EPIDEMIOLOGIC, PATHOGENIC AND EVOLUTIVE ASPECTS IN ENTEROCOLITIS WITH ESCHERICHIA COLI / EPIDEMIOLOGIC

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Abstract: E. Coli species are members of the Enterobacteriaceae family. The enteropathogenic strains are classified into six groups: enterotoxigenic, enteroinvasive, enteropathogenic, enteroaggregative, diffuse adherent and shigatoxin – producer of E. Coli. All these strains are capable to produce acute enterocolitis in children, representing a major cause of acute diarrhoea especially in children from the developing countries. They can produce, due to the different pathogenic mechanisms, various clinical manifestations, from acute, non – bloody diarrhoea to bloody diarrhoea. Its evolution may be accompanied by complications like: severe acute dehydration or hemolytic – uremic syndrome.

Keywords: enterocolitis, children, E. Coli, complications, dehydration.

Rezumat: Speciile de E. Coli sunt membri ai familiei Enterobacteriaceae. Tulpiile enteropatogene sunt clasificate în șase grupuri: E. Coli enteropatogen, enteroinvaziv, enterotoxigen, producător de toxină shiga, enterogragregat și difuz adherent. Toate aceste tulpii sunt capabile să producă enterocolită acută la copii, reprezentând un factor major de diaree acută la copii din țări în curs de dezvoltare. POT determina, în funcție de mecanismul patogenic, aspecte clinice mergând de la diaree apusă, posibil cu evoluție prelungită, până la diaree sanguinoanelată. Evoluția poate fi greață de complicații ca de exemplu: sindromul acut de dehidratare sau sindromul hemolitic uremic.

Cuvinte cheie: enterocolita, copii, E. Coli, complicații, dehidratare

E Coli species are members of the Enterobacteriaceae family. The enteropathogenic strains of E. Coli are classified into six major groups, taking into account the pathogenic mechanisms and sero-grouping: E. Coli enteropathogenic (EPEC), enteroinvasive (EIEC), enterotoxigenic (ETEC), shiga toxin producer (known as enterohemoragic O 157: H 7) (STEIC), enterooagregative (EaggEc) and diffusely adherent (DAEC). (4, 6, 10)

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Enterocolitis with ETEC

Epidemiology. ETEC represents a major cause of acute diarrhea in children from the developing countries and causes travellers’ diarrhea in adults. Within the developed countries, ETEC enterocolitis is unusual in children. It occurs in almost 20-30% of the enterocolitis causes within the developing countries, being the most frequent pathogen bacterial agent of enterocolitis in children, as well as EPEC. Most usually, the disease is faecally-orrally transmitted, or by water consumption and strongly contaminated food (1).

Pathogenesis. In order to produce the disease, ETEC colonizes the small intestine and then it is attached to the intestinal mucous surface by the help of the fimbriae; this process does not cause detectable morphological changes within the architecture of the brush border, but it allows the bacterium to release the enterotoxins (thermolabile and thermostable) in the immediate neighbourhood of the enterocytary brush border, where the receptors for these toxins can be found. The thermolabile toxin is similar structurally, functionally and antigenically with the choleric toxin, it stimulates adenylate cyclase at the same time with the increase of the cyclic adenosine monophospat and the consecutive increase of the intestinal secretion of water and electrolytes. The thermostable toxin is a small molecule distinct from the thermolabile toxin which stimulates guanylate cyclase, increasing the quantity of cyclic adenosine monophospat (6). Two endogen ligands of the thermostable toxin have been described: guanylin and uroguanylin. The existence of these two ligands suggests the fact that the thermostable toxin exercises the diarrhoeic effects by the alteration of the normal mechanism of the water and electrolytes secretion (by molecular mimetism with the above mentioned endogen agents). (10) Uroguanylin also interferes at renal level regarding the water and salt secretion, as a response to the salt oral charge. A large part of the ETEC strains produces the EAST1, a thermostable toxin, similar with that mentioned above, for the first time described in EaggEc.(5)

