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Optimization of Diagnosis and Treatment Strategies for Vomiting Syndrome in Infants

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Abstract
The aim of this study is to analyze current approaches to the diagnosis and management of gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD) in infants during the first year of life. The paper presents data from Russian and international studies addressing the prevalence and structure of risk factors, including perinatal pathology, intrauterine infections, and birth trauma as contributors to gastrointestinal dysfunction. Particular attention is given to the clinical features of congenital hypertrophic pyloric stenosis, persistent regurgitation syndrome, and their differentiation from other congenital or functional gastrointestinal disorders. Diagnostic modalities discussed include esophagogastroduodenoscopy, radiological imaging, 24-hour pH monitoring, scintigraphy, and esophageal manometry. The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN, 2005) guidelines are reviewed, emphasizing a stepwise treatment strategy: parental counseling and psychological support, postural therapy, and dietary interventions with specialized anti-reflux formulas. In cases of treatment resistance, pharmacological therapy with prokinetics or acid-suppressive drugs is recommended, while surgical correction using fundoplication remains the method of choice in severe and complicated cases. The paper highlights findings from clinical trials indicating that GERD symptoms may resolve, but histological esophagitis often persists, increasing the risk of complications such as strictures, Barrett's esophagus, and even adenocarcinoma. The conclusion stresses the importance of raising awareness among primary care pediatricians, ensuring timely diagnosis, implementing international treatment standards, and providing long-term follow-up for infants at risk of complicated GERD.
Key words: vomiting syndrome; gastroesophageal reflux (GER); gastroesophageal reflux disease (GERD); pyloric stenosis; pylorospasm; functional gastrointestinal disorders; dietary therapy; anti-reflux formulas; diagnostics; infant treatment.

Chaqaloqlarda qusish sindromini tashxislash va davolash taktikasini optimallashtirish

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Annotatsiya
Ushbu tadqiqotning maqsadi chaqaloqlarda hayotning birinchi yilida gastroezofageal reflyuks (GER) va gastroezofageal reflyuks kasalligi (GERK)ni tashxislash va davolashning zamonaviy yondashuvlarini tahlil qilishdan iborat. Ishda perinatal patologiya, homiladorlik davridagi infeksiyalar va tug‘ruq jarohatlari kabi xavf omillari, ularning ovqat hazm qilish tizimi buzilishlarida tutgan o‘rni haqidagi mahalliy va xorijiy tadqiqotlar natijalari yoritilgan. Tug‘ma pilorostenoz, qaytalanuvchi qusish sindromi va ularni boshqa tug‘ma hamda funksional kasalliklardan differensial tashxislash masalalari batafsil ko‘rib chiqilgan. Diagnostika usullari qatoriga ezofagogastroduodenoskopiya, rentgenologik tekshiruv, 24 soatlik pH-monitoring,

scintigrafiya va qizilo‘ngach manometriyasi kiradi. Evropa bolalar gastroenterologiyasi, gepatologiyasi va ovqatlanish jamiyatining (ESPGHAN, 2005) tavsiyalari bosqichma-bosqich davolashni o‘z ichiga oladi: ota-onalarga maslahat berish va psixologik qo‘llab-quvvatlash, postural terapiya, maxsus antireflyuks aralashmalardan foydalanish. Agar davolash samara bermasa, prokinetik va sekresiyani kamaytiruvchi dorilar qo‘llanadi, og‘ir hollarda esa fundoplikatsiya usuli bilan jarrohlik muolajasi tavsiya qilinadi. Klinik tadqiqotlar shuni ko‘rsatadiki, GERK simptomlari yo‘qolishi mumkin, ammo qizilo‘ngachning shikastlanishi uzoq vaqt davom etib, striktura, Barrett qizilo‘ngachi va hatto adenokarsinoma kabi og‘ir asoratlarni keltirib chiqaradi. Xulosa sifatida, pediatrlarning, ayniqsa birlamchi bo‘g‘indagilarning, ushbu patologiyaga nisbatan hushyorligini oshirish, zamonaviy diagnostika usullarini keng joriy qilish va xavf guruhi chaqaloqlarini uzoq muddat kuzatib borish zarurligi ta’kidlanadi.

Kalit so‘zlar: qusish sindromi; gastroezofageal reflyuks (GER); gastroezofageal reflyuks kasalligi (GERK); pilorostenoz; pilorospazm; funksional ovqat hazm qilish buzilishlari; parhez terapiyasi; antireflyuks aralashmalari; tashxis; chaqaloqlarni davolash.

