Early Symptom Identification, Diagnosis, and Treatment Strategies for Clostridium Difficile Infection

Acquired During Hospitalization in Adults Ages 18 and Over

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By

Sarena L. Sloot, RN, BSN, FNP-S

WASHINGTON STATE UNIVERSITY

COLLEGE OF NURSING

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To the Faculty of Washington State University:

The members of the Committee appointed to examine the master's project of

SARENA L. SLOOT find it satisfactory and recommend that it be accepted.

Lorna Schumann, PhD, ACNP-BC, NP-C,
ACNS-BC, CCRN, ARNP, FNP, ACNP, FAANP

Mel Haberman, PhD, RN, FAAN

Billie Severtsen, MN, PhD
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Early Symptom Identification, Diagnosis, and Treatment Strategies for *Clostridium difficile* Infection Acquired During Hospitalization in Adults Ages 18 and Over

By Sarena L. Sloot, RN, BSN, FNP-S

Chair: Lorna Schumann

Abstract

*Clostridium difficile* acquired infection (CDI) is a significant cause of morbidity and mortality for hospitalized patients in the United States, as well as a large financial burden for both patients and healthcare facilities. Evidence based practice recommendations currently focus on preventative measures such as contact precautions, environmental decontamination, and antimicrobial stewardship in order to prevent horizontal transmission, however there are few available strategies that allow healthcare providers to promptly identify, diagnose, and treat patients with CDI early in the disease process. Recommendations for areas of research include clearly defining patient symptoms to trigger provider suspicion of CDI, streamlining diagnostic testing modalities, standardizing pharmacologic treatment interventions, and exploring the role of alternative preventative therapies such as monoclonal antibodies and bio-therapeutics. Through early symptom identification strategies, diagnostic testing modalities, and evidence based treatment recommendations, providers can decrease patient morbidity and mortality and improve overall outcomes.

Keywords: *Clostridium difficile*, CD, CDI, identification, symptom, testing, treatment.
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Early Symptom Identification, Diagnosis and Treatment Strategies for *Clostridium Difficile* Infection Acquired During Hospitalization in Adults Ages 18 and Over.

**Introduction**

*Clostridium difficile* (CD) is an anaerobic, gram-positive, spore-forming bacillus that attaches to the mucosa of the colon and when given the proper host environment, produces toxins that result in mucosal disease. Acquisition occurs by oral ingestion of spores which resist acidity of the stomach. Spores germinate into vegetative bacteria within the small intestine. When normal colonic flora is altered by exposure to antimicrobials an environment in which CD is able to multiply and produce endotoxins that lead to disease is created (Guide to the Elimination of *Clostridium difficile* in Healthcare Settings, 2008). The endotoxins created by this reaction are coined either A or B strains of the infectious organism, however studies indicate that both strains cause the same spectrum of disease (Cookson, Fritsche, Limaye & Turgeon, 2000). *Clostridium difficile* infection (CDI) is defined by the presence of symptoms such as mild to moderate diarrhea with either a stool test positive for CD toxins or toxigenic CD, or colonoscopic or histopathologic findings revealing pseudo membranous colitis (Dubberke, Olsen, McDonald, & Reske, 2008). Active CDI can lead to toxic dilation of the colon, sepsis, and death (Caro, Lahue, & O’Brien, 2007).

Risk factors for CDI include advanced age, immune status, duration of hospital stay, and exposure to antimicrobial agents (Kwok, McFarland, & Mulligan, 1989). Other risk factors noted in literature review were high severity of illness, exposure to other patients with CDI, and receipt of gastric acid suppressants (Butler et al., 2011).
Emerging evidence also notes that irritable bowel disease, solid organ transplant, gastrostomy or jejunostomy tube placement, and peripartum women, are also at increased risk (Lo Vecchio & Zacur, 2012).

CDI is a significant cause of morbidity and mortality for hospitalized patients in the United States, as well as a large financial burden for both patients and healthcare facilities. CDI accounts for 20%-30% of cases of antibiotic-associated diarrhea and is named as the most commonly recognized cause of infectious diarrhea in healthcare settings in adult populations (Cohen et al., 2010). National surveillance data within the United States indicates that the incidence of hospital discharges with CDI doubled between 2000-2003 with a disproportionate increase for persons older than 64 years of age (Caro, Lahue, & O’Brien 2007). Recent literature also indicates that 13 out of every 1000 hospitalized inpatients will be either infected or colonized with CDI (Guide to the Elimination of Clostridium difficile in healthcare settings, 2008). In addition, recent studies indicate that, as many as 250,000 hospitalizations in the United States in 2005 were complicated by CDI associated disease (Dubberke, Fraser, McDonald, Olsen, & Reske, 2008). Evidence shows that an estimated 45.5% of CDI are identified at greater than 48 hours after admission, causing 72.5% of identified infections to be considered healthcare-associated rather than community associated or chronic colonization, which further compounds early identification, testing, and appropriate treatment (Guide to the Elimination of Clostridium difficile in Healthcare Settings, 2008).

