

The effect of higher protein human milk fortifier on  
growth in preterm infants

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# Table of Contents

|   |              |
|---|--------------|
| <b>Table of Contents</b>  | <b>ii</b>    |
| <b>List of Tables</b>   | <b>viii</b>  |
| <b>List of Figures</b>  | <b>x</b>     |
| <b>Abbreviations of commonly used words and units of measurement</b>                    | <b>xii</b>   |
| <b>Abstract</b>   | <b>xv</b>    |
| <b>Declaration</b>  | <b>xvii</b>  |
| <b>Acknowledgements</b>   | <b>xviii</b> |
| <br>  |              |
| <b>Chapter 1 Literature review</b>  | <b>1</b>     |
| <b>1.1 The preterm infant</b>   | <b>2</b>     |
| 1.1.1 Incidence of preterm birth is increasing  | 2            |
| 1.1.2 Consequences of preterm birth   | 2            |
| 1.1.3 Consequences of prematurity into adult life                                       | 3            |
| 1.1.4 Predictors of morbidity in adult life   | 4            |
| 1.1.5 Poor neurodevelopment is associated with poor in-hospital growth                  | 6            |
| <b>1.2 Nutrition of the preterm infant</b>  | <b>8</b>     |
| 1.2.1 The immaturity of the preterm infant makes nutritional management difficult       | 8            |
| 1.2.2 Protein must be administered early and safely to encourage growth and weight gain | 9            |
| 1.2.3 High protein enteral feeding is the goal  | 11           |
| 1.2.4 Human milk is recommended for preterm infants                                     | 12           |
| 1.2.5 Major clinical concerns with enteral nutrition – necrotising enterocolitis        | 12           |
| 1.2.6 Nutritional content of breast milk  | 13           |
| 1.2.7 Breast milk fortification for preterm infant growth                               | 14           |
| 1.2.8 RCT of protein in human milk fortifier (HMF)                                      | 15           |
| 1.2.8.1 Nutritional interventions of studies summarised in Table 1.2                    | 17           |
| 1.2.8.2 Outcomes of studies summarised in Table 1.2                                     | 24           |
| 1.2.8.3 Quality of studies summarised in Table 1.2                                      | 24           |
| 1.2.8.4 Summary of findings of studies in Table 1.2                                     | 25           |
| 1.2.9 Good quality nutrition is vital to achieving good quality growth                  | 26           |
| 1.2.10 The challenge of fortifying direct breast feeds                                  | 27           |
| <b>1.3 Body composition</b>   | <b>28</b>    |
| 1.3.1 Importance of determining body composition  | 28           |
| 1.3.2 Body composition measurement methods  | 28           |
| 1.3.2.1 Imaging techniques  | 29           |

|  |           |
|--|-----------|
| 1.3.2.2 Techniques using a two compartment model   | 30        |
| 1.3.3 Intervention studies and body composition assessment in preterm infants summarised                                 | 32        |
| 1.3.3.1 Included publications  | 33        |
| 1.3.3.2 Participants summarised in Table 1.4   | 33        |
| 1.3.3.3 Nutritional Interventions summarised in Table 1.4  | 33        |
| 1.3.3.4 Body composition assessment summarised in Table 1.4  | 34        |
| 1.3.3.5 Outcome assessments summarised in Table 1.4  | 34        |
| 1.3.3.6 Quality of trials summarised in Table 1.4  | 35        |
| 1.3.3.7 Summary of findings summarised in Table 1.4  | 36        |
| <b>1.4 Rationale for thesis</b>  | <b>42</b> |
| <b>1.5 Aims of this project</b>  | <b>42</b> |
| <br>   |           |
| <b>Chapter 2 Developing resistivity constants and validating Bioelectrical Impedance Spectroscopy in preterm infants</b> | <b>45</b> |
| 2.1 Introduction   | 45        |
| 2.2 Bioelectrical Impedance Spectroscopy principles  | 46        |
| 2.3 Trial aim  | 50        |
| 2.3.1 Overview of trial design   | 50        |
| 2.4 Trial protocol   | 51        |
| 2.4.1 Participants   | 51        |
| 2.4.2 Eligibility criteria   | 51        |
| 2.4.2.1 Inclusion  | 51        |
| 2.4.2.2 Exclusion  | 51        |
| 2.5 Trial methodology  | 52        |
| 2.5.1 Timeline   | 52        |
| 2.5.2 Baseline blood sample  | 52        |
| 2.5.3 BIS measurements   | 52        |
| 2.5.4 Anthropometric measurements  | 53        |
| 2.5.5 Calculation of tracer dose   | 54        |
| 2.6 Sample analyses  | 55        |
| 2.6.1 Pre-analysis   | 55        |
| 2.6.2 Transportation   | 55        |
| 2.6.3 Bromide analysis by High Performance Liquid Chromatography assay   | 56        |
| 2.6.3.1 Sample preparation   | 56        |
| 2.6.3.2 HPLC conditions  | 57        |
| 2.6.3.3 Quantification of bromide  | 57        |
| 2.6.3.4 Calculation of ECW volume  | 58        |
| 2.6.3.5 Deuterium analysis by Fourier Transform Infrared Spectrophotometer   | 58        |
| 2.6.4 BIS analysis   | 59        |

