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Surgical treatment of gastroesophageal reflux disease in children with neurological disorders accompanied by impaired swallowing

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The article is dedicated to the issue of gastroesophageal reflux treatment in infants with neurological disorders, which remains insufficiently studied and unsettled. Bronchopulmonary complications in patients with gastroesophageal reflux are life-threatening, cause frequent aspiration pneumoniae and spontaneous apneas; therefore, operative correction is required in critical situations. The article presents results of operative treatment of 22 patients with different nervous system pathologies accompanied by gastroesophageal reflux disease. The authors have developed practical recommendations on the selection of surgical treatment tactics. The control group consisted of 10 infants and preschoolers with gastroesophageal reflux disease and central nervous system lesion, whose parents refused operative treatment for various reasons.
***Keywords**: pediatrics, pediatric surgery, gastroesophageal reflux disease, cerebral palsy, pseudobulbar syndrome, bulbar syndrome, gastrostomy, Nissen fundoplication.*

INTRODUCTION

Numerous publications in recent years [1-4] indicate a considerable increase in the rate of gastroesophageal reflux disease (GERD) all over the world. The modern trials proved that children with GERD considerably more often develop sinusitis, laryngitis, otitis, bronchial asthma, recurrent pneumonia, bronchiectases, tooth enamel damage and, in infancy, apnea [1, 5-7]. The best studied and proven is the association of GERD with bronchial asthma; according to different authors, its rate in children varies across a wide range – from 9 to 80% [6, 8].
The main cause of sever GERD is disturbed innervation of the upper gastrointestinal tract's segments. This pathology is very often revealed at different nervous system diseases accompanied by deglutitive problem, such as severe perinatal central nervous system lesions with the formation of cerebral palsy and hydrocephaly, and at Parkinson's disease, post-polio syndrome, disseminated sclerosis, Guillain–Barré syndrome, space-occupying cerebral lesions etc. [1, 8-10] due to the unity of innervation of muscles of soft palate, pharynx, epiglottis, esophagus with vagus nerve, topographical proximity of vagus and glossopharyngeal nerves' nuclei [11]. Combined lesion of pathways and/or nuclei and trunks of these cranial nerves results in the formation of pseudobulbar or bulbar palsy of pharyngeal muscles depending on the type of neurologic pathology. Therefore, it becomes difficult to swallow bolus and saliva; they stagnate and ballot in oropharynx; it causes esophagus-to-stomach passage disorder. Partial reflux to the upper respiratory tract causes chronic respiratory infections. Morphofunctional immaturity of the vegetative nervous system observed in children with perinatal brain damage of different genesis also aggravates GERD course. All these factors may considerably aggravate the patients' condition.
Anti-reflux therapy for patients with GERD is symptomatic; it is primarily aimed at improving quality of life. The patients are virtually doomed to lifelong intake of anti-reflux drugs. According to foreign trials, relapse of disease symptoms is diagnosed 6 months after the end of the anti-reflux therapy in 50% of patients, after 12 months – in 87-90% [2, 12].
Indications to surgical treatment of gastroesophageal reflux are:

1) Recurrent character of the disease, persistent vomiting;

2) Inefficacy of the conducted drug therapy (more than 2 weeks);
3) No possibility of feeding children due to the altered innervation of palate or upper gastrointestinal tract's segments (bulbar/pseudobulbar palsy);
4) GERD complications (stenosing reflux-esophagitis, Barrett's esophagus);
5) Respiratory complications (recurrent aspiration pneumonia, bronchial asthma, bronchitis) [3, 4].

Various techniques of GERD operative treatment may be employed: Toupet operation (wrapping of the anterior wall of stomach around esophagus by 270^{o}) or Thal operation (wrapping of the anterior wall of stomach around the cardioesophageal sphincter by 180^{o}). The most frequent anti-reflux operation is Nissen fundoplication. This is the most frequently used method at gastroesophageal reflux in children with neurologic pathology; this allows recovering anti-reflux barrier as completely as possible in order to prevent further aspiration pneumonias [4, 13, 16].

