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EXPLORATORY STUDY ON THE USE OF COLOSTRUM THERAPY IN A BRAZILIAN MATERNITY HOSPITAL'S NEONATAL UNIT

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ABSTRACT: Exploratory study of colostrum therapy use in very low birth weight newborns in a neonatal unit by the analysis of medical records. The 108 patients under study were predominantly female (56,5%), had a mean weight and gestational age at birth of 1091.9 g (SD = 263.7g) and 29 weeks/2 days (SD = 2 weeks/6 days), respectively. Colostrum therapy was used for 29.5% of the patients mostly by oral administration (96.4%). The use of colostrum therapy was significantly associated with low gestational age and weight at birth and with neonatal death ($p = 0.001$, $p < 0.001$ and $p < 0.001$). As there was no established protocol to guide colostrum therapy prescription in the neonatal unit, the therapy was apparently chosen to be used for more immature or sicker babies, with a greater morbidity or mortality risk.

KEY WORDS: Colostrum; Low birth weight newborn; Preterm newborn.

ESTUDO EXPLORATÓRIO SOBRE A UTILIZAÇÃO DA COLOSTROTERAPIA EM UNIDADE NEONATAL DE UMA MATERNIDADE BRASILEIRA

RESUMO: Estudo exploratório para verificar a utilização da colostroterapia em recém-nascidos de muito baixo peso, em unidade neonatal de maternidade de médio porte, por meio da avaliação de prontuários. Dos 108 prontuários avaliados, 56,5% dos neonatos eram do sexo feminino, com média de peso e idade gestacional ao nascimento de 1091,9 g (DP = 263,7g) e 29 semanas/2dias (DP = 2semanas/6dias), respectivamente. A colostroterapia foi utilizada em 25,9% dos pacientes, sendo que em 96,4% dos casos a administração foi por via oral. O uso de terapia colostral foi associado significativamente a variáveis neonatais como idade gestacional, peso ao nascer e óbito neonatal ($p = 0,001$, $p < 0,001$, e $p < 0,001$). Não havendo protocolo estabelecido para guiar a prescrição da colostroterapia, esta ocorreu principalmente para prematuros de menor peso, mais imaturos ou mais doentes, com maior risco de morbidade e mortalidade.

PALAVRAS-CHAVE: Colostro; Recém-nascido prematuro; Recém-nascido de baixo peso.

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INTRODUCTION

Neonatal mortality is strongly influenced by the population's social development and by the availability of adequate healthcare support. Prenatal and delivery attention improvements, as well as quality neonatal care could help to avoid at least 1.7 million of the 2.5 million deaths that occur in the first 28 days of life each year. Over 80% of neonatal deaths occur among low birth weight newborns (birth weight under 2,500 grams), of which a third are small for gestational age (SGA) term newborns and two thirds are preterm newborns[1].

Prematurity is characterized by the occurrence of birth before the completion of 37 weeks of gestation. Around 15 million preterm babies are born worldwide annually[2], and Brazil is among the ten countries with the highest preterm birth frequencies. This is considered an epidemic taking into account that in 2016 nearly 317,000 babies were born prematurely[2,3]. It is a worrisome reality, given that preterm delivery is one of the main causes of neonatal morbidity and mortality[4]. Besides that, the preterm newborns (PTN) who are also SGA have a mortality risk 100 times higher when compared to term newborns without intrauterine growth restriction[5].

It is known that the newborn´s characteristic immunological immaturity is even more pronounced among PTN and very low birth weight newborns (VLBWN), being intrinsically related to high rates of neonatal infection occurrence, that can be up to 10 times higher than those of term and adequate birth weight babies[6]. These infants usually are hospitalized during their first days of life, sometimes in intensive care facilities, which increases the risk of infection by being exposed to invasive procedures or pre-existing diseases, but also by the lack of access to human milk (HM) immune protection caused by prolonged mother-infant detachment[6-8]. Many short and long-term complications are common in PTN, such as respiratory distress, metabolic disorders, feeding difficulties, sepsis, necrotizing enterocolitis, intra/periventricular hemorrhages, hypoxic-ischemic encephalopathy and periventricular leukomalacia.[2, 9, 10]. Cognitive and developmental delay have been described and observed in 30 to 40% of PTN with birth weight lower than 1,000 grams, as well as severe neurosensorial disabilities such as blindness, deafness and cerebral palsy[10].

