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LOCAL PREOPERATIVE THERAPEUTIC ACTIONS IN HIRSCHSPRUNG`S DISEASE IN NEWBORNS AND INFANTS.

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Summary
The author presents the results of an original study of the problem of local preoperative treatment of Hirschprung disease (HD) in newborns and infants. The study was based on the analysis of data of preoperative bowel preparation in 52 newborns and infants with HD. As a result the more comprehensive and efficient tactics of preoperative bowel preparing was elaborated, which includes prolonged intubation and decompression of the colon; biological decontamination and detoxification by administration of enterosorbents, favoring indigenous microflora development with dysbacteriosis liquidation through administration of probiotics (eubiotics).

Introduction. Analysis of the literature data states that the chapter of colon dysbacteriosis in neonates and infants in HD is under debate [3, 6]. Most authors demonstrate that chronic retention of the intestinal transit and emptying due to the intramural innervation damage induces changes of the local-regional microbial medium resulting in obstructive enterocolitis [2, 4, 6]. Aggressive enterocolitis presents multiple metabolic disorders, alters synthesis and intestinal absorption processes, contributing to spread of septic-pyemic processes etc. [1, 2]. These processes evolve extremely severely in neonates with acute forms of HD, since the pathology in question impedes normal colonization of the digestive tract with aerobic and anaerobic flora [8]. As a result 68.5 % of neonates with HD have severe dysbacteriosis with underlying obstructive enterocolitis, from the first days of life, which reaches critical proportions at the end of the late neonatal period. Under these conditions the average value of the indigenous bacterial colonies logarithm decreases (bifidum- and lactobacteria) per 1 gr of faeces (Lg CB/gr) [6].

Recent researches attest that reduction of the titer of these two bacteria induces quantitative growth of facultative pathogenic and pathogenic flora, enhancing the risc for development of general and limitrophe inflammatory complications [2, 4]. The importance of colonic biocenosis study in HD in newborns and infants for an adequate preoperative preparation results from the above mentioned facts. The results of recent publications denote that only an adequate diagnostic-curative strategy, based on objective clinical and laboratory tests, can save the lives of these children, giving them the chance to be radically operated [8, 9].

Management of incidence and mortality caused by enterocolitis shows that, thanks to early diagnostic and curative measures, in the last 30 years, a number of pediatric surgery clinics have managed to reduce lethality from 30 % to 1-10%, with respective complication incidence of 17 to 38 % [3, 5, 10]. The results are largely due to early diagnosis of HD and enterocolitis, awareness of the disease etiopathogenesis mechanisms, which have been so far incompletely elucidated, undertaking of general and local-regional curative actions [4, 5, 11]. It is to be noted that newborns and infants have a relatively imperfect immunobiological potential of local protection, being undermined by factors such as deficiency of the intestinal fermentative system, incomplete morpho-functional development of the microvilli of the intestinal mucosal lining, reduction of the function of the mucosa adhesion to microorganisms, etc. [3, 12].

Immaturity and morphological congenital defect of intramural innervation of the colon are not the last causes in the pathogenesis of enterocolitis [3, 4, 9]. Currently many aspects of etiopathogenisis, diagnosis and treatment of enterocolitis caused by HD are at the stage of study and improvement based on the new concepts.

The problem of preoperative preparation of children with Hirschsprung`s disease, especially in the group of newborns and infants, has been current so far. Local preparation of this contingent of children presents particular interest.

Purpose of this article is to develop a more rational and effective tactics of preoperative preparation of the colon in Hirschsprung's disease in neonates and infants.

Materials and methods. In the surgical wards of the newborns and thoraco-abdominal ones of the National Center of Pediatric Surgery "Natalia Gheorghiu" MSPI IM and C, during 2006 and 2012, 52 neonates and infants with an age limit of 48 hours to 12 months were evaluated, being hospitalized for Hirschsprung`s disease. Children were divided into 4 groups by age: 2-30 days (9 children - 16.2%), 1-3 months (14 children - 24.3%), 3-6 months (12 children - 33, 8%), 6-12 months (17 children - 25.7%).