There have been no trials on the operative treatment technique selection tactics for children with GERD and neurologic pathology in Russian medical literature.

The aim of this study is to develop an operative treatment algorithm for children with GERD and neurologic pathology.

PATIENTS AND METHODS

The trial involved 32 children from 2 months to 6 years of age with severe central nervous system (CNS) lesions combined with GERD. Before admission to the surgical department, all children had been treated at the childhood pathology department or the neuropsychiatry and psychosomatic pathology department of the FSBI "SCCH" in 2008-2012. The group under study consisted of 22 children (average age – 4±3 years), who received an operation; the control group consisted of 10 children comparable in age and sex, whose parents refused operative treatment for various reasons (tb. 1).

Table 1. Age and sex spread of the examined patients

Age groups	**Group under study, n=22 (%)**		**Control group, n=10 (%)**	
	Girls	Boys	Girls	Boys
Infancy (from 29 days to 12 months of age)	6 (35.3)		3 (30)	
	5	1	0	3
Babyhood (1-3 years of age)	7 (32)		2 (20)	
	4	3	2	0
Preschool period (3-7 years of age)	3 (13.6)		1 (10)	
	2	1	0	1
Primary school age (7-12 years)	4 (18.2)		0	
	2	2	0	0
Secondary school age (12-16 years)	2 (9.1)		4 (40)	

The examination revealed cerebral palsy (CP) in 4 patients (12.5%) of the group under study. Hereditary pathology including mitochondrial, metabolic and autoimmune disorders [CHARGE association, subacute necrotizing encephalomyelopathy (Leigh's disease), Cornelia de Lange syndrome, type I neurofibromatosis (Recklinghausen's disease), Down's syndrome] was revealed in 6 (27.3%) patients of the group under study and 2 (20%) patients of the control group. The group under study also included 2 children (9.15%) with types II and III mucopolysaccharidoses.

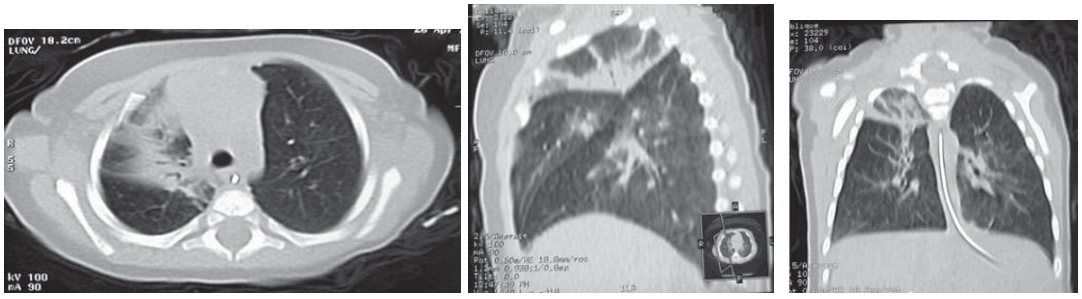
The group under study included 5 (22.7%) patients with hypoxic-ischemic or hypoxic-traumatic CNS lesion, the control group – 3 (30%) such patients. Diagnosis "Psychomotor retardation" was established in 5 (22.7%) patients over 1 year of age in the group under study and in 5 (50%) of children in the group under study (tb. 2).