|   |           |
|---|-----------|
| 2.6.4.1 Prediction of body water volumes  | 60        |
| 2.6.4.2 Calculation of apparent resistivity coefficients  | 61        |
| 2.6.5 Statistical analyses  | 61        |
| <b>2.7 Results</b>  | <b>62</b> |
| 2.7.1 Participant characteristics   | 62        |
| 2.7.2 Cross-validation between predicted and measured body water volumes                                    | 63        |
| <b>2.8 Discussion</b>   | <b>69</b> |
| <br>  |           |
| <b>Chapter 3 Methods of a randomised controlled trial of increased protein fortification of breast milk</b> | <b>72</b> |
| <b>3.1 Objectives and hypotheses</b>  | <b>73</b> |
| 3.1.1 Primary hypothesis  | 73        |
| 3.1.2 Secondary hypothesis  | 73        |
| <b>3.2 Safety outcomes</b>  | <b>74</b> |
| <b>3.3 Trial design</b>   | <b>74</b> |
| <b>3.4 Ethical approval</b>   | <b>74</b> |
| <b>3.5 Participants</b>   | <b>75</b> |
| 3.5.1 Settings and location   | 75        |
| 3.5.2 Eligibility criteria  | 75        |
| 3.5.2.1 Inclusion criteria  | 75        |
| 3.5.2.2 Exclusion criteria  | 76        |
| 3.5.3 Recruitment   | 76        |
| <b>3.6 Randomisation</b>  | <b>77</b> |
| 3.6.1 Sequence generation   | 77        |
| 3.6.2 Allocation concealment mechanism  | 77        |
| 3.6.3 Implementation  | 77        |
| <b>3.7 Interventions</b>  | <b>78</b> |
| 3.7.1 Balancing the energy intakes  | 79        |
| 3.7.2 Administration of intervention  | 79        |
| 3.7.3 Concomitant care  | 80        |
| 3.7.4 Criteria for discontinuing allocated intervention   | 81        |
| 3.7.5 Criteria for adding additional protein  | 81        |
| 3.7.6 Participant withdrawal request  | 82        |
| 3.7.7 Education and support of care staff   | 82        |
| 3.7.8 Calculation and ordering of Poppet dose   | 83        |
| 3.7.8.1 High protein fortifier  | 83        |
| 3.7.8.2 Standard protein fortifier  | 83        |
| 3.7.9 Preparation of Poppet trial fortifier   | 86        |
| 3.7.10 Blinding   | 87        |
| 3.7.11 Monitoring nursery compliance  | 89        |

