



Oropharyngeal administration of mother's colostrum: a literature review

Colostroterapia: uma revisão da literatura

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Abstract

Introduction: Premature births are considered a public health problem. Estimates indicate that approximately 30% of preterm newborns present complications inherent to this condition due to an immature immune response, as well as the immaturity of their digestive tract, which cause important long-term sequelae, such as growth deficit, delay in neurodevelopment, impairment of vision and hearing, with irreparable damage to children's health. Colostrum therapy is an admittedly safe technique that uses maternal colostrum to provide preterm infants with early immunological protection. This article aims to answer the following question: what is the impact of colostrum therapy on the health of premature infants? *Objective:* To review the evidence on the benefits of colostrum therapy for preterm infants. *Methodology:* Narrative review of the literature. The search for the articles was done in the databases of Pubmed, Cochrane, Virtual Health Library, Medline EBSCO, Proquest, Embase and Banco de Teses da Capes, without language restriction or publication period. Gray literature included unpublished theses, dissertations and abstracts. The descriptors used in the search strategy were: human milk, premature and colostrum. In addition, the terms "colostrumtherapy", "colostrum oropharyngeal administration" and "colostrum oral administration" were used. *Results:* The results of eight studies were included in this review, being seven controlled and one observational. Different endpoints were measured in the studies, with approaches related to nutrition and growth, clinical outcomes, assessment of oral mucosa colonization of the newborn, and evaluation of immune development mediators, such as serum immunoglobulin A and

lactoferrin secreted in the urine. When comparing the groups that received the colostrum with the control groups, the findings are positive, such as a shorter time to reach the full enteral diet, a higher mean weight at 36 weeks of life, a protective effect for sepsis development, and better breastfeeding rates at hospital discharge than children who did not receive colostrum therapy. *Conclusions:* Although there is no strong evidence of the clinical impact of colostrum therapy, it does not pose a risk for children. More evidence is needed on the impact of colostrum therapy on the prevention of clinical outcomes of higher incidence in premature infants to support the widespread implantation of this practice in neonatal units.

Keywords: Human milk. Preterm newborn. Colostrum.

Resumo

Introdução: os nascimentos prematuros são considerados um problema de saúde pública. Estimativas indicam que aproximadamente 30% dos recém-nascidos pré-termo apresentam complicações inerentes a esta condição, decorrentes de uma resposta imunológica imatura, bem como da imaturidade de seu trato digestivo, que ocasionam importantes sequelas em longo prazo, como déficit de crescimento, atraso no neurodesenvolvimento, comprometimento da visão e audição, com danos irreparáveis à saúde infantil. A colostroterapia é uma técnica reconhecidamente segura que utiliza o colostro materno com a finalidade de proporcionar aos recém-nascidos prematuros proteção imunológica precoce. Este artigo pretende responder à seguinte questão: qual o impacto da colostroterapia na saúde dos prematuros? *Objetivo:* revisar as evidências sobre os benefícios da colostroterapia para os recém-nascidos prematuros. *Metodologia:* revisão narrativa da literatura. A busca dos artigos foi feita nas bases de dados Pubmed, Cochrane, Biblioteca Virtual em Saúde, Medline EBSCO, Proquest, Embase e Banco de Teses da Capes, sem restrição de linguagem ou período de publicação. A literatura cinza incluiu teses, dissertações e resumos não publicados. Os descritores utilizados na estratégia de busca foram: leite humano, prematuro e colostro. Além destes, foram utilizados os termos “colostroterapia”, “*colostrum oropharyngeal administration*” e “*colostrum oral administration*”. *Resultados:* foram incluídos nesta revisão os resultados de nove estudos, sendo oito controlados e um observacional. Diferentes desfechos foram medidos nos estudos, com enfoques relacionados à nutrição e

