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Review

Vomiting in neonates

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Abstract

Vomiting is a common clinical sign in the paediatric age group, including neonates. It is the forced expulsion of gastric content through the mouth and must be differentiated from gastro-oesophageal reflux. Vomiting in neonates is usually a non-specific clinical sign and may correspond to gastrointestinal abnormalities, but it can also signal systemic disorders such as infectious pathologies, intracranial injuries with intracranial hypertension, and endocrine and metabolic diseases. Physicians should be able to recognize life-threatening causes of vomiting in order to avoid serious complications. This review considers congenital gastrointestinal malformations, infections and other less common causes of vomiting in neonates.

Keywords

Vomiting, neonates, gastro-oesophageal reflux, congenital gastrointestinal malformations, acquired intestinal obstructive causes, infection.

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Introduction

Vomiting is the forceful extrusion of gastric content and it is never normal in neonates [1]. In neonates, vomiting is usually a non-specific clinical sign and may correspond to the initial presentation of infectious pathologies (respiratory infection, pyelonephritis, meningitis, septicaemia), digestive abnormalities (hypertrophic pyloric stenosis, intestinal invagination, intestinal stenosis or atresia, volvulus, incarcerated hernia), intracranial injuries with intracranial hypertension and endocrine and metabolic diseases [1, 2].

It is important to differentiate between vomiting and regurgitation [3]. Regurgitation is a physiological process by which gastric content is brought back into the oesophagus or oral cavity without the abdominal and diaphragmatic muscular activity that characterizes vomiting [1, 3]. This situation is associated with gastro-oesophageal reflux disease (GORD). The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) defines GORD as a pathological condition that occurs when gastro-oesophageal reflux is associated with clinical signs that affect daily functioning and/or complications such as discomfort, irritability, feeding difficulties and poor weight gain [4, 5]. It is important to make the differential diagnosis as soon as possible in order to guide both treatment and management. Most cases of GORD can be treated conservatively with body positioning and avoidance of overfeeding. Proton pump inhibitors are, when necessary, the recommended pharmacological agents [5, 6].

Objectives and methods

This review was performed to summarize and describe the causes of vomiting in neonates. A systematic review was carried out on the PubMed database using: "Vomiting" [MESH] AND "newborn" [MESH], and "Vomiting" [MESH] AND "neonate" [MESH]. We used PubMed metadata to filter articles by publication date (2007-2022), language (English or Portuguese) and type of article (excluding case reports/images). This literature source retrieved 327 articles. After exclusion by title (articles focusing on gestation period and labour, on children and adolescents or where vomiting was not one of the main topics), 88 articles were screened for eligibility. A further 64 articles were excluded by abstract (case reports and studies not related to the neonatal period), leaving 24 articles that were fully assessed.

Type of vomiting

Vomiting can be classified according to its cause or its characteristics [1, 2]. We can classify vomiting as projectile or non-projectile. Projectile vomiting refers to forceful vomiting and is usually associated with pyloric stenosis or increased intracranial pressure [1, 2]. Vomit itself can also be classified based on its quality: bilious, bloody or non-bilious/non-bloody [2, 7]. The latter is characterized by yellow vomiting and often contains remnants of previously ingested food. Bilious vomiting is dark green and usually pathological [1, 2]. In this type of vomit, we must think of congenital gastrointestinal (GI) obstruction beyond the duodenal ampulla of Vater, where the common bile duct empties [2, 7]. The most common cause of bloody vomiting in neonates is swallowing of maternal blood during breastfeeding [2] but it can also be caused by swallowing of the neonate's own blood, for example during vigorous suctioning, after orotracheal tube insertion or after trauma during nasogastric tube insertion or nasal aspiration. Less common causes are Mallory-Weiss syndrome (neonates with GORD), treatment with corticosteroids and indomethacin and also haemorrhagic disease, which is rare if adequate vitamin K is administered. Bloody vomiting is brighter red in lesions more proximal in the GI tract, whereas darker red can indicate an old GI haemorrhage [1, 2].

Main causes of vomiting in neonates

The main causes of vomiting in neonates are listed in **Tab. 1**.

