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Rapid communication

Analysis of clinical outcomes of oropharyngeal colostrum administration in very low-birth-weight preterm newborns

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A B S T R A C T

Objectives: Colostrum is the first secretion produced by the mammary glands and is present through the seventh day after birth. Colostrum has important immunomodulatory components and protective factors that contribute to the protection and development of newborns. The oropharyngeal administration of colostrum (OAC) has been proposed as a potential nutritional option for very low-birth-weight (VLBW) newborns (<1500 g). This study aimed to analyze the clinical outcomes of VLBW infants receiving OAC.
Methods: This is a retrospective longitudinal study with nonprobability sampling of VLBW infants on the OAC protocol. VLBW infants for whom no OAC data were available, who received no dose, or who died within the first 7 d of life were excluded. The Mann–Whitney test was used to compare quantitative variables and the Wilcoxon test to assess the evolution of anthropometric values with a significance level of 5% ($P < 0.05$).
Results: Enteral nutritional therapy was commenced after 1 d (median: 1 d; interquartile range [IQR], 1–1 d). Full enteral feeding was achieved after 11 d (median: 11.0 d; IQR, 9.0–16.0 d). Birth weight was recovered after 11 d (median: 11 d; IQR, 7.0–14.0 d). OAC was commenced at 3 d of life, and 32.5 doses (IQR, 21.0–44.0 d) were given in total. There were significant differences in the evolution of anthropometric characteristics during hospitalization, with a tendency to recover birth weight more quickly the higher the number of doses administered ($P = 0.07$). Time to full enteral feeding was significantly longer and time to recovery of birth weight significantly shorter when OAC was commenced ≤3 d after birth ($P = 0.023$).
Conclusions: OAC was associated with a shorter time to recover birth weight and time to full enteral feeding.
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Introduction

According to the World Health Organization (WHO), >1 in 10 births in the world were premature in 2010, or approximately 15 million [1]. Brazil is among the 10 countries with the highest number of premature births in the world. In 2017, 10.5% of births in the country were premature [2,3]. Prematurity is birth at a gestational age (GA) of <37 wk. The lower the GA and birth weight, the greater the risk of morbidity and mortality [4]. In such scenarios, breast milk is considered the main factor for maturation of an infant's systems and weight gain [2,5].

Human milk (HM) is recognized by the WHO as the most complete food for infants. HM is also valued for its potential protective effects and fostering better recovery of infants in antenatal intensive care. Colostrum is the first secretion produced by the mammary glands and present until the 7th d of life. A transitional food between the intrauterine period and extrauterine life [6,7], colostrum contains important immunomodulatory components and protective factors that contribute to infant development [5,6–10], including immunobiologics, immunoglobulins, growth factors, lactoferrin, and anti- and proinflammatory cytokines. When in contact with the oral mucosa, colostrum interacts with local lymphoid tissue and can modulate an inflammatory response in newborns [11].

In light of the importance of timely exposure to maternal colostrum, the oropharyngeal administration of colostrum (OAC) has been used for very low-birth-weight newborns (VLBW; <1500 g). The idea is that oral mucosa is capable of absorbing small amounts of colostrum, serving as a form of immunotherapy [10,12]. Typically, 0.2 mL is divided between the two cheek mucosa and massaged for absorption. In addition, raw expressed HM, ideally expressed at the bedside, is recommended and should be

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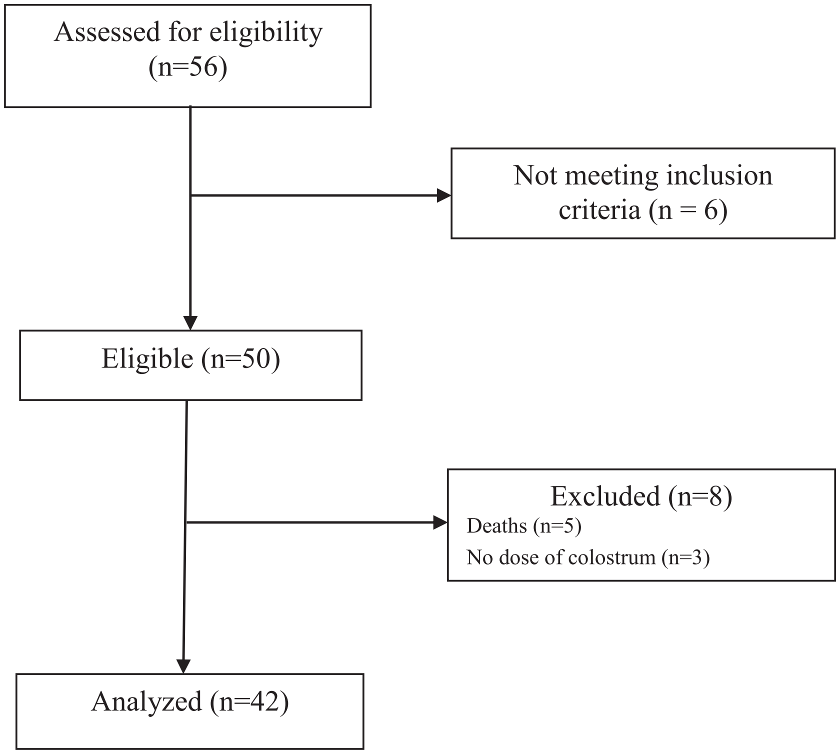

