Breast milk and kangaroo care in the Neonatal Intensive Care Unit (NICU), simple interventions, and great results.

Maria Bertha Romo Almanza*

Guadalupe Victoria Maternity Hospital, Mexico

Abstract

Currently the rate of premature births as well as the survival of these babies has increased, becoming a serious global health problem.

In the Guadalupe Victoria Maternal and Child Hospital in Atizapan Mexico, around 3,500 births are attended each year, of which 419 patients required hospitalization for various reasons, the main one being: prematurity, as we are in a developing country where resources are often insufficient, strategies must be sought so that the culture of prevention can reduce the length of hospital stay by reducing the risk of morbidity and mortality. It is important to mention that the Hospital has the accreditation as a Hospital that is friendly to the child and the mother, being in favor of feeding with breast milk, and insofar as the patient's conditions allow it to start with kangaroo care. Strategies that manage to influence in a positive way the evolution of hospitalized children.

The World Health Organization (WHO) estimates that the incidence in the premature birth is around 11.1%. Frequency in places with low income is between 12%-18%, finding that Asia and Africa are areas with high rates. In Mexico, a rate of 7.3% is reported in agreement. To the records of the same organization.

Prematurity is considered a multifactorial syndrome which has multiple etiologies. Some of the main maternal risk factors are: malnutrition, little weight gain in pregnancy, infections and extreme maternal ages, short intergenetic period and/or obstetric complications, use of assisted reproductive techniques, multiple pregnancies.

These premature new-borns, compared to term babies, have a higher morbidity and mortality rate. Being the second most common cause of death in children less than 5 years of age and it is the first cause in developed countries. Associated with higher risk of development of multiple pathologies in adult life; Therefore, safe strategies are sought, not only to improve their survival, but also their quality of life, thinking about the possible scenarios that could arise, with the purpose that by providing bioactive factors (human milk,) colonization with microbiome adequate, (kangaroo breast method) and avoiding colonization with pathogenic bacteria responsible for sepsis, (correct hand hygiene) to intervene positively influencing achieving an adequate metabolic programming in the development of each one.

Conclusion: Simple and low-cost interventions that have a high impact on the evolution of critically ill hospitalized new-borns, both in their stay and in their future development, two of these actions are: feeding with human milk as well as establishing the program Kangaroo breast as a treatment.

Keywords: Breast milk, Kangaroo care, NICU, Inmunonutrition, Nutrigenetics, Microbiome.

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Introduction

Currently the rate of premature births as well as the survival of these babies has increased, becoming a serious global health problem [1].

In the Guadalupe Victoria Maternal and Child Hospital in Atizapan Mexico, around 3,500 births are attended each year, of which 419 patients required hospitalization for various reasons, the main one being: prematurity, as we are in a developing country where resources are often insufficient, strategies must be sought so that the culture of prevention can reduce the length of hospital stay by reducing the risk of morbidity and mortality. It is important to mention that the Hospital has the accreditation as a Hospital that is friendly to the child and the mother, being in favour of feeding with breast milk, and insofar as the patient's conditions allow it to start with kangaroo care. Strategies that manage to influence in a positive way the evolution of hospitalized children. That is why in addition, mothers are asked to extract and collect milk from their admission, which is used in all areas, and there is support to pasteurize it in another unit, it is worth mentioning that only in the month of January 6388 ml were collected in the NICU area 8814 in the intermediate care area, that is to say 15.2 liters, this in reserve which allows the feeding to be almost exclusively human milk, this if the conditions of the patients allow it.

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Prematurity is considered a multifactorial syndrome which has multiple etiologies. Some of the main maternal risk factors are: malnutrition, little weight gain in pregnancy, infections and extreme maternal ages, short intergenetic periods and/or obstetric complications, use of assisted reproductive techniques, multiple pregnancies [1,3-7].

These premature new-borns, compared to term babies, have a higher morbidity and mortality rate. Being the second most common cause of death in children less than 5 years of age and it is the first cause in developed countries [8]. Associated with higher risk of development of multiple pathologies in adult life; Therefore, safe strategies are sought, not only to improve their survival, but also their quality of life, thinking about the possible scenarios that could arise, with the purpose that by providing bioactive factors (human milk,) colonization with myocrobiota adequate, (kangaroo breast method) and avoiding colonization with pathogenic bacteria responsible for sepsis, (correct hand hygiene) to intervene positively influencing achieving an adequate metabolic programming in the development of each one.