Оптимизация диагностики и тактики лечения синдрома рвоты у младенцев

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Аннотация
Целью исследования является анализ современных подходов к диагностике и лечению гастроэзофагеального рефлюкса (ГЭР) и гастроэзофагеальной рефлюксной болезни (ГЭРБ) у детей первого года жизни. В работе представлены данные отечественных и зарубежных исследований, посвящённых частоте и структуре факторов риска, роли перинатальной патологии, внутриутробных инфекций и родовых травм в формировании нарушений пищеварительного тракта. Рассмотрены особенности течения врождённого пилоростеноза, синдрома упорных срыгиваний и их дифференциальная диагностика с другими врождёнными и функциональными заболеваниями желудочно-кишечного тракта. Подробно освещены методы обследования, включая эзофагогастродуоденоскопию, рентгенологическое исследование, pH-метрию, сцинтиграфию и манометрию нижнего пищеводного сфинктера. Представлены современные рекомендации Европейского общества детской гастроэнтерологии, гепатологии и питания (ESPGHAN, 2005), предусматривающие поэтапный подход к лечению срыгиваний, начиная с психологической поддержки родителей, постуральной терапии и диетических мер с использованием специализированных антирефлюксных смесей. При отсутствии положительного эффекта показано применение прокинетиков, антисекреторных препаратов и, в тяжёлых случаях, хирургической коррекции методом фундопликации. Особое внимание уделено результатам клинических исследований, указывающих на необходимость длительного наблюдения за детьми с ранними проявлениями ГЭРБ в связи с риском формирования осложнений, таких как эзофагит, стриктуры пищевода и пищевод Барретта. Делается вывод о необходимости повышения настороженности врачей первичного звена в отношении данной патологии, широкого внедрения современных диагностических методик и международных стандартов лечения.
Ключевые слова: синдром рвоты; гастроэзофагеальный рефлюкс (ГЭР); гастроэзофагеальная рефлюксная болезнь (ГЭРБ); пилоростеноз; пилороспазм; функциональные нарушения ЖКТ; диетотерапия; антирефлюксные смеси; диагностика; лечение младенцев.

Digestive tract disorders in infants are predominantly functional in nature and mainly result from immaturity of motor and secretory functions. Motor dysfunctions include physiological gastroesophageal reflux (GER), impaired gastric accommodation and antropyloric motility, and

intestinal dyskinesia. Secretory immaturity is characterized by variable gastric, pancreatic, and intestinal lipase activity, low pepsin activity, and insufficient disaccharidase activity, particularly lactase [1]. These factors lead to regurgitation, colic, meteorism, and dyspepsia, which are not associated with organic pathology and usually do not affect overall health.

The primary mechanisms of regurgitation involve immaturity of the esophageal and gastric sphincter apparatus, insufficient lower esophageal sphincter (LES) tone, delayed gastric emptying, and transient LES relaxations triggered by weak swallowing or gastric distension. Pathological GER is promoted by short and immature LES, reduced esophageal clearance, and increased intra-abdominal or intragastric pressure. GER often worsens in the upright position. Functional maturation of the LES explains the typically benign course of GER in infancy.

Risk groups include preterm and morpho-functionally immature infants, those deprived of early breastfeeding, and those receiving total parenteral nutrition. Epidemiological data show that over 65% of infants under four months regurgitate daily, though fewer than 20% of parents find this concerning. Prevalence varies by country (15% in France, 22% in the USA, ~40% of pediatric consultations in Australia). Most cases resolve spontaneously by 12–18 months, though early treatment may accelerate improvement.

A large Italian prospective study (>2800 infants under six months) reported functional GI symptoms in over 50% of children: regurgitation (>20%), colic (~20%), constipation (>15%), vomiting (6%), and diarrhea (4%). Low birth weight and short gestation were significant risk factors. Poor growth occurred in ~15% of affected infants.

Additional risks include intrauterine hypoxia, intrapartum asphyxia, postnatal hypoxia, CNS damage, and severe infections. These conditions may exacerbate functional GI disorders but tend to diminish with growth and maturation. However, congenital malformations, perinatal pathology, and hereditary GI diseases may require specific therapeutic or surgical interventions.

Privorotsky V.F. identified unfavorable early-life factors in children with GERD, including perinatal pathology in more than 71% of cases, burdened allergic history in less than 50%, and early artificial feeding in over 36% of patients [2].

