REVISTA BIO CIENCIAS
http://revistabiociencias.uan.edu.mx
https://doi.org/10.15741/revbio.11.e1723

ISSN 2007-3380

Artículo original/Original Article

Colostrum as part of the treatment in symptomatic neonatal hypoglycemia.

Calostro como parte del tratamiento en hipoglucemia neonatal sintomática.

Contreras Garduño, K.A.[1]**(orcid.org/0009-0008-7058-4546), Rojas Mayorquín, A.E. (orcid.org/0000-0002-4517-8975)*

[1] *Noor Clinic, Blvd. Bosque Real No 85, Colonia Bosque Real, Huixquilucan, C.P.52774, Estado de México, México 2 Universidad de Guadalajara, Departamento Materno Infantil, Centro Universitario de Tlajomulco (CUTLAJO) Carretera Tlajomulco, Santa Fé Km. 3.5 No.595, Lomas de Tejeda, C. P. 45641, Tlajomulco de Zúñiga, Jalisco, México.*

Please cite this article as/Como citar este artículo: Contreras Garduño, K.A., Rojas Mayorquín, A.E. (2024). Colostrum as part of the treatment in symptomatic neonatal hypoglycemia. Revista Bio Ciencias, 11, e1723. https://doi.org/10.15741/revbio.11.e1723

Article Info/Información del artículo
Received/Recibido: July 07th 2024.
Accepted/Aceptado: October 09th 2024.
Available on line/Publicado: October 31th 2024.

ABSTRACT

Neonatal hypoglycemia (NH) is a common condition, though its diagnosis and management remain controversial. The establishment and maintenance of breastfeeding can be compromised in NH patients. To prevent neurological damage, intravenous glucose infusion is typically suggested for patients with symptomatic NH. However, intraoral administration of colostrum as an intervention has been slightly explored. Here, we present a case of a newborn with symptomatic NH who responded positively to an initial intervention of oral colostrum administration. Colostrum therapy in NH management represents a low-cost, noninvasive intervention that promotes the breastfeeding establishment.

KEYWORDS: Hypoglycemia, Neonatal, Colostrum, Colostrum therapy, Breastfeeding.

***Corresponding Author:**

Katia Andrea Contreras-Garduño. Noor Clinic, Blvd. Bosque Real No 85, Colonia Bosque Real, Huixquilucan, 52774, Estado de México, México Teléfono: +(52)552115 7925. E-mail: kacgpedia@gmail.com

Revista Bio ciencias
ISSN 2007-3380

RESUMEN

La hipoglucemia neonatal (NH) es una condición frecuente cuyo diagnóstico y manejo siguen siendo controversiales. El establecimiento y mantenimiento de la lactancia pueden verse afectados en pacientes con NH. Para evitar daño neurológico, se recomienda infusión intravenosa de glucosa en pacientes con NH sintomática. La administración intraoral de calostro como intervención ha sido poco explorada. Reportamos el caso de un recién nacido con NH sintomática cuya primera intervención fue la administración oral de calostro con una respuesta favorable. La calostroterapia en el manejo de NH es una intervención de bajo costo, no invasiva y favorece el establecimiento de la lactancia.

PALABRAS CLAVE: Hipoglucemia, neonatal, calostro, calostroterapia, lactancia.

Introduction

Neonatal hypoglycemia (NH) is a widespread metabolic condition in newborn (NB) care. Its incidence is difficult to estimate accurately due to ongoing controversy regarding its definition (Hosagasi *et al.,* 2018; Karbalivand *et al.,* 2022). Globally, the incidence is estimated to range from 1.3 to 5 cases per 1,000 live NB, with higher frequencies reported in developing countries (Khan *et al.,* 2010). In healthy NBs, its incidence ranges from 3.4% (Bromiker *et al.,* 2019) to 16.9% (Zhou *et al.,* 2015). In contrast, in NBs with risk factors such as low birth weight, prematurity, and severe neonatal asphyxia, frequencies as high as 77.8%, 55.6%, and 42.9%, respectively, have been reported (Zhou *et al.,* 2015). In a tertiary hospital in Mexico City, the incidence was reported to be 5.9% in late preterm NBs and 11.4% in term NBs with low birth weight for gestational age (Castillo, 2013). Similarly, in a tertiary hospital in Zapopan, Jalisco, an incidence of 16.9% was reported in NBs with risk factors (Quiroz-Lamadrid *et al.,* 2020).

Symptomatic and persistent NH can lead to long-term neurological deficits. Hypoglycemia persisting beyond 48 hours of life is defined as persistent NH and entails the clinician to rule out congenital syndromes, inborn errors of metabolism, or endocrinological disorders (**Table 1**) (Abramowski *et al.,* 2023).

Revista Bio ciencias
ISSN 2007-3380

Table 1. Causes of persistent neonatal hypoglycemia.