In diagnosing HD and EC we relied on the results of compulsory and additional clinical and laboratory examinations, the basic criteria of their selection being: diagnostic informativeness, accessibility, clinical and economic rationality. Diagnostic algorithm included general and local-regional clinical examination, radiological and neurophysiological imaging, histomorphology of the rectal biopsies and microbiocenosis of faeces.

Table 1

Distribution of patients by age, sex and location of the aganglionic area

Groups of patients	Age	Number of examined patients		Distribution by sex		Location of the aganglionic area			
		Abs.	%	Male	Female	Infrarectal	Recto-sigmoidal	Sigmoidal	Subtotal colonic
I	2-30 days	9	17,3	6	3	1	5	1	2
II	1-3months	14	26,9	9	5	3	6	3	2
III	3-6months	12	23,1	8	4	4	5	3	0
IV	6-12months	17	32,7	12	5	6	9	2	0
TOTAL		52	100	35	17	14	25	9	4

Based on these examinations, 28 (53.8%) of 52 children with HD were diagnosed with obstructive EC: 17 (32.7%) - were diagnosed preoperatively, 7 (13.5%) - were diagnosed postoperatively and 4 (7.7%) - were diagnosed pre-and postoperatively. In 17 (60.7%) children EC manifested in the first 14 days of life, being hospitalized for emergency in territorial and republican medical institutions with diarrhea, hyperthermia, meteorism, vomiting, abdominal enlargement and signs of peritoneal excitement that evolved with underlying severe constipation.

Elucidation of specific clinical and laboratory features of obstructive EC in the context of HD in neonates and infants, as well as the efficiency of various diagnostic and therapeutic methods was based on the monitoring of the 28 children with EC, pre-, intra- and postoperatively.

According to the methods of preoperative preparation of the colon, the patients were divided into 2 groups.

Group I comprised children in whom the colon preparation for the operation required intubation and mechanical purging by means of enemas twice a day, using 1% NaCl solution up to the complete emptying of the intestine off faeces.

Conservative treatment was simultaneously performed. It aimed at correction of side effects of chronic colostasis through antibiotic therapy, fluid resuscitation, vitamin therapy, etc.

In group II the long-term intubation of the colon was carried out, with the passage of the probe on the level of the suprastenotic area, providing colon disimpaction and local administration of enterosorbent and eubiotic preparations. Antibiotic therapy was not used preoperatively in this group of children.

Assessment of veracity of mean values difference (P) was based on Fischer-Student criterion.

Discussions. Confirmation of HD based on multimodal clinical and laboratory examination, indicates the need for further laboratory testing to elucidate the state of the colonic microbial medium. This informative diagnostic plan involves checking quantitative and qualitative characteristics of intestinal dysbacteriosis.

Analysis of the obtained examination shows that intestinal microflora is subjected to serious complications in all 28 children with HD and EC manifestations. The degree of dysbacteriosis varied from mild forms (10.0%) and mildly severe (16.6%), to severe (46.6%) and extremely severe (26.6%).

Table 2 summarizes the quantitative and qualitative characteristics of colonic biocenosis in children with HD + EC, compared to the age norm and children with HD with no EC manifestations.

Data included in Table 2 show that colonic microflora undergoes serious changes in both groups of assessed children, especially those with obstructive enterocolitis. It is to be noted the veridical decrease ($P < 0.001$) of bifido- and lactobacteria titer, high titres of Staphylococcus aureus, Clostridium difficile, protei, klebsiela.

Obstructive enterocolitis evolved particularly aggressively in children with Clostridium difficile, the disease developing fulminantly with signs of intoxication and exicosis. Biopsies of the resected colon segments affected by enterocolitis, reveal profound histomorphological inflammatory changes in all layers, the severity of which is directly dependent on the duration of illness, secretory wearing down of enterocytes and enteroendocrine cells, translocation of microflora in improper places through the walls of the damaged intestine.

In developing curative strategy and tactics of newborns and infants with HD complicated by obstructive enterocolitis we have taken into account the above-mentioned etiopathogenic aspects stressing the following:

- Catheterization of aganglionic area with suprastenotic bowel intubation and providing bowel intestine emptying and prolonged decompression.
- Administration of enterosorbents and probiotics (eubiotics) per os and retrograde infusion through the rectocolic tube, which provides biological decontamination and detoxification, favoring indigenous acidophilic microflora development.
- General syndrome treatment (infusion, metabolism correction, immunocorrection etc).