ao crescimento, desfechos clínicos, avaliação da colonização da mucosa oral do recém-nascido, além da avaliação de mediadores do desenvolvimento imunológico, como imunoglobulina A sérica e lactoferrina secretadas na urina. Ao comparar os grupos que receberam a colostroterapia com os controles, os achados são positivos, como menor tempo para se atingir a dieta enteral plena, maior peso médio em 36 semanas de vida, efeito protetor para desenvolvimento de sepse e melhores taxas de aleitamento materno na alta hospitalar do que as crianças que não receberam a terapia com colostro. *Conclusões:* apesar de não existirem fortes evidências do impacto clínico da colostroterapia, esta não oferece risco para as crianças. São necessárias mais evidências sobre o impacto da colostroterapia na prevenção dos desfechos clínicos de maior incidência em prematuros para apoiar a implantação generalizada desta prática nas unidades neonatais.

Palavras-chave: Leite humano. Colostro. Recém-nascido prematuro.

Introduction

Complications related to prematurity are the largest cause of neonatal deaths in Brazil, and data from 2011 show that 11.7% of the births occurring in the country are premature.¹ Due to body immaturity and low birth weight, premature infants tend to need incubators and invasive procedures to ensure their growth and development outside the womb, which increases the risk of infection.² In this context, it is common for many premature babies not to be breastfed in the first days of life, and, in many cases, due to factors involving prematurity and low weight, breastfeeding is not even established. In this way, in addition to presenting an increased risk of infection due mainly to immunological immaturity, premature infants often lack the protection provided by breast milk, especially by colostrum, which could be a protective factor and guarantee better recovery of the child hospitalized in a neonatal intensive care unit. Colostrum contains a significant amount of immunobiological aspects such as secretory immunoglobulin A, growth factors, lactoferrin, anti- and proinflammatory cytokines. When in contact with oral mucosa, colostrum interacts with local lymphoid tissue and is able to modulate the inflammatory response of newborns (NB). The colostrum of the mother of premature babies contains higher concentrations of immunobiological factors when compared to mature breast milk.³

Given the worst prognosis of preterm infants, a new strategy has been studied to maintain their health, especially of those with very low birth weight (birth weight <1500 grams), known as colostrum therapy or oropharyngeal administration of mother's colostrum, which deals with the

use of raw maternal colostrum as an immune therapy, without nutritional function, for premature and / or very low birth weight infants.⁴ The technique consists in the administration of 0.2 milliliter of maternal colostrum (0.1 ml on each side of the oral cavity) at the frequency of every three hours, for five consecutive days, beginning between 24 and 96 hours of the child's life.

Lymphoid tissue in the oropharynx is important for both gastrointestinal and immunological development and is stimulated by direct contact with breast milk, meaning that the route of the oropharyngeal mucosa in preterm infants may facilitate the immunological maturation of these children.⁵ Colostrum is the secreted fluid in the first days after delivery, for a maximum of seven days. It is a yellowish, thick, viscous fluid that fills the alveolar cells in the last trimester of gestation. It is produced when the tight junctions of the breast epithelial tissue are opened, allowing the passage of many protective components derived from maternal immunity, from the bloodstream to the milk.⁶ Studies have shown that the oropharyngeal administration of maternal colostrum in the first hours of life stimulates the development of the intestinal microbiota of the very low-weight newborn, and may be related to a better prognosis of these children.^{7,8}

Considering the importance of the above for health and child development, especially in situations of prematurity, in addition to the fact that research on colostrum therapy is still incipient, this study intends to review the available national and international literature trying to respond to the following question: what is the impact of oropharyngeal administration of mother's colostrum on the health of premature infants?

Methodology

This is a narrative review of the literature. There was no restriction of publication period or language in the selection of studies. The inclusion criteria were human studies that characterized the use of maternal colostrum as therapy, regardless of the research design. Gray literature was also searched through unpublished works such as thesis, dissertations and abstracts.

The search of the studies was done in the databases of Pubmed, Cochrane, Virtual Health Library, Medline EBSCO, Proquest, Embase and Banco de Teses da Capes. The keywords used were "human milk", "premature" and "colostrum". The terms "colostrum therapy", "*colostrum oropharyngeal administration*" and "*colostrum oral administration*" were also used.

The search strategy used in the review is described in Figure 1, according to the recommendations of each database.