Congenital hyperinsulinism
Congenital syndromes
Beckwith-Wideman syndrome
Soto syndrome
Costello syndrome
Endocrine disorders
Congenital hypopituitarism
Congenital adrenal hyperplasia
Hypothyroidism
Inborn errors of metabolism
Maple syrup disease
Glycogenosis
Galactosemia
Hereditary fructose intolerance
Fatty acid oxidation defects

Magnetic resonance imaging (MRI) studies have shown that NH can cause neurological damage. A report of neurological follow-up in four patients, aged 9 to 12 months, revealed lesions predominantly in the occipital regions, which were identified through an MRI performed before day 50 of life (Filan *et al.,* 2006). In these cases, 3 of the 4 patients had hyperinsulinism, a risk factor for more severe hypoglycemia. In contrast, a follow-up of 35 NBs with symptomatic NH using early MRI (before 6 weeks of life) and neurodevelopmental assessment (after 18 months of age) showed that the pattern of neurological damage is more variable and not limited to occipital regions (Burns *et al.,* 2008).

Recently, increasing evidence has debated the neurodevelopmental implications of transient (lasting less than 48 hours) and asymptomatic NH (Adamkin, 2017; Cacciatore *et al.,* 2022). Low glucose levels (<40 mg/dL) may be part of normal metabolic adaptation in the first hours of a NB (Adamkin, 2017). However, NH screening and interventions can hinder the establishment and maintenance of breastfeeding. Hypoglycemia screening in healthy infants is associated with an increased likelihood of formula supplementation (Mukhopadhyay *et al.,* 2020), which can delay the lactogenesis onset (Haninger & Farley, 2001; Wight, 2021). In addition to the well-established risk factors for NH outlined in Table 2 (Wight, 2021), recent studies have identified other factors that increase the risk, such as cesarean birth (Turner *et al.,* 2019; Chen *et al.,* 2022) and hypothermia (Chen *et al.,* 2022; Zhao *et al.,* 2020). Furthermore, recent research highlights protective factors against NH, such as prolonged skin-to-skin contact with the mother (Chen *et al.,* 2022; Chiruvolu *et al.,* 2017; Dalsgaard *et al.,* 2019; WHO Immediate KMC Study Group *et al.,* 2021).

Revista Bio ciencias
ISSN 2007-3380

Table 2. Risk factors for neonatal hypoglycemia.

Maternal conditions
Gestational diabetes or pre-existing diabetes
Preeclampsia
History of macrosomic babies
Substance abuse
Treatment with beta-agonists
Treatment with oral hypoglycemic agents
Administration of intravenous glucose during childbirth
Neonatal conditions
Intrauterine growth restriction
Low birth weight or low weight for gestational age
High weight for gestational age (>90th percentile)
Macrosomia
Discordant twin
Children of mothers with poorly controlled diabetes
Prematurity (<35 weeks of gestation)
Perinatal stress (asphyxia or severe acidosis)
Hypothermia, Polycythemia, or Erythroblastosis fetalis
Beckwith-Wiedemann syndrome
Midline defects or microphallus
Suspected neonatal sepsis or respiratory distress
Inborn errors of metabolism
Neonate admitted to the Intensive Care Unit

In symptomatic patients with glucose levels below 40 mg/dL (Adamkin & Committee on Fetus and Newborn, 2011) or below 50 mg/dL (Thornton *et al.,* 2015), according to the criteria of the American Academy of Pediatrics (AAP) and the Pediatric Endocrine Society (PES), respectively, treatment with intravenous glucose infusion is well-established (Adamkin & Committee on Fetus and Newborn, 2011; Thornton *et al.,* 2015). Recently, oral dextrose gel has been proposed as a noninvasive and low-cost treatment effective in NH management (Edwards *et al.,* 2022; Roberts *et al.,* 2023; del Carmen *et al.,* 2023). Dextrose gel has even been suggested as a prophylactic method in NBs with risk factors, with potential benefits including preventing NH, reducing maternal-newborn separation, supporting breastfeeding, and preventing neurological damage (Edwards *et al.,* 2022; Roberts *et al.,* 2023). However, these studies are not yet conclusive, and larger-scale studies with longer follow-up periods are required (Edwards *et al.,* 2022).

For over a decade, the effects of colostrum administration compared to interventions like infant formula in NBs of mothers with diabetes have been explored (Tozier, 2013). Prenatal extraction of colostrum and its postnatal administration to NBs has been shown to reduce the NH risk in NBs with risk factors (Johnsen *et al.,* 2021; Foudil-Bey *et al.,* 2021; Forster *et al.,* 2017). However, no study has yet explored the metabolic response to the intraoral administration

Revista Bio ciencias
ISSN 2007-3380

of maternally extracted colostrum in managing symptomatic NH. Here, we present the clinical case of an NB with symptomatic NH who received oral colostrum as an initial intervention when resources for intravenous glucose administration were not immediately available.

