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Introductory Chapter: *Clostridium difficile* Infection

Overview

Shymaa Enany

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1. Introduction

Clostridium difficile (*C. difficile*) is an anaerobic, spore-forming Gram-positive bacillus that was first described in 1935 as part of the intestinal microflora in neonates, even so it was not identified as a causative agent of human disease until 1978 [1]. The clinical presentation of *C. difficile* infection (CDI) could be asymptomatic, mild or moderate diarrhea and fulminant colitis [2, 3].

2. Epidemiology of CDI

Center of Disease Control and Prevention showed an elevation in the incidence and the severity of CDI [4]. More than 250,000 person need to be hospitalized due to CDI, and around 14,000 people die from it in the United States every year [5]. Among hospitalized patients, the incidence of CDI differs every year and from location to another. It has been elevating, to nearly 15 per 1000 hospital dismissal [6] and around 20 cases per 100,000 individual in the community [7]. *C. difficile* can only colonize the gut when the normal intestinal microflora is changed by the usage of antibiotics and that was proved by the 16S ribosomal RNA sequencing [8]. Therefore, the antibiotics usage remains the most important risk factors for *C. difficile* infection. Many antibiotics are associated with the CDI such as ampicillin, amoxicillin, cephalosporins, clindamycin, fluoroquinolones, trimethoprim and sulfonamides [9]. Another risk factor for CDI is the age; the severity of the infection increases as the age increases [10]. Poor hand hygiene has also previously been shown to play a part in CDI transmission [11]. Hospitalization considers also a main risk factor as it brings together many CDI risk factors in one place such as the use of antibiotics, the spore contaminated media, inappropriate hand hygiene and the elderly patients [12].

3. *C. difficile* virulence factors

C. difficile has many virulence factors including toxins, sporulation, surface layer proteins and adherence. It produces many toxins such as the enterotoxin TcdA, the cytotoxin TcdB and the binary toxin CDT [12]. These toxins cause disruption of the actin cytoskeleton and tight junction and cause a decrease in the transepithelial resistance, fluid accumulation and damage of the intestinal epithelium [13].

4. Diagnosis of CDI

Diagnosis of *C. difficile* is easily done in the laboratory and usually performed for the patients suffering from diarrhea. Currently, CDI is diagnosed by several available diagnostic tests such as enzyme immunoassay (EIA), EIA for *C. difficile* glutamate dehydrogenase (GDH) or by DNA-based tests which recognize the genes of *C. difficile* toxin in the stool sample. Additional diagnostic tests are available like toxigenic cultures and cell culture neutralization assays [14].

Stool culture for *C. difficile* requires anaerobic culture and is not widely available [9]. Radiography suggestive of CDI includes polypoid mucosal thickening, haustral fold thickening or gaseous distention of the colon; however, radiographic features are not sensitive and not CDI specific [15]. Another diagnostic method is the endoscopy which is rarely required, but it may be helpful in case of doubt of CDI from the clinical signs with all the laboratory tests showed negative results or in patients with inflammatory bowel disease [16].

5. Prevention and treatment of CDI

Since there is no effective vaccine for the CDI control, prevention of the CDI has been a demand and it has focused on barrier methods and environmental hygiene in a trial for prohibiting *C. difficile* spores and for the reduction of the CDI risk factors: isolation of CDI patient in private room, gowns and gloves usage, hand hygiene and the use of sporicidal solution for rooms [12]. Moreover, altering the antibiotic prescribing could be a good way for preventing CDI spreading, since the possibilities of some antibiotics to stimulate CDI are smaller than others. Furthermore, the use of probiotics to prevent CDI could be a safe method. Probiotics usually formed of live microorganisms which give a lot of health benefits to the patient. These microorganisms work through direct activity against *C. difficile* through the inhibition of the bacterial adherence, the modification of the response of the host and the induction of production of specific IgA antitoxin [17, 18].

The treatment of CDI has not shown a big variation. For the acute infections, metronidazole and oral vancomycin has been the mainstay of treatment since 1970. Fidaxomicin was approved in 2011 by the Food and Drug Administration for CDI treatment [19]. Treatment of the first recurrent CDI infection is recommended with a repeat course of either metronidazole

or vancomycin, and this regime is proved to be successful in 50% of patients [20]. Second recurrent infection can be treated with fidaxomicin which proved to prevent further episodes of *C. difficile* [21]. The fecal microbial transplantation is one of the bacterio-therapy used to prevent CDI. It is referring to the infusion of fecal suspension from a healthy person to reinstating the gut microbiota of the recipient.

6. Conclusion

Since the CDI causes common and serious problems, many researchers have focused on improving the prevention and the treatment of CDI. In this book, we have focused on studying the pathogenesis and the virulence factors of *C. difficile* including toxins and trying to explore the different diagnostic tools and preventive therapeutic methods.

Author details

Shymaa Enany

Address all correspondence to: shymaa21@yahoo.com

Microbiology and Immunology Department, Faculty of Pharmacy, Suez Canal University, Egypt

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