Sadowska–Krawczenko I. et al. studied the relationship between the frequency of GER in preterm newborns (more than 100 infants with gestational age <40 weeks) and intrauterine infection, intrauterine growth restriction (IUGR), pneumonia, respiratory distress syndrome, and intraventricular hemorrhage. According to 24-hour pH monitoring performed in all infants, acid GER was detected in more than 22% of cases (about 27 patients). Nearly 50% of these infants had IUGR, while among those without IUGR, GER was identified in only >16% of cases [5].

These researchers also investigated the effect of antenatal corticosteroid therapy on GER frequency in 96 preterm newborns (gestational age >35 weeks). Among 20 infants whose mothers received antenatal corticosteroids, acid GER occurred in ~40% (8 of 20). In the group of 76 infants without antenatal corticosteroid exposure, GER was detected in over 16% (13 of 76) [6].

Birth trauma of the nervous system may cause persistent regurgitation and vomiting, making timely diagnosis and treatment of CNS damage critical. Despite advances in obstetrics, the frequency of such pathology remains high—between 10–22%, accounting for more than 10% of perinatal mortality. Spinal cord injuries at birth occur in 10–30% of all deaths related to spinal injury. Most frequently (>56%), patients present with signs of vertebral, vertebral artery, and spinal cord injury, while <40% have combined spinal and brain lesions. Cervical injuries are the most common (up to 84.8%), due to the significant mechanical load borne by the cervical spine even during normal delivery. Predisposing factors include premature rupture of membranes, precipitous labor, weak uterine contractions, breech presentation, macrosomia, and others. Clinical findings in such infants may include torticollis, the characteristic “short neck” symptom with transverse folds, and tension of the cervico-occipital muscles. Involvement of the vertebral arteries in cervical dislocation often leads to vascular spasm, cerebral circulatory disturbances, and hypoxia. Radiographic vertebral displacement is detected in ~20% of neonates with birth trauma (Mikhailov M.K., 1983). In >10% of children with cervical spine injury, atlantoaxial subluxation is revealed, particularly in the Cruveilhier joint. Displacements of C1 relative to C2 may be sagittal or rotational.

However, radiological assessment of the atlantoaxial joint in lateral view is recommended only after ossification centers of the anterior arch of the atlas appear (around day 60–120 of life) [7].

Persistent regurgitation and vomiting resistant to dietary therapy require differential diagnosis with congenital GI malformations, primary neuronal disorders of the enteric nervous system (achalasia, congenital esophageal stenosis, congenital pyloric stenosis [CPS], intestinal pseudo-obstruction), myopathies, and allergic or infectious-inflammatory GI diseases. Among congenital anomalies, CPS is relatively common, ranking after musculoskeletal and cardiovascular malformations [8].

The population frequency of CPS is ~5 per 1000 live births, with a male-to-female ratio of 5:1. Timely diagnosis is crucial, as CPS carries risks of aspiration pneumonia, progressive malnutrition, enterocolitis, electrolyte imbalance, and other complications associated with early-life intestinal obstruction.

At the Samarkand State Medical University, a comprehensive study of ~140 patients with CPS admitted to the Bishkek City Children's Emergency Hospital between 1987 and 2002 was conducted. The majority of patients (>81%) were admitted at 2–4 months of age, while <6% were neonates. Projectile vomiting of gastric contents without bile was the main symptom in all patients. In more than 71% of cases, vomiting appeared between 14–28 days of life, and in <6% during the first days after birth. During the first week, infants exhibited persistent regurgitation and periodic vomiting of curdled milk without bile. With disease progression and gastric dilation, projectile vomiting occurred between 14–28 days, with vomitus volume exceeding single feed volume. The frequency reached up to 5 episodes/day, fewer than the number of daily feedings.

Prolonged vomiting led to weight loss and progressive malnutrition: upon admission, >30% had grade II hypotrophy and >52% grade III. In ~83% of patients, projectile vomiting persisted for 14–50 days before hospitalization, resulting in dehydration and, in some cases, metabolic alkalosis.

As the disease progresses, **more than 87% of children demonstrate reduced urination frequency (2–6 times per day vs. the normal 15–30 times),** which serves as a valuable diagnostic indicator. All patients show decreased daily urine output; in over 11% of cases, diuresis does not exceed 15–30 ml compared to the normal 600–700 ml/day. **Bowel function is also impaired:** more than 40% of infants with congenital pyloric stenosis (CPS) pass stool only once every 4–8 days, more than 22% once daily, and about 35% have 1–2 small bowel movements per day. On clinical examination, a thickened pylorus could be palpated in more than 32% of children, confirming the diagnosis of CPS. This finding indirectly highlights insufficient or inattentive examination by community pediatricians at home.

