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Case Report

Effectiveness of Powdered Human Milk in the Nutrition of a Premature Newborn with Prenatal Exposure to Toxic Substances: A Clinical Case Report

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Abstract

Introduction: Human milk feeding is fundamental for the optimal development of premature neonates, providing the necessary nutrients for their growth and recovery. However, in cases of extreme prematurity and prenatal exposure to toxic substances of the mother, complications may arise that hinder the ability to feed through sucking-swallowing or natural breastfeeding. This clinical case evaluates the effectiveness of powdered human milk (PHM) as a nutritional intervention in a premature newborn with prenatal exposure to toxic substances and multiple complications.

Case Presentation: A female infant born at 32.3 weeks of gestation, weighing 1331g, is presented with a complex diagnosis including respiratory distress syndrome (RDS), congenital syphilis, pneumonia, hepatosplenomegaly, microcephaly, patent ductus arteriosus, bacterial sepsis, and bronchopulmonary dysplasia. Prenatal exposure to methamphetamines and the infant's rejection of conventional milk formulas led to the need to explore nutritional alternatives for her recovery, such as feeding with PHM.

Methods: The PHM was administered to the patient starting from 30 days of life. The human milk was collected from healthy donors, processed through spray drying, and subjected to rigorous quality controls to ensure its safety and effectiveness. Feeding was administered via an orogastric tube, adjusted to meet the nutritional requirements of the premature infant.

Results: The administration of PHM resulted in a significant improvement in the newborn from the first feeds. Gastrointestinal tolerance, abdominal distension, and haematochezia, which had emerged with the intake of commercial formulas, were solved with the introduction of PHM. The patient gained weight, increasing from 1331g at birth to 2034g after 56 days of PHM feeding. Haematological and biochemical parameters also stabilised, with improvements in haemoglobin, platelet, and electrolyte levels.

Conclusion: The PHM facilitated a rapid improvement in the premature patient affected by prenatal exposure to toxic substances and associated complications. The good tolerance to PHM and the clinical recovery observed in this case highlight the potential of this unique food as a key tool for the nutrition of premature infants in complex hospitalised situations. These results suggest the need for further research to refine nutritional protocols for neonates with a past exposure to toxic substances and to implement the feeding of premature neonates with PHM in hospitals.

Keywords: *Human Milk Powder; Nutrition; Premature Neonate; Recovery; Toxic Substance*

Abbreviations

µg: Micrograms; CPAP: Continuous Positive Airway Pressure; CUCEI: University Centre for Exact Sciences and Engineering; dL: Decilitres; FiO2: Fraction of Inspired Oxygen; g: Grams; h: Hours; Kg: kilograms; max: Maximum; mg: Milligrams; min: Minimum; mL: Millilitres; NICU: Neonatal Intensive Care Unit; PHM: Powdered Human Milk; RDS: Respiratory Distress Syndrome; Toxic Substances: Use of Illicit Drugs and Controlled Medications; UDG: Universidad de Guadalajara

Introduction

Feeding a premature neonate with human milk is the primary source for the infant to obtain the necessary nutrients and energy required to carry out vital functions. However, complications can prevent neonates from being fed through coordinated sucking-swallowing [1]. This frequently occurs when the infant is premature and has not developed this reflex or presents complications that require admission to a Neonatal Intensive Care Unit (NICU) [2]. There is a higher risk in newborns born to mothers who consume toxic substances, as they tend to be born before 32 weeks of gestation due to exposure to these substances during pregnancy. This situation complicates their recovery and, especially, enteral feeding, which often leads to the placement of a nasogastric tube to nourish the neonate to initiate digestive processes and colonize the intestines with beneficial microbiota lately [3,4].

The purpose of this clinical study was to assess the effectiveness of powdered human milk (PHM) as an intervention to improve nutritional status and health recovery in high-risk premature infants. This case report focuses on a female patient at 32.3 weeks of gestation, born to a mother who used toxic substances (positive for methamphetamines), with a low birth weight of 1331g considered for the gestational age, diagnosed with RDS, congenital syphilis [5]. CDC scenario 1, neonatal pneumonia, hepatosplenomegaly, microcephaly, patent ductus arteriosus, bacterial sepsis, and bronchopulmonary dysplasia. This case study aims to contribute a new and effective alternative for feeding with PHM in at-risk neonates, to help optimize clinical care strategies in similar scenarios.