Clinical evolution. The clinical manifestations include nausea, abdominal pain, numerous aqueous explosive stools in large quantities, without mucous or blood. The disease is usually self-limited, evolving for a period of 3-5 days, rarely a week. The most severe cases may evolve towards the acute syndrome of dehydration. (10)

Enterocolitis with EPEC

Epidemiology. EPEC represents a major cause of diarrhoea in the developing countries, almost 30-40%

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of the enterocolitis cases, especially in infants under the age of 6 months are caused by EPEC. It may cause epidemic outbreaks in the newborn sections, whose incidence and severity have decreased lately. Due to the difficulty of the serotypes, the incidence of the enterocolitis with EPEC seems to be underestimated (1).

Pathogenesis. The EPEC virulence is determined by the attaching mechanism to the intestinal mucous, accomplishing the so-called injuries of “fixation and destruction”, which consist in the microvilli destruction and the intimate adherence of the microorganism to the intestinal cells. The affected enterocyte will suffer marked changes of cytoskeleton, including the actin polymers accumulation. The pathogenesis of the enterocolitis with EPEC follows three stages: the located adherence which will lead the germ in contact with the enterocyte, the transduction of the signal which leads to the intracellular calcium and to the phosphorylation of proteins and finally, the intimate adherence of the germ to the enterocyte. The marked loss of the microvilli determines the decrease of the absorption function of the small intestine, causing diarrhea. It seems that EPEC may also cause diarrhea by a secreror mechanism similar with ETEC (2, 7).

Clinical evolution. Generally, EPEC causes acute diarrhoea but the severe cases may present long evolution including complications such as: dehydration, malnutrition and zinc deficiency. The chronic diarrhoea accompanied by malnutrition occurs mainly in the children from the developing countries. The main clinical manifestations consist in vomiting, aqueous diarrhoea, reduced fever, general bad mood. The stools may contain mucous but they do not contain blood. Regarding the severe cases evolution, the syndrome of acute dehydration may occur (10).

Enterocolitis with EIEC

Epidemiology. The enterocolitis with EIEC occurs especially within the epidemic outbreaks, as a result of the contaminated food ingestion. EITEC enterocolitis outbreaks may occur in the developing countries, where this bacterium is isolated with a larger frequency. Within the developing countries, EITEC determines 5% of the diarrhoea sporadic cases and it is involved in almost 20% of the bloody diarrhoea cases.(1)

Pathogenesis. EIEC shares many characteristics, including the Shigella virulence factors. It determines injuries of the colon, ulcerations, bleeding, mucous and submucous edema, polymorphonuclear inflammatory infiltrate. The invasion process of mucous implies the following stages, which are similar to the invasion process accomplished by Shigella:

1. cell penetration
2. intracellular multiplication
3. intra and intercellular distribution
4. death of the host cell (10)

All bacterial genes necessary to the host cell invasion are situated at the level of a plasmid which can be encountered in Shigella, as well. This plasmid contains the *ipa* and *ipg* genes which codify different proteins which facilitate the EIEC penetration into the host cell. The *spa* and *mxi* genes codify a series of proteins which accomplish the type III secretion apparatus, necessary for the invasins production. This type III secretion apparatus may be encountered in many other bacteria, its major function being to transport proteins from the bacterial cytoplasm into the host cytoplasm (1, 6).

Clinical evolution. EIEC produces aqueous diarrhoea which is clinically impossible to differentiate from the secretory diarrhoea produced by ETEC. A small number of patients developed forms of dysentery with fever, general bad mood, colic abdominal pain, rectal tenesmus, stools in small quantity which contain mucous, leucocytes and blood (10).