The associated morbidity is well known: late sepsis, necrotizing enterocolitis, retinopathy of prematurity, bronchopulmonary dysplasia, and neurodevelopmental problems, among others. There is evidence that they are at higher risk of developing cardiovascular and metabolic diseases in adulthood, as well as chronic lung disease and allergies [9-11]. It has been commented on the association that adults with chronic pulmonary obstructive disease have with a history of prematurity and development of bronchopulmonary dysplasia, so it has been considered that they may have the same pathophysiology.

It is clear that adequate nutrition during the earliest stage of life (Immunonutrition) is of great importance for the growth and maturation of organs and tissues, especially those premature new-borns. Remembering the term: Nutrigenetics: Humans are not genetically identical, and they live in different environments, the response of each person to the food they receive may not be equivalent. Therefore, this term refers to the intervention that may exist between the gene-nutrient and how the response will be individually based on its genome, since there is genetic polymorphism [11]. Being one of the reasons why human milk is the one that covers all nutritional needs, since it provides adequate amounts of micro and macronutrients for growth and development. In addition to carrying several bioactive components, which contribute for the development and maturation of immune system.

Its composition is dynamic and varies according to maternal age, number of pregnancies, Body Mass Index (BMI), maternal diet, time of day, lactation period and other environmental factors [12-14].

Bioactive factors in human milk

Antioxidants are among the most studied and understood, which can help counteract the negative effect of oxidative stress in new-borns [15]. Other bioactive components to consider are: growth factors and hormones, which regulate energy intake and organ maturation. Cytokines have a protective effect against infections and the ability to reduce the inflammatory process, which in the long term can contribute to the protection against the development of cardio metabolic diseases [16]. Human milk-fed preterm infants exhibit lower rates of metabolic syndrome, high blood pressure, or insulin resistance in adolescence compared to formula-fed infants. Human milk is known as the best scavenger of free radicals [17-19].

Antioxidants in human milk

Endogenous antioxidants can be classified as enzymatic (*i.e.* Superoxide Dismutase (SOD), catalase or Glutathione Peroxidase (GPx), small non-enzymatic molecules (such as Glutathione (GSH), or hormones with antioxidant capacity (such as melatonin)) [20,21]. In addition to endogenous antioxidants, several foods, mainly vegetables and fruits, contain antioxidants such as vitamins, carotenoids and polyphenols, among others.

Antioxidants provide a line of defense against disease and can be critical in the management of infants with critical prematurity. Human milk-fed new-borns have less oxidative stress, evidenced by lower levels of biomarkers of oxidative damage compared to formula-fed babies. Proposing that this may be related to reduction of synthesis for free radicals [22]. The total antioxidant capacity is higher in colostrum compared to mature milk and their activity decreases throughout the breastfeeding period

Glutathione is the main low molecular weight intracellular antioxidant; it participates in the regeneration of other antioxidants such as vitamin C and E or their active forms, in human milk it has been found with a concentration of 10.4 to 43.1 nmol/mg [23].

Melatonin

Endocrine product secreted by the pineal gland, plays a physiological role in neuroimmunomodulation, is synthesized from tryptophan *via* serotonin, regulates circadian rhythm, also has pleiotropic actions, and exhibits a protective effect against cellular aging. As a direct destroyer of radicals, as well as stimulating the expression of SOD, catalase and GPs. In addition, it seems to have a neuroprotective role in premature patients due to its effects on the modulation of the neuroinflammatory pathway [24].

Antioxidant	Activity	Range
Superoxide dismutase	Eliminates superoxide anion	2.01-6.26 nmol/min/mL
Catalase	Eliminates hydrogen peroxide	1.84-26.1 nmol/min/mL

Glutathione peroxidase	Eliminates hydrogen peroxide	6.6-17.7 mM/min/L
Glutathione	Regeneration of other antioxidants	10.4-43.1 nmol/mg of protein
Melatonin	Free radical scavenger, antioxidant expression	<10-23 ng/L

Table 1. Endogenous antioxidants in human milk.

Growth Factors

Many premature patients may present with growth retardation, poor physical development, and neurological deficits.

In the post-birth period, growth retardation is commonly the result of inadequate nutritional support, as well as associated pathologies. Human milk provides factors that play an important role in the growth, maturation and integrity of various organs, particularly in the gastrointestinal tract. They help in ripening and have anti-inflammatory effects [25-27]. These factors promote proliferation and differentiation in their immature cells, and the highest concentrations are found in colostrum [28-29].