During the neonatal period, the most severe causes of bilious vomiting episodes are congenital obstructive intestinal malformations [1, 8], and therefore the presumptive diagnosis should always be GI obstruction. An observational study including 163 neonates with bilious vomiting found that 75 (46%) of these neonates had a surgical condition [8]. In these cases, vomiting is frequently associated with a distended and tender abdomen. Another study showed that among 391 neonates referred to the Paediatric Emergency Department with bilious vomiting, 113 (28.9%) had a surgical cause [9]. On the other hand, projectile non-bilious vomiting occurs when the obstruction level is high,

Table 1. Causes, pattern and type of vomiting in neonates (adapted from: Shields and Lightdale, 2018, and Chandran and Chitkara, 2008 [1, 2]).

Causes	Pathology	Pattern	Type of vomiting
Mechanical/obstruction causes	Congenital GI atresia/stenoses	Acute/chronic	Bilious/non-bilious
	Hypertrophic pyloric stenosis	Acute	Non-bilious
	Malrotation with volvulus	Cyclic	Bilious
	Hirschsprung's disease	Acute/chronic	Bilious/non-bilious
	Meconium ileus	Acute/chronic	Bilious
	Anorectal malformation	Acute/chronic	Bilious/non-bilious
Infectious causes	Necrotizing enterocolitis	Acute	Bilious/non-bilious
	Sepsis	Acute	Non-bilious
	Pyelonephritis	Acute	Non-bilious
	Pneumonia	Acute	Non-bilious
	Acute gastroenteritis	Acute	Non-bilious (may progress to bilious)
Metabolic/inborn errors of metabolism causes	Organic acidemias	Cyclic	Bilious/non-bilious
	Urea cycle disorders	Cyclic	Bilious/non-bilious
	Galactosaemia	Cyclic	Bilious/non-bilious
Central nervous system causes	Intracranial haemorrhage	Acute/chronic	Non-bilious
	Brain tumour	Acute/chronic	Non-bilious
	Meningitis	Acute/chronic	Non-bilious
	Hydrocephaly	Acute/chronic	Non-bilious
Other causes	Milk protein allergy/food protein-induced enterocolitis syndrome	Acute	Bilious/non-bilious (may have blood)
	Adrenal insufficiency	Cyclic/chronic	Non-bilious
	Hepatobiliary disease	Acute	Non-bilious
	Medical drug intoxication	Acute	Non-bilious

GI: gastrointestinal.

for example in vomiting associated with pyloric stenosis or duodenal obstruction [2].

In this section, we describe in detail some of the most frequent pathologies that involve the need for a quick diagnosis.

Obstructive causes

Duodenal atresia

Duodenal atresia occurs in about 1 in 10,000 neonates and represents more than 60% of intestinal atresias [10]. On antenatal ultrasound, the condition is related to polyhydramnios in about 50% of cases [11]. This pathology is associated with Down's syndrome in 30% of cases and with cardiac defects in 25% [11, 12].

Neonates with this condition present the typical signs of intestinal obstruction: vomiting, abdominal distension and absence of intestinal transit [2]. Vomit can be non-bilious or bilious, depending on whether the obstruction is proximal or distal to the insertion of the bile duct [2, 11]. In one-third of infants, the obstruction is proximal [11].

Diagnosis of duodenal atresia can be confirmed by performing an abdominal X-ray, which will demonstrate a typical double-bubble appearance [11, 12]. Any suspicion of this diagnosis mandates an operative intervention, ideally performed in the first few days of life [11, 12].

Hypertrophic pyloric stenosis

Hypertrophic pyloric stenosis occurs due to hypertrophy of the circular muscles of the pylorus, with obstruction of the lumen. It is the most common GI disease among infants, occurring as an isolated condition or with other congenital malformations [13]. It is more frequent at 3-6 weeks of life [2]. In this condition, vomiting is usually projectile and non-bilious and the baby is hungry after vomiting [13, 14]. The classic presentation is a small dehydrated infant with signs of poor weight progression, alkalosis and electrolyte changes

[2]. Furthermore, vomiting is not accompanied by diarrhoea or fever. Some known risk factors include a family history of hypertrophic pyloric stenosis, male gender, young maternal age, first pregnancy, maternal smoking and receiving erythromycin in the first 2 weeks of life [2, 13]. At the physical examination, an olive-like mass can be detected in the right upper abdomen, at the location corresponding to the pylorus. This mass is being reported less frequently because of earlier diagnosis by ultrasound. The treatment is generally surgical via laparoscopy (Ramstedt's pyloromyotomy) [2, 13, 14].