Fig. 1. Data collection flowchart, Rio de Janeiro, 2020.

administered whenever possible, because pasteurization and refrigeration impair its immunologic potential [10,12,13].

The objective of this study was to analyze the clinical outcomes of VLBW infants who received OAC at the maternity teaching hospital of the Federal University of Rio de Janeiro in Brazil. The study hypothesis is that early OAC, namely, earlier administration and a greater number of doses, is associated with better clinical outcomes.

Methods

This retrospective longitudinal study used data on VLBW infants admitted to the neonatal intensive care unit (NICU) at the Maternity School of Federal University of Rio de Janeiro between January and December 2018 who received OAC. Nonprobability sampling was used, enabling all eligible patients to be included in the study. All VLBW infants who received OAC per the OAC protocol were included in the study. VLBW infants for whom no OAC data were available, who did not receive AOC, or who died within the first 7 d of life were excluded. Data were collected from medical records and the NICU's protocols using a specific digital form.

The institution's OAC protocol [14] (prepared in 2018) recommends OAC for all VLBW infants (<1500 g), except for those with serious swallowing disorders, significant saliva accumulation, and restrictions on breast milk [15]. Colostrum is administered in the first 7 d of life, often given before the prescribed diet. OAC consisted of applying 0.1 mL colostrum to the right and left oral mucosa (total of 0.2 mL) in the direction of the oropharynx, without removing the syringe from the mouth during the change of side, then massaging each cheek for at least 10 s. The colostrum is either expressed by the mother at the bedside or taken from the institution's HM bank. The evaluation of OAC considered how soon after birth colostrum was administered and the total number of doses given [14].

The independent variables considered were anthropometric (birth weight, length at birth, head circumference at birth), sociodemographic (maternal age, maternal complications, GA at birth, sex of infant), clinical (first- and fifth-min Apgar [appearance, pulse, grimace, activity, and respiration] scores and postnatal complications), and OAC (time since birth at first OAC and total number of doses). The dependent variables were time to start of enteral feeding, time to reach full enteral feeding, length of stay, recovery of birth weight, and time of ventilator support.

Weight according to GA at birth was classified using the INTERGROWTH-21st international standard curve of postnatal growth [16,17] as proposed by the WHO. At the time of discharge, anthropometry data were evaluated according to the INTERGROWTH-21st international standard curve of postnatal growth of preterm infants up to 64 postconceptional wk [16,17], performance of the respiratory tract according to the total number of days that ventilator support was required, evolution of enteral feeding (time to initiation, initial diet, and time to reach full enteral feeding, defined as the time to reach full calorie intake), total length of stay, time to recover birth weight, and type of feeding at hospital discharge (exclusive breastfeeding, mixed, or formula).

The normality of distributions was tested using the Shapiro–Wilk test. The descriptive statistical analysis was represented by the median and interquartile range (IQR; P25–P75) due to the presence of sample asymmetry. Categorical data were summarized with absolute and relative frequencies. The Mann–Whitney test was used to compare the quantitative variables and the Wilcoxon test to assess the evolution of anthropometric values with a significance level of 5% ($P < 0.05$). The analyses were performed using SPSS Statistics 23 for Windows.

Results and discussion

During the period studied, 56 VLBW infants were born, of whom 50 were considered eligible for the study and had OAC prescribed according to the protocol. Eight of these VLBW infants were excluded (five due to death and three because they did not receive any dose of colostrum), resulting in a cohort of 42 VLBW infants (Fig. 1).

