Yurkiv O.I., PhD
Bucovinian State Medical University, Ukraine
Юрків О.І., кандидат медичних наук
Буковинський державний медичний університет, Україна

PECULIARITIES OF CLINICAL SYMPTOMS AND DIAGNOSIS OF GASTROINTESTINAL TRACT DISORDERS IN INFANTS WITH PERINATAL PATOLOGY HISTORY

ОСОБЛИВОСТІ КЛІНІЧНОЇ СИМПТОМАТИКИ ТА ДІАГНОСТИКИ ПОРУШЕНЬ ШЛУНКОВО-КТШКОВОГО ТРАКТУ У ДІТЕЙ ГРУДНОГО ВІКУ ПРИ ПЕРИНАТАЛЬНІЙ ПАТОЛОГІЇ В АНАМНЕЗІ

Annotation: A comprehensive clinical and paraclinical examinations of infants with perinatal pathology history suffering from the disorders of the functional state of gastrointestinal tract were conducted. Intestinal microbiocenosis changes were revealed; they are most likely to extend liver and bile-excreting tract dysfunction. Early diagnosis of the detected changes makes possible to improve functional state of intestine in infants and ignore dysbiosis signs.

Keywords: infants, gastrointestinal tract, microbiocenosis of intestine.

Анотація: Проведено комплексне клініко-параклінічне обстеження дітей грудного віку з перинатальною патологією в анамнезі, що мають порушення функціонального стану шлунково-кишкового тракту. Виявлені зміни мікробіоценозу кишечника, які імовірно поглиблюють дисфункцію печінки та жовчовивідних шляхів. Своєчасна діагностика виявлених змін надає змогу покращити функціональний стан кишечника у немовлят та нівелювати ознаки дисбіозу.

Ключові слова: діти грудного віку, шлунково-кишковий тракт, мікробіоценоз кишечника.

Introduction. Nowadays, one of the most common pathological conditions in children is a disorder of the composition and function of large intestine microflora developing under the influence of various unfavourable factors. In infants dysbiotic disorders occur more frequently than in adults; that is determined by morphological and functional immaturity of the gastrointestinal tract (GIT) in this age. There exists a point of view that severe clinically significant forms of dysbiotic disorders in the first years of life can be regarded as a prerequisite to the development of inflammatory bowel disease [1, p.42-48].

The peculiarities of infant age are an increased activity of metabolic processes and relative functional imperfection of bodily organs, including hepatobiliary system (GBS) and gastrointestinal tract, what stipulates the necessity of ensuring early diagnostics and adequate correction in the treatment of perinatal pathology and restorative therapy in the future. The peculiar features of the GIT functional state in children of infant age are hydrochloric acid lack and proteolytic enzymes in the stomach, decreased secretion of bile by the liver, and increased oxygen concentration in the large intestine [2, p. 54-61].

Normal intestinal microflora fulfills several especially important vital bodily functions. One of them is the formation of colonization resistance in the intestine in the

neonatal period, which prevents from exogenous pathogenic microorganisms colonization and their excessive proliferation. It provides human body's resistance to infections, caused by various pathogenic microorganisms. Normal microflora agents of GIT provide protection from exogenous infectious agents through the synthesis of different substances, inhibiting the growth and multiplication of pathogens as well as by means of successful fight between them for the places of attachment to the surface of mucous membrane of the intestine and source of nutrition. Another mechanism of ensuring colonization resistance of normal intestinal microflora agents is the one associated with their ability to cause significant non-specific stimulation of humoral and cellular immunity [3, p. 56]. Intestinal autoflora stimulates intestinal peristalsis and is involved in hepatic-intestinal circulation of the most important bile components.

Contributing background to the development of dysbiotic intestinal disorders in infants with perinatal pathology is connected changes in the functional state of the liver and biliary tract. Occurrence of unfavourable risk factors even during the labour leads to adaptation disorders of varying degrees of severity in newborns; that requires treatment and care of the infant separately from the mother under the supervision of medical personnel. This causes colonization of the newborn body with microflora, which is not always physiological and leads to disturbances in the formation of intestinal mucin layer. Mucous intestinal microflora is stable and is represented by bifidobacteria and bacteroides attached directly to the membrane of epithelial cells, facultative anaerobes (lactobacilli) and aerobes. All microorganisms are united into exopolysaccharide-mucin matrix and form a special biofilm, covering the intestinal mucous membrane [4, p.118]. Adhesion effectiveness and vital activity of symbiont microflora depends on the peculiarities of protective mucin layer formation.