Materials and Methods

Patient description

The patient is a female one month old (36.5 weeks corrected), currently hospitalised in the Neonatal Intensive Care Unit (NICU) of the Neonatology Service at Hospital Civil "Fray Antonio Alcalde" in Guadalajara, Jalisco, Mexico. The patient is on nasal CPAP 5x5 with FiO_2 35%, with vital signs within normal parameters for her age, not requiring inotropic support, exhibiting poor tolerance to enteral feeding, and with normal diuresis and stools.

Sociodemographic background

The mother had no prenatal care and was in her fourth pregnancy with no history of miscarriages. Rapid tests were positive for syphilis, leading to the initiation of treatment with benzathine penicillin, 2.4 million units intramuscularly. Toxicological screening revealed the presence of amphetamines. The mother has no known chronic illnesses or relevant surgical history.

Physical examination

On physical examination, the patient is active and responsive to stimuli, with adequate hydration and normal skin and mucous membrane coloration. Microcephaly is present with a normotensive anterior fontanelle, and an orogastric tube is in place. A globular abdomen is observed with hepatosplenomegaly confirmed by X-ray, as shown in figure 1, which displays an increase in the size of the liver and spleen.

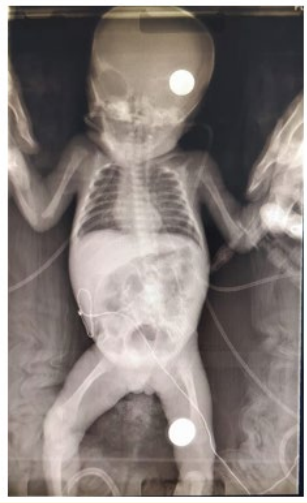

Figure 1: *X-ray of the premature patient showing evident visceromegaly and hepatosplenomegaly in the thoracic cavity.*

Previous interventions

The patient had a serious health condition at birth, thus she was kept fasting for the first two days with an infusion of 10% glucose IV. From the third day, parenteral nutrition was initiated for 10 days, adjusted to her weight. On day 12, enteral nutrition was started with 2 mL every 3 hours via orogastric tube with a formula for premature infants. Due to intolerance to the formula, enteral feeding was discontinued, and parenteral nutrition was resumed for 5 days. Enteral nutrition was then restarted with extensively hydrolysed formula, which led to symptoms such as abdominal distension, gastric reflux, haematochezia, and atopic eczema, attributed to an allergy to cow milk protein.

Penicillin was administered in meningeal doses and amikacin for 10 days, due to a positive result for congenital syphilis and a procalcitonin level of 5.98. Desquamation of palms and soles, visceromegaly, and pancytopenia were also observed.

Clinical analysis

The clinical analyses at 30 days of life for the patient show the following results: haemoglobin of 14.55 g/dL, haematocrit of 30.43%, platelets of 46,780/µL, leukocytes of 8,830/µL, serum creatinine of 0.21 mg/dL, total bilirubins of 3.31 mg/dL, chloride of 116 mg/dL, and sodium of 153 mg/dL. These results and the clinical assessment of the patient are illustrated in figure 2. During their stay in the NICU, the patient received a platelet transfusion on day 9 of life, which resulted in a significant increase in the platelet count, reaching 309,700/µL by day 13, and remaining within normal ranges. However, by day 14, the patient developed thrombocytopenia that persisted for 24 days, leading to a second platelet transfusion. This second transfusion resulted in an improvement and stabilisation of platelet levels.

Additionally, on day 16, a red blood cell concentrate transfusion was performed at 15 mL/kg/day due to anaemia, as shown in figure 2A. Following this, the patient exhibited respiratory pauses of less than 20 seconds, leading to the application of nasal CPAP, attributed to the anaemia, along with nasal prongs at 2 litres per minute with an FiO_2 of 30%, maintaining adequate tolerance.