Intestinal malrotation

The incidence of intestinal malrotation in neonates is estimated at 1:6,000 live births and is the third most common cause of neonatal intestinal obstruction [11, 15]. It may occur as an isolated malrotation during fetal development or it may be associated with other congenital abnormalities [16]. The main concern of malrotation is that abnormal fixation of the midgut can result in torsion of the narrow mesentery and midgut volvulus, consequently threatening both the venous and later arterial flow to the intestine [11, 12]. Clinically, malrotation can vary from asymptomatic throughout the patient's life to intestinal and vascular obstruction symptoms or intestinal necrosis in the first days of life [11, 16]. The first manifestation is usually bilious vomiting accompanied by abdominal distension, and less frequently can occur with constipation and GI haemorrhage [12, 16].

Diagnosis should be suspected when an asymmetric gas pattern on abdominal X-ray is found and is confirmed by performing an upper GI contrast study [16]. If volvulus is present, this may show a "bird-beak" as a complete obstruction at the level of the proximal to mid-duodenum or a "cork-screw" when duodenojejunal flexure lies to the right (small bowel passes from posterior to anterior). When these findings are present, an immediate laparotomy is indicated due to the risk of volvulus [12, 16]. Mortality depends on the bowel and is approximately 3% [17].

Hirschsprung`s disease

Hirschsprung's disease is defined by aganglionosis in the intestinal nerve plexus, which causes overcontraction of the affected segment, resulting in intestinal obstruction and failure to pass meconium [18]. The estimated prevalence is 1:5,000 live births [18]. One must suspect this condition with a clinical scenario of bowel obstruction, delayed passage of meconium after 48 hours of birth, abdominal distension and bilious vomiting, which improves with rectal examination or rectal washout [14, 18]. The lack of ganglion cells in submucosal and myenteric plexus in histopathology confirms the diagnosis [11, 15]. Subsequent treatment consists of continued rectal decompression with washouts, followed by early neonatal surgical correction [11].

Meconium ileus

Meconium ileus is the accumulation of viscous intestinal content and a thick mucous secretion that adheres to the crypts of the terminal ileum and caecum, causing a luminal obstruction [11, 16]. This condition is one of the most common causes of neonatal intestinal obstruction (9-33%) [16] and has been associated with intestinal atresia (20-30%) [11]. It is usually associated with cystic fibrosis, being the first manifestation of this disease in 15% of neonates [11, 16]. The presentation is with abdominal distention, failure to pass meconium and vomiting. Abdominal X-ray may suggest the diagnosis if dilated bowel loops proximal to the impaction are present, classically with a "bubbly" appearance of the distended intestinal loops. A contrast enema may be undertaken to relieve the obstruction. If decompression is not successful or if intestinal atresia is present, resection and anastomosis or temporary stoma formation will be required [11].

Anorectal malformation

If not noted, an anorectal malformation can lead to bilious vomiting and abdominal distension. Inspection of the anus is part of the routine examination of any newborn and should not be missed, as delay in surgical correction can lead to intestinal perforation. Surgical correction by angioplasty or diverting colostomy may be performed in the first 24-48 hours [11].

Infectious causes

Other causes of vomiting in neonates are digestive or extra-digestive infectious diseases [1, 2]. Vomiting is a non-specific symptom, and in a neonate with no other complaints we should think

of infection: pyelonephritis, sepsis, meningitis, pneumonia or gastroenteritis [2].

Necrotizing enterocolitis

Necrotizing enterocolitis affects 5-12% of neonates with very low weight at birth, being the main cause of death due to GI disease, mainly if associated with prematurity [19]. The signs can be insidious: at first, they include feeding intolerance and irritability, but quickly progress to bilious vomiting and abdominal distension, with pneumatosis intestinalis and/or portal venous gas detected by X-ray/ultrasonography [11, 19]. Treatment during the early stages includes bowel rest, fluid therapy and broad-spectrum antibiotics. Surgery is required if intestinal perforation occurs and the mortality rates are estimated to be 20-30%. Some observational studies report that probiotics may reduce both the incidence and mortality [19]. An exclusive human milk diet has also proved to be protective of the occurrence of necrotizing enterocolitis [20].

Inborn errors of metabolism causes

Inborn errors of metabolism, such as organic acidaemias, urea cycle defects and defects with carbohydrate metabolism, should be considered for neonates with progressive vomiting [1, 2]. After exclusion of the most frequent aetiologies, a metabolic disease should be suspected if there is continued vomiting, neurological symptoms and growth or developmental delay [1, 2]. In these cases, we should inquire about newborn screening test results, history of consanguinity or sudden infant death, feeding difficulties, weight loss associated with dietary intake or episodes with alterations in consciousness [21]. In the physical examination, attention must be paid to hypotonia, dehydration with tachycardia, poor perfusion or hypotension, which should be treated aggressively [21].