Hepatocyte growth factors, epidermal and neuronal growth factor, neurotrophic factor playing a critical role in the development and maintenance of the central nervous system, in neuronal survival and proliferation, insulin binding increases erythropoiesis and therefore hematocrit, but still Its exact function is not known, CD14 proteins, acts as a co-receptor for the detection of bacterial lipopolysaccharides. It has two forms, one is a soluble form (sCD14) and another is anchored to the cell membrane (mCD14). This membrane is expressed primarily in monocytes, macrophages and neutrophils also provides against subsequent allergic manifestations [30].

Growth factors	Main tissue sythesized	Range (μg/ml)	Main neonatal functions
Epidermal-GF	Submandibular slivary gland	24-37	Intestinal mucosa maturation and healing, nutrient absorption, protein synthesis
Neuronal-GF	Cerebral cortex and hippocampus	2.8-934	Nervous system maturation, learning, and memory
Insulin-like-GF	Placenta and digestive system	5-35	Retinal vascularization, brain maturation
Vascular endothelial-GF		505-650	Angiogenesis

Table 2. Growth factors in breast milk.

Adipokines

Components involved in the regulation of food intake and energy balance can modulate the metabolic development of diseases in adulthood such as obesity type 2 diabetes mellitus or insulin resistances [31].

Adipokines	Tissue synthesized	Range (ng/ml)	Preterm infants	Main neonatal functions
Leptin	White adipose placenta mammary	0.2-10.1	↑/?	Anorexigenic t-lymphocyte responses
Adiponectin	Adipocytes	4.2-87.9	≈/?	Orexigenic regulation of lipid/glucose metabolism improvement of insulin sensitivity anti-inflammatory actiions
Resistin	Immune cells epithelial cells	0.2-1.8	↑/?	Regulation of glucose homeostasis inhibition of adipocyte differentiation inflammatory response
Ghrelin	Stomach pituitary other	0.07-6	?	Orexigenic gastric motility and secretiion adipogenesis anti-inflammatory actions
Obestatin	Stomach small intestine	0.4-1.3	?	Anorexigenic body weight regulation
Nesfatin	Neurons pancreas other	0.008-0.01	?	Anorexigenic production of body fat
Apelin	Heart lung other	43-81	?	Regulation of cardiovascula r system fluid homeostasis angiogenesis regulation of insulin secretion

Table 3. Adipokines in human breast milk.

Adapted from Catli et al. Arrows indicate comparison with full-term newborns or inconclusive data requiring investigation [31].

Cytokines in human milk

They are small proteins synthesized by almost all nucleated cells. Its role in the inflammatory response is divided into cytosines that promote inflammation or protect against infection and those that decrease inflammation [32].

Ant-inflammatory cytokines

Transforming Growth Factor-B (TGF-B) IL-7 and IL-10, IL 7, crosses the intestinal barrier and constitutes the formation of thymus, as well as the development of T lymphocytes. Regarding IL-10, its role is controversial, but it has been found that low levels of IL-10 in breast milk increase the risk of developing necrotizing enterocolitis [33].

Inflammatory cytokines

Most of them, such as Tumor Necrosis Factor Alpha (TNF-a), IL-1B, IL-6, IL-8 and interferon gamma, their role has not yet been well defined. They are found in greater amounts in human milk of mothers of premature infants than in term births [34].

Stem cells

It is suggested that up to 6% of the cells present in human milk are stem cells and mesenchymal stem cells, and these may have a role in the development of immune cells, including regulatory T lymphocytes, which may produce tolerance to non-inherited maternal antigens and suppress anti maternal immunity. They induce microchimerism of pregnancy, leading to intestinal tissue repair and development of immune protection against infectious diseases [35].

Leukocytes in human milk

Present in high amounts in colostrum, 1010 maternal leukocytes per day, [36] their role is not clear, reports have been made where a significantly lower proportion of macrophages is observed in the milk of mothers with babies who developed allergy to protein from the cow's milk, in contrast to a higher content of neutrophils, eosinophils or lymphocytes, which were associated with a lower risk of presenting an allergy to cow's milk proteins [37]. On the role of these cells is still far from understood, their mechanism to pass to the stomach, and intestinal barriers, as well as access to the infant or its mechanism of action, more research is required to clarify these aspects of inflammation and immunity development.

Human milk microbiome

It is well known that human milk is not sterile, colonization with non-pathogenic microbiota is essential for metabolic and immunological maturation of the new-born, it begins at birth, and its most important changes occur during the first year of life, The microbiome is constantly changing and It is influenced by hormones, cytosines and chemokines, after birth the continuous transfer during lactation and is considered the main cause of variability between infants exclusively breastfed and those fed formula during the first months of life [38,39].