- Administration of antibiotics is mandatory in fulminant forms with a severe evolution, with ulcerative mucosal lesions caused by Clostridium difficile or other representatives of anaerobic and facultative anaerobic infection.
- Progress of EC with the suspected passage of the disease into the irreversible phase is an indication for surgery - application of **colostomy.**

Table 2

Quantitative and qualitative characteristics of microbiocenosis in HD + EC

Type of microbes	Norm Lg CB/g	Control group (MH+EC) n=28		Witnesses (MH) n=24		P
		Lg CB/g				
		M	m	M	m	
Colibacillus (Total nr.) including fermentative activity: Normal Hemolytic (%) Lactose-negative (%)	 7,0-8,0 7,0-8,0 0% < 5%	 4,48 4,37 23,4 25,6	 ± 0,11 ± 0,17 ± 1,62 ± 1,23	 5,4 5,86 15,8 16,3	 ± 0,23 ± 0,13 ± 1,52 ± 1,6	 <0,001 <0,001 <0,001 <0,01
Bifidobacterium	10-11	4,2	± 0,12	6,1	± 0,14	<0,001
Lactobacillus	6-7	3,9	± 0,14	5,2	± 0,21	<0,001
Bacteroides spp	7-8	4,2	± 0,1	6,1	± 0,2	<0,001
Streptococcus saprophytes	7-8	5,2	± 0,2	6,2	± 0,1	<0,001
Enterococcus	5-7	3,8	± 0,4	5,2	± 0,3	<0,001
Other conditionally pathogenic enterobacteria	0	3,6	± 0,2	2,8	± 0,4	<0,001
Staphilococcus aureus	0	4,8	± 0,3	3,1	± 0,1	<0,001
Staph. saprofiticus, epidermis	< 4	6,6	± 0,2	4,8	± 0,3	<0,001
Non-fermentative bacteria	< 4	5,8	± 0,3	4,6	± 0,1	<0,001
Candida	0	5,7	± 0,2	3,2	± 0,3	<0,001
Clostridium difficile	< 3	5,4	± 0,3	2,8	± 0,1	<0,001
Proteus spp.	0	4,3	± 0,2	3,2	± 0,1	>0,05
Klebsiella spp.	0	4,87	± 0,3	2,8	± 0,3	<0,001

Testing of colonic microflora sensitivity to antibacterial action (Table 3) shows that 86.2 ± 3.8% of facultative pathogenic microorganisms detected in feces of newborns and infants with HD that were to be operated, manifested resistance and only 13.8 ± 3.8% - had sensitivity to antibacterial remedies under study (P < 0.001). In this research we have established the fact that representatives of all microbial colonies detected in the colonic lumen of children with HD tolerated easily the antibiotic action, therefore it was very hard to suppose which one of them will dominate the microbial association and determine potential suppurative-inflammatory complications in the postoperative period.

From the above mentioned it is easy to imagine how much we can rely on antibacterial chemotherapy to combat obstructive enterocolitis, peritonitis, wound suppuration and other complications in the structure of postoperative morbidity in neonates and infants operated for HD. The fact that most colonies appreciated by us as receptive to the action of antibiotics in reality had only a minimal or moderate degree of sensitivity accounts for the effectiveness of the use of antibiotics in preventing limitrophe and generalized suppurative-inflammatory complications in the postoperative period.

This fact raises questions about the efficacy of antibiotics in preventing complications mentioned above, especially in combating microbial association consisting of anaerobic and aerobic colonies.

From the above mentioned it is clear that the decisive role in the prophylaxis of purulent-septic complications in these operations does not belong to antibacterial therapy.

For this reason we have undertaken a clinical trial aimed at developing biological principles of preoperative cleansing of the colon, which would not rely on sterilization, but on the restoration of intestinal biocenosis. Bowel intubation was performed for this purpose, with probe passing through the aganglionic region, up to the suprastenotic segment. In this position the probe was fixed on the time period needed for implementation of therapeutic actions necessary for preoperative preparation. Using method of the continuous colon intubation enabled us to ensure bowel disimpaction and decompression by lavage fluid drainage and colonic content. Natrii chloride 1% solution was used as a remedy for lavage, whose osmotic properties do not permit its absorption from the intestinal lumen, thereby preventing endogenous intoxication.