Table 1 shows that in all cases analyzed, there was at least one maternal complication, primarily hypertensive pregnancy disorders (53.7%), followed by infections (29.3%). More than one third of the infants (35.7%) were twins, and a high proportion were delivered by Cesarean section (76.2%). Most infants (54.8%) were very preterm, and there was a high rate of adequacy of birth weight for GA.

OAC is a therapy for VLBW infants; thus, 21.3% of infants were extremely premature, 54.8% were very premature, and 23.8% were moderately preterm. The distribution of premature births in the GA subgroups is remarkably similar worldwide, which suggests a biologic basis [1].

In relation to the evolution of nutritional therapy (Table 1), OAC generally commenced on the first day of life (median: 1 d; IQR, 1–1 d). Most infants received expressed HM and infant formula (90.5%), achieving full enteral feeding around the 11th d (median:

Table 1
Sociodemographic, gestational, birth and clinical characteristics of very low birth weight newborns (Rio de Janeiro, 2020)

Variables	Median (Q25–75)/%
Mother's age, y (n = 42)	28.0 (23.0–34.0)
Maternal complications, % (n = 42)	
Hypertensive syndromes (n = 22)	53.7
Infectious (n = 12)	29.3
Diabetes mellitus (n = 7)	17.1
Type of pregnancy, % (n = 42)	
Single fetus (n = 27)	64.3
Twin (n = 15)	35.7
Type of delivery, % (n = 42)	
Vaginal (n = 10)	23.8
Cesarean section (n = 32)	76.2
Sex, % (n = 42)	
Male (n = 26)	57.8
Female (n = 16)	35.6
GA at birth, wk (n = 42)	30.0 (28–25)
Classification of prematurity, % (n = 42)	
Extreme (GA ≤28 wk; n = 9)	21.4
Very premature (28 wk < GA < 32 wk; n = 23)	54.8
Moderate and late (GA ≥32 wk; n = 10)	23.8
Apgar first min (n = 42)	7.0 (4.8–8.0)
Apgar fifth min (n = 42)	8.0 (7.0–9.0)
Birth weight, % (n = 42)	
SGA (n = 3)	7.1
AGA (n = 39)	92.9
Length at birth, % (n = 42)	
AGA (n = 34)	81.0
SGA (n = 5)	11.1
Very small for GA (n = 3)	6.7
Head circumference at birth, % (n = 42)	
AGA (n = 3)	92.9
Microcephaly (n = 1)	2.4
Severe microcephaly (n = 2)	4.8
Ventilatory support, d (n = 40)	1.0 (0.0–4.8)
Start of enteral diet, d (n = 42)	1.0 (1.0–1.0)
Type of feeding initiated, % (n = 42)	
EHM (n = 2)	4.8
Formula (n = 2)	4.8
Mixed (EHM + formula; n = 38)	90.5
Reach of full enteral feeding, d (n = 39)	11.0 (9.0–16.0)
Recovery of birth weight, d (n = 39)	11.0 (7.0–14.0
Length of hospitalization, d (n = 42)	37 (19.75–67.00)
GA at NICU discharge, wk (n = 38)	35.5 (34.0–39.2)
Type of breastfeeding at NICU discharge, % (n = 38)	
Exclusive breastfeeding (n = 11)	26.9
Artificial breastfeeding (n = 7)	17.1
Mixed breastfeeding (n = 23)	56.1

AGA, appropriate for gestational age; Apgar, appearance, pulse, grimace, activity, and respiration; EHM, expressed human milk; GA, gestational age; NICU, neonatal intensive care unit; SGA, small for gestational age.

11.0 d; IQR, 9.0–16.0 d). Birth weight was also recovered around the 11th d (IQR: 7.0–14.0 d), and the median length of hospitalization was 37 d (IQR, 19.75–67.00). Median commencement of OAC was at 3 d of life, and the mean total number of doses was 32.5 (IQR, 21.0–44.0). The type of feeding at the time of discharge in most cases was mixed (56.1%), followed by exclusive (26.9%) breastfeeding and formula (17.1%).

Early enteral nutrition therapy is known to be positive for preterm infants, and especially VLBW infants. Enteral nutrition therapy should be started as soon as possible (within 6 to 12 h of birth), if clinically stable, because commencement on the first d of life is considered feasible [18,19]. The data found in our study are consistent with recent recommendations in so far that the diet was started on the first d of life.