|   |            |
|---|------------|
| <b>3.8 Outcomes and assessment</b>  | <b>89</b>  |
| 3.8.1 Primary outcome – weight gain   | 89         |
| 3.8.2 Secondary safety outcomes   | 90         |
| 3.8.2.1 Biochemistry metabolic markers  | 90         |
| 3.8.3 Secondary efficacy outcomes   | 90         |
| 3.8.3.1 Length gain.  | 91         |
| 3.8.3.2 Head circumference gain   | 92         |
| 3.8.3.3 Small for gestational age (SGA)   | 92         |
| 3.8.3.4 Body composition  | 92         |
| 3.8.3.5 Other clinical outcomes   | 93         |
| <b>3.9 Data collection</b>  | <b>93</b>  |
| <b>3.10 Sample size</b>   | <b>95</b>  |
| <b>3.11 Sample analysis – breast milk</b>   | <b>95</b>  |
| 3.11.1 Principles of MilkoScan Minor  | 95         |
| 3.11.2 Set up   | 96         |
| 3.11.3 Analysis   | 96         |
| 3.11.4 Sample collection  | 96         |
| 3.11.5 Standardising MilkoScan Minor  | 97         |
| 3.11.6 Mean protein concentration   | 98         |
| <b>3.12 Sample analysis – blood spot</b>  | <b>101</b> |
| <b>3.13 Sample analysis – urine</b>   | <b>101</b> |
| <b>3.14 Statistical analysis</b>  | <b>101</b> |
| <b>3.15 Data management</b>   | <b>102</b> |
| <b>3.16 Trial Management Committee</b>  | <b>103</b> |
| <b>3.17 Serious Adverse Event Committee</b>   | <b>103</b> |
| <br>  |            |
| <b>Chapter 4 Effectiveness of higher protein fortifier on preterm infant growth</b> | <b>105</b> |
| <b>4.1 Participant flow</b>   | <b>105</b> |
| 4.1.1 Randomisation error   | 106        |
| <b>4.2 Maternal characteristics at randomisation</b>                                | <b>108</b> |
| <b>4.3 Birth characteristics at randomisation</b>                                   | <b>109</b> |
| <b>4.4 Infant characteristics at randomisation</b>                                  | <b>111</b> |
| <b>4.5 Trial entry</b>  | <b>112</b> |
| <b>4.6 Dietary intake in the first 28 days</b>                                      | <b>114</b> |
| <b>4.7 Primary outcome – rate of weight gain</b>                                    | <b>115</b> |
| <b>4.8 Key secondary outcomes</b>   | <b>117</b> |
| 4.8.1 Length gain   | 117        |
| 4.8.2 Head circumference gain   | 117        |
| 4.8.3 Per protocol analyses   | 119        |
| 4.8.4 Small for gestation at trial end  | 120        |
| 4.8.5 Fat free mass as a proportion of body weight                                  | 121        |

|  |            |
|--|------------|
| 4.8.6 Weight, length and head circumference at trial end   | 123        |
| <b>4.9 Discussion</b>  | <b>124</b> |
| 4.9.1 Was the intervention successful?   | 124        |
| 4.9.2 Did the intervention increase the rate of weight gain?   | 125        |
| 4.9.3 Did the differences in weight and length at birth and trial start impact on the primary outcome? | 125        |
| 4.9.4 Comparison with similar published trials   | 126        |
| 4.9.5 Delivery system  | 128        |
| 4.9.6 Strengths  | 128        |
| <br>   |            |
| <b>Chapter 5 Biochemistry, feeding, respiratory and clinical outcomes</b>                              | <b>131</b> |
| <b>5.1 Blood chemistry safety outcomes</b>   | <b>131</b> |
| 5.1.1 BUN measurements from randomisation to week 3  | 131        |
| 5.1.2 Base excess measurements from randomisation to week 3  | 134        |
| 5.1.3 Albumin measurements from randomisation to week 3  | 134        |
| 5.1.4 Creatinine from randomisation to week 3  | 134        |
| 5.1.5 Glucose from randomisation to week 3   | 134        |
| 5.1.6 pH from randomisation to week 3  | 134        |
| 5.1.7 Amino acid measures  | 138        |
| <b>5.2 Urine chemistry outcomes</b>  | <b>138</b> |
| 5.2.1 Urinary urea, creatinine and albumin   | 139        |
| <b>5.3 Feeding outcomes</b>  | <b>140</b> |
| 5.3.1 Infants who had feeds withheld   | 140        |
| 5.3.2 Feeding tolerance  | 140        |
| 5.3.3 Incidence of Necrotising Enterocolitis and supplementation                                       | 141        |
| <b>5.4 Respiratory outcomes</b>  | <b>142</b> |
| 5.4.1 Mean hours of ventilator mediated support  | 143        |
| <b>5.5 Other clinical outcomes</b>   | <b>144</b> |
| <b>5.6 Discussion</b>  | <b>146</b> |
| <br>   |            |
| <b>Chapter 6 General discussion</b>  | <b>150</b> |
| <b>6.1 Key findings</b>  | <b>151</b> |
| <b>6.2 Strengths</b>   | <b>152</b> |
| <b>6.3 Limitations</b>   | <b>153</b> |
| <b>6.4 Implications</b>  | <b>153</b> |
| <b>6.5 Future directions</b>   | <b>154</b> |
| <br>   |            |
| <b>References</b>  | <b>155</b> |





