PATHOGENIC ASPECTS IN ACUTE DIARRHOEA

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Abstract: *In general, all types of diarrhoea results from an alteration of water and electrolytes transport, at intestinal level, including an alteration of the absorption and secretion of water and electrolytes. Due to age particularities, infants have an increased risk for acute dehydration syndrome, in comparison with adults. Diarrhoea is produced by four mechanisms: secretory, osmotic, altered motility and mucosal inflammation. The pathogens had to overcome the host defence mechanisms in order to produce the disease. These defence mechanisms are: gastric acidity, intestinal motility, commensal microflora and local and systemic immune defence mechanisms. The complex interactions between the host defence mechanisms and the bacterial virulence factors determined four mechanisms that produce bacterial diarrhoea: invasive, cytotoxic, toxigenic and through adherence.*

Keywords: *Diarrhoea, dehydration, mechanism, infant.*

Rezumat: *În esenţă, toate tipurile de diaree rezultă din tulburarea transportului de apă şi electroliţi la nivel intestinal, inclusiv a proceselor de absorbţie şi secreţie a acestora. Datorită particularităţilor legate de vârstă, sugarul prezintă un risc mai mare decât adultul şi copilul mare de a prezenta sindrom acut de deshidratare. Mecanismele de producere a diareei sunt: secretor, osmotic, prin alterarea motilităţii şi inflamaţia mucoasei. Pentru a produce boala, agentul patogen trebuie să depăşească mecanismele de apărare ale gazdei reprezentate de: aciditatea gastrică, motilitatea intestinală, secreţia de mucus, microflora saprofită intestinală şi mecanismele imune locale (IgA secretor) şi sistemice de apărare. Interacţiunile complexe dintre mecanismele de apărare ale gazdei şi factorii de agresiune bacteriană au dus la individualizarea a patru mecanisme de producere a enterocolitei bacteriene: invaziv, citotoxic, toxigenic şi prin aderenţă.*

Cuvinte cheie: *diaree, deshidratare, mecanism, sugar.*

In general, all types of diarrhoea results from an alteration of water and electrolytes transport, at intestinal level, including an alteration of the absorption and secretion of water and electrolytes.

The small intestine absorbs almost the entire quantity of fluids, necessary to the organism. The affection of this segment of the digestive tube will bring about severe diarrhoeas that will rapidly lead to an acute syndrome of dehydratation.

Absorption efficiency of the small intestine is of 93%, and the absorption of the entire digestive tube is of about 98%, in normal conditions in adult people; thus, out of 9 litres of fluid (7 coming from endogenous secretions and 2 from ingestion), around 150-200 ml will be released through stools. It is estimated that the water absorption efficiency is similar in children (1). In the case of an affection of the small intestine, the water absorption efficiency at chronic level increases 2-3 times. Diarrhoea may result either from an affection of the small intestine, or of the colon or of both of them, the latter being the most severe possibility (2).

Infants present a higher risk in developing acute syndrome of dehydratation than adults, because water turnover at the level of the digestive tube is two times larger than the extra cellular water, as against adults and the intestinal mucosa of the little babies tends to be more permeable than in adults, resulting large quantities of water in pathologic conditions. Enterocolitis in infants is aggravated by the increased losses of fluids (due to the larger corporal area in relation with the weight), as well as by fever that frequently occurs in this age group (3).

Water is absorbed at the level of the digestive tube through a passive mechanism, according to the osmotic gradients which exist on both sides of the cellular membranes, followed either by inorganic substances (sodium, potassium), or by organic ones (glucose, peptide, amino acids), substances that are actively absorbed.

At digestive level, absorption is accomplished through three main mechanisms:

1. sodium absorption through Na/K ATP-ase. This mechanism is present in the entire intestine, but is predominant at colon level and is usually affected in infectious enterocolitis;
2. co-transportation of sodium and glucose, amino acids or peptides, mechanism operating at small intestine level and not at colon level. This mechanism remains intact in the majority of acute infectious diarrhoea cases;
3. absorption of NaCI in cationic exchange (Na^+ cu H^+) and anionic (Cl^- cu HCO_3^-). This mechanism is

present in the entire small intestine, being predominant in ileum.

The presence of glucose increases up to three times the water and sodium absorption; this concept lies at the basis of oral rehydratation used in the therapy of acute enterocolitis. In normal conditions, the processes of water and electrolytes absorption are predominant in comparison with their secretion (4).

The mechanisms that produce diarrhoea are:

- *secretor* – through the decrease of absorption and increase of absorption (cholera, enterotoxigenic *Escherichia coli*, *Clostridium difficile*, neuroblastom),
- *osmotic* – maldigestion, transportation disorders, ingestion of solutions with high osmolarity (lactose deficiency, laxative abuse),
- *motility alteration* – in thyrotoxicosis, irritable bowel syndrome, postvagotomy, dumping syndrome: early or late,
- *mucosa inflammation* – in the celiac disease, different infections (*Salmonella*, *Shigella*, *Yersinia*, rotavirus).(2)

In order to produce the disease, the pathogen agent had to overcome the host defence mechanisms. These defence mechanisms are: gastric acidity, intestinal motility, commensal microflora and local (secretory IgA) and systemic immune defence mechanisms (5).

