

Recommendations for the Development of New Hospital Guidelines due to the Effects of Antibiotics on *Clostridium difficile* Colitis

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What is *Clostridium difficile*?

- ▶ Gram-positive, anaerobic, spore forming
- ▶ Ability to produce exotoxins
- ▶ Naturally present in approx. 5% of populations microbiota
- ▶ It becomes pathogenic when *C. difficile* exploits an uninhabited niche

C. difficile virulence factors

- ▶ Attachment of the bacterium to the mucin and cells lining colon
- ▶ Damage occurs due to toxins and a yellowish layer forms on surface of the colon
- ▶ Damage causes an inflammatory response
- ▶ Pseudomembrane forms

C. difficile toxins

- ▶ Two large AB-type toxins
 - ▶ TcdA
 - ▶ TcdB
- ▶ TcdA
 - ▶ Mucosal cells become unable to control fluid movement
 - ▶ Slower working than TcdB
- ▶ TcdB
 - ▶ Collapses the actin cytoskeleton of the tissue cells
 - ▶ Some strains only produce TcdB

TcdA Mechanism

- ▶ Stimulation leads to cytokines and other inflammatory proteins
- ▶ Attraction of neutrophils
- ▶ Results in mucosal-cell destruction
- ▶ Fluid movement is not able to be controlled
- ▶ Pathway for TcdB to enter
- ▶ Targets G proteins
 - ▶ Responsible for many regulatory functions in mammals

TcdB Mechanism

- ▶ Damages the tissue on the underside of the mucosal membrane and intestinal wall
- ▶ Extensive damage can lead to LPS or bacteria from colon to enter into the bloodstream and cause septic shock

How *C. difficile* may be transmitted

- ▶ Survival through spores
 - ▶ Can survive for up to 5 months
 - ▶ Sanitization is important
- ▶ Transmitted by:
 - ▶ Environmental surface contamination
 - ▶ Staff or infected patients carrying it around on their hands

Symptoms

- ▶ Mild to Moderate
 - ▶ Watery diarrhea three or more times a day
 - ▶ Mild abdominal cramping and tenderness
- ▶ Severe
 - ▶ A few of the symptoms include:
 - ▶ Watery diarrhea ten to fifteen times a day
 - ▶ Severe abdominal cramping and pain
 - ▶ A stay in an intensive care unit
 - ▶ Endoscopic examination showing the presence of pseudomembranes

Antibiotic Risk Factors

- ▶ 96% of people received antibiotics within the last 14 days of their first symptoms
- ▶ All had received antibiotics within the last 3 months
- ▶ Fluoroquinolones
 - ▶ Associated with a higher risk
- ▶ Important because many people are taking antibiotics
 - ▶ Ex. Acne antibiotics
- ▶ Increased antibiotic use associated with new hypervirulent strain BI/NAP1/027

Diagnostic Testing

- ▶ Best specimen for testing is watery, loose, or unformed stool
- ▶ Cell Cytotoxicity Assay
- ▶ Enzyme Immunoassay
- ▶ Culture
- ▶ Glutamate dehydrogenase
- ▶ Polymerase Chain Reaction

Current Treatment Options

- ▶ Antibiotics
 - ▶ Metronidazole
 - ▶ Vancomycin
 - ▶ Fidaxomicin (Dificid)
- ▶ Colectomy
 - ▶ Used in severe cases
- ▶ Fecal Microbiota transplantation

Fecal Microbiota Transplantation (FMT)

- ▶ Process of delivering stool from a healthy donor to a patient
- ▶ Routes of administration
 - ▶ Enema
 - ▶ Colonoscopy
 - ▶ Upper GI tract via ingestion
- ▶ Preferred due to decrease in probability of a relapse occurring
- ▶ Goal: Help the body reestablish its normal microbiota
 - ▶ *Bacteroidetes* and *Firmicutes*
- ▶ Administration: mix fecal matter with nonbacteriostatic saline solution and then strain or blend to remove unwanted particulate
- ▶ Good option for people with compromised immune systems
- ▶ 83% - 90% efficiency

Why *C. difficile* Is a Concern

- ▶ Increasing resistance of patients to antibiotics
- ▶ Costing approximately \$3.2 billion annually
- ▶ Many people today are taking antibiotics for many things making them susceptible

Solutions

- ▶ Education
 - ▶ Physicians
 - ▶ Patients
- ▶ Prevention of Transmission
 - ▶ Handwashing, gloves, gown
- ▶ Hospital Layout
 - ▶ Single rooms or patients with *C. difficile* in same room
- ▶ Hospital Cleaning Staff Responsibilities
 - ▶ Sporocidals, 1:10 dilution of concentrated sodium hyperchlorite (bleach)

Solutions continued...

- ▶ FMT in a Pill
 - ▶ Reduction of transmission through instruments
- ▶ Continued Care Practices
 - ▶ Bringing hospital guidelines to the home of the patient
- ▶ Further Development of Care
 - ▶ Research to gain a better understanding

Conclusion

- ▶ It is a disease that can be controlled
 - ▶ Education
 - ▶ Understanding of risks associated with antibiotics
 - ▶ Maintaining a clean environment

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