Table 2. Neurologic pathologies in the examined children

Disease	Number of patients (n=32)	
	Group under study, n=22 (%)	Control group, n=10 (%)
Cerebral palsy	4 (18.2)	0
Metabolic, mitochondrial, genetic disorders	6 (27.3)	2 (20)
Mucopolysaccharidosis	2 (9.15)	1 (10)
Hypoxic-ischemic/traumatic lesion of the central nervous system (children of 0-1 years of age)	5 (22.7)	3 (30)
Psychomotor, motor retardation	5 (22.7)	4 (40)

All children from 2 months to 2 years of age were tube-fed and received standard conservative therapy: proton-pump inhibitors, antacids, prokinetics. On neurologist's orders, the children received neurometabolic, neurotrophic, sedative and anticonvulsive therapy. Despite the conducted treatment, 23 children (71.9%) had aspiration pneumonia episodes 1-4 times per year in anamnesis (pic. 1). The children's examination plan consisted of general clinical (blood, urine) analyses, biochemical blood analysis, radiographic contrast study of the gastrointestinal tract's upper segment and esophagogastroduodenoscopy (EGDS). The children were examined by a pediatrician and a neurologist. Children over 3 years of age underwent a 24-hour-logn pH-metry.

Pic. 1. Computer tomography of the chest cavity: Lots of inflammatory infiltration of lung tissue in the upper lobe of the right lung (1); vascular interstitial pattern is amplified, preferably in the upper lobe of the right lung in upper back moderately deformed parts on the right and left segments in segments by single coarse pleuropulmonary adhesions (2). Bronchus traced to the level subsegmental branches walls are thickened, preferably in the right upper lobe (3). Painting sided pneumonia. Signs of bronchopulmonary dysplasia (6 points)



In order to assess the esophageal pH-gram, we used the criteria developed by T.R. DeMeester et al. [17]. In case the total duration of intraesophageal pH reduction below 4.0 was longer than 4% of the trial duration and the DeMeester index exceeded 14.7, we diagnosed pathologic acid gastroesophageal reflux. Esophageal pH increase over 7.5 more than 27 times per day with the DeMeester index below 5 was diagnosed as pathologic alkaline gastroesophageal reflux.

All patients underwent Nissen fundoplication: closure of diaphragmatic peduncles and formation of a cuff of the anterior wall of stomach (wrapping of the wall of stomach around the cardioesophageal sphincter by 360^{o}), sutural fixation to esophagus; the last suture is stitched fixing the wall of esophagus (pic. 2).

Pic. 2. Laparoscopic Nissen fundoplication

Children with the pronounced CNS lesion, dysphagia, convulsive syndrome and frequent bronchopulmonary complications underwent gastrostomy with laparoscopic Nissen fundoplication and formation of a tight cuff. Children with no pronounced CNS lesion and no dysphagia (with mild CP, hypoxic-ischemic CNS lesion, perinatal CNS lesion, psychomotor retardation) underwent only laparoscopic Nissen fundoplication. Incurable patients (3; 13.6%) from the group under study with bulbar and pseudobulbar palsies underwent tracheostomy in order to rule out aspiration pneumonias and for palliative purposes.
Technically, gastric fistula was established after laparoscopic Nissen fundoplication: we pulled up the wall of stomach, dissected all its layers and established a gastric fistula into the stomach through the performed incision in the anterior abdominal wall.
Statistical manipulation of the obtained results was conducted using a personal computer IBM-PC, software Statistica 6. Significance error probability (p) was assessed according to the generally accepted criteria (the statements with error probability $p \leq 0.05$ were considered significant).

TRIAL RESULTS AND DISCUSSION

According to our examination, 7 patients (31.8%) of the group under study and 3 patients (30%) of the control group underwent cesarean obstetric operation. 30% of the examined children were born prematurely (different grades): in the group under study, 2 (9%) children was born with grade I prematurity, 3 (13.6%) – grade II, 1 (4.5%) – grade III, 1 (4.5%) – grade IV. In the control group, 1 (10%) child was born with grade I prematurity, 2 (20%) – grade II. Other children were born in term (tb. 3).
We observed emesis and/or regurgitation in all the examined patients. Degree of manifestation of the regurgitation syndrome was different – from non-abundant (several times a day) to persistent emesis after each feeding.
Dysphagia was observed in 13 patients (59%) in the group under study and 5 patients (50%) in the control group. Continuous emesis resulted in body weight reduction in 19 (86.4%) of the children in the group under study and in 8 (80%) – in the control group. Respiratory symptoms (cough, bronchites, pneumonias) were observed in 19 (86.4%) children in the group under study and 4 (40%) – in the control group.
Vomit mass blood admixture was observed only in 3 (13.7%) patients from the group under study (tb. 4).