Materials and methods: Case presentation

The patient was a full-term male NB at 37 weeks of gestation, with low birth weight for gestational age according to World Health Organization charts (2440 grams). He was the product of the first pregnancy of a healthy 35-year-old mother. The pregnancy was normal, with spontaneous labor onset. The birth was a natural, unmedicated vaginal delivery, allowing for immediate skin-to-skin contact and breastfeeding within the first 30 minutes of life. A natural childbirth without medical intervention refers to the absence of obstetric analgesia, anesthesia, synthetic oxytocin, or any other interventions that could interfere with the natural labor progression. The mother-child dyad was released fourteen hours after birth, with no dehydration evidence.

At 44 hours of life, the patient was brought to the emergency department following a phone report of hypoactivity and reduced interest in feeding. Since the typical timeframe for the onset of lactogenesis II (mature milk production) ranges between 48 and 120 hours postpartum, the mother was still in the colostrum lactation phase, the newborn milk (Neville *et al.,* 2001). On examination, the patient was hypoactive but had stable vital signs, no clinical signs of dehydration, and had lost 200 grams (8% of his birth weight). Other than hypoactivity and reduced feeding (hyporexia), no additional neurological symptoms were observed. A glucose level measured via dextrostix test showed 25 mg/dL, then confirmed through a serum glucose level of 36 mg/dL. It was also found with multifactorial hyperbilirubinemia; ruling out polycythemia, neonatal sepsis, and hypernatremic dehydration as causes of hypoactivity.

While the patient was being administered intravenous glucose, the mother was assisted in colostrum extraction. Sixteen milliliters of colostrum were manually expressed (Figure 1), stored at room temperature, and immediately spoon-fed to the newborn. Manual extraction of colostrum in the first few days postpartum is recommended. Before extraction, it is important to wash hands thoroughly, gently massage the breasts, and stimulate the oxytocin reflex. The thumb should be positioned above the nipple and areola, with the index finger below, opposite the thumb. A gentle pressing motion should be applied toward the chest wall, avoiding squeezing the nipple to prevent obstruction of the milk ducts (Figure 1). The motion should be repeated until colostrum drips, and the process should last 5 to 7 minutes per breast. Due to the dense consistency and small volume of colostrum, it is advisable to collect it in a small container or spoon.

Upon noticing immediate clinical improvement (increased activity and interest in eating) after the intervention, serum glucose was taken at the time of accessing an intravenous line (forty-three minutes after oral colostrum intake), which was reported to be 302 mg/dL. During the breastfeeding clinical assessment, two notable findings were identified: ankyloglossia in the NB and Raynaud's phenomenon in the nipples of the mother, both of which may have hindered optimal breastfeeding since hospital discharge. During the hospital stay, the breastfeeding technique was

Revista Bio ciencias
ISSN 2007-3380

corrected, and the patient was referred for subspecialty evaluation of ankyloglossia. A frenotomy was performed on an outpatient basis, and Raynaud's phenomenon was managed with physical measures. Intravenous glucose was no longer required for the patient.

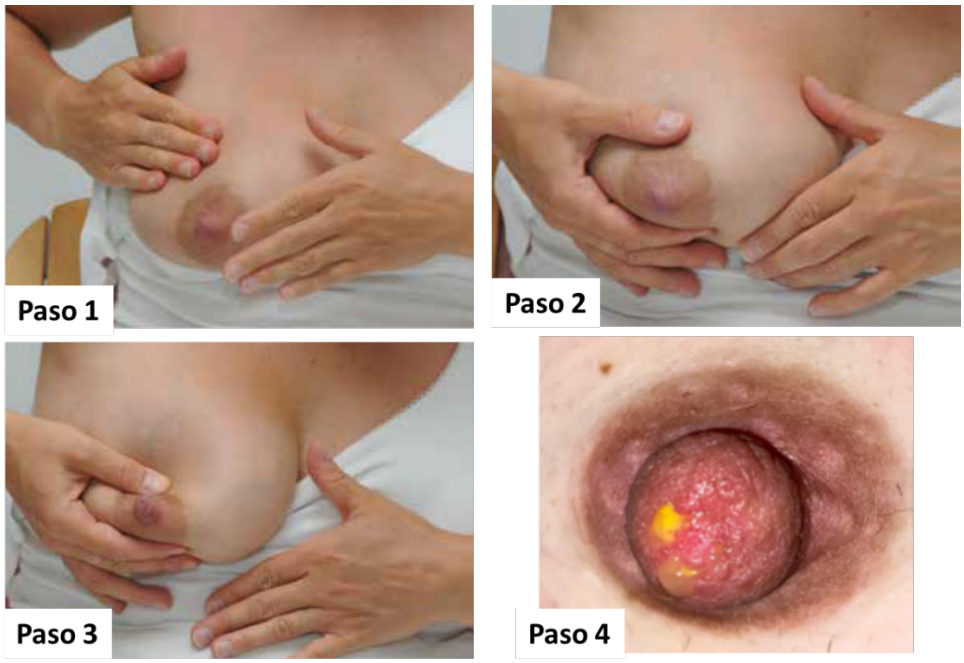

Figure 1. Manual colostrum extraction technique. Step 1) Gently massage the breasts; Step 2) Place the thumb on the breast above the nipple and areola, and the index finger underneath, opposite the thumb; Step 3) Gently press towards the ribs and release the pressure; Step 4) Repeat the movement (press and release) until the first drops are seen. (Data retrieved from Antenatal Hand Expressing. Maternity Services Lothian 2023).