Breastfeeding (BF) is the most natural and safe way of feeding young children and constitutes the purest form of health promotion. Human milk (HM) is a unique combination of lipids, carbohydrates, minerals, proteins, vitamins, enzymes and living cells whose benefits are already well known and unquestionable[8]. Lactation progresses through three well-identified periods, which are characterized by the production of colostrum, transitional milk and mature milk[8]. It is known that colostrum, which is produced in small proportions since the second trimester of pregnancy, has a high concentration of proteins and minerals, and a low concentration of fats and lactose. Its most important feature is the presence of a large number of protective factors such as secretory immunoglobulin A, lactoferrin and anti/pro-inflammatory cytokines[11, 12]. Thus, it has the potential to actively influence the development of the newborn's immune system[12, 13].

For the PTN, the promotion of BF has been defended based on the immunological properties of HM, its role in gastrointestinal maturation, the formation of the mother-child bond and the better neurobehavioral performance shown by breastfed children[8]. HM exerts a protective effect on premature infants against severe infections and necrotizing enterocolitis[14]. Thus, the first choice food for preterm infants is their own mother's milk, what can be offered following hand or pump extraction if the child is unable to get it directly from the breast[8].

Recent evidence has shown that even VLBWN who are clinically unable to receive enteral nutrition can benefit from the administration of colostrum drops in the oropharynx, which would allow oligosaccharides and cytokines to be absorbed by the mucosa, forming a protective barrier by blocking adhesion of pathogens to epithelial cells, and amplifying the newborn's immune response[15]. The therapeutic use of the mother's own colostrum - so called colostrum therapy - is also described by its application in small volumes for oral hygiene or gastric lavage[7, 9].

Bearing in mind that this seems to be a safe and viable practice[9], it is necessary to assess the use and impact

of this new assistance strategy. Taking these elements into account, it was decided to determine the frequency of use of colostrum-therapy in VLBWN in a neonatal unit of a medium-sized maternity hospital in southern Brazil, and to evaluate its association with neonatal variables.

METHODS

This is an exploratory, retrospective and analytical study, with a quantitative approach carried out based on data collected from patient records.

Based on a report from the electronic medical record system of a maternity hospital in southern Brazil, premature neonates born with birth weight below 1,500 grams (VLBWN) in the years 2015 and 2016 were selected for the study.

From the electronic records of the selected subjects, the following data were transcribed into proper form: sex, birth weight, gestational age, twinning, use of colostrum therapy (form of administration and time of onset), occurrence of infections, length of hospital stay, outcome (discharge, death or transfer), weight and type of food at discharge. Those who died in the early neonatal period (up to 06 full days after delivery) and those who had incomplete data essential to the study were excluded from analysis.

The type of feeding at discharge was considered to be "exclusive BF" to the subject who was being fed exclusively with breast milk, "mixed BF" if receiving breast milk and infant formula, and "Weaned" if receiving only infant formula[14].

The public maternity hospital that hosted the study is a Baby-Friendly Hospital under the administration of the State Health Department and is a tertiary reference center for maternal and child healthcare. It is also a state reference center for Human Milk Banks and Kangaroo Mother Care Method of the National Ministry of Health. It has 105 beds, 75 of which are obstetric and 30 neonatal, hosting an average of 505 monthly deliveries during the period of study (64.3% of vaginal deliveries), resulting in the birth of an average of 510 newborns each year, 8.8% being low birth weight newborns (LBWN) and 6.4% PTN.