Table 3. Prematurity grades of the examined children

Prematurity grade	Group under study, n=22 (%)	Control group, n=10 (%)
Grade I prematurity (corresponds to the age of 35-37 weeks and body weight of 2,001-2,500 g)	2 (9.1)	1 (10)
Grade II prematurity (corresponds to the age of 32-34 weeks and body weight of 1,501-2,000 g)	3 (13.6)	2 (20)
Grade III prematurity (corresponds to the age of 29-30 weeks and body weight of 1,001-1,500 g)	1 (4.5)	0
Grade IV prematurity (corresponds to the age of 28 weeks or less and body weight of 2,001-2,500 g)	1 (4.5)	0

Table 4. Clinical manifestations of gastroesophageal reflux in the examined children (n=32)

Clinical manifestations of gastroesophageal reflux	Group under study before the operative treatment, n=22 (%)	Control group, n=10 (%)
Regurgitation or emesis	22 (100)	10 (100)
Dysphagia	13 (59)	5 (50)

Body weight reduction	19 (86.4)	8 (80)
Vomit mass blood admixture	3 (13.7)	0
Anemia	5 (22.7)	2 (20)
Respiratory symptoms	19 (86.4)	4 (40)

According to the general clinical analyses, anemia was observed in 5 (22.7%) patients from the group under study and 2 (20%) – from the control group. The conducted analyses did not reveal any other specific abnormalities.
According to the EGDS (we employed Savary-Miller classification, 2008 to appraise the results; tb. 5), grade I esophagitis was observed in 8 patients (36.4%) from the group under study; another 8 patients (36.4%) had symptoms of grade II esophagitis. Grade III esophagitis was observed in 2 patients (9%), grade IV – in 4 patients (18.2%). According to the EGDS, grade I and II esophagites were revealed in 6 (60%) and 4 (40%) patients from the control group, respectively. Grade III and IV refluxes were not observed in the control group.

Table 5. Esophagitis grade in the patients according to the EGDS (Savary-Miller reflux-esophagitis classification, 2008)

Esophagitis grade	**Group under study before the operation, n=22 (%)**	**Control group, n=10 (%)**
Grade I	8 (36.4)	6 (60)
Grade II	8 (36.4)	4 (40)
Grade III	2 (9)	0
Grade IV	4 (18.2)	0

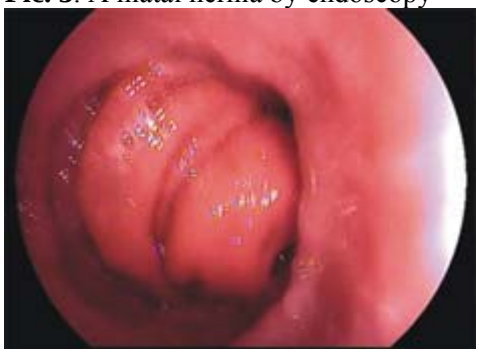
Grade of esophagitis was not the only criterion for the treatment tactics selection. Determining the operative treatment method and conservative therapy scheme, we considered the patient's somatic condition, neurological and nutritive status and respiratory complications (if present).
The children over 3 years of age underwent a 24-hour-long pH-metry: 9 out of 22 children and 5 out 10 patients in the group under study and the control group, respectively. According to the conducted studies, acid gastroesophageal refluxes (GER; number of refluxes with pH<4 more than 50 times per day, DeMeester index over 14.7) were observed in 5 (55.5%) patients. The average time with intraesophageal pH<4 per day - 25±10 minutes, the average DeMeester index – 15.5±0.7. Alkaline GER (number of refluxes with pH>7.5 more than 27 times per day, DeMeester index below 5) were observed in 1 (11%) patient. The average time with intraesophageal pH>7.5 per day - 18±0.6 minutes, the average DeMeester index – 3±1. Mixed GER were observed in 3 (33%) patients. In the control group, acid and mixed GER were observed in 2 patients (40%), alkaline reflux – in 1 patient (20%). The average time with intraesophageal pH<4 per day - 15±0.6 minutes. The average DeMeester index in those patients was similar to the DeMeester index in the children from the group under study (tb. 6).

