _____

Actual total 24 hour feed volume fed (mls) _____ (ml/kg) _____

Feed volume deficit in 24 hours (mls) _____

FEED TYPE: (EBM, PTF, Mixed) _____

APPENDIX 7 STUDY NO ---------- BABY _____

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH

DATA SUMMARY FORM

BABY	STUDY NO.
SEX(M/F)	FEED TYPE(BM, PTF,TF, MIXED)
BIRTH WEIGHT(GRAMS)	FEEDING REGIMEN(CFR/SFR)
REGAINED BIRTH WEIGHT(DAYS)	ORAL FEEDS STARTED(HOURS)
DAYS TO FULL FEEDS(DAYS)	FEED VOLUMES(MLS/KG)
WEIGHT GAIN(g/kg/day)	AT 24 HRS(1500g - 1999g) _____
DAY 28 WEIGHT(g)	AT 48 HRS(1000g - 1499g) _____
	AT 7 DAYS _____

APPENDIX 8 Client No----------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH.

NUTRITIONAL COMPOSITION OF COMMERCIAL MULTICOMPONENT HUMAN MILK FORTIFIER FM85 FROM NESTLE.

The 5g quantity (usually added to 20mls of expressed breast milk) contains:

Macronutrients	
Energy, kcal	18
Protein, g	0.8
Fat, g	0.015
Carbohydrate, g	3.6
Minerals	
Calcium, mg	51
Phosphorus, mg	34
Magnesium, mg	2
Sodium, mmol	1.2
Chloride, mmol	0.5
Potassium, mmol	0.3
Iron, mg	0
Zinc, mcg	0
Copper, mcg	0
Manganese, mcg	0
Vitamins	
Vitamin A, mcg	0
Vitamin E, mg	0
Vitamin K1, mcg	0
Vitamin D, mcg	0
Vitamin C, mg	0
Thiamine, mcg	0
Riboflavin, mcg	0
Vitamin B6, mcg	0
Vitamin B12, mcg	0
Niacin, mg	0
Folic acid, mcg	0
Biotin, mcg	0
Pantothenic acid, mg	0
Increment in osmolality, mOsm	105

APPENDIX 9 Client No----------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH.

FEEDING TABLES (1000g – 1450g)

DAYS (*mls/kg/day*)	3- HOURLY FEED VOLUMES									
	WEIGHTS(grams)									
	1000g	*1050g*	*1100g*	*1150g*	*1200g*	*1250g*	*1300g*	*1350g*	*1400g*	*1450g*
D1(*80*)	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5
D2(*100*)	12.5	13	13.5	14	15	15.5	16	16.5	17.5	18
D3(*120*)	15	16	16.5	17	18	18.5	19.5	20	21	21.5
D4(*140*)	17.5	18	19	20	21	22	22.5	23.5	24.5	25
D5(*160*)	20	21	22	23	24	25	26	27	28	29
D6(*180*)	22.5	23.5	24.5	25.5	27	28	29	30	31.5	32.5
D7(*200*)	25	26	27.5	28.5	30	31	32.5	33.5	35	36

FEEDING TABLES (1500g - 2000g)

DAYS (*mls/kg/day*)	3- HOURLY FEED VOLUMES										
	WEIGHTS(grams)										
	1500g	***1550g***	***1600g***	***1650g***	***1700g***	***1750g***	***1800g***	***1850g***	***1900g***	***1950g***	***2000g***
D1(*60*)	11	12	12	13	13	13	14	14	14	15	15
D2(*80*)	15	16	16	17	17	18	18	19	19	20	20
D3(*100*)	19	19	20	21	21	22	23	23	24	24	25
D4(*120*)	23	23	24	25	26	26	27	28	29	29	30
D5(*140*)	26	27	28	29	30	31	32	32	33	34	35
D6(*160*)	30	31	32	33	34	35	36	37	38	39	40
D7(*180*)	34	35	36	37	38	39	41	42	42	44	45
D8(*200*)	38	39	40	41	43	44	45	46	48	49	50

APPENDIX 10 Client No---------

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH

BELL'S STAGING FOR NECROTISING ENTEROCOLITIS [21]

Stage 1

- History of perinatal stress
- Systemic signs of ill-health: temperature instability, lethargy,apnoea
- Gastrointestinal manifestations: poor feeding, increased volume of gastric aspirates, vomiting, mild abdominal distension and fecal occult blood(no fissure)

Stage 2

Any feature of stage 1 plus:

- Persistent occult of gross intestinal bleeding, marked abdominal distension.
- Abdominal radiograph: intestinal distension, bowel wall edema, unchanging bowel loops, pneumatosis intestinalis, portal vein gas.

Stage 3

Any of the features of stage 1 and 2 plus:

- Deterioration in vital signs; evidence of shock or severe sepsis and marked intestinal hemorrhage.
- Abdominal radiograph- any features of stage 2 plus pneumoperitoneum.

NB: The radiographs will be viewed by a consultant radiologist.

APPENDIX 11 Client No————

EFFECT OF A STANDARDISED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY- LOW BIRTH WEIGHT NEONATES AT KNH

MODIFIED BALLARDS SCORE FOR GESTATIONAL ASSESSMENT [20]

Neuromuscular Maturity

	-1	0	1	2	3	4	5
Posture							
Square Window (wrist)	>90°	90°	60°	45°	30°	0°	
Arm Recoil		180°	140°-180°	110°-140°	90-110°	<90°	
Popliteal Angle	180°	160°	140°	120°	100°	80°	<90°
Scarf Sign							
Heel to Ear							

Physical Maturity

Skin	sticky friable transparent	gelatinous red, translucent	smooth pink visible veins	superficial peeling &/or rash, few veins	cracking pale areas rare veins	parchment deep cracking no veins	leathery cracked wrinkled
Lanugo	none	sparse	abundant	thinning	bald areas	mostly bald	
Plantar Surface	heel-toe 40-50mm -1 <40mm -2	>50mm no creases	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole	
Breast	imperceptible	barely perceptible	flat areola no bud	stippled areola 1-2mm bud	raised areola 3-4mm bud	full areola 5-10mm bud	
Eye/Ear	lids fused loosely -1 tightly -2	lids open pinna flat stays folded	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear stiff	
Genitals male	scrotum flat, smooth	scrotum empty faint rugae	testes in upper canal rare rugae	testes descending few rugae	testes down good rugae	testes pendulous deep rugae	
Genitals female	clitoris prominent labia flat	prominent clitoris small labia minora	prominent clitoris enlarging minora	majora & minora equally prominent	majora large minora small	majora cover clitoris & minora	

Maturity Rating

score	weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

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Ref: KNH-ERC/ 01/ 138

8th February 2008

Dr. Eric K. Ngetich
Dept. of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Ngetich

RESEARCH PROPOSAL: "EFFECTS OF A STANDARDIZED FEEDING REGIMEN ON EARLY NEONATAL GROWTH IN LOW AND VERY LOW BIRTH WEIGHT NEONATES AT K.N.H: A PILOT RANDOMIZED CONTROLLED TRIAL" (P340/11/2007)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your revised research proposal for the period 8th February 2008 – 7th February 2009.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M. Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
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