PUBMED, BVS, EMBASE, COCHRANE

Search 1: milk, human AND colostrum AND infant premature

Search 2: "colostrum oropharyngeal administration"

BANCO DE TESES DA CAPES, PROQUEST:

Search 1: "colostrum oropharyngeal administration"

MEDLINE EBSCO:

Search 1: milk, human AND colostrum AND infant premature

Search 2: "colostrum oropharyngeal administration"

Search 3: "colostrum oral administration"

Figure 1. Search strategies used in each revised database.

Results and Discussion

In total, the search in all databases resulted in 465 studies. After reading titles and abstracts, 37 studies were selected, regardless of language. Of these, twenty four were excluded for duplicate reasons, three for not bringing results that added to this review and, therefore, these were considered as theoretical support for the basis of the manuscript and discussion of the findings. In addition, two publications of research protocols were located, being a systematic review protocol⁹ and a randomized clinical trial.¹⁰ At the end of the selection, eight studies were described in the present review (Table 1). The flowchart (Figure 2) describes the selection of studies.

Table 1. Description of the studies included in the revision.

Author/Year	Study type	Objective / Intervention	Population	Main findings
Rodríguez et al., 2010 ¹⁷	Almost experimental	To test method security and feasibility; AOF* of 0.2 ml colostrum every two hours for 48 consecutive hours, starting after 48 hours of life.	5 NB** of extreme low-weight (<1000g), <28 weeks of gestation, with adequate weight for IG#.	There were no episodes of apnea, bradycardia, hypotension or other adverse effects associated with AOF* of maternal colostrum, demonstrating safety of the method.
Lee et al., 2015 ¹⁵	Randomized clinical trial, double-blind.	AOF* of 0.2 ml of maternal colostrum or sterile water every 3 hours for 72 hours, between 48 and 96 hours after birth.	48 premature NB <28 weeks	The group that received colostrum had less clinical sepsis and a shorter total antibiotic duration. There were no significant differences in other clinical outcomes.

continue

Author/Year	Study type	Objective / Intervention	Population	Main findings
Rodríguez et al., 2011 ¹²	Randomized clinical trial	AOI* of 0.2 ml of colostrum (intervention) or sterile water (placebo group) every 2 hours for 48 hours, starting at 48 hours of life.	16 NB** with extreme low-birth weight (<1000 g) and / or <28 weeks of IG#, with weight at birth suitable for IG#	There were no differences in immunological markers found between or within the groups. A large and moderate effect size was observed for urinary lactoferrin and urinary secretory IgA for infants treated with colostrum, suggesting that the results could have reached statistical significance if the sample was larger. The most convincing finding was that the children in the group who received colostrum reached full enteral feeding (150 mL / kg / day) 10 days earlier compared to children in the placebo group.

continue

Author/Year	Study type	Objective / Intervention	Population	Main findings
Alvarez et al., 2015 ⁷	Non-randomized clinical trial	AOF* of 0.2 ml colostrum every 4 hours, beginning the procedure in the first 24 hours of life, and continuing until the 15th day of life.	38 NB** <38 + 6 weeks IG# and / or <1500g	Serum IgA increased significantly in the intervention group in the first month of life (p = 0.026). AOF* of colostrum favors the development of the immune system of premature and very low-weight NB** by increasing IgA at one month of life.
McFadden, 2012 ^{9,14}	Randomized clinical trial	It evaluated the colonization of the oral mucosa of the NB** AOF* of colostrum or sterile water	29 NB** with IG# between 26 and 34 weeks	The most common organism identified was the negative <i>Staphylococcus</i> , but other organisms were identified. Although there were no harmful effects of colostrum use, there was no change in colonization at weeks 2 and 3 of life.