Also the intralumenal presence of the rectal tube allows local administration of enterosorbents and eubiotics on the focal level, contributing to dysbacteriosis correction and enterocolitis control, based on biological mechanisms of protection.

Table 3

Redistribution of microorganisms revealed in feces of children with chronic constipations depending on their sensitivity to antibiotics

Identified microorganisms		Sensitivity to antibiotics					
		Control group (MH+EC) n=28			Witnesses (MH) n=24		
		sensible	resistant	Total	sensible	resistant	Total
S. aureus	Abs	11	67	78	33	24	57
	%	14,1	85,9	93,9	58,3	41,7	68,7
Klebsiella spp.	Abs	7	69	76	13	30	43
	%	9,2	90,8	91,5	30,8	70,2	51,8
Ps Aeruginosa	Abs	3	51	54	11	17	28
	%	5,5	94,4	65	38,8	61,1	33,7
Proteus spp.	Abs	6	71	77	24	32	56
	%	7,8	92,2	92,7	43,7	56,3	67,5
E. coli	Abs	26	57	83	35	47	83
	%	31,3	68,7	100	42,8	57,2	100
Enterobacter spp.	Abs	11	64	75	51	30	81
	%	14,6	85,3	90,3	63,6	36,4	97,6
M±m	Abs	10,7±3,3	63±3,3	73,8±4,1	27,8±6,1	30,0±4,1	58±8,7
	%	13,8±3,8	86,2±3,8	100	46,2±5,1	53,8±5,1	100
P_{1-2}	Abs	<0,05	<0,001	>0,05	<0,05	<0,001	>0,05
	%	<0,001	<0,001	-	<0,001	<0,001	-

Administration of eubiotics alters the intestinal pH to acidosis, the latter benefiting the indigenous microflora development.

Attaching to the mucosal layer of the intestine, lactobacilli that are part of eubiotics reduce inflammatory processes, stimulate local factors of biological protection and destroy conditioned pathogenic and pathogenic flora thereby preventing postoperative purulent - septic complications . The advantage of the method described is keeping indigenous intestinal microflora and, parallel with this, suppression of pathogenic flora, which could lead to inflammation of anastomosis or obstructive enterocolitis. Using eubiotics has practically no contraindications, age limits to its application, the range of therapeutic dose is wide. No negative consequences were recorded after long-term administration of the preparation.

Enterosorbent administration was indicated in mechanical cleansing of the colon off biological impurities and microbial colonies. In our opinion the most successful enterosorbent applied in neonates and infants is enterosgel. Having a high coefficient of adsorption, the preparation accumulates on its surface intestinal wastes, catabolism products, bacterial endotoxins, proper oligopeptides and microorganisms, removing them from the body.

Laboratory testing of the preparation allowed us to conclude that the maximal curative effect manifests within 30min after its administration, maintaining up to 8 hours, which led us to administer it orally and by enema 3 times / 24 hours. Among the negative actions we have to mention its ability to adsorb not only pathogenic and facultative pathogenic colonies, but also those favorable for maintaining the intestinal biocenosis balance (lactobacilli, bifidumbacteria, E. coli). Its combination with eubiotics conditions the prophylaxis of adverse action on the titre of local bifidumbacteria and lactobacilli. Improvement of intestinal biocenosis in the group of patients receiving eubiotic + enterosgel is a reliable evidence.

The above mentioned tactics of treatment in HD complicated by enterocolitis enabled us to achieve a positive effect in the absolute majority of cases (93.3%) through the conservative methods and to operate programmed the children in the neonatal period and infancy. Application of colostomy was performed according to vital indications in 4 (13.3%) cases. HD complicated by enterocolitis at a frequency of 40.5%, had a lethality of - 6.6%.