More than 100 types of viable bacteria/Ml have been documented including 65% of phyla Protebacteruas and 34% of phyla Fhirmicutes, in terms of genera; the most common are Staphylococcus, Streptococcus, Lactobacillus, Enterococcus, Lactococcus, Weissella, Veillonella and Bifodobacterium [40-42].

This microbiota is also related to other factors, ethnic group, place of residence, form of birth, maternal food intake. Few studies have reported differences between the human milk microbiome; some include more Bifidobacterium in term milk and more Enterococcus in preterm milk [36].

Kangaroo care

Once we get into the topic of Microbiota and microbiome, it is very important to comment on the kangaroo care program within the strategies to have a better development of low-weight hospitalized newborns, and the benefits that children can have.

It consists of holding a newborn in ventral skin-to-skin contact with its mother, and receives its name for simulating marsupial care, being recommended as a feasible, natural and profitable intervention, which is considered as a gold standard in treatment quality medical that should be provided to all babies, regardless of geographic location or socioeconomic status. The beneficial effects of this program have been widely studied, allowing meta-analysis to be carried out, there are 2 reviews in Cochrane, one focused on the health of late-term or late preterm newborns, while the second includes low-birth weight newborns birth [43,44].

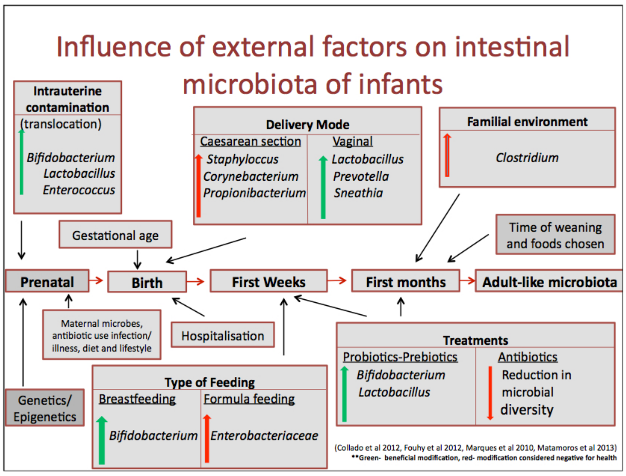
Among the benefits reported is at the physiological level: achieving adequate homeostasis (temperature regulation, cardiohemodynamic stability, and respiratory, blood glucose stability) which is reflected at the hospital level in reducing the risk of suffering serious pathologies, including sepsis and death.

At the behavioral level, sleep directly influences its neurodevelopment, the duration of breastfeeding and the degree of exclusivity of said feeding, it is also very important as an effective therapy for pain relief during procedures, improves neurological development and father binomial attachment-son. However, the adoption of this practice despite everything reported is variable. Uncertainty remains as to whether continuous KC should be recommended in all settings or whether there is a critical onset period, optimal dose, or duration [45].

Implications in daily practice

The evidence for KC care to promote homeostasis is strong, especially in developing countries, where it is suggested that this method can reduce mortality [46], the best evidence focuses on the intermittent use of this program, and while homeostatic benefits should theoretically persist when applied continuously there is a leak in the design of the study, in any case there are still limitations to conclude the adequate time that the baby should spend in KC to achieve the maximum benefits. Feldman et al provide evidence that an average of 1 hour per day can impart lasting benefits, but evidence is lacking whether a shorter or longer period could yield different results. Being very important the medical criteria, the pathology of the newborn and the availability of the parents to carry out this program [47,48].

In addition to what was previously mentioned in these children, the development of an adequate microbiome is very important, there are multiple studies in this regard and the following conclusions have been reported when analyzing newborn feces (Figure 1).



Figue 1. Collado et al. 2012.

The most abundant phylas (or families) in the intestinal tract of healthy neonates in the first 2 weeks of life are: proteobacteria (46%), firmicutes (45%), actinobacteria (2%) and bacteroidetes (7%) very important because as there is no balance, dysbiosis occurs.

This microbiome then contributes to proper digestive health, intervenes in the production of short chain fatty acids, synthesis of vitamin K, is related to the development of the immune system, protecting us against infections and pathologies, and contributes to intellectual and mental development. They are directly related to protection against obesity (Reinhardt 2009) and against allergic, gastrointestinal, autoimmune and metabolic diseases.