The first line of defence encountered by the germs is the gastric acidity, with important bactericide proprieties in a pH < 4. The part of the gastric acidity in antimicrobian defence is to diminish the number of viable bacteria that reach the small intestine. The microorganisms that survive as a result of the action of the gastric juice are included in the mucosal layer, facilitating their movement along the digestive tube through the peristaltic movements and their release. When the intestinal motility is diminished or absent, the pathogenic germs included in the mucosal layer may become capable of producing enterocolitis. The acceleration of the intestinal peristaltism that occurs in certain enteral infections might represent an attempt from the part of the host to release the intestinal pathogenic germs. Besides its part of including pathogenic microorganisms, the mucosa accomplishes a non specific barrier against the bacterial colonization and proliferation of the intestinal mucosa, an efficient barrier in toxins inhibition, too. The exfoliated cells of the intestinal mucosa, placed in the mucosal layer may include germs that will be released subsequently. The mucosa also contains analogues of area receptors, of lucidic nature that may prevent the microbial invasion, occupying the receptors used by bacteria, for the adhesion to the intestinal mucosa epithelium (2).

The intestinal saprophyte microflora represents the next line of defence. The commensal flora is made up mainly of anaerobe germs, which produce short-chain fat acids and lactic acid – toxic substances for the majority of the enteric bacterial pathogens. Regarding breast-fed infants, this line of defence is intensified by the presence of the anaerobe lactobacilli, which generate fermentation products – true toxins for the pathogen bacteria. A proof in the support of the importance of the saprophyte flora for the organism's defence is the pseudomembranous colitis with *Clostridium difficile*, consecutively to the prolonged large spectrum antibiotherapy that strongly reduces the intestinal and systemic flora (2).

The most complex host defence mechanism is represented by the local and systemic immunity.

The interaction between these host defence mechanisms and the virulence of the pathogen agent is responsible for the severity and the clinical manifestation of diarrhoea (3).

The pathogens germs produce acute enterocolitis by the help of two basic mechanisms: *inflammatory* (through the direct invasion of the intestinal mucosa or cytotoxins production) and *non-inflammatory* (through adherence or enterotoxins production) (4). The bacteria developed a large variety of virulence factors in order to overtake the host defence mechanisms. The complex interactions between the host defence mechanisms and the factors of bacterial aggression brought about the individualization of four mechanisms of bacterial enterocolitis production:

1. *invasive* – After infection, the germ proliferates in the intestinal lumen and adhere to the intestinal cells, a process which is favoured by a number of active mechanisms (chemotaxy, specific bacterial adherence or specific structures of pili and fimbriae type). Subsequently, invasion follows, producing inflammatory lesions of the mucosa, up to ulceration and the release of a complex of substances with secretagogue part (metabolites of arahydonic acid, kinines). Example: *Salmonella, Shigella, Vibrio parahaemolyticus, Yersinia enterocolitica, Campylobacter jejuni.*
2. *cytotoxic* – by the production of cytotoxins that perturb the cellular functions through the direct alteration of the intestinal mucosa area, being capable of inducing the cellular death. Cytotoxins exercise an intense effect of protein synthesis inhibition, a secretogenous effect of stimulating the production of inflammation mediation, some of them having neurotoxic effects. Example: *E.coli enterohemoragic* and *enteropathogenic, Shigella, Clostridium difficile.*
3. *enterotoxigenic* – through the production of enterotoxins with polypeptide structure that alter the cellular hydroelectrolitic balance, without affecting the morphological cellular integrity. After having been linked to a specific enterocytary receptor, enterotoxins act on adenylate cyclase (in some cases, they act on guanylate cyclase) with the subsequent increase of the intracellular mediators, cyclic adenosine monophosphatase and cyclic guanosine monophosphatase. These mediators contribute to the opening of the selective channels for anions of the secretory cells from the intestinal luminal membrane, stimulating the intestinal secretion of water and electrolytes. Example: *Enterotoxigenic E. Coli*

Aeromonas, Shigella, Vibrio cholerae, Yersinia enterocolitica, Vibrioni non 01.

4. *through adherence* – where the pathogenic germs penetrate the glycocalyx, adhere to the enterocytes area and produce the moderate aplatisation of microvilli. This action affects the functionality of the brush border of the enterocyte and diminishes the absorptive capacity of this area. Example: *Enteropathogenic E. Coli enterohemoragic, enteroaggregative and diffuse adherent.*(6)

The factors of bacterial virulence act in specific regions of the intestine. Thus, enterotoxins act mainly at the level of the small intestine, but they may affect the colon, as well; the enteroadherence mechanism is active both in the small intestine and in colon and the effects of cytotoxins and the direct invasion of mucosa operate especially at the level of colon. As we noticed, the same bacterium may act on more pathogenic mechanisms (2).

BIBLIOGRAPHY

1. William F. Ganong, Lange – Review of Medical Physiology. 21th Edition. The McGraw-Hill Companies 2003.471:517;
2. Wyllie R., Williams J. S. – Pediatric gastrointestinal and liver disease. Third edition. Saunders Elsevier 2006. 151:169, 557:575, 1165:1174;
3. Neamţu M., Cazan C – Patologie digestivă la copil. Note de curs. Editura Universităţii "Lucian Blaga" din sibiu 2005. 22:20, 74:84, 91:103;
4. Behrman, Kliegman, Jenson – Nelson Textbook of Pediatrics. 17th Edition. Saunders 2004. 861:865, 912:933, 953:954, 1274:1276.
5. Gherghina I, Matei D, Aloman Monica, Iusan Mirela, Ioniţă Eliza – Actualităţi în diareea acută la sugar şi copilul mic. 2004. www.emcb.ro.
6. Ciofu E., Ciofu C. – Pediatria. Tratat ediţia I. Editura medicală 2001. 490:549.