The neurological development of the patient during his pediatric follow-up has been favorable, achieving developmental milestones in the expected ranges for his age. Currently, the patient is 8 years 10 months old and is in the third year of elementary school with excellent school performance and adequate neurological development. He was exclusively breastfed until he was six months old and was weaned at 5 years of age. The breastfeeding experience of the mother was satisfactory, meeting her own breastfeeding goals.

Observations and discussion

NH is one of the most feared clinical entities in NBs and is a frequent cause of separation from the mother-infant dyad in the first days of life (Wight, 2021; Giouleka *et al.,* 2023). In the case presented here, the patient had several risk factors for hypoglycemia and difficulty establishing

Revista Bio ciencias
ISSN 2007-3380

breastfeeding: gestational age of 37 weeks, low weight for gestational age, ankyloglossia, early discharge home, and the presence of Raynaud syndrome in the mother.

The therapeutic response to colostrum (colostrum therapy), with a glycemic control of 302 mg/dL forty-three minutes after intervention, demonstrates the NB remarkable ability to compensate for low glucose levels through different metabolic pathways (Wight, 2021). Colostrum is an exceptional fluid, concentrated, rich in proteins, lactoferrin, fat-soluble vitamins, minerals, growth factors, and cells. In addition to its immunological properties, colostrum comprises a high content of other macronutrients that aid in counter-regulating NH (Lawrence & Lawrence, 2022). It is estimated to provide approximately 55 cal/dL, along with its immune components (Bardanzellu *et al.,* 2017). Almost a decade ago, research showed that colostrum from mothers with obesity contained higher concentrations of glucose, fat, and caloric content (Fujimori *et al.,* 2015), as well as leptin and adiponectin (Fujimori *et al.,* 2017). The elevated expression of these substances in the colostrum of mothers of NBs at risk for NH could have significant biological implications for the metabolic regulation of NBs. The colostrum use as a therapeutic intervention in NH, as well as these findings, merits further investigation.

Although there are already several studies exploring oral dextrose gel administration as part of treatment for asymptomatic HN (Hosagasi *et al.,* 2018; Wight, 2021; Edwards *et al.,* 2022; del Carmen *et al.,* 2023; Gregory *et al.,* 2020; Meneghin *et al.,* 2021; Harding *et al.,* 2021; Stanzo *et al.,* 2020), and that it has even been shown to be a cost-effective intervention compared to standard treatment (Glasgow *et al.,* 2020), there are trials that suggest it is not a superior intervention to offering formula milk (Coors *et al.,* 2018). Continuing to feed the infant as an intervention has been little studied (Dalsgaard *et al.,* 2019; Tozier, 2013; Johnsen *et al.,* 2021; Gregory *et al.,* 2019). The AAP suggests continuing to feed the infant with asymptomatic HN <25mg/dL at initial screening in infants younger than 4 hours, and <35mg/dL in NBs from 4 to 24 hours of extrauterine life (Hosagasi *et al.,* 2018). Feeding with a breast milk substitute does not have the same benefits as continuing to feed human milk, and few studies denote these implications for both nutritional and immunological content as well as the physiological breastfeeding process (Tozier, 2013; Johnsen *et al.,* 2021; Van Kempen *et al.,* 2020). Breastfeeding and regulating maternal metabolism will be critical in the metabolic programming of the NB (Elbeltagi *et al.,* 2023).

In this case, we did not have any other resources in the emergency department as immediate as colostrum, Hence, we started treatment with colostrum. Since there was an immediate clinical response to colostrum ingestion, it was decided not to continue intervening. Intravenous access in a pediatric patient, especially in small patients such as NBs, can be a challenge for not-so-trained personnel (Cuper *et al.,* 2012). Colostrum collection is a no-cost alternative that, in the hands of someone trained, can be obtained immediately.

Interventions in an NB can become barriers to the establishment of breastfeeding. The lack of breastfeeding counseling at discharge is also a challenge to resolve. The mother of the patient we report describes returning to the hospital with a condition that put the health of her baby at risk as an experience that diminished her confidence in her ability to breastfeed. Good communication with the mother explaining the risks her baby presented for NH developing, as well

Revista Bio ciencias
ISSN 2007-3380

as showing proper breastfeeding technique and making colostrum part of the NB treatment, was helpful in regaining her confidence.