Nutritional intervention with PHM

Ethical and legal aspects

After analysing the case and obtaining the necessary permissions from the hospital's ethics and biosafety committee with document No. HCG/CEI-0907/22 and research registration 141/22, as well as the informed consent with Folio No. 002, and based on the General Health Law [6] and the Helsinki Declaration [7], the informed assent letter, based on the United Nations Convention on the Rights of the Child [8] and confidentiality letter signed by the parents or legal guardian, in accordance with the current criteria established in the Federal Law on Protection of Personal Data Held by Private Parties [9], enteral feeding is then commenced. This involves powdered human milk from clinically healthy donor mothers who authorised the use of their milk and were previously assessed through clinical analyses.

Collection and processing of the milk

The milk was collected aseptically in the neonatal unit care facilities of the "Fray Antonio Alcalde" Civil Hospital in Guadalajara and processed by spray drying to convert it into powder at the Human Milk Research Laboratory of CUCEI/UDG. This process preserves the nutritional content, biological properties, and sanitary quality of the liquid human milk, ensuring a shelf life of over two years at room temperature without the need for additives or preservatives. It provided a unique alternative for feeding hospitalised premature infants [10].

Quality control of PHM

To ensure the quality of PHM, nutrients (proteins, lipids, carbohydrates, total solids, non-fat solids, salts, and amino acids), which retain 90% of the nutrients compared to fresh milk. Additionally, the product's sanitary quality is ensured through analysis of indicator microorganisms and pathogens [11], as well as toxicological monitoring of the donated milk to ensure it is free from cocaine, methamphetamines, amphetamines, opiates, marijuana, and benzodiazepines [12].

Feeding plan

To feed the patient with exclusive human milk during the first months of life, in accordance with WHO [13] recommendations and the country's current regulations [14], a feeding plan with PHM via orogastric tube was designed, tailored to the nutritional needs of the premature patient. Due to the risks of contamination of breast milk with toxic substances for the neonate, the mother authorised the use of PDH for her daughter, ensuring the newborn's right to exclusive breastfeeding, given the difficulty the patient had in being fed with her own mother's milk.

Results and Discussion

The consumption of toxic substances during pregnancy and breastfeeding constitutes a serious public health issue. Substances such as cocaine, methamphetamines, and certain controlled medications can cross the placental barrier, directly affecting the foetus. Likewise, once born, these substances can reach significant concentrations in breast milk, putting the neonate's health at risk [15].

A study by Amezcua., *et al*. (2023) reported that mothers who used abused drugs during pregnancy often had preterm deliveries between 31 and 37 weeks of gestation [12]. Additionally, Dr. Gunatilake from the University of Arizona College of Medicine highlighted that the use of amphetamines and cocaine during pregnancy can cause congenital defects, inadequate fetal growth, premature separation of the placenta, neonatal withdrawal syndrome, and even death [16].

This clinical case involved a nutritional intervention with PHM in a premature patient, the daughter of a mother with a toxicological profile positive for amphetamines, congenital syphilis, respiratory distress, and allergy to cow's milk protein. The patient's clinical

condition was assessed in collaboration with the neonatology department, nutrition team, and the Human Milk Research Laboratory of the Universidad de Guadalajara, Jalisco, Mexico.

Clinical findings that led to this decision included gastrometabolic intolerance to commercial dairy formulas. The patient was fed with a special formula for preterm infants from the second day of life but exhibited abdominal distension of more than 2 cm after feeds and evident haematochezia. Due to the premature development of the gastrointestinal tract, it was decided to suspend enteral feeding and administer parenteral nutrition for 10 days. Subsequently, enteral nutrition was reintroduced with extensively hydrolysed formula at a dose of 2 mL every 3 hours. Although the patient initially appeared to tolerate the formula well, by the third day, abdominal distension, haematochezia, irritability, and atopic eczema recurred, characteristic symptoms of cow's milk protein allergy.

This condition, as shown in a study conducted by Sorensen., *et al*. (2021), induces dysbiosis in the gastrointestinal metabolism of infants, increasing the risks of intestinal infections and delaying recovery in patients with other complications [17]. Given these findings and as a last resort for feeding, an amino acid formula was administered on day 25 of life (2 mL every 3 hours), with clinical values showing platelet counts of 82,380/µL (Figure 2B), leukocytes of 17,720/µL (Figure 2C), and stable serum electrolytes, except for phosphorus at 7 mg/dL, as shown in table 1. The patient initially showed apparent tolerance and a reduction in symptoms. However, on the fourth day of feeding, haematochezia reappeared.