## List of Tables

|  |     |
|--|-----|
| Table 1.1 Table of excluded studies.....   | 17  |
| Table 1.2 Randomised controlled trials of preterm infants with high protein fortification intervention and growth as a key outcome ..... | 19  |
| Table 1.3 Advantages and disadvantages of current body composition assessment methods.....   | 32  |
| Table 1.4 Summary of randomised controlled nutritional intervention trials with body composition measurements.....                       | 37  |
| Table 2.1 Data cleaning parameters for raw BIS files .....   | 59  |
| Table 2.2 Clinical characteristics of infants .....  | 63  |
| Table 2.3 Characteristics of cross-validation group .....  | 64  |
| Table 2.4 Resistivity coefficients for prediction participants, validation participants and all participants .....                       | 65  |
| Table 2.5 Measured and predicted body water values in validation group using resistivities derived from the predicted group.....         | 66  |
| Table 3.1 Trial solutions recipe .....   | 83  |
| Table 4.1 Maternal demographics* .....   | 109 |
| Table 4.2 Primary reason for preterm birth .....   | 110 |
| Table 4.3 Multiple birth demographics .....  | 110 |
| Table 4.4 Administration of steroids and delivery demographics .....   | 111 |
| Table 4.5 Birth demographics .....   | 112 |
| Table 4.6 Trial entry summary.....   | 113 |
| Table 4.7. Daily intake for the first 28 days of trial .....   | 114 |
| Table 4.8 Primary outcome – mean weight gain per week .....  | 115 |

|  |     |
|--|-----|
| Table 4.9 Key secondary outcomes – mean length and head circumference gain per week..... | 117 |
| Table 4.10 Weekly weight, length and head circumference gains – per protocol             | 120 |
| Table 4.11 SGA at trial end .....  | 121 |
| Table 4.12 Fat free mass as a proportion of body weight .....                            | 122 |
| Table 4.13 Anthropometric growth measures at trial end.....                              | 124 |
| Table 5.1 BUN values from randomisation to week 3 .....                                  | 133 |
| Table 5.2 Base excess measurements from randomisation to week 3 .....                    | 135 |
| Table 5.3 Blood amino acid measures at week 3.....                                       | 138 |
| Table 5.4 Urine Urea, creatinine and albumin.....  | 139 |
| Table 5.5 Feeding tolerance outcome .....  | 141 |
| Table 5.6 Incidence of Necrotising enterocolitis and supplementation .....               | 141 |
| Table 5.7 Need for respiratory support and incidence of chronic lung disease...          | 143 |
| Table 5.8 Hours of IPPV, CPAP and HHFNC .....  | 144 |
| Table 5.9 Other clinical outcomes .....  | 145 |

