Clostridium Difficile Infection (CDI)

Introduction

Clostridium difficile is an anaerobic spore-forming gram-positive bacillus. It is ubiquitous in the environment especially in the soil. *C. difficile* is the most common cause of infectious colitis in hospitalized patients and is often associated with antibiotic use. The strain of *C. difficile* that produces toxin A and B is most virulent and is associated with severe disease. Non-toxin producing strains are not pathogenic.

Transmission

The primary mode of transmission is via the fecal-oral route. Patients are exposed to *C. difficile* through direct contact with:

- Health-care workers whose hands are transiently colonized with spores
- Contaminated environment
- Asymptomatic carriers

C. difficile Infection (CDI) Definition

- 3 or more passages of unformed stools in 24 hours
  AND
- A stool test positive for toxigenic *C. difficile*, and detection of toxin in stool
  or
- Colonoscopic or histopathologic findings of pseudomembranous colitis

Risk Factors Associated with CDI

- Antibiotics
  - Typically 4-9 days after initiation, but may occur up to 10 weeks after initiation
  - Most commonly implicated:
    - Clindamycin
    - Fluoroquinolones
    - Third generation cephalosporins

    Note: fluoroquinolones associated with hypervirulent C. diff strain
  - Increased risk with multiple antibiotics or multiple doses

    Note: A single dose of antibiotics (e.g. surgical prophylaxis) may also increase risk of CDI
- Hospitalization
  - > 72 hours
  - Increased risk with prolonged stays > 28 days
- Advanced age
  - > 60 years - 10-fold increased risk
- Gastrointestinal surgery or manipulation
- Acid-reducing agents (proton pump inhibitors, histamine-2 receptor antagonist)

Testing

- Cytotoxicity assay
  - Previous gold standard
  - Sensitivity approx. 80%
  - Time to reporting 48-72 hours
- Enzyme immunoassay (EIA) for antigen detection and toxin production
  - Rapid time to reporting
  - Sensitivity of test still problematic
- Molecular detection of toxin – PCR assay
  - Improved sensitivity and specificity
  - Current testing method in use at KGH

    Note:

    1. With PCR assay, no need to repeat testing if negative as previously recommended with EIA method.

    2. Test of cure not recommended as test may remain positive for 3-4 weeks after resolution of clinical symptoms. Treatment of recurrences should be based on clinical symptoms.

Clinical Manifestation of CDI

- May range from asymptomatic *C. difficile* colonization to life-threatening pseudomembranous colitis (Table 2)
- Onset of symptoms usually occurs within 2-3 days after acquisition of *C. difficile*
- Diarrhea may contain mucous or occult blood (frank blood not typical of CDI)

Table 1 – Severity and Complications of CDI (*Adapted from reference 2)*

Disease Severity	Diarrhea	Symptoms	Physical Exam	Other Diagnostic Findings
Asymptomatic colonization	--	--	Normal	Normal
Mild CDI	+	Usually no systemic symptoms	Usually normal	Normal
Early colitis	+++	Nausea ↓ appetite	Fever (low-grade) ± mild abdominal tenderness	Patchy erythema (nonspecific)
Pseudomembranous colitis	+++	Nausea Fatigue Abdominal discomfort	Fever Abdominal tenderness, distension	Pseudomembranes (yellow plaques) Leukocytosis with left shift
Fulminant colitis	+++ (may be absent in ileus or toxic megacolon)	Nausea Abdominal discomfort / pain	Fever (high) Abdominal tenderness, distension	Endoscopy contraindicated in severely-ill Leukocytosis Colonic dilatation, mucosal thickening, perforation on radiography

-- = none; + = mild; +++ = profuse

Infection Control Precautions for Acute Care (CDI proven or highly suspected)

- Move patient to a single-bed room. If not feasible, use a dedicated commode which is kept at the patient's beside
- Post appropriate signage outside patient's room
- Wear gown and gloves for patient care
- Wash hands with soap and water when leaving patient's room
    - **Note: alcohol-based hand cleanser is not effective against *C. difficile* spores**

Precautions for patients at home:

- If diarrhea persists, use own bathroom, or clean bathroom after each use
- Wash hands with soap and water after toileting and before eating

Treatment

Antibiotic Therapy

- Discontinue antibiotics if possible
- If antibiotic treatment necessary, consider using antibiotics with lower CDI potential (e.g. cotrimoxazole, tetracyclines, aminoglycosides)
    - Minimize duration of antimicrobial therapy and number of antibiotics

Table 2 – Treatment of CDI dependent on severity *(Adapted from reference 1)*

Severity Classification	Supportive Data	Recommended Treatment
First mild-moderate episode	WBC ≤ 20 x 10^9 /L Serum creatinine (SCr) < 1.5x base-line value	Metronidazole 500mg PO/NG TID x 10-14days If NPO, use metronidazole 500mg IV Q8H x 10-14 days
Severe episode	WBC > 20 x 10^9 /L SCr ≥ 1.5 x baseline value Sepsis/hemodynamically unstable Deterioration on metronidazole	Vancomycin 250mg PO QID x 10-14 days.
First recurrence		Same as for initial episode Consider vancomycin 250 mg regimen if recurrence is severe
Second recurrence		Vancomycin 125mg PO/NG QID x 10-14 days Consider 250 mg regimen if severe disease
More than 2 recurrences		Consider tapered vancomycin Consider specialist consult
Episode with complications	ileus, toxic megacolon	Metronidazole 500mg IV Q8H x 10-14 days, **plus** Vancomycin 500mg in 1L normal saline perfused via rectal tube at 3mL/min x 10-14 days

Note: Metronidazole should not be used for more than 2 consecutive courses or in a tapering regimen due to cumulative risk of neurotoxicity.

Binding Resins and Antimotility Agents

- Avoid cholestyramine, colestipol and other ion-exchange binding resins
    - These products bind to vancomycin, rendering it less effective in eradicating CDI
    - Addition of these agents do not prevent future episodes
- Discontinue antidiarrheals as they prevent elimination of *C. difficile* toxins and delivery of metronidazole or vancomycin to the site of action
    - Antidiarrheals include:
        - Attalpulgite (Kaopectate™)
        - Loperamide (Imodium™)
        - Diphenoxylate-atropine (Lomotil™)

Probiotics

- Insufficient evidence to recommend routinely for primary prevention of CDI
    - *Lactobacillus* and *Saccharomyces boulardii* may decrease incidence of mild diarrhea associated with antibiotic use
- A small study demonstrated probiotic-containing yogurt may decrease risk of CDI in patients > 50 years of age
    - Larger trials are warranted to confirm the results
- Limited evidence supports use of *Saccharomyces boulardii* in addition to vancomycin therapy for secondary prophylaxis in patients with recurrent CDI
- Potential risks of bloodstream infections in immunocompromised patients
- Lack of product standardization

Fecal transplant

- May be considered in recalcitrant cases; consultation with specialist recommended

References

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