Weeks of life	Phosphorus (mg/dL)	Calcium (mg/dL)	Chloride (mmol/L)	Potassium (mmol/L)	Sodium (mmol/L)
Birth	4.2	8.1	96	4	137
1	4.5	10.7	96	4.4	140
2	3.8	9.1	101	5.9	138
3	2.9	9.7	107	4.2	139
4	7.0	9.4	109	4.3	143
5	4.3	10.6	116	4.1	153
6	4.5	9.3	105	3.9	137
7	6.5	9.8	101	4.5	136
8	5.8	9.2	107	4.1	135
9	5.4	9.2	101	3.3	134
Reference value	2.7-4.5	8.4-10.2	98-107	3.50-5.10	135-145

Table 1: *Serum electrolyte concentrations in patient evaluated over 9 weeks.*

Note: The analyses were performed using spectrophotometric and colourimetric methods.

Considering these multiple instances of clear intolerance to milk formulas and after obtaining permission from the hospital and the child's legal guardian, as well as having the informed consent read and signed in the presence of two witnesses, the feeding with PHM was initiated. A feeding plan was developed in coordination with the neonatal nutrition department, based on the preterm infant's needs, tolerance, and clinical progress, as outlined in the clinical practice guidelines for feeding preterm infants [18].

Feeding with PHM commenced on day 30 of life, with stable values of procalcitonin at 0.21 ng/mL, haemoglobin at 14.55 g/dL, platelets at 46,780/µL, leukocytes at 8,830/µL (indicating resolved bacterial sepsis and no presence of new infectious processes), serum creatinine at 0.21 mg/dL, and total bilirubins at 3.31 mg/dL. These results are shown in figure 2A-2D. The review of serum electrolytes showed

values within normal ranges, as observed in table 1. Feeding was initiated via an orogastric tube with a dose of 4 mL every 3 hours (140 mL/kg/day). The patient displayed good gastrometabolic tolerance (with a total balance of 43.8, diuresis of 3.8 mL/kg/h, and actual fluids of 138.5 mL/kg/day), without abdominal distension or haematochezia, and showed good progress, leading to a progressive increase in the doses.