Central nervous system causes

Increased intracranial pressure

A less common cause of chronic vomiting is increased intracranial pressure, which can occur by mass effect (e.g. intracranial haemorrhage, brain tumour) or pseudotumour cerebri [1, 2].

For intracranial haemorrhage, the most common clinical features in newborns are anaemia, hypotension and shock, followed by neurological symptoms (seizure, apnoea, lethargy) with or without nausea and vomiting [22]. Vomiting with positional changes or waking from sleep to vomit are warning signs for these conditions. Findings of the Cushing's triad (bradycardia, hypertension and irregular breathing) should induce urgent evaluation for increased intracranial pressure [1].

Other causes

Milk protein allergy/food protein-induced enterocolitis syndrome

Milk protein allergy typically presents in infants after exposure to the allergen, usually proteins included in formula milk [1, 23]. Symptoms develop within 2 hours after exposure and the most frequent clinical signs are vomiting, urticaria, angioedema, lethargy or respiratory symptoms. When a non-immunoglobulin E-mediated type of food hypersensitivity is the case, the pattern can be different: food protein-induced enterocolitis syndrome. The signs occur 2-6 hours after intake and the most common are irritability, feeding intolerance, intermittent vomiting and diarrhoea. Occasionally, patients may present with compromise in weight progression or iron deficiency anaemia, and examination of stools reveals occult blood with polymorphonuclear cells, lymphocytes and eosinophils [1, 2, 23].

Treatment involves removal of the allergen from the diet, replacing protein milk with hydrolysed formula or L-amino-acid-based formulas. The symptoms usually resolve in 3-10 days [2].

Adrenal insufficiency

Adrenal insufficiency can result from adrenal destruction (primary adrenal insufficiency or deficiency) or can be due to hormone deficiency that leads to the impaired synthesis and release of adrenocorticotrophic hormone from the pituitary gland or of corticotrophin-releasing hormone from the hypothalamus [24]. Congenital hyperplasia of the adrenal gland due to deficiency of the enzyme 21-hydroxylase is the most common cause of adrenal insufficiency [1]. It is an autosomal recessive disorder involving deficiencies in enzymes for the synthesis of cortisol, aldosterone or both [24]. The phenotype depends on the type and severity of the enzyme defect. Patients often present with chronic vomiting, refusal to eat, dehydration, poor weight progression and

also, on physical examination, signs of virilization of the female genitals and skin hyperpigmentation may be observed [1, 24]. Blood results may depict hyponatraemia and hyperkalaemia [1]. The diagnosis is established using measurements of cortisol and aldosterone [24]. Treatment comprises correction of dehydration and initiation of glucocorticoids and then mineralocorticoids [24].

Conclusion

Vomiting is a common but non-specific clinical entity in neonates that may involve a variety of different organ systems and, in some cases, finding the aetiology can be challenging.

It is important to differentiate between vomiting and GORD to guide the treatment and management. Most cases of GORD can be treated conservatively with body positioning and avoidance of overfeeding.

The evaluation of vomiting should be targeted to the medical history, type of vomit and physical examination findings, especially abdominal examination and evaluation of weight loss. Acid-base fluid and electrolyte imbalances must always be considered when assessing a neonate who has a history of vomiting.

Congenital or acquired intestinal obstructive syndromes are the most common and serious causes of vomiting in neonates and need emergency treatment. Serious extra-intestinal causes of vomiting include brain tumours, meningitis and inborn errors of metabolism.

It is important to recognize red flags for urgent evaluation of vomiting, including nocturnal vomiting that awakens the patient, weight loss, haematemesis (especially in the first episode of vomiting), recurrent bilious emesis, abdominal distention, absent tympanic bowel sounds and mental status changes.