For a proper breastfeeding technique, the mother must be in a comfortable position. The baby should be positioned in front of the breast of the mother, held firmly with the body aligned, preventing the baby from turning his head and positioning the nose in front of the nipple (figures 2 and 3). The nipple is placed in front of the nose of the infant so that the baby can look for it and widely open the mouth. The mouth of the infant should be wide open before bringing the baby close to the breast. The mother should make sure that the latch-on is deep and prevent the baby from grasping the nipple alone. This will avoid pain due to poor latch-on. Once at the breast, the baby should keep its mouth open and make a firm seal around the breast, and preferably the chin of the baby should touch the breast of the mother. A NB should have a breastfeeding frequency of at least 8 feedings per day, with each feeding lasting between 20 and 40 minutes.

Figure 2. In the comfortable mother position, the body of the baby is aligned. The use of a pillow or cushion is optional (own photos).

Figure 3. In the comfortable mother position, the body of the baby is aligned, facing the breast in a deep latch, the baby's mouth wide open, baby's chin close to the mother's breast (own photos).

Revista Bio ciencias
ISSN 2007-3380

Conclusions

Oral colostrum administration is a no-cost, non-invasive intervention that supports the establishment of breastfeeding and supports the confidence of the mother in her ability to feed her baby. Studies are needed to demonstrate the efficacy of colostrum therapy as part of interventions in the prevention and treatment of symptomatic NH. The clinical benefits of colostrum administration in preterm infants have been reported (Kumar et al. 2023). All first-contact pediatricians must have the knowledge to support manual colostrum extraction, which can be useful to prevent NH or even to provide immediate care in case of metabolic disturbance. It is also important to know to detect conditions that could complicate the establishment of lactation, as in this case ankyloglossia in the infant and Raynaud syndrome in the mother. The case we report demonstrates to us the value of adopting hospital practices for the management of HN that facilitate exclusive breastfeeding (Perez et al., 2019; Stewart et al., 2016), especially with high-risk NBs (Wight, 2021; WHO Immediate KMC Study Group et al., 2021; Tozier, 2013).

Author contribution

Work conceptualization, Contreras K; development of the methodology, observation, discussion, and conclusions, Contreras K and Rojas A. All authors of this manuscript have read and accepted the published version of the manuscript.

Financing

This research did not receive external funding.

Statement of Informed Consent

Informed consent was obtained from the mother, father, and patient involved in the study.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

Abramowski, A., Ward, R., & Hamdan, A. H. (2023). Neonatal Hypoglycemia. In *StatPearls*. StatPearls Publishing.

Adamkin D. H. (2017). Neonatal hypoglycemia. *Seminars in fetal & neonatal medicine*, *22*(1), 36–41. https://doi.org/10.1016/j.siny.2016.08.007

Adamkin, D. H., & Committee on Fetus and Newborn. (2011). Postnatal glucose homeostasis

in late-preterm and term infants. Pediatrics, 127(3), 575–579. https://doi.org/10.1542/peds.2010-3851

Bardanzellu, F., Fanos, V., & Reali, A. (2017). “Omics” in Human Colostrum and Mature Milk: Looking to Old Data with New Eyes. *Nutrients*, *9*(8), 843. https://doi.org/10.3390/nu9080843

Bromiker, R., Perry, A., Kasirer, Y., Einav, S., Klinger, G., & Levy-Khademi, F. (2019). Early neonatal hypoglycemia: incidence of and risk factors. A cohort study using universal point of care screening. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*, *32*(5), 786–792. https://doi.org/10.1080/14767058.2017.1391781

Burns, C. M., Rutherford, M. A., Boardman, J. P., & Cowan, F. M. (2008). Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics*, *122*(1), 65–74. https://doi.org/10.1542/peds.2007-2822

Cacciatore, M., Grasso, E. A., Tripodi, R., & Chiarelli, F. (2022). Impact of glucose metabolism on the developing brain. *Frontiers in endocrinology*, *13*, 1047545. https://doi.org/10.3389/fendo.2022.1047545

Castillo Martínez, J. (2013). “Incidencia de hipoglucemia neonatal transitoria asintomática en recién nacidos prematuros tardíos y de término con bajo peso al nacer”. [Trabajo de grado de especialización. Universidad Nacional Autónoma de México]. https://repositorio.unam.mx/contenidos/367725

Chen, Y. S., Ho, C. H., Lin, S. J., & Tsai, W. H. (2022). Identifying additional risk factors for early asymptomatic neonatal hypoglycemia in term and late preterm babies. *Pediatrics and neonatology*, *63*(6), 625–632. https://doi.org/10.1016/j.pedneo.2022.04.011

Chiruvolu, A., Miklis, K. K., Stanzo, K. C., Petrey, B., Groves, C. G., McCord, K., Qin, H., Desai, S., & Tolia, V. N. (2017). Effects of Skin-to-Skin Care on Late Preterm and Term Infants At-Risk for Neonatal Hypoglycemia. *Pediatric quality & safety*, *2*(4), e030. https://doi.org/10.1097/pq9.0000000000000030