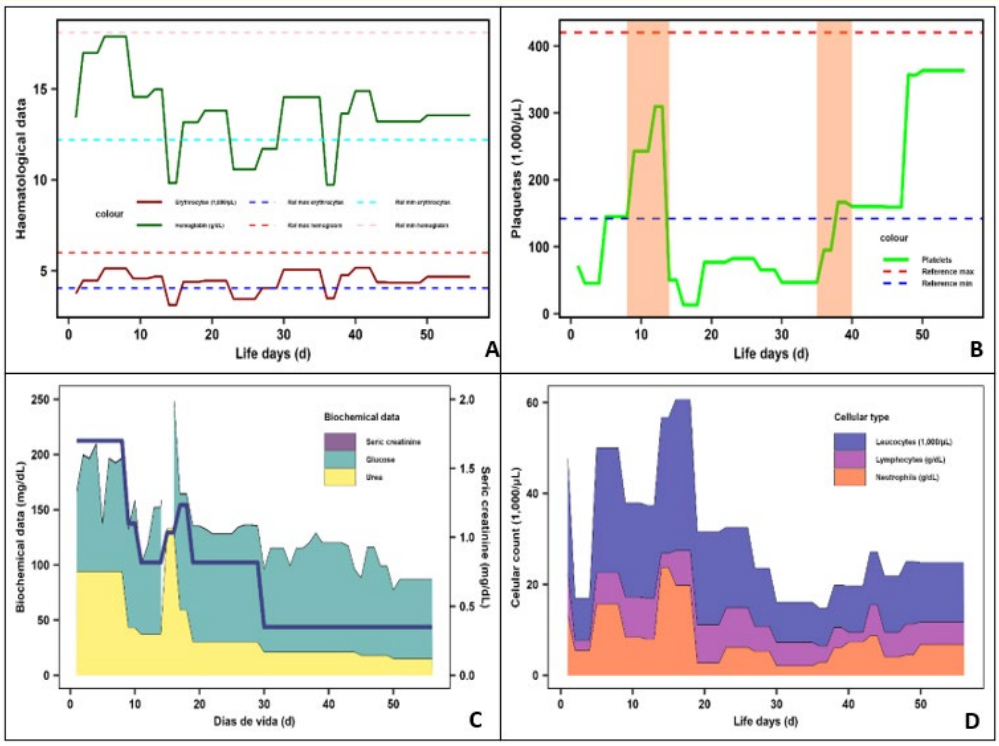

Figure 2: *Clinical assessment of the patient during the first 56 days of life. In figure A, the haematogram values are shown, with the green line corresponding to haemoglobin (min 12.2, max 18.1 g/dL) and the red line corresponding to erythrocytes (min 4.04, max 6.13 thousand/µL). In figure B, the values for platelets (min 142, max 424 thousand/µL) are observed; the boxes within the graph correspond to the transfusions administered to the patient. In figure C, the biochemical data for serum creatinine (min 0.5, max 1.2 mg/dL), glucose (min 60, max 120 mg/dL), and urea (min 15, max 39 mg/dL) are shown. In figure D, the values for leucocytes (min 4.6, max 10.2 thousand/µL), lymphocytes (min 10, max 50 g/dL), and total neutrophils (min 37, max 80 g/dL) are shown.*

A clinical trial conducted by Dr. Karine da Rosa., *et al*. (2020) from the hospital de Porto Alegre, Brazil, exhibited that early oral stimulation in preterm infants, during a short transition period from tube feeding to full oral intake, showed beneficial results in the tolerance of breast milk and better nutrient absorption [19].

On the fourth day of feeding with PHM, the patient was placed on fasting due to the onset of apneas and hypotension, requiring emergency intubation for RDS associated with prematurity. After 18 hours, extubating was performed and high-flow nasal cannula

was placed, with enteral feeding resumed progressively and based on nutritional needs. This feeding process is illustrated in figure 3B, showing the progress of enteral feeding and the reduction of parenteral nutrition.

A study conducted by Dr. Granger and colleagues at the Clinical and Translational Research Institute in the United Kingdom identified that feeding preterm infants with breast milk from an early stage provides numerous nutritional and immunological benefits. As exposure to the human milk microbiome increases immune levels and reduces the risk of developing necrotising enterocolitis, as well as mitigating various morbidities that jeopardise the health of the neonate during this period [20].

On the 10th day of treatment, the patient showed adequate tolerance to PHM, with no abdominal distension. Bowel movements improved significantly, changing from green and pasty stools to a soft, mustard-yellow consistency, like those of an infant exclusively breastfed, as noted in the UNICEF guidelines for infant feeding [21].

The patient continued to progress well. Haematological values stabilised within normal ranges, urea levels decreased from 21 to 15 mg/dL over the course of 20 days, and platelets and serum electrolytes stabilised (these values can be seen in table 1), indicating good fluid management and no signs of anaemia.

Regarding weight gain, the neonate was born weighing 1331g, decreased to 1147g by day nine, and remained within this range for 10 days due to rejection of the formula. From day 20 onwards, weight gain commenced, and after the administration of PHM, the neonate gained 260g in 8 days, the progression of weight can be seen in figure 3A.

Research led by Dr. Yu Li and her team at Weifang University in China., displayed that pasteurised donor milk significantly reduces the risk of diseases and the need for parenteral nutrition in preterm infants. However, it was observed that this donor milk is less effective than commercial formulas for weight gain and growth in preterm infants. Therefore, it is recommended to add fortifiers to compensate for nutrient deficiencies [22].