Enterocolitis with STEC

Epidemiology. STEC was identified in 1983 as a cause of hemorrhagic colitis and uremic hemolytic syndrome (9). The infection may also be asymptomatic and the majority of the disease cases are determined by the O157: H7 serotype, which represents the most common cause of hemorrhagic colitis in the Unites States (10). The most severe manifestations occur in children, aged between 6 months and 10 years old, as well as in the elderly. STEC is transmitted by interpersonal contact, as well as by water and contaminated food (apple juice, non pasteurized dietetic products, insufficient thermally treated beef, mayonnaise, sausages) because of its very high virulence; thus only a small inoculum is necessary in order to produce the disease. The infection reservoir is represented by the cattle’s intestine, which remain asymptomatic. STEC causes about 10000-20000 infections per year in the USA, being the cause of approximately 250 deaths, yearly. (1)

Pathogenesis. Most severely, STEC affects the colon, where it produces edema, ulcerations, bleedings, fibrins deposits, neutrophilic infiltration and microvascular thromboses. The pseudomembranous colitis may also be encountered. The major virulence factor of STEC is shiga toxins of type 1 and 2, the majority of the STEC strains being capable of synthesising both of them. Shiga toxin type 1 is identical with the inhibiting exotoxin of the serotype 1 protein synthesis of the Shigellei dysenteriae, while shiga toxin type 2 presents similarities with Shigellei toxins, not being identical with these ones. Each toxin is made of a sub unit – A which is uncovalently linked to a pentamer made of 5 units B. The B sub units are linked to globotriosylceramide, a glycosphingolipid receptor of the host cell. The A sub unit enters the enterocyte through endocytosis, where it produces changes at the messenger RNA level (depurination), causing the alteration of the proteic synthesis and the host cell death in the end.

Toxins will enter the systemic circulation where they activate the coagulation, determine intravascular hemolysis, microthromboses and ischemia, as well as the mediators’ elaboration of inflammation by the host organism. Other virulence factors of STEC are: the capacity of producing injuries of “fixation and

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destruction”, similar with EPEC, enterohemolysin and autoagglutinitant adhesin (10).

Clinical evolution. Patients may be asymptomatic or may present diarrhoea of the easy form of aqueous diarrhoea up to severe hemorrhagic diarrhoea. The gastro-intestinal affection is characterised by abdominal pain, with initial aqueous diarrhoea, bloody diarrhoea subsequently, sometimes even with massive bleeding. Unlike the dysentery syndrome produced by Shigella or EIEC, in the case of STEC, fever is unusual. The symptoms may last for few days, rarely weeks. The majority of patients evolve without complications, but 5-10% of the children may present systemic complications of uremic hemolytic syndrome, type, characterised by acute renal insufficiency, thrombocytopenia and hemolytic anemia. Rarely, thrombotic thrombocytopenic purpura may occur (11).

Enterocolitis with EAggEc and DAEC

Epidemiology. Initially, they were regarded as one single entity. They represent one of the causes of prolonged diarrhoea in children from the developing countries, especially in those above 12 months years old. They may also determine acute diarrhoea and are involved in the travellers’ diarrhoea and in the chronic diarrhoea in AIDS (2).

Pathogenesis. Characteristically, EggEc produces a mucous biofilm at the level of the intestinal mucous, shortening of villi and determining hemorrhagic necrosis and inflammatory response. The pathogenesis of the enterocolitis with EggEc includes three stages: adherence to the intestinal mucous, augmentation of the mucous secretion and the production of toxins and inflammation which cause injuries of the mucous and the alteration of the intestinal secretion mechanism. The diarrhoea determined by EggEc is secretory predominant. The pathogenesis of the enterocolitis with DAEC is not completely characterised, but it seems that it resembles to those with EggEc.(8)

Clinical evolution. The typical manifestations consisted in aqueous diarrhoea, reduced vomiting or even absent, reduced or absent fever. The stools contain mucous in large quantity and regarding a third of patients, they may contain blood. The aqueous diarrhoea usually lasts more then two weeks, becoming complicated with retard of increase and malnutrition (10)

BIBLIOGRAPHY