Although colostrum therapy was already used in the neonatal unit, this method was not used during the study period in respect to a specific protocol for the prescription, collection, storage and administration of colostrum in the form of non-nutritive therapy for the neonate.

The data collected in the form were then transcribed to EpiData Entry 3.1 and analyzed with EpiData Analysis 2.2.3, using descriptive statistical methods as frequency distributions and central tendency measures (means and standard deviation). For the analysis of the association between the use of colostrum therapy and neonatal variables, Student's t test was used to compare means, and the Chi-square test was used to assess the statistical significance of the differences between proportions, assuming a level significance of 0.05. In case of a cell in the contingency table having an expected frequency below 5, Fisher's exact test was applied.

The research project was approved by the hospital's reference Research Ethics Committee (Registry Nr. 2.230.563).

RESULTS

From the 202 patients initially selected for this study, 94 were excluded, 89.4% associated with early neonatal death and 10.6% for incompleteness of essential data.

The hundred and eight neonates studied had a mean birth weight of 1091.9 g (SD = 263.7 g) and a mean gestational age of 29 weeks / 2 days (SD = 2 weeks / 6 days). The first colostrum offer occurred on average of 42.9 (SD = 22.5) hours after birth. The mean length of hospitalization of the VLBWN, who survived and were discharged, was 53.5 (SD = 20.0) days. The mean discharge weight was 2024.4 g (SD = 145.1 g). Colostrum Therapy was used in 28 patients (25.9%). Table 1 shows other neonatal and colostrum therapy characteristics.

From the study group, 11 neonates died after the first week of life, and 29 were transferred to other hospitals, 10 and 12 of which received colostrum therapy, respectively. Referral to other institutions made it impossible to follow up for the occurrence of infection or death after the transfer.

The comparative analysis between the groups of VLBWN who received and not received colostrum therapy showed that gestational age (27 weeks / 3 days vs 29

weeks / 3 days) and birth weight (931.4 g vs 1151.6 g) were significantly lower in treated patients (Table 2). Likewise, neonates undergoing colostrum therapy evolved more frequently to death (Table 3).

The use of colostrum therapy was not significantly associated with other variables studied, such as sex, presence of infections, hospital stay and exclusive BF at discharge.

Table 1. General characteristics of the VLBWN sample and of colostrum therapy (n = 108)

Characteristics	N	%
Gender		
Female	61	56,5
Male	47	43,5
Twin pregnancy		
No	89	82,4
Yes	19	17,6
Colostrum therapy		
No	28	25,9
Yes	80	74,1
Colostrum way of administration		
Oropharyngeal	27	96,4
Gastric irrigation	1	3,6
Infection		
No	38	35,2
Yes	70	64,8
Outcome		
Discharge	68	63,0
Transference	29	26,8
Death	11	10,2
Type of feeding at discharge		
Exclusive BF	30	44,1
Mixed BF	31	45,6
Weaned	7	10,3

BF – Breastfeeding

Table 2. Colostrum therapy and its association to continuous variables

	Colostrum therapy	Total	Meania	SD	95%CI	p
Gestational age[1]						
	Yes	28	27,5	2,8	26,4 - 28,6	0,001
	No	80	29,5	2,6	28,9 - 30,1	
Birth weight[2]						
	Yes	28	921,4	278,3	813,4 - 1029,3	0,000
	No	80	1151,6	231,9	1100,0 - 1203,2	
Lenght of stay[3]						
	Yes	06	56,8	21,3	34,5 - 79,2	0,672
	No	62	53,2	20,0	48,1 - 58,3	

1 – Gestational age at birth, in weeks.

2 – Birth weight, in grams.

3 – Duration of hospitalization of discharged patients, in days.

Statistical significance assessed by t Test.