The first option for nutrition in newborns is the mother's own colostrum, preferably fresh. The second option is pasteurized (donated) HM, and the third is infant formula for premature infants. In 2012, the initial diet of 94.1% of preterm infants at the study institution was infant formula [20]. In the present study, 90.5% of infants started enteral feeding with HM and formula. This difference suggests that the introduction of OAC for VLBW infants may have been instrumental in increasing early contact with HM. In another study, OAC was associated with higher rates of HM enteral feeding by the sixth wk of life and at the time of hospital discharge [21].

Time until full enteral feeding (median: 11; IQR, 9–16) was compatible with the recommendation that full enteral feeding is reached in 7 to 15 d after birth [19]. Median OAC initiation was at 3 d of life. Although priority is given to starting OAC on the first day of life [14], this can be hampered by different factors. In our study, 10% to 20% of mothers were unable to supply colostrum for administration, colostrum was generally not available in the milk bank for administration before 2 d of life, and 75% to 80% of scheduled administrations were actually performed [12].

Growth is seen as an indicator of well-being, especially in preterm infants. For this to occur, nutrition must be a key part of intensive care, especially in those born with a GA of <32 wk [5,18,22]. In our study, birth weight was recovered around the 11th d of life. This is compatible with other reports, which have found initial weight loss followed by recovery of birth weight at 10 d to 20 d of life [5,18,23].

When clinical outcomes were compared against the total number of doses of colostrum administered (Table 2), no significant difference was found. However, there was a tendency for birth weight to be recovered in fewer days when a higher number of doses was given (P = 0.07). When the outcomes were compared against the commencement of OAC (Table 2), a significant difference was found in relation to full enteral feeding and recovery of birth weight when OAC was started early (≤3 d). Time to full enteral feeding was significantly longer and time to recovery of birth weight was significantly shorter when OAC was commenced within 3 d (P = 0.023).

In the literature, OAC has been positively associated with a shorter time to full enteral feeding, greater weight gain at 36 wk of life, reduced hospitalization, higher rate of breastfeeding at the time of hospital discharge, and potential positive influence on the amount of expressed HM offered [24–29]. Other studies have not found OAC to have a significant influence on time to recovery of birth weight, time to commencement of enteral feeding, time to full enteral feeding, or type of diet initiated [21,24,26,28].

Table 2
Comparison of clinical outcomes of very low birth weight newborns according to total number of doses of oropharyngeal administration of colostrum and start in days of oropharyngeal administration of colostrum (Rio de Janeiro, 2020)

Variables	Number of doses <32.5	Number of doses ≥32.5	*P*-value	Start ≤3 d of life	Start >3 d of life	*P*-value
Start of enteral diet, d	1.0 (1.0–1.0)	1.0 (0.5–1.0)	0.178	1.0 (1.0–1.0)	1.0 (1.0–1.0)	0.772
Ventilatory support, d	1.0 (0–3.5)	0.5 (0–5.8)	0.913	1.0 (0–5.5)	1.0 (1.0–2.0)	0.480
Reach of full enteral feeding, d	14.0 (9.0–20.0)	10.5 (8.3–14.5)	0.158	13.0 (9.0–16.0)	8.0 (6.0–10.0)	0.013
Recovery of birth weight, d	13.0 (10.0–14.8)	10.0 (6.0–13.0)	0.070	10.5 (7.0–13.0)	14.0 (13.0–16.5)]	0.023
Length of NICU stay, d	40.0 (23.5–9.0)	34.0 (17.0–68.0)	0.900	40.0 (21.5–68.0)	31.0 (12.0–64.5)	0.421

NICU, neonatal intensive care unit.

Regarding the attainment of full enteral feeding, the data from the present study are divergent. A randomized study in which infants were given OAC or a placebo showed that the group that received colostrum reached full enteral feeding 10 d earlier [24], but another study also observed a shorter time [29]. No studies that compared the time of commencement of OAC were found.

Otherwise, OAC provides perceptible gains to the mother and child in the clinical setting. Breastfeeding and bonding are encouraged from the first moments of life, because mothers' involvement in the care of their preterm infant is encouraged at the NICU, enabling them to participate actively in the treatment of their own child [27].

Conclusions

In this study, OAC was found to be associated with a shorter time to recover birth weight and a shorter time to full enteral feeding. OAC is a major challenge for multiprofessional health teams providing care for VLBW infants despite the limited evidence for its positive effects on clinical outcomes. Further studies are needed of the impact of OAC on clinical outcomes to elucidate its effects, which are still considered inconclusive, and also to develop its expanded implementation in neonatal units.

Conflict of Interest

The authors have no conflicts of interest to declare.

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