continue

Author/Year	Study type	Objective / Intervention	Population	Main findings
Sohn et al., 2016 ⁸	Randomized clinical trial	It evaluated the colonization of the oral mucosa of the NB** AOF* 0.1 ml of colostrum every 2 hours for 46 hours.	12 RN** <; 1500g; age <; 7 days; intubation in 48 hours after birth.	The oral microbiota markedly changed over the 96-hour period in all NBs**. Colonization patterns differed between groups with <i>Planococcaceae</i> , the dominant family at 48 and 96 hours in the colostrum group and <i>Moraxellaceae</i> and <i>Staphylococcaceae</i> , dominant at 48 and 96 hours, respectively, in the control group.
Oliveira, 2014 ²	Control case	Administration of 1.0 ml of colostrum every 6 hours.	108 NB** with IG# between 24 and 34 weeks	Children who received colostrum had higher rates of breastfeeding (even if not exclusive), higher than those who did not receive colostrum.

continue

Author/Year	Study type	Objective / Intervention	Population	Main findings
Seigel et al., 2013 ¹³	Retrospective Cohort	AOF* of 0.1 ml of maternal colostrum every 4 hours for 5 days, starting within the first 48 hours of life.	369 RNs with extreme low-weight at birth (280 were born before the colostrum therapy protocol was implanted - "PCC"; and 89 after - "CC")	Mortality and percentage of children with necrotizing surgical necrotizing enterocolitis and spontaneous perforations were statistically similar between the groups. The CC weighed on average 1,666g in 36 weeks <i>versus</i> 1,380g for the PCC (p <0.001). In a multivariate analysis with birth weight as covariate, weight at 36 weeks was significantly greater in newborns receiving colostrum.

*AOF= oropharyngeal administration; **NB= newborn; #IG= gestational age; IgA= immunoglobulin A; PCC=group prior to implantation of the colostrum protocol; CC = group after the implantation of the colostrum protocol.

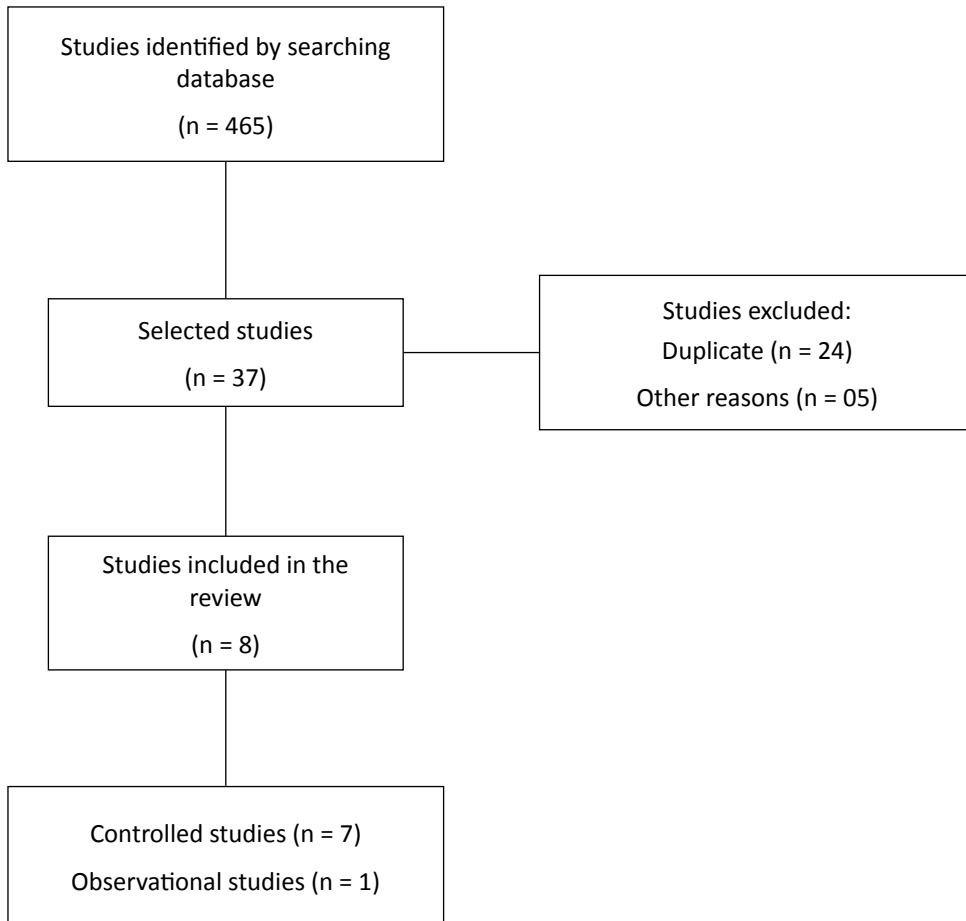


Figure 2. Flowchart of the search for articles in scientific literature.