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References

1. Shields TM, Lightdale JR. Vomiting in Children. Pediatr Rev. 2018;39(7):342-58.
2. Chandran L, Chitkara M. Vomiting in children: reassurance, red flag, or referral? Pediatr Rev. 2008;29(6):183-92.
3. Mousa H, Hassan M. Gastroesophageal Reflux Disease. Pediatr Clin North Am. 2017;64(3):487-505.
4. Rosen R, Vandenplas Y, Singendonk M, Cabana M, DiLorenzo C, Gottrand F, Gupta S, Langendam M, Staiano A, Thapar N, Tipnis N, Tabbers M. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2018;66(3):516-54.
5. Sanchez JB, Jadcherla SR. Gastroesophageal Reflux Disease in Neonates: Facts and Figures. Neoreviews. 2021;22(2):e104-17.
6. Chabra S, Peeples ES. Assessment and Management of Gastroesophageal Reflux in The Newborn. Pediatr Ann. 2020;49(2):e77-81.
7. Parashette KR, Croffie J. Vomiting. Pediatr Rev. 2013;34(7):307-21.
8. Mohinuddin S, Sakhuja P, Bermundo B, Ratnavel N, Kempley S, Ward HC, Sinha A. Outcomes of full-term infants with bilious vomiting: observational study of a retrieved cohort. Arch Dis Child. 2015;100(1):14-7.
9. Nundeekasen S, Dalrymple H, Moustafa A, Thomas G, Carmo KB. How should the neonatal retrieval team respond to the neonate referred with bilious vomiting? J Paediatr Child Health. 2022;58(5):774-81.
10. Best KE, Tennant PW, Addor MC, Bianchi F, Boyd P, Calzolari E, Dias CM, Doray B, Draper E, Garne E, Gatt M, Greenlees R, Haeusler M, Khoshnood B, McDonnell B, Mullaney C, Nelen V, Randrianaivo H, Rissmann A, Salvador J, Tucker D, Wellesly D, Rankin J. Epidemiology of small intestinal atresia in Europe: a register-based study. Arch Dis Child Fetal Neonatal Ed. 2012;97:F353-8.
11. Burge DM. The management of bilious vomiting in the neonate. Early Hum Dev. 2016;102:41-5.
12. Adams SD, Stanton MP. Malrotation and intestinal atresias. Early Hum Dev. 2014;90(12):921-5.
13. Galea R, Said E. Infantile Hypertrophic Pyloric Stenosis: An Epidemiological Review. Neonatal Netw. 2018;37(4):197-204.
14. Peters B, Oomen MW, Bakx R, Benninga MA. Advances in infantile hypertrophic pyloric stenosis. Expert Rev Gastroenterol Hepatol. 2014;8(5):533-41.
15. Verma A, Nain Rattan K, Yadav R. Neonatal intestinal obstruction: a 15-year experience in a tertiary care hospital. J Clin Diagn Res. 2016;10(2):SC10-13.
16. Vargas MG, Miguel-Sardaneta ML, Rosas-Téllez M, Pereira-Reyes D, Justo-Janeiro JM. Neonatal Intestinal Obstruction Syndrome. Pediatr Ann. 2018;47(5):e220-5.
17. Gohary Y, Alagtal M, Gillick J. Long-term complications following operative intervention for intestinal malrotation: a 10-year review. Pediatr Surg Int. 2010;26:203-6.
18. Duess JW, Hofmann AD, Puri P. Prevalence of Hirschsprung's disease in premature infants: a systematic review. Pediatr Surg Int. 2014;30(8):791-5.
19. Meister AL, Doheny KK, Travagli RA. Necrotizing enterocolitis: It's not all in the gut. Exp Biol Med (Maywood). 2020;245(2):85-95.

20. Altobelli E, Angeletti PM, Verrotti A, Petrocelli R. The Impact of Human Milk on Necrotizing Enterocolitis: A Systematic Review and Meta-Analysis. Nutrients. 2020;12(5):1322.
21. Kwon KT, Tsai VW. Metabolic emergencies. Emerg Med Clin North Am. 2007;25(4):1041-60.
22. Tabibian S, Motlagh H, Naderi M, Dorgalaleh A. Intracranial hemorrhage in congenital bleeding disorders. Blood Coagul Fibrinolysis. 2018;29(1):1-11.
23. Munblit D, Perkin MR, Palmer DJ, Allen KJ, Boyle RJ. Assessment of Evidence About Common Infant Symptoms and Cow's Milk Allergy. JAMA Pediatr. 2020;174(6): 599-608.
24. Patti G, Guzzeti C, Di Iorgi N, Allegri AEM, Napoli F, Loche S, Maghnie M. Central adrenal insufficiency in children and adolescents. Best Pract Res Clin Endocrinol Metab. 2018;32(4):425-44.