Intestinal microbiota (bacteria, viruses, protozoa and others) effect on the human body can be local and systemic. Local effect includes trophic function, through which energy is supplied to epithelial cells of human tissues, based upon utilization of low-molecular metabolites within the Krebs' cycle, the metabolites are obtained as the result of mucus monosaccharide fragments detachment, glycocalyx and products of exogenous origin at the expense of extracellular glycosidases of saccharolytic anaerobes followed by fermentation of these sugars.

Besides, breaking up extracellular polysaccharides and glycoproteins by extracellular glycosidases of microbial origin leads to monosaccharides (glucose, galactose, etc.) formation. Another important effect is the stimulation of local immunity, first of all – the production of secretory immunoglobulin (IgA) [4, p.120]. Participation of the liver in IgA transportation largely determines the intensity of local immunoreactivity in gastrointestinal mucous membrane and other organs. Unconjugated IgA reaches the liver, on the sinusoidal membrane of hepatocytes it joins the secretory component and is transported through hepatocytes into bile. The most important function of IgA is the ability to form immune complexes with circulating macromolecules of alimentary, bacterial and other origin. Secretory component of hepatocytes can bind to these complexes, so their transmission from blood to bile and excretion from the body become possible.

The **purpose of the scientific work** was to study peculiarities of formation of intestinal microecology in infants with perinatal pathology in the neonatal period.

Materials and methods of research. The main study group consisted of 25 infants with perinatal pathology history; the infants had clinical symptoms of gastrointestinal tract disorders; group of comparison numbered 25 infants without these disorders. Diagnostic complex included determination of secretory immunoglobulin A (sIgA), alpha-1-antitrypsin (A1-AT) and albumin in the faeces, which indicate inflammation process in the intestine. Complex of additional paraclinical examination of infants included the analysis of intestinal micro-ecological environment.

The analyses of human intestinal micro-ecological environment were carried out according to standard microbiological methods at the Department of Clinical Immunology and Allergology at Bukovinian State Medical University. Determination of secretory immunoglobulin A (sIgA), alpha-1-antitrypsin (A1-AT) and albumin in the faeces was conducted on the base of the German-Ukrainian laboratory "BUKINTERMED" with the company reagents. Analysis of the obtained results was made by means of application programs package «STATGRAPHICS Plus 5.1» using conventional statistical methods of research.

Results and discussion. The retrospective study of infant development maps at birth showed that in children of the first group in 12 (48%) cases intrauterine growth retardation by hypotrophic type was diagnosed; neonatal encephalopathy was detected in 13 (52.0%) cases. Exploration of pregnancy and delivery peculiar characteristics of mothers in the main group showed that most of them had some complications. In 3 (12.0%) mothers this very pregnancy was third and fourth. 4 (16.0%) children were born by means of cesarean section. Comparative characteristics of peculiar features of clinical symptoms on the part of gastrointestinal tract in children of the second experimental group are presented in Table 1

Table 1

Comparative characteristics of peculiar clinical symptoms on the part of gastrointestinal tract in children of the first and second experimental groups

Clinical symptoms		
	I group (N=25)	II group (N=25)
Regurgitation (n/%)	1 (4,0%)	1 (4,0%)
Flatulence (n/%)	7 (28,0%)	2 (8,0%)
Large liver mass (n/%)	1 (4,0%)	-
Poor / weak sucking (n/%)	5 (20,0%)	1 (4,0%)
Abdominal distension (n/%)	1 (4,0%)	-
liquid stool (n/%)	4 (16,0%)	-
Constipation (n/%)	8 (32,0%)	1 (4,0%)
Crying (n/%)	4 (16,0%)	-
Abdominal pain (n/%)	6 (24,0%)	-

At the time of the study regurgitation was detected in one infant that constitutes 4.0%. Frequent symptoms in the infants of this group were flatulence, constipations and abdominal pain, which constitute 7 (28.0%), 8 (32.0%) and 6 (24.0%) cases respectively. Isolated cases of regurgitation, flatulence, poor sucking and constipation were observed in children of the second group.

Developmental factors concerning disorders of the intestinal functional state in infants were severe illnesses, they had suffered from, and with which they were repeatedly admitted for treatment to the pediatric hospitals. Thus, 3 (12.0%) children recovered from acute obstructive bronchitis, 3 (12.0%) suffered from enterocolitis; in 2 (8.0%) cases tracheobronchitis was in past history; 1(4.0%) infant recovered from upper respiratory tract infections (URTI) and in 1 (4.0%) case salmonellosis was revealed in the past history. Children were treated in accordance with existing protocols and clinical guidelines, including antibiotic therapy, nonsteroidal anti-inflammatory, bronchospasmolytic and anticonvulsant medical preparations that, along with the basic pathology, contributed to an increased risk of intestinal disorders development.