Most of the studies on colostrum therapy are recent, with publications starting in 2009. Only one study prior to this period, carried out by Gutiérrez & Fernández,¹¹ was identified in the search but not included in the review, considering that it does not match the technique currently defined as colostrum therapy. The study was a randomized clinical trial that evaluated the effect of colostrum on the prevention and treatment of diarrhea and necrotizing enterocolitis in premature infants. Some aspects deserve to be commented on in this study, such as the administration of colostrum, which was made by nursing bottle or by catheter, as well as the fact that cow's milk was offered to

the control group. The group receiving colostrum had less necrotizing enterocolitis and diarrhea than the control group, showing the positive effect of colostrum administration. In more current studies, the administration of colostrum as therapy occurs in small volumes in contact with the oral mucosa at times systematized during the first days of life of the preterm newborns.

More recent articles have reported different outcomes, and although all studies include populations of preterm infants, gestational age cut-off points and weight ratings vary in the samples. Two studies found a positive impact of colostrum administration on nutritional and growth-related outcomes in preterm infants with extremely low-weight (<1,000 grams) as the shortest time to achieve the full enteral diet and the highest mean weight at 36 weeks of age.^{12,13} These findings are very important, as they have a direct impact on hospitalization time and post-discharge hospital feeding. Two other studies focused on the evaluation of the oral mucosa colonization of the NB, finding some effects; and another study measured serum immunoglobulin A secreted in the urine because of its effect on the immunological development of the preterm infant, with positive findings.^{7,8,14}

Considering the findings of most studies, the authors report that the positive effects of colostrum therapy are still inconclusive. Methodological problems, such as the small number of participants in most samples or short follow-up time of some studies, limit the results found. Only one study found a protective effect of colostrum therapy in preterm infants for the development of clinical sepsis, with favorable results in the group receiving maternal colostrum, even after adjustment for possible confounding factors. The same study also measured urinary excretion of immunoglobulin A and lactoferrin, which were increased in the intervention group for up to two weeks, suggesting an endogenous continuation of production, as well as supporting the practice to improve immunological maturation.¹⁵ However, the study evaluated only 48 patients, which limits the fact that these results are expanded for the preterm population in general.

Otherwise, colostrum therapy provides an invaluable gain to the mother-infant pair if it is considered that breastfeeding and the bond created between mother and child are stimulated from the very first moments of life of the newborns at risk, since the mother can actively participate in the treatment and recovery of the child. One of the studies included in this review showed that children exposed to colostrum therapy had a higher rate of breastfeeding at hospital discharge than those who did not receive colostrum therapy.

Although there is already a review¹⁶ on the topic discussed, this study contributes to describe the first studies on the topic, since it involves studies conducted in Brazil, besides including studies with different designs, providing the reader with an updated systematization of the data available for a critical evaluation of the construction of knowledge about the theme over the years.

Conclusion

Although there is no strong evidence of the clinical impact of colostrum therapy, it does not pose a risk for children. More evidence is needed on the impact of colostrum therapy on the prevention of clinical outcomes of higher incidence in premature infants to support the widespread implantation of this practice in neonatal units.

Collaborators

Lopes JB participated in the study design and preparation of the manuscript; Soldateli B participated in the study design and drafting of the manuscript; de Oliveira LD participated in the conception of the study and the preparation of the manuscript.

Conflict of interests: The authors declare no conflict of interest.

References

1. Silveira M, Matijasevic A, Horta B, Bettiol H, Barbieri MA, Silva AA, et. al. Prevalência de nascimentos pré-termo conforme grupos de peso ao nascer: revisão sistemática, análise colaborativa de estudos brasileiros e comparação com resultados do SINASC. *Rev. Saúde Pública*. 2013; 47(5):992-1003.
2. Oliveira A. Estudo da viabilidade da administração orofaríngea de colostro para recém-nascidos pré-termo: colostroterapia [dissertação]. [Ribeirão Preto]: Universidade de São Paulo; 2014.
3. Meier PP, Engstrom JL, Patel AL, Jegier BJ, Bruns NE. Improving the use of human milk during and after the NICU stay. *Clin Perinatol*. 2010; 37(1):217-245.
4. Sociedade Brasileira de Pediatria. O que é Colostroterapia?. Sociedade Brasileira de Pediatria [Internet]. [acesso em: 29 nov. 2016]. Disponível em: http://www.sbp.com.br/fileadmin/user_upload/pdfs/Colostroterapia.pdf
5. Cleminson JS, Zalewski SP, Embleton ND. Nutrition in the preterm infant: what's new?. *Curr Opin Clin Nutr Metab Care*. 2016; 19(3):220-225.
6. Neville M. Anatomy and physiology of lactation. *Pediatr Clin North Am*. 2001; 48(1):13-34.
7. Álvarez EM, Cabanillas MVJ, Caballero MP, López LS, Kajarabille N, Castro JD, et al. Efectos de la administración de calostro orofaríngeo en recién nacidos prematuros sobre los niveles de Inmunoglobulina A. *Nutr Hosp*. 2015; 33(2):232-238.
8. Sohn K, Kalentra KM, Mills DA, Underwood MA. Buccal administration of human colostrum: impact on the oral microbiota of premature infants. *J Perinatol*. 2016; 36(2):106-111.
9. Nasuf AW, Ojha S, Dorling J. Oropharyngeal colostrum in preventing mortality and morbidity in preterm infants. *Cochrane Database of Systematic Reviews*. 2015; 10(CD011921). Disponível em: <http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD011921/pdf>

10. Rodriguez NA, Vento M, Claud EC, Wang CE, Caplan MS. Oropharyngeal administration of mother's colostrum, health outcomes of premature infants: study protocol for a randomized controlled trial. *Trials*. 2015; 16:1-14.
11. Gutiérrez LJ, Fernández VO. El calostro humano em la prevención de la diarrea y de la enterocolitis necrosante. *Bol Med Hosp Infant*. 1980; 37(1):23-30.
12. Rodriguez NA, Groer MW, Zeller JM, Engstrom JL, Fogg L, Du H, et al. A randomized controlled trial of the oropharyngeal administration of mother's colostrum to extremely low birth weight infants in the first days of life. *Neonatal Intensive Care*. 2011; 24(4):31-35.
13. Seigel JK, Smith PB, Ashley PL, Cotten CM, Herbert CC, King BA, et al. Early administration of oropharyngeal colostrum to extremely low birth weight infants. *Breastfeed Med*. 2013; 8(6):491-495.
14. McFadden B. Oral colonization in the preterm neonate: effect of oral care [tese] [Internet]. Denton: Texas Woman's University; 2012. [acesso em: 29 nov. 2016]. Disponível em: <https://twu-ir.tdl.org/twu-ir/handle/11274/192>
15. Lee J, Kim HS, Yung YH, Choi KY, Shin SH, Kim EK, et al. Oropharyngeal colostrum administration in extremely premature infants: an RCT. *Pediatrics*. 2014; 135(2):357-378.
16. Gephart SM, Weller M. Colostrum as oral immune therapy to promote neonatal health. *Adv Neonatal Care*. 2014; 14(1):44-51.
17. Rodriguez NA, Meier PP, Groer MW, Zeller JM, Engstrom JL, Fogg L. A pilot study to determine the safety and feasibility of oropharyngeal administration of own mother's colostrum to extremely low birth weight infants. *Adv Neonatal Care*. 2010; 10(4):206-212.

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