Coors, S. M., Cousin, J. J., Hagan, J. L., & Kaiser, J. R. (2018). Prophylactic Dextrose Gel Does Not Prevent Neonatal Hypoglycemia: A Quasi-Experimental Pilot Study. *The Journal of pediatrics*, *198*, 156–161. https://doi.org/10.1016/j.jpeds.2018.02.025

Cuper, N. J., de Graaff, J. C., van Dijk, A. T., Verdaasdonk, R. M., van der Werff, D. B., & Kalkman, C. J. (2012). Predictive factors for difficult intravenous cannulation in pediatric patients at a tertiary pediatric hospital. *Paediatric anaesthesia*, *22*(3), 223–229. https://doi.org/10.1111/j.1460-9592.2011.03685.x

Dalsgaard, B. T., Rodrigo-Domingo, M., Kronborg, H., & Haslund, H. (2019). Breastfeeding and skin-to-skin contact as non-pharmacological prevention of neonatal hypoglycemia in infants born to women with gestational diabetes; a Danish quasi-experimental study. *Sexual & reproductive healthcare : official journal of the Swedish Association of Midwives*, *19*, 1–8. https://doi.org/10.1016/j.srhc.2018.10.003

Covas, M., Qintana, D., Oviedo, B., Medina, M., Gurrea, M., Miyar, A., & Alda, E. (2023). Hipoglucemia neonatal: eficacia de la glucosa gel en el tratamiento de la hipoglucemia precoz en recién nacidos con factores de riesgo. Ensayo clínico aleatorizado. *Andes Pediatrica, 94*(1), 70-77. doi:http://dx.doi.org/10.32641/andespediatr.v94i1.4220

Edwards, T., Liu, G., Battin, M., Harris, D. L., Hegarty, J. E., Weston, P. J., & Harding, J. E. (2022). Oral dextrose gel for the treatment of hypoglycaemia in newborn infants. *The Cochrane*

database of systematic reviews, *3*(3), CD011027. https://doi.org/10.1002/14651858.CD011027.pub3

Elbeltagi, R., Al-Beltagi, M., Saeed, N. K., & Bediwy, A. S. (2023). Cardiometabolic effects of breastfeeding on infants of diabetic mothers. *World journal of diabetes*, *14*(5), 617–631. https://doi.org/10.4239/wjd.v14.i5.617

Filan, P. M., Inder, T. E., Cameron, F. J., Kean, M. J., & Hunt, R. W. (2006). Neonatal hypoglycemia and occipital cerebral injury. *The Journal of pediatrics*, *148*(4), 552–555. https://doi.org/10.1016/j.jpeds.2005.11.015

Forster, D. A., Moorhead, A. M., Jacobs, S. E., Davis, P. G., Walker, S. P., McEgan, K. M., Opie, G. F., Donath, S. M., Gold, L., McNamara, C., Aylward, A., East, C., Ford, R., & Amir, L. H. (2017). Advising women with diabetes in pregnancy to express breastmilk in late pregnancy (Diabetes and Antenatal Milk Expressing [DAME]): a multicentre, unblinded, randomised controlled trial. *Lancet (London, England)*, *389*(10085), 2204–2213. https://doi.org/10.1016/S0140-6736(17)31373-9

Foudil-Bey, I., Murphy, M. S. Q., Dunn, S., Keely, E. J., & El-Chaâr, D. (2021). Evaluating antenatal breastmilk expression outcomes: a scoping review. *International breastfeeding journal*, *16*(1), 25. https://doi.org/10.1186/s13006-021-00371-7

Fujimori, M., França, E. L., Fiorin, V., Morais, T. C., Honorio-França, A. C., & de Abreu, L. C. (2015). Changes in the biochemical and immunological components of serum and colostrum of overweight and obese mothers. *BMC pregnancy and childbirth*, *15*, 166. https://doi.org/10.1186/s12884-015-0574-4

Fujimori, M., França, E. L., Morais, T. C., Fiorin, V., de Abreu, L. C., & Honório-França, A. C. (2017). Cytokine and adipokine are biofactors can act in blood and colostrum of obese mothers. *BioFactors (Oxford, England)*, *43*(2), 243–250. https://doi.org/10.1002/biof.1339

Giouleka, S., Gkiouleka, M., Tsakiridis, I., Daniilidou, A., Mamopoulos, A., Athanasiadis, A., & Dagklis, T. (2023). Diagnosis and Management of Neonatal Hypoglycemia: A Comprehensive Review of Guidelines. *Children (Basel, Switzerland)*, *10*(7), 1220. https://doi.org/10.3390/children10071220

Glasgow, M. J., Edlin, R., & Harding, J. E. (2020). Cost-Utility Analysis of Prophylactic Dextrose Gel vs Standard Care for Neonatal Hypoglycemia in At-Risk Infants. *The Journal of pediatrics*, *226*, 80–86.e1. https://doi.org/10.1016/j.jpeds.2020.06.073