Table 3. Colostrum therapy and its association to categorical neonatal variables

		Colostroterapia				
	Total	No	%	Yes	%	p
Gender						
Female	61	47	77,0	14	23,0	0,646 *
Male	47	33	70,2	14	29,8	
Infection						
No	70	56	80,0	14	20,0	0,056 *
Yes	38	24	63,2	14	36,8	
Exclusive BF						
Yes	30	27	90,0	3	10,0	1,000 **
No	38	35	92,1	3	7,9	
Death						
Yes	11	1	9,1	10	90,9	0,000 **
No	97	79	81,4	18	18,6	

* - Chi-square Test

** - Fisher's Exact Test

BF – Breastfeeding

DISCUSSION

The results of this study showed a low frequency of use of colostrum therapy among VLBWN (25.9%) during the study period, which may be associated not with the lack of knowledge of the technique on the part of the neonatal care team, but with the inexistence, at the time, of a protocol for its application in the unit. In an American maternity hospital, when 89 extremely low birth weight neonates born after the introduction of a protocol for oropharyngeal colostrum delivery were evaluated, it was observed that 85% of them were benefited by the treatment[16], which reinforces the importance of standardizing procedures of care.

It was found in this research that, regarding the form of administration of colostrum therapy, the practice used coincided with that proposed by most of the authors, who consider the oropharyngeal route as the most appropriate for this immunotherapy[9, 11, 15, 17, 18]. As in preterm infants in the first days of life, the possibility of

enteral feeding is limited, oropharyngeal administration of a small amount of colostrum is the most used way of delivery, through the use of a syringe inserted into the side of the newborn's mouth and directed to the oropharynx, with subsequent injection of the volume proposed in each protocol[9, 11, 17-19]. The use oropharyngeal mucosa to offer colostrum has been well tolerated by PTN, who keep their vital signs stable during the procedure, with no need for interruption of therapeutics[9, 15, 19]. Another alternative would be oral hygiene with colostral drops which, in addition to the benefits already associated with this therapy, could alter the microbiota of the mouth and reduce colonization with pathogenic microorganisms[20].

The earlier initiation of colostrum therapy seems to contribute to efficiently and sustainably stimulate the PTN immune system, as it would guarantee greater number of doses, with a consequent greater concentration of its important immunomodulatory components[22, 23]. In this study, we observed a mean age at the beginning of therapy of 42.9 hours of life, which is in accordance with data in the literature. A Brazilian study, carried out in Minas Gerais, describes that the application of the protocol starts approximately 44 hours after birth[19]. In other publications on the topic, the therapy is offered for the first time between 48 and 96 postnatal hours[11, 15,16]. Much earlier offer is described in an American article, where the median age for the beginning of treatment in 133 VLBWN is 24 hours[21]. A recent publication, evaluating PTN with gestational age less than 32 weeks, reports that non-nutritional use of colostrum occurs in an average age of 32 hours[22]. In a pilot study, conducted in California, to assess the impact of colostrum therapy on the composition of the oral microbiota in premature infants, the median onset of administration was 39 hours[19].

Comparing the duration of hospitalization of the VLBWN who received colostrum therapy with those who did not, we failed to identify a significant difference in the length of hospital stay of the studied neonates. The favorable impact of oropharyngeal colostrum application on the length of hospital stay is described in a study, which assesses 99 PTN with a gestational age of up to 32 weeks, where treated newborns had a 16-day reduction in hospital length of stay median compared to the untreated[18]. The decrease in the need for prolonged hospitalization would be advantageous, not only for the baby and his family, but also for the health care system, since it contributes to the reduction of costs and optimization of bed use in neonatal units[18, 23].

The bioactive compounds of human colostrum and their possible effects on the oral and tracheal microbiota, and on stimulating the development of immunity in PTN, suggest a beneficial effect on protection against infections[11, 20, 22, 24]. However, the presence of infection was not significantly associated with immunological therapy with colostrum in this research. Literature reports on this outcome are conflicting. Seigel et al.[16], Sharma et al.[17], Romano-Keeler et al.[18], Ferreira et al.[19] and Abd-Elgawad et al.[25] find no difference in the incidence of necrotizing enterocolitis and/or neonatal sepsis between the group that receive oropharyngeal application of colostrum and another which did not received it. On the other hand, Lee et al.[11] detected a significant decrease in clinical sepsis in their study group. Despite the biological plausibility of colostrum administration for protection against infections, there are many methodological variations among published scientific articles, with no standardization of doses, intervals and duration of treatments, thus, the positive effects of this practice on the infection are still inconclusive[23].