Discussion

As described in the literature review, simple strategies such as providing human milk and kangaroo care in hospitalized newborns have a positive influence on the evolution of these infants, below are the graphs of hospitalized newborns (Figures 2-4).

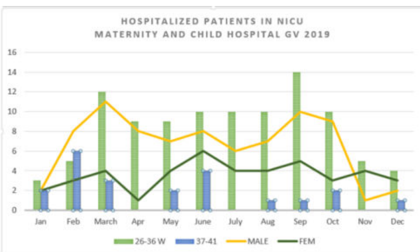
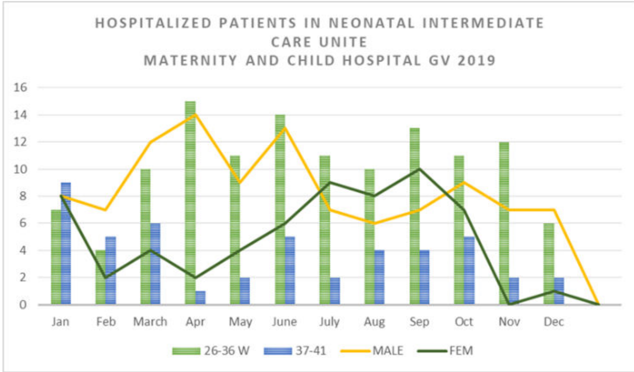


Figure 2. This graph show that there was a greater number hospitalized patients in the months March and September with gestational age comprised between 26 and 36 weeks of gestation, predominantly males



Figue 3. The graph shows hospitalized patients in the intermediate care area, with a higher number of admissions on April and September months, coinciding in gestational age with those who required intensive care, but there was a variation in sex since during the months from July to September, female patient admissions predominated.

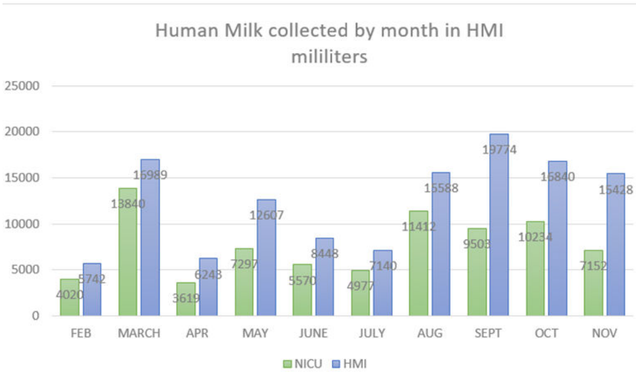


Figure 4. This last figure shows the milk collection per month. Observing that during the month of March and September the largest collection occurred. Births per year around 3500; Hospitalized patients NICU: 123+294 (Intermediate care)=417 (11.9%); BM Harvested in 10 months 77,624 ml (77 liters).

It should be noted that all babies who are in health conditions that allow it enter kangaroo care, where mothers stay for at least 30 minutes 3-4 times a day as they enter the care area to breastfeed intermediate. In that year 2019 the NICU mortality rate was 8.5% and National rate 10%.

Conclusion

There are simple, effective, low-cost and quality interventions that, when implemented in continuous medical practice in Neonatal Intensive care units, can positively influence the treatment of critically ill premature newborns in the neonatal care area. can positively influence their evolution during the hospital stay and metabolically program, perhaps intervening favorably in the epigenetics of each infant, having said this we can conclude that human milk is a complex diet and the gold standard for the nutrition of the newborn born as it provides bioactive components, participates in growth, is a defense barrier against oxidative stress and infections, is a dynamic fluid and changes continuously according to the needs of newborns, together with macronutrients, human milk contributes to a correct maturation and development of org years and tissues. However, it should be included in the investigation how the maternal diet can influence in all aspects.

Regarding kangaroo care, the benefits are widely known by including physiological aspects, pain control, and development of both healthy and sick newborns. The time that the child should stay with his parents is still under study. To obtain the greatest benefits already commented at least one hour a day, but evidence is lacking as to whether shorter or longer periods of time can have the same result.

On the other hand, it should be considered in each hospital center to provide facilities for mothers to stay with infants.

It is also important to comment that during the year 2020, year of the SARS Cov 19 pandemic, there were no documented cases of patients infected by said pathology in the Unit, so it could be argued that simple strategies continue to be protective factors against much pathology.

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*Correspondence to:

Maria Bertha Romo Almanza

Guadalupe Victoria Maternity Hospital

Mexico

Tel: +525540562778

E-mail: betyca5@hotmail.com