In cases of persistent regurgitation, evaluation begins with **upper gastrointestinal endoscopy (esophagogastroduodenoscopy, EGD)**, which in most cases establishes the diagnosis. Endoscopic findings in CPS include a dilated stomach with pronounced mucosal folds in the antral region and varying degrees of pyloric canal stenosis, which fails to open during air insufflation [8]. Radiographic evaluation in an upright position reveals a markedly enlarged stomach, often extending to the level of the pelvis or below the umbilicus. Contrast studies with barium suspension demonstrate delayed gastric emptying up to 6 hours post-ingestion [10].

Differential diagnosis between CPS and pylorospasm can be challenging. Pathognomonic criteria include the character and volume of vomiting, urination frequency, presence of constipation, and visible gastric peristalsis. The diagnosis is confirmed based on EGD or barium contrast radiography. In pylorospasm, gastric emptying delay may last up to 8 hours, while in pyloric stenosis, it extends up to 24 hours.

According to **ESPGHAN guidelines (2005), treatment of regurgitation is structured in several stages.**

1. **First stage:** Parental counseling and psychological support.
2. **Second stage:** Postural therapy — the mother feeds the infant in a semi-upright position (45–60°), holding the baby for at least 20–30 minutes afterward, both day and night.
3. **Third stage:** Adequate dietary therapy.
    - In **breastfed infants**, efforts focus on a calm environment for the mother, normalization of feeding regimen, avoiding overfeeding and aerophagia. Breast milk

thickeners may be used (e.g., *HiPP Organic Rice Cereal*, Austria). Infants older than 60–120 days can receive one teaspoon of rice porridge before each feeding.

- In **formula-fed infants**, careful attention must be paid to feeding regimen, adequacy of formula type, and volume corresponding to the child's age and body weight. Dietary therapy is initiated with **casein-predominant formulas** (*Malyutka Plus*, Nutricia; *Similac*, Abbott Laboratories; *Enfamil AR*, Mead Johnson). Casein slows gastric emptying and reduces GER frequency compared to whey hydrolysates, as confirmed by scintigraphy [12].

If no improvement is observed, **specialized anti-reflux (AR) formulas** are prescribed. Their viscosity is increased with thickeners such as locust bean gum, rice, or corn starch.

- Gum-containing AR formulas: *Nutrilon AR* (Nutricia), *Humana AR* (Humana GmbH), *Frisovom* (Friesland), *Nutrilak AR* (Nutritek).
- Starch-based AR formulas: *Enfamil AR* (Mead Johnson), *Semper Lemolac*.

An example is *Nutrilon AR*, which contains predominantly casein (casein:whey ratio 80:20), reduced fat content (3.1 g/100 ml) to accelerate gastric emptying, β-palmitic acid, and 0.4 g/100 ml gum, which does not cause diarrhea [11,13].

It is recommended that these formulas completely replace the previously used milk formula, with long-term use indicated in order to achieve a stable therapeutic effect. In cases of moderately severe regurgitation, particularly when accompanied by colic and flatulence, the use of preventive formulas for infants with minimal functional gastrointestinal disturbances is advisable: *Nutrilon Comfort* (containing potato starch and a GOS+FOS prebiotic blend); *Gallia Digest Premium* (containing a mixture of potato and corn starch, as well as GOS) [14]. However, the effect of thickened formulas in gastroesophageal reflux (GER) with increased gastric acidity is inconsistent, as confirmed by pH monitoring and scintigraphy. The number of reflux episodes may either increase or decrease, and esophageal acidity varies with the infant's body position. The duration of prolonged refluxes remains unchanged or may even increase significantly. These findings are consistent with observations that increasing the volume and osmolarity of feeds raises the frequency of transient lower esophageal sphincter relaxations and produces fluctuations in lower esophageal sphincter pressure, often to nearly undetectable levels [15]. A worsening cough may also be observed when formulas containing thickeners are used.

If dietary therapy proves ineffective, subsequent stages of regurgitation management should include pharmacological treatment with prokinetics, H_2-histamine receptor blockers, and proton pump inhibitors (although not all of these drug classes are registered for neonatal use in Russia).