Gregory, K., Turner, D., Benjamin, C. N., Monthe-Dreze, C., Johnson, L., Hurwitz, S., Wolfsdorf, J., & Sen, S. (2020). Incorporating dextrose gel and feeding in the treatment of neonatal hypoglycaemia. Archives of disease in childhood. Fetal and neonatal edition, 105(1), 45–49. https://doi.org/10.1136/archdischild-2018-316430

Harding, J. E., Hegarty, J. E., Crowther, C. A., Edlin, R. P., Gamble, G. D., Alsweiler, J. M., & hPOD Study Group (2021). Evaluation of oral dextrose gel for prevention of neonatal hypoglycemia (hPOD): A multicenter, double-blind randomized controlled trial. PLoS medicine, 18(1), e1003411. https://doi.org/10.1371/journal.pmed.1003411

Haninger, N. C., & Farley, C. L. (2001). Screening for hypoglycemia in healthy term neonates: effects on breastfeeding. Journal of midwifery & women's health, 46(5), 292–301. https://doi.org/10.1016/s1526-9523(01)00180-5

Hosagasi, N. H., Aydin, M., Zenciroglu, A., Ustun, N., & Beken, S. (2018). Incidence of hypoglycemia in newborns at risk and an audit of the 2011 American academy of pediatrics guideline

Revista Bio ciencias
ISSN 2007-3380

for hypoglycemia. Pediatrics and neonatology, 59(4), 368–374. https://doi.org/10.1016/j.pedneo.2017.11.009

Johnsen, M., Klingenberg, C., Brand, M., Revhaug, A., & Andreassen, G. (2021). Antenatal breastmilk expression for women with diabetes in pregnancy - a feasibility study. International breastfeeding journal, 16(1), 56. https://doi.org/10.1186/s13006-021-00393-1

Karbalivand, H., Iyare, A., Aponte, A., Xianhong, X., Kim, M., & Havranek, T. (2022). Hypoglycemia screening of asymptomatic newborns on the 2nd day of life. Journal of neonatal-perinatal medicine, 15(2), 311–316. https://doi.org/10.3233/NPM-210861

Khan, I., Muhammad, T., & Khan, M. (2010). Frequency and Clinical Characteristics of Symptomatic Hypoglycemia in Neonates. Gomal Journal of Medical Sciences, 8(2). Retrieved from https://www.gjms.com.pk/index.php/journal/article/view/329/326

Kumar, J., Meena, J., Ranjan, A., & Kumar, P. (2023). Oropharyngeal application of colostrum or mother's own milk in preterm infants: a systematic review and meta-analysis. Nutrition reviews, 81(10), 1254–1266. https://doi.org/10.1093/nutrit/nuad002

Lawrence RA & Lawrence RM. (2022). Breastfeeding : A Guide for the Medical Profession. Ninth ed. Philadelphia PA: 360 Elsevier. https://www.clinicalkey.com/dura/browse/bookChapter/3-s2.0-C20140021363

Maternity Services Lothian (2023). Antenatal Hand Expressing. accessed 2024 at: 362 https://www.anchb.scot.nhs.uk/media/lhwljysc/hand-expressing-2023-updated.pdf

Meneghin, F., Manzalini, M., Acunzo, M., Daniele, I., Bastrenta, P., Castoldi, F., Cavigioli, F., Zuccotti, G. V., & Lista, G. (2021). Management of asymptomatic hypoglycemia with 40% oral dextrose gel in near term at-risk infants to reduce intensive care need and promote breastfeeding. Italian journal of pediatrics, 47(1), 201. https://doi.org/10.1186/s13052-021-01149-7

Mukhopadhyay, S., Wade, K. C., Dhudasia, M. B., Skerritt, L., Chou, J. H., Dukhovny, D., & Puopolo, K. M. (2020). Clinical impact of neonatal hypoglycemia screening in the well-baby care. Journal of perinatology : official journal of the California Perinatal Association, 40(9), 1331–1338. https://doi.org/10.1038/s41372-020-0641-1

Neville, M. C., Morton, J., & Umemura, S. (2001). Lactogenesis. The transition from pregnancy to lactation. Pediatric clinics of North America, 48(1), 35–52. https://doi.org/10.1016/s0031-3955(05)70284-4

Pérez G, Meritano J, Rubio C, Gutierrez S, Mariani M, Brener P, Sabatelli D, Scaramutti M. (2019). Comité de Estudios Feto-Neonatales. Hipoglucemia neonatal: revisión de las prácticas habituales. Archivos Argentinos de Pediatría , 117 Supl 5:S195-S204. http://dx.doi.org/10.5546/aap.2019.S195

Quiros-Lamadrid D, Guzmán-Anaya GA, Almonte Lemus LA, Ceja-Mejia OE, Arias-Uribe BN, Ruelas-Arana E, Gutierrez-375 Padilla JA, Gallego-Tapia AR, López-Romero JA, Mercado-Cerda JI. (2020). Hipoglucemia del recién nacido de 376 riesgo en las primeras 24 horas de vida. Revista Médica MD, 11(2):87-91. 377 https://revistamedicamd.com/aj./webmaster/getfile/a9473f7fc728bfb1ab088104f198c300/