CDI has been associated with an attributable mortality rate of 6.9% after 30 days of disease, and contributed indirectly to another 7.5% of deaths within the healthcare
setting within this timeframe. The attributable mortality rate at one year is estimated at 16.7% (Caro, Lahue, & O’Brien, 2007). One study of 278 intensive care patients had a 30-day mortality rate of 30.6%, yielding an attributable mortality of 6.1% for patients with CDI and associated disease (Doherty, Kenneally, Rosini, & Skrupky, 2007). This data suggests that a large percentage of the United States’ inpatient population has the potential to experience negative outcomes due to CDI associated disease.

**Problem Statement**

There are few available strategies outside of infection prevention control techniques that allow healthcare providers to identify, diagnose, and treat patients at risk for CDI in a time sensitive fashion. Some strategies are contact precautions, environmental decontamination, and antimicrobial stewardship. Providers are challenged to identify CDI infection early and respond with appropriate treatment, which is believed to decrease patient morbidity and mortality.

The purposes of this paper are to examine the evidence pertaining to the early symptom identification, diagnosis, and treatment strategies related to CDI. The population of interest is adults over the age of 18 identified as contracting hospital acquired CDI during an inpatient admission. The concepts of interest are early symptom identification strategies, (strategies are defined as screening processes and algorithms), diagnostic testing modalities and treatment recommendations of hospital acquired CDI.
Literature Search Strategies

Literature search was initiated using the WSU online library. An advanced cross sectional search of databases was performed. The initial key words used during the cross search were “Clostridium difficile,” “screening,” “strategies,” “early symptoms,” “identification,” “adult,” “inpatient,” “treatment” and “test.” Databases searched included PubMed, American Medical Association, CINAHL (EBSCO), Cochrane Library (Wiley) and PsycInfo, and Springer Protocols. One hundred and seventy one articles were returned and then narrowed by “peer reviewed,” and “published within the past 5 years.” This resulted in 42 article retrieved, 28 articles reviewed, and 15 analyzed in accordance with discussion problem statement and organized into three sections: early symptom identification strategies (2 articles), diagnostic testing modalities (4 articles), and treatment recommendations of hospital acquired CDI (9 articles). The Clinical Practice Guidelines for Clostridium Difficile Infection in Adults by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) (2010) were considered and integrated into the sections of this paper as the current evidence based practice guideline. Current recommendations specify that CDI is effectively managed when discovered early, detected with appropriate laboratory examination, transmission precautions taken, and appropriate pharmacological measures followed (Centers for Disease Control, 2011).

Theoretical Framework

The Research Center for Symptom Management at the University of California at San Francisco developed a model to guide advancement of knowledge in regards to
symptom management in any disease process and subsequently improve provider practice and patient outcomes (See Figure 1). If symptom control is not achieved patient outcomes are adversely affected. Providers are challenged to create symptom management strategies that are useful and relevant to the healthcare setting (Lee & Miaskowski, 2011).

The symptom management model gives person, environment, and health/illness focused direction to symptom experience. Three components are subsumed in these three broader domains: symptom experience, symptom management strategies, and outcomes (Lee & Miaskowski, 2011). The symptoms experience evaluation of interest in CDI are liquid stools of greater than 500 milliliters on a single occurrence and the presence of greater than 3 liquid stools in one 24 hour timeframe within the inpatient setting (Coignard et al., 2007). The components of symptom management of interest in CDI are what symptoms need to be recognized early to constitute prompt diagnosis (Coignard et al., 2007) and what diagnostic tests should be performed and when should they take place (Jessee, 2011). Symptom outcomes of interest are decreased morbidity and mortality of adult inpatients, and improved functional status through symptom identification, management, and treatment (Forster, Oake, Roth, Taljaard, & Walraven, 2010).

**Literature Review**

**Symptom Identification**

The initial priority for adult inpatients with CDI is the early identification of the disease process itself. Description of CDI criteria include the presence of diarrhea, defined as passage of 3 or more un-formed stools in 24 or fewer consecutive hours, a stool test result positive for the presence of toxigenic CDI or its toxins, or colonoscopic
or histopathologic findings demonstrating pseudomembranous colitis. The same criteria is used to diagnose recurrent CDI (SHEA & IDSA, 2010). Guidelines do not however, suggest any clear identification criteria or symptomology that should by providers to identify CDI in early stages to decrease horizontal transmission, treat early, and thus improve patient outcomes. Using the symptom management theory as a theoretical framework, literature was examined to determine what symptomology can be used to aid providers in early identification of CDI.

Hardy, Hawkey, Gossain, Pillay, and Thomblinson (2010) conducted an 18 month study of 439 