Table 6. 24-hour-long pH-metry results of the patients

24-hour-long pH-metry results	Group under study before the operation, 9 patients out of 22 (%)	Control group, 5 patients out of 10 (%)
Acid gastroesophageal refluxes (GER)	5 (55.5)	2 (40)
1) Average time with intraesophageal pH<4 per day (minutes)	25±10	20±10
2) Average DeMeester index	15.5±0.7	15.5±0.7
Alkaline GER	1 (11)	1 (20)
1) Average time with intraesophageal pH>7.5 per day (minutes)	18±0.6	15±0.6
2) Average DeMeester index	3±1	3±1
Mixed GER	3 (33)	2 (40)

On the basis of the obtained data, all patients with dysphagia in the group under study (13; 59%) underwent combined operative treatment: laparoscopic Nissen fundoplication, laparoscopically assisted establishment of gastric fistula (with the priority given to the RF patent #2012125906 "Method of establishment of gastric fistula at laparoscopic fundoplication in children" of 13.06.12). 9 patients (41%) without dysphagia underwent only laparoscopic Nissen fundoplication. 5 of the operated patients had hernia of esophageal opening (pic. 3). According to the EGDS, we were the first to reveal and histologically confirm Barrett's esophagus in 2 patients (9%).

Pic. 3. A hiatal hernia by endoscopy



According to the follow-up examination of the patients from the group under study and the control group (6-12 months later), we observed body weight deficit in 1 (4.5%) out of 19 (86.4%) patients from the group under study, $p<0.02$; body weight reduction was observed in 8 (80%) children from the control group.

We observed regurgitation in all (100%) children from the group under study before the operation and from the control group: regurgitation/emesis reduced down to 9.1% in the group under study after the operation; we did not observe any changes in the control group in the setting of the conducted conservative treatment (100%); $p<0.05$. Respiratory symptoms (cough, bronchites) reduced in the group under study from 86.4% (n=19) to 27% (n=6), $p<0.05$, while in the non-operated children respiratory symptoms remained at 40% (n=4) despite the conducted conservative therapy. The follow-up examination revealed anemia in 1 out of 5 patients in the group under study and 2 (20%) patients in the control group.

The children (92% of the patients of the group under study) who had undergone gastrostomy, continued receiving food by gastric fistula 1 year after the operative treatment. Dysphagia

leveled only in 1 child after improvement in the somatic condition and neurologic status. Gastric fistula was closed in that patient at rehospitalization (tb. 7).
According to the 24-hour-long pH-metry within the follow-up examination of the patients from the group under study, we revealed reduction in the frequency of acid refluxes (number of refluxes with pH<4 more than 50 times per day and DeMeester index over 14.7); the average time with intraesophageal pH<4 was 13.0±0.7 minutes, the average DeMeester index – 15.5±0.7. After the operation, the number of mixed refluxes reduced from 33 to 11%. We did not observe alkaline refluxes (number of refluxes with pH>7.5 more than 27 times per day and DeMeester index below 5) in the examined children in the postoperative period (tb. 8).