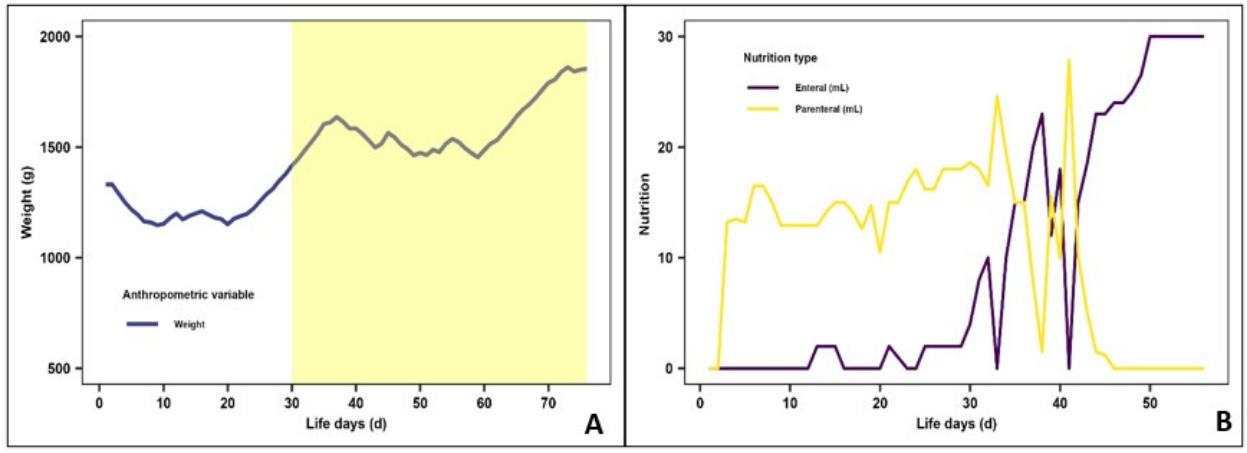

Figure 3: *Assessment of weight gain and enteral feeding plan with powdered human milk. Figure A shows the progressive weight gain from birth to patient discharge. Figure B illustrates the changes in feeding from parenteral to enteral.*

In this case, the results obtained with feeding PHM show similarities with those reported by Li., *et al.* (2022). Although the recovery and stabilisation of the patient was achieved in less time compared to premature infants who received commercial milk formula, weight gain was slower. For these reasons, on day 50 of life, once the patient was stable, it was decided to fortify the PHM with a commercial liquid fortifier to enhance weight gain.

After 56 days of feeding with PHM, the patient made a full recovery, without the need for supplemental oxygen, and was discharged from the neonatal intensive care unit with a weight of 2034g (Figure 3A), being transferred to the growth and development area for continued monitoring. The patient continued to be fed with PHM for an additional 40 days, and at 4.2 months of age, was transitioned back to commercial formula with good acceptance and weight gain.

The patient was followed up for 12 months to assess allergies, progress, and complications. In neurodevelopmental follow-up, improvements were observed improvement in motor and cognitive development, as well as muscle tone, evidenced by adequate control and coordination of the limbs and a more effective response to stimuli, compared to other preterm children exclusively fed with commercial formula and born to mothers who used toxic substances. However, a slow motor development process was noted, attributable to the central nervous system sequelae caused by prenatal exposure to illicit drugs. Currently, the child is in good health, correcting her posture with the help of rehabilitation, and without any presence of cow milk protein allergy or other food allergies.

It is crucial to conduct further studies to evaluate the long-term effects of feeding preterm patients with PHM. These developments pave the way for future research into potential nutritional alternatives that ensure the health and well-being of neonates, as well as suggest and review nutritional management protocols for preterm infants with a history of prenatal exposure to toxic substances. These results highlight the importance of personalised nutrition and the potential of PHM as an innovative food for the recovery of these patients.

Conclusion

This case report shows that feeding with PHM is an effective strategy to improve the nutritional status and health recovery of preterm neonates exposed to toxic substances during gestation. The patient exhibited adequate gastrometabolic tolerance to PHM consumption, and thanks to the use of human milk, the patient's haematological and biochemical parameters stabilised, allowing for discharge from the NICU in less time and significant weight gain. This highlights the effectiveness of personalised nutrition with PHM. This illustrates that PHM is a key alternative for the recovery and well-being of preterm neonates, particularly those affected by maternal toxic substances.

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Conflict of Interest

The authors declare that they have no conflicts of interest related to this research. No funding has been received, and no relationships have been established that could influence the design, execution, analysis, or publication of the study's results.

Informed Consent Statement

This study was also approved by the Ethical Research Committee 08 June 2022, with registration number HCG/CEI-0907/22 and research registration 141/22.

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