## List of Figures

|  |     |
|--|-----|
| Figure 2.1 Extrapolation of resistance at 0 kHz and at infinite kHz is achieved by plotting measured values of resistance versus reactance on a curve..... | 49  |
| Figure 2.2 Correlation of predicted and measured TBW in the validation group...  | 67  |
| Figure 2.3 Bias and limits of agreement between predicted and measured TBW in the validation group. ....   | 67  |
| Figure 2.4 Correlation of predicted and measured ECW in the validation group. .  | 68  |
| Figure 2.5 Bias and limits of agreement between predicted and measured ECW in the validation group. ....   | 68  |
| Figure 3.1 Medication labels used to order Poppet fortified (worked example) ....  | 85  |
| Figure 3.2 Trial product tins labels. ....   | 88  |
| Figure 3.3 Protein content of breast milk from each mother by days post partum.  | 99  |
| Figure 3.4 Protein concentration of EBM decreases as days post-partum increases .....  | 100 |
| Figure 4.1 Participant flow.....   | 107 |
| Figure 4.2 Predicted mean weekly weights by group .....  | 116 |
| Figure 4.3 Predicted mean weekly lengths by group .....  | 118 |
| Figure 4.4 Predicted mean weekly head circumferences by group .....  | 119 |
| Figure 4.5 Fat free mass as a proportion of body weight for the first 4 weeks of the trial.....  | 123 |
| Figure 5.1 BUN from randomisation to week 3... ..  | 133 |
| Figure 5.2 Base excess from randomisation to week 3.....   | 135 |
| Figure 5.3 Albumin from randomisation to week 3 .....  | 136 |
| Figure 5.4 Creatinine from randomisation to week 3.....  | 136 |

|  |     |
|--|-----|
| Figure 5.5 Glucose from randomisation to week 3..... | 137 |
| Figure 5.6 pH from randomisation to week 3 .....     | 137 |

## **Abbreviations of commonly used words and units of measurement**

|         |   |
|---------|---|
| ABS     | Australian Bureau of Statistics                     |
| ADP     | Air-displacement plethysmography                    |
| ANZCTR  | Australian and New Zealand Clinical Trials Registry |
| ANZNN   | Australian and New Zealand Neonatal Network         |
|         |   |
| BIS     | Bioelectrical Impedance Spectroscopy                |
| BUN     | Blood Urea Nitrogen                                 |
| BW      | Birth Weight  |
|         |   |
| CA      | Corrected Age                                       |
| CI      | Confidence Interval                                 |
| CIS     | Clinical Information Services                       |
| CONSORT | Consolidated Standard of Reporting Trials           |
| CPAP    | Constant Positive Airway Pressure                   |
| CRF     | Case Report Form                                    |
| CT      | Computed Tomography                                 |
|         |   |
| DHA     | Docosahexaenoic acid                                |
| DMAC    | Data Management and Analysis Centre                 |
| DXA     | Dual Energy X-ray Absorptiometry                    |
|         |   |
| EBM     | Expressed Breast Milk                               |
| ECW     | Extracellular Water                                 |
| EDD     | Estimated Delivery Date                             |

|           |   |
|-----------|---|
| FFM       | Fat Free Mass                                   |
| FM        | Fat Mass  |
| FMC       | Flinders Medical Centre                         |
| g         | Grams   |
| g/kg/day  | Grams per kilogram of body weight per day       |
| GA        | Gestational Age                                 |
| HFOV      | High Frequency Oscillation Ventilation          |
| HHFNC     | Humidified High Flow Nasal Cannula therapy      |
| HMF       | Human Milk Fortifier                            |
| ICW       | Intracellular Water                             |
| IQ        | Intelligence Quotient                           |
| IPPV      | Intermittent Positive Pressure Ventilation      |
| IVF       | In-Vitro Fertilisation                          |
| IVH       | Intraventricular Haemorrhage                    |
| LCPUFA    | Long Chain Polyunsaturated Fatty Acids          |
| LM        | Lyell McEwin Hospital                           |
| MDI       | Motor Development Indices                       |
| ml        | Millilitre                                      |
| MRI       | Magnetic Resonance Imaging                      |
| MeSH      | Medical Subject Heading                         |
| ml/kg/day | Millilitres per kilogram of body weight per day |
| mm/d      | Millimetres per day                             |
| NEC       | Necrotising Enterocolitis                       |
| NED       | Neonatal Early Discharge                        |