Notwithstanding no statistically significant association between colostrum therapy and the type of feeding at the time of discharge was observed in this study, American authors describe that the use of colostrum, via the oropharyngeal route in the first days of life, can help guarantee the maintenance of the supply of the breast milk until the moment of hospital discharge[21]. The mother receiving information about the benefits of colostrum for the preterm infant stimulates the performance of breast milk expression early and frequently, which is essential for the establishment and maintenance of lactation, and can facilitate an optimal milk production, and thus guarantee exclusive BF at the time of discharge.[12] In addition, the mother's participation in the care of the hospitalized premature child and skin-to-skin contact, as in the Kangaroo Mother Care Method, favor an increase in the bond of the dyad and improve the psycho-affective development of the newborn[12, 21].

The observation that the frequency of deaths was significantly higher in the group of our patients who received colostrum therapy, apparently counterweights the premise that the existence of growth factors, immunoglobulins, lactoferrin, cytokines and other components in human colostrum could have an immunomodulatory effect[24] and would increase the survival of these patients. According to a review of Cochrane Library, which includes six studies with 335 neonates, colostrum therapy does not decrease neonatal mortality[26]. A recent systematic review, encompassing nine randomized controlled trials, reveals that although the risk of death among neonates receiving therapy with colostrum is 37% lower than in the untreated group, this result is also not statistically significant[23].

In the present study, colostrum therapy was applied more frequently to neonates of lowest weight and gestational age at birth, which could justify the higher mortality observed in the treated group. The absence of an established protocol to guide clinical practice could, therefore, have enabled assisting neonatologists to decide for the prescription of therapy especially for premature infants of less weight, more immature or more ill, motivated by an eventual compassionate attitude.

The neonatal intensive care environment is recognized to be very stressful, not only on the care of vulnerable patients, but especially on the need of making quick and difficult decisions, which often include the use of all available measures to save a life[27, 28]. Extremely premature newborns usually face weeks or months of hospitalization, undergoing multiple frequent painful procedures, with a heavy iatrogenic burden on non-survivors, and a huge financial burden on their families and society[27]. Physicians' attitudes towards neonates with poor prognosis can greatly influence their decisions regarding the course of treatment and the care to be provided in this situation[28].

Although there are different circumstances and cultures, it is clear that when planning the implementation of certain types of health interventions, it is essential to establish guidelines for clinical practice, that is, the creation of specific protocols that encourage and guide the adoption of treatment to ensure better results[28–30].

This idea would be very important to bring advances to the use of colostrum therapy in our service. Nevertheless, there is a lack of evidence regarding the reduction of neonatal infections and mortality in preterm infants; another aspect to be considered about colostrum therapy is its advantage in stimulating the early initiation of breast milk extraction and the formation of the mother-child bond, which are essential for the establishment and maintenance of lactation, and for the success of breastfeeding process of premature babies[9, 12].

Among the limitations of this study, we can highlight the loss of cases due to the incompleteness of data in medical records and the significant number of subjects who were transferred to other hospital units, which was determinant to the lack of data on outcomes of interest.

CONCLUSION

The frequency of use of colostrum therapy in VLBWN was 25.9%, the preferred route for the supply of colostrum was oral, and the patients treated were mainly premature infants of lower weight and gestational age, and probably more ill and therefore, with greater risk of dying.

Considering that colostrum therapy seems to be a safe and promising practice in reducing infections and neonatal mortality, there is an evident need to implement a clinical protocol to guide the medical decision in favor of this treatment, allowing a greater number of neonates to receive the benefits of colostrum.

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