Examination of all infants in the first group revealed clinical symptoms of abdominal dysfunctions, among which there are: constipation – in 8 (32.0%) infants, predisposition to the liquid stool – in 4 (16.0%) infants; signs of flatulence with abdominal distension, intestinal colic and characteristic infant pose with adduction of the legs – in 7 (28.0%) cases. 5 (20.0%) children had appetite abnormalities (dysorexia); in 1 (4.0%) case regurgitation was observed. Clinical manifestations of jaundice were noted in 1 (4.0%) infant; enlargement of the liver was also observed in 1 (4.0%) case. 4 (16.0%) children experienced nervousness and constant crying. In addition, macroscopically the faeces of infants contained mucus and undigested food. Coprogram in most cases was characterized by a high content of neutral fat, amount of epithelium and white blood cells.

The results of special additional methods of research, including albumin level, A1-AT and sIgA in children of the first group showed significant differences compared to the control group II. The obtained results are presented in Table 2.

Table 2

Albumin level, A1-AT and sIgA in the feces of 5-month-old infants (M±m)

Indices	Indices recommended norm	I group	II group
A1-AT (mg/g)	< 268	540,2±27,01*	113,9±5,69
Albumin (mg/g)	<9,2	9,7±0,48*	3,3±0,16
sIgA (mg/g)	510-2040	2538,7±126,93*	1087,7±54,38

Note: * – probable difference of indices in compared groups, $p<0,05$

According to the data given in Table 2 infants with clinical signs of intestinal dysfunctions had stool with much higher level of albumin, A1-AT and sIgA as compared with children in the control group. Taking into consideration the interpretation of indices concerning the enhancement of intestinal mucosa permeability against the background of local inflammation, decrease in the activity of proteolytic enzymes, namely, chymotrypsin, trypsin, elastase, hyaluronidase, protease of leukocytes, macrophages,

microorganisms, etc. can explain loss of appetite in children and lack of tolerance to food – features accompanying the presence of intestinal dysfunctions. The increased level of sIg A in the faeces of infants in IIA group may be caused by an allergic reaction of the intestinal mucosa, probably against the background of artificial feeding, but one can not exclude the presence of an allergic component of local immunity as one of the pathogenesis links of the intestinal mucosa inflammation.

Thus, there is a situation in which on the one hand, microbial imbalance causes local inflammation development, on the other hand – the presence of inflammation with an allergic component contributes to the long-term intestinal dysfunctions, supporting clinical symptoms. The peculiarities of microbiocenosis of large intestine cavity in children are presented in Table 3.

Table 3

Peculiarities of microbiological composition of large intestine in children of infant age (lg CFU/g)

Indices	Experimental groups	
	I group	II group
	M± m	M± m
ANAEROBES:		
Bifidobacteria	5,56±0,28*	9,74±0,49
Bacteroids	9,58±0,48	9,48±0,47
Lactobacteria	7,54±0,38*	8,66±0,43
Peptococci	8,79±0,44*	7,45±0,37
Peptostreptococci	8,93±0,45*	4,43±0,22
Clostridia	-	-
AEROBES:		
Colon bacilli	9,65±0,48*	6,28±0,31
Hemolytic escherichia coli	-	-
Enteropathogenic escherichia coli	-	-
Enterococci	-	-
Staphylococci	5,29±0,26	-
Bacilli protei	6,54±0,33	-
Fungi of the genus Candida	3,34±0,17	-

Note: *Probable difference between groups of observation, $p<0,05$

In accordance with the data presented in Table 3 the infants possessing the signs of intestinal dysfunctions, were also characterized by a decreased bifidobacteria and lactobacteria content, increased peptococci, peptostreptococci and Escherichia coli content, Staphylococcus presence, protei, and fungi of the genus Candida.

In the absence of timely correction in the neonatal period clinical manifestations of dysbiosis in the future may take considerable clinical severity.

Conclusion. Dysbiosis gastrointestinal manifestations in infants are a consequence of perinatal pathology in the neonatal period that usually occur in combination with functional disorders of other organs and systems, including, hepatobiliary one. Early signs of the appearance of gastrointestinal tract dysbiosis may be detected by means of diagnostic research complex and prevented by early administration of correcting therapy (prebiotics, probiotics, functional food). Prospects for further research consist in studying pathogenic mechanisms of intestinal dysfunctions development, diagnostics and correction methods.

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