|        |   |
|--------|---|
| NICU   | Neonatal Intensive Care Unit                          |
| PDI    | Psychomotor Development Indices                       |
| Poppet | Providing Optimal Protein for Prems via Enteral Tubes |
| RCT    | Randomised Controlled Trial                           |
| RR     | Relative Risk   |
| SCBU   | Special Care Baby Unit                                |
| SD     | Standard Deviation                                    |
| SGA    | Small for Gestational Age                             |
| SOP    | Standard Operating Procedure                          |
| TBW    | Total Body Water                                      |
| TGA    | Therapeutic Goods Administration                      |
| UR     | Unit Registration Number                              |
| VLBW   | Very Low Birth Weight                                 |
| WCH    | Women's and Children's Hospital                       |
| WMD    | Weighed Mean Difference                               |

## **Abstract**

Preterm infants are difficult to adequately nourish due to their immature organ systems and prematurity related illnesses. Human milk is accepted as the preferred feed for the preterm infant but needs to be supplemented with protein, carbohydrate, vitamins and minerals to meet the metabolic needs of the infant. Currently available commercial fortifiers do not meet the recommended protein intakes suggested in the literature. This thesis tested the hypothesis that preterm infants fed a human milk fortifier with a protein content of 1.8 grams protein per 100 ml expressed breast milk would experience greater weight gain than infants fed the current nursery practice amount – 1.0 grams protein per 100 ml expressed breast milk.

Criteria for eligibility of infants in this study were birth at 28–32 weeks gestation and a planned breast milk diet. Power analysis indicated that to detect a clinically significant weight gain increase of 3.31 grams per day, 60 infants in total would be required. After parental consent was obtained, 60 infants were randomised into the study between February 2012 and February 2013, with 31 in the High protein group and 29 in the Standard group. Multiple births were randomised as individual infants. Infants in the High protein group received a human milk fortifier (FM-85, Nestle) enriched with Protifar (Nutricia) which provided 1.8 grams protein per 100 ml expressed breast milk. Infants in the Standard group received a human milk fortifier (FM-85) that was equivalent to standard care and provided 1 gram protein per 100 ml expressed breast milk. The Standard diet was made isocaloric to the High Protein by the addition of carbohydrate (PolyJoule, Nutricia). The study period for infants began at randomisation and ceased when the naso-gastric tube



was removed. Infants were weighed daily by care staff and weekly by trained research personnel. Length and head circumference – important measures of growth – were assessed weekly. Lean mass gain, which is better associated with adult metabolic health outcomes than adipose tissue gain in the in-hospital period, was also assessed weekly. Blood and urine chemistry markers were assessed weekly and every two weeks, respectively, as an assessment of protein nutritional status. A weekly sample of breast milk was collected if supply was abundant. Lean mass was assessed using Bioelectrical Impedance Spectroscopy, which was validated for use in preterm infants as part of this thesis. Breast milk was assessed for protein content to ensure that intake calculations were based on true, not assumed values.

There were no differences in the primary outcome of weight gain or the secondary outcomes of length gain, head circumference gain or small for gestational age at discharge status. There was a significant trend for increased lean mass as a percentage of body weight in the high protein infants ( $p=0.03$ ). Blood urea nitrogen and urine urea measurements were significantly higher in the High protein infants. Base excess measurements were significantly decreased in High protein infants however no infants experienced metabolic acidosis.

Increasing the protein content of human milk fortifier to 1.8 grams protein did not increase weight gain, length gain or head circumference gain in preterm infants born at 28–32 weeks gestation. While the intervention was well tolerated it is the conclusion of this thesis that the protein content of human milk fortifier does not need to be increased to 1.8 grams protein per 100 ml expressed breast milk. Further studies are required to determine the optimal macronutrient content of human milk fortifier to improve preterm growth.

## **Declaration**

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Jessica Reid

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