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RECOMMENDATIONS FOR THE MANAGEMENT OF SYMPTOMATIC *CLOSTRIDIUM DIFFICILE* INFECTION (CDI)

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Definition of symptomatic *Clostridium difficile* infection (CDI)

Symptomatic *Clostridium difficile* infection is manifested by the appearance of clinical symptoms (most often diarrhoea) in a patient with confirmed presence of *Clostridium difficile* toxins or toxigenic *Clostridium difficile* strains in faecal specimen or pseudomembranous colitis, revealed in colonoscopy.

Etiology. Infection is caused by toxigenic *Clostridium difficile* strains. *Clostridium difficile* infection affects most frequently patients treated with antimicrobials or anticancer drugs within 8 weeks prior to the onset of CDI symptoms. However, there are also cases of community-acquired *Clostridium difficile* infection, thus, the absence of aforesaid drug use does not exclude CDI.

Risk factors for CDI progression. In addition to factors enumerated above, advanced age of patient (>64 years old) constitutes the most important risk factor for symptomatic *Clostridium difficile* infection and its severe and complicated course. Furthermore, other important risk factors include duration of hospitalization and contact with *Clostridium difficile*-infected persons during stay in hospital, use of inhibitors–H2, proton pump inhibitors and HIV infection.

Clinical course of CDI. Infection with toxigenic *Clostridium difficile* strains may be of asymptomatic course, however, it may also be manifested by symptoms ranging from mild diarrhoea to fulminant and fatal pseudomembranous colitis. In addition to diarrhoea, the following symptoms may occur: fever, pain or discomfort in the region of abdominal cavity and peripheral leukocytosis. Extraintestinal symptoms, including arthritis or bacteremia, appear on a rare basis.

Severe course of CDI may result in complications such as dehydration, electrolyte disturbances, hypoalbuminemia, megacolon toxicum, perforation of large intestine, sepsis, multiple organ dysfunction syndrome and death.

CDI diagnostics. If CDI is suspected in a patient, a specimen of diarrheal faeces (unformed) should be collected for laboratory testing. Examination of faecal specimen for CDI in asymptomatic patients is not recommended, except for the purpose of epidemiological investigations.

A standard diagnostic procedure should involve two stages, including: detection of *C. difficile* antigen by determining glutamate dehydrogenase (GDH) in faecal specimen, using immunoenzymatic method, and then, performing cell cytotoxicity assay for GDH-positive specimens. Such procedure is characterized by relatively the highest diagnostic sensitivity and specificity and rather low costs, however, it is time-consuming.

Detection of toxins A and B of *C. difficile* in faecal specimen, using immunoenzymatic method, is a rapid and inexpensive diagnostic technique. It should not be forgotten, however, that its sensitivity does not exceed 60%. Thus, in case of negative test results, diagnostics should be further extended.

Molecular biology techniques (PCR) are also applied in testing for *C. difficile* infection. Having considered their high costs, however, they are not used in a routine clinical diagnostics.

Provided aforesaid diagnostic methods fail, CDI may be also diagnosed on a basis of colonoscopy, revealing pseudomembranous colitis with typical histopathologic presentation of this disease.

Treatment of primary CDI. Metronidazole is the drug of choice in the treatment of CDI cases presenting mild or moderate course of disease. It is applied in a dosage of 500 mg p.o. 3 times a day for 10-14 days.

Vancomycin is the drug of choice in primary infection of severe course. It should be administered in a dosage of 125 mg p.o. 4 times a day for 10-14 days. Provided there are cases of considerable severe course, in which aforesaid treatment is not effective, oral dosage of vancomycin may be increased to 500 mg 4 times a day together with vancomycin per rectum as a retention enema in a dosage of 500 mg in 100 ml solution

administered enterally every 6 hours. Additionally, metronidazole in a dosage of 500 mg i.v. every 8 hours should be used in severe CDI cases.

In extreme instances, severe course of CDI may require surgical intervention, i.e. subtotal colectomy with preservation of the rectum.

Treatment of recurrent CDI. First CDI recurrence should be treated in a manner adopted in primary infection. Successive recurrences should be treated using vancomycin. Following first 10-14 days of treatment with oral vancomycin in a dosage of 125 mg 4 times a day, treatment may be extended by using 125 mg 2 times a day for a week, and then, 125 mg 1 time a day for a week, and finally 2-3 times in a week for the next 2-8 weeks.

Recommended and contraindicated adjunctive therapies. In addition to antibiotic therapy, treatment of severe CDI requires electrolyte disturbances to be rebalanced. If *C. difficile* infection is confirmed, the use of drugs inhibiting peristaltic reflex is absolutely contraindicated due to a risk of paralytic ileus and megacolon toxicum.

Use of probiotics, comprising *Saccharomyces boulardii,* does not have a considerable impact on CDI treatment, however, it may probably prevent the recurrence of disease.

Prevention of CDI. There are no existing recommended methods of CDI prevention in patients treated with antibiotics.

Received: 9.03.2015
Accepted for publication:25.03.2015

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