Table 7. Clinical manifestations in the group under study and the control group patients

Clinical manifestations	**Group under study after the operative treatment, n=22 (%)**	**Control group, n=10 (%)**
Regurgitation or emesis	2 (9.1)	10 (100)
Dysphagia	12 (54.5)	4 (40)
Body weight reduction	1 (4.5)	8 (80)
Vomit mass blood admixture	0	0
Anemia	1 (4.5)	2 (20)
Respiratory symptoms	6 (27)	6 (60)

Table 8. 24-hour-long pH-metry results in the group under study

24-hour-long pH-metry result	**Before the operation, 9 patients out of 22 (%)**	**After the operation, 9 patients out of 22 (%)**
Acid gastroesophageal refluxes (GER) 3) Average time with intraesophageal pH<4 per day (minutes) 4) Average DeMeester index	5 (55.5) 25±10 15.5±0.7	2 (22) 13±0.7 15.5±0.7
Alkaline GER 3) Average time with intraesophageal pH>7.5 per day (minutes) 4) Average DeMeester index	1 (11) 18±0.6 3±1	0
Mixed GER	3 (33)	1 (11)

Table 9. Esophagitis grade in the group under study according to the EGDS (Savary-Miller reflux-esophagitis classification, 2008)

Esophagitis grade	**Before the operation, n=22 (%)**	**After the operation, n=22 (%)**
Grade 0	0	15 (68.2)
Grade I	8 (36.4)	4 (18.2)
Grade II	8 (36.4)	0
Grade III	2 (9)	0
Grade IV	4 (18.2)	3 (13.6)

According to the EGDS (tb. 9), we did not reveal symptoms of esophagitis 6-12 months after the operation in 15 patients (68.2%). Grade I esophagitis was observed in 4 patients (18.2%), before the operation – in 8 patients (31.8%). No grade II reflux symptoms were observed. Grade IV

esophagitis symptoms were observed in 3 (13.6%) patents (before the operation – in 4 patients; 18.2%). Grade IV esophagitis was diagnosed in 2 children with Barrett's esophagus and in 2 patients with peptic esophageal stenosis, who would later undergo esophageal bougienage under anesthesia. The follow-up examination observed positive dynamics and increase in the diameter of esophagus. We did not observed endoscopic symptoms of metaplasia at the confocal laser endomicroscopy 6 months after the operation and the course of conservative therapy in the patients with Barrett's esophagus (see tb. 8).

Nissen fundoplication was reperformed to 2 patients due to displacement of the cuff. We did not observe any other complications in the catamnesis. All patients had been receiving antacids (aluminum phosphate etc.), proton-pump inhibitors (esomeprazole, abeprazole, omeprazole) and prokinetics (domperidone) for a long time.

In the course of the conducted examinations of patients with GERD and neurologic pathology, we developed an operative treatment algorithm for this group of patients. Children with marked CNS lesion, dysphagia, convulsive syndrome and frequent bronchopulmonary complications underwent gastrostomy with laparoscopic Nissen fundoplication with formation of a tight cuff. Children without marker CNS lesion and dysphagia (with mild CP, hypoxic-ischemic CNS lesion, perinatal CNS lesion, psychomotor retardation) underwent only laparoscopic Nissen fundoplication. In order to rule out aspiration pneumonias, we conducted tracheostomy in the incurable patients for palliative purposes.

The follow-up examination in the group under study 6-12 months later revealed the children's body weight increase, improvement in the somatic condition and reduction in the number of the children's and their parents' complaints.

CONCLUSIONS

Bulbar and pseudobulbar palsies in children with neurologic pathology are crucial to the establishment of gastric fistula, as the anti-reflux operation alone does not resolve the primary problem – swallowing disorder accompanied by sputum and gastric content aspirations.

The operative treatment on the basis of the developed algorithm in combination with the conservative therapy is significantly more effective that the conservative treatment alone.

Laparoscopic Nissen fundoplication in combination with the laparoscopically assisted gastrostomy for children with dysphagia, marked convulsive activity or organic CNS lesion (severe CP, hereditary and metabolic pathology, mucopolysaccharidosis) minimizes traumatization of tissues and reduces duration of anesthetic management.

Operative treatment considerably improves somatic condition of the patients with neurologic pathology, nutritive status, prevents aspiration complications and facilitates child care.

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