Conclusions:

1. As a multifactorial pathomorphologic and pathophysiologic complication, enterocolitis presents a common complication (42.8%) of HD in neonates and infants.
2. Enterocolitis as a complication of HD can be suspected in all cases of diarrhea, flatulence, vomiting, dyspeptic disorders being preceded or evolving intermittently with severe constipation, which is rebellious to conservative treatment. Clinical suspection of HD complicated by enterocolitis indicates the need of special laboratory management to establish early the correct etiopathogenic diagnosis.
3. The key moments in the etiopathogenic treatment of HD complicated by enterocolitis are: prolonged intubation and decompression of the colon; biological decontamination and detoxification by administration of enterosorbents, favoring indigenous microflora development with dysbacteriosis liquidation through administration of probiotics (eubiotics).
4. Administration of antibiotics, application of colostomy, complex intensive care are indicated in the advanced stage of the disease, as radical curative measures aimed at speeding the body's biological potential to normalize and stabilize.

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CISTOADAPTOMETRIA LA COPII CU UROLITIAZĂ.

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Summary

CYSTOADAPTOMETRY IN CHILDREN WITH NEPHROLITHIASIS.

In view of studying the function of the urinary bladder, at thirty nine children with ages between four and fifteen years old, diagnosed with urotiliasis, 39 (thirty nine) cystoadaptomerys were performed and in about 60% (sixty percent) of the cases bladder hypotony was found. In order to improve the treatment of the bladder hypotony, stimulant drugs of the urinary tract peristalsis, such as Neostigmina, Cerucal, Neiromedina, were added to the treatment, which showed satisfying results.

Este bine cunoscut faptul că vezica urinară ca parte constituenta a sistemului urinar are un rol primordial în urodinamică, aprecierea funcţiei căreia ne reflectă starea motilităţii întregului tract urinar.

Metode: Pentru a aprecia funcţia vezicii urinare s-a efectuat cistoadaptometria la 39 copii cu urolitiază, cu vîrsta cuprinsă între 4-15 ani (preponderent 9-12 ani). Fetiţe au fost -26, baieţei -13. La 30 din copii s-a depistat concrement în rinichi, la 5 copii concrement al vezicii urinare, iar la 4 copii concrement în ureter.

Rezultate: Hipotonie a vezicii urinare s-a apreciat la 23 de copii, normotonie la 11 copii, iar hipertonie la 6 copii. Aşadar la majoritatea pacienţilor cu urolitiază s-a depistat hipotonie (cca 60%), ce duce la stazarea urinei, astfel contribuind la formarea calculilor. Cistoadaptometrograma la un copil de 13 ani cu urolitiază a înregistrat o hipotonie pronunţată (fig.1). Hipertonie s-a apreciat la copiii cu concrement în vezica urinară (pe fon de cistită). Din 11 copii cu normotonie la 8 s-au depistat semne vădite de hidrocaliconefroză. Nu se exclude faptul că la aceşti pacienţi urolitiaza e cauzată de obstrucţia joncţiunii pielo-ureterale (JPU). Deseori este greu de apreciat dacă concrementul a stat la baza apariţiei hidronefrozei sau că acesta s-a format pe fondalul obstrucţiei JPU.

La toţi pacienţii luaţi în studiu s-a depistat infecţie urinară. Evaluarea ritmului micţional a decelat frecvenţa de 2-3 micţii în 24 ore la 18 copii.

Discuţii: Litiaza urinară poate apărea la orice vîrstă, dar afectează preponderent persoanele de vîrstă reproductivă 20 – 50 ani. Mai rar se identifică la bătrîni şi copii.

Se cunosc multiple teorii ale litogenezei – teoria cristalizării (suprasaturaţiei urinare) şi îmbibiţiei. În mod normal urina uneori conţine cristale mici, adesea de oxalaţi de calciu dihidrat, dar numai 5-10% din aceşti indivizi vor dezvolta calculi renali. Probabil aceste cristale se formează în ducturile colectoare papilare şi sunt eliminate înainte de a creşte în dimensiuni şi a fi blocate în lumen. Datorită unor factori intrinseci sau exrinseci precum scăderea diurezei, eliminarea excesivă de săruri în urină, echilibrul stabilit anterior se dereglează, favorizînd depunerea de săruri.