A particularly interesting and innovative study by World Medical Association investigated the course of gastroesophageal reflux disease (GERD) in infants during their first year of life. The study included 19 infants who, after two weeks of ineffective postural therapy and feeding adjustments, were divided into two groups. The "placebo" group consisted of 10 infants who received no drug therapy, while the second group (9 infants) was treated with secretion inhibitors and prokinetics. In the placebo group, the dynamics of the clinical picture were assessed using the *Infant Gastroesophageal Reflux Questionnaire* (IGERQ), as well as morphological changes in esophageal mucosa based on biopsy samples obtained at 2, 4, 6, and 12 months. In the absence of pharmacological treatment, esophagitis persisted, and morphological normalization of the esophageal mucosa did not occur during the first year of life, despite the disappearance of GER symptoms [16,17]. The lack of improvement in tissue morphology corresponding to clinical remission raises the issue of subclinical persistence of esophageal damage, which in the long term may predispose to serious GERD complications such as strictures, Barrett's esophagus, and/or esophageal adenocarcinoma.

The lifelong complications of GERD demand close scientific attention. This includes population-based epidemiological studies, the identification of high-risk groups (with onset in early childhood), and long-term studies of family cohorts with documented infantile GERD [19]. GERD should be suspected when reflux manifests as regurgitation and vomiting unresponsive to trial therapy, or when accompanied by complex clinical features suggesting complicated GER.

Clinical symptoms of complicated GER requiring urgent intervention include hematemesis, growth retardation, and persistent extra-esophageal manifestations (crying, cough, hoarseness, laryngospasm, recurrent otitis media, otalgia, rhinitis; vocal fold ulcers, granulomas, and polyps; subglottic laryngeal stenosis; bronchial obstruction; sleep disturbances, etc.). It should also be noted that esophageal motility disorders seen in children with esophagitis (not secondary to other diseases) resolve after the esophagitis has healed. This supports the view that GER, in such cases, represents an independent disease [20,21].

Diagnostic methods for suspected pediatric GERD include esophagogastroduodenoscopy (EGD) with biopsy of the esophageal and gastric mucosa, X-ray fluoroscopy, radioisotope assessment of gastric emptying, radioisotope diagnosis of esophageal metaplasia (when indicated), lower esophageal sphincter manometry, and 24-hour pH monitoring of the esophagus and stomach.

Currently, laparoscopic fundoplication is considered the primary surgical method for correcting pathological GER in children. Indications for surgery include persistent vomiting, malnutrition, growth retardation, respiratory disorders, hiatal hernia, peptic esophageal stricture, Barrett's esophagus, and reflux esophagitis resistant to medical therapy. Each year, the thoracic surgery department of Specialized Pediatric Surgery Clinic of SamSMU evaluates and treats 60–70 children with GER. From 1991 to 2005, more than 700 fundoplications were performed.

Despite the complex and diverse pathologies often masked as functional gastrointestinal disorders, pediatricians' attitudes toward GER and GERD development in infants remain relatively superficial. An analysis of the frequency of specialized formula use in infants during their first year of life, based on medical records and parental reports, showed that pediatricians prescribed formulas containing thickeners four times less often than parents themselves (0.7% vs 2.8%, respectively) [18]. These figures are inconsistent with the previously noted high prevalence of functional gastrointestinal disorders in infants, which clearly warrant dietary and pharmacological therapy.

The aim of our publication is to draw pediatricians'—particularly those in primary care—attention to the problem of GER and GERD development in infants, to encourage broader implementation of ESPGHAN recommendations on regurgitation therapy, and to promote the use of modern diagnostic methods available for evaluating children with this condition [22].

Conclusion. Functional gastrointestinal disorders in infants, such as regurgitation and vomiting, mainly reflect immaturity of motor and secretory functions. While often self-limiting, they may also signal congenital malformations, perinatal pathology, or neurological injury, requiring timely differentiation. Gastroesophageal reflux (GER) is common and generally benign, but a subset of infants develop pathological GERD, associated with prematurity, intrauterine growth restriction, or birth trauma. Accurate diagnosis is essential to prevent complications like malnutrition, dehydration, and aspiration. Modern tools—endoscopy, pH monitoring, radiographic studies, and manometry—help distinguish physiological reflux from organic disease.

Management should follow a stepwise approach: parental counseling, postural therapy, dietary adjustments with anti-reflux formulas, pharmacological treatment when indicated, and surgical intervention in refractory cases. Greater adherence to ESPGHAN recommendations and early recognition by pediatricians can improve outcomes, reduce complications, and support normal growth and development in infants with regurgitation and vomiting.

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