Roberts, L., Lin, L., Alsweiler, J., Edwards, T., Liu, G., & Harding, J. E. (2023). Oral dextrose gel to prevent hypoglycaemia in at-risk neonates. The Cochrane database of systematic reviews, 11(11), CD012152. https://doi.org/10.1002/14651858.CD012152.pub4

Stanzo, K., Desai, S., & Chiruvolu, A. (2020). Effects of Dextrose Gel in Newborns at Risk for

Neonatal Hypoglycemia in a Baby-Friendly Hospital. Journal of obstetric, gynecologic, and neonatal nursing: JOGNN, 49(1), 55–64. https://doi.org/10.1016/j.jogn.2019.11.006

Stewart, C. E., Sage, E. L., & Reynolds, P. (2016). Supporting 'Baby Friendly': a quality improvement initiative for the management of transitional neonatal hypoglycaemia. Archives of disease in childhood. Fetal and neonatal edition, 101(4), F344–F347. https://doi.org/10.1136/archdischild-2015-308950

Thornton, P. S., Stanley, C. A., De Leon, D. D., Harris, D., Haymond, M. W., Hussain, K., Levitsky, L. L., Murad, M. H., Rozance, P. J., Simmons, R. A., Sperling, M. A., Weinstein, D. A., White, N. H., Wolfsdorf, J. I., & Pediatric Endocrine Society (2015). Recommendations from the Pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children. The Journal of pediatrics, 167(2), 238–245. https://doi.org/10.1016/j.jpeds.2015.03.057

Tozier P. K. (2013). Colostrum versus formula supplementation for glucose stabilization in newborns of diabetic mothers. Journal of obstetric, gynecologic, and neonatal nursing: JOGNN, 42(6), 619–628. https://doi.org/10.1111/1552-6909.12260

Turner, D., Monthé-Drèze, C., Cherkerzian, S., Gregory, K., & Sen, S. (2019). Maternal obesity and cesarean section delivery: additional risk factors for neonatal hypoglycemia?. Journal of perinatology : official journal of the California Perinatal Association, 39(8), 1057–1064. https://doi.org/10.1038/s41372-019-0404-z

van Kempen, A. A. M. W., Eskes, P. F., Nuytemans, D. H. G. M., van der Lee, J. H., Dijksman, L. M., van Veenendaal, N. R., van der Hulst, F. J. P. C. M., Moonen, R. M. J., Zimmermann, L. J. I., van 't Verlaat, E. P., van Dongen-van Baal, M., Semmekrot, B. A., Stas, H. G., van Beek, R. H. T., Vlietman, J. J., Dijk, P. H., Termote, J. U. M., de Jonge, R. C. J., de Mol, A. C., Huysman, M. W. A., … HypoEXIT Study Group (2020). Lower versus Traditional Treatment Threshold for Neonatal Hypoglycemia. The New England journal of medicine, 382(6), 534–544. https://doi.org/10.1056/NEJMoa1905593

WHO Immediate KMC Study Group, Arya, S., Naburi, H., Kawaza, K., Newton, S., Anyabolu, C. H., Bergman, N., Rao, S. P. N., Mittal, P., Assenga, E., Gadama, L., Larsen-Reindorf, R., Kuti, O., Linnér, A., Yoshida, S., Chopra, N., Ngarina, M., Msusa, A. T., Boakye-Yiadom, A., Kuti, B. P., … Massawe, A. (2021). Immediate "Kangaroo Mother Care" and Survival of Infants with Low Birth Weight. The New England journal of medicine, 384(21), 2028–2038. https://doi.org/10.1056/NEJMoa2026486

Wight, N. E., & Academy of Breastfeeding Medicine (2021). ABM Clinical Protocol #1: Guidelines for Glucose Monitoring and Treatment of Hypoglycemia in Term and Late Preterm Neonates, Revised 2021. Breastfeeding medicine: the official journal of the Academy of Breastfeeding Medicine, 16(5), 353–365. https://doi.org/10.1089/bfm.2021.29178.new

Zhao, T., Liu, Q., Zhou, M., Dai, W., Xu, Y., Kuang, L., Ming, Y., & Sun, G. (2020). Identifying risk effectors involved in neonatal hypoglycemia occurrence. Bioscience reports, 40(3), BSR20192589. https://doi.org/10.1042/BSR20192589

Zhou, W., Yu, J., Wu, Y., & Zhang, H. (2015). Hypoglycemia incidence and risk factors assessment in hospitalized neonates. The journal of maternal-fetal & neonatal medicine: the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 28(4), 422–425. https://doi.org/10.3109/14767058.2014.918599

Revista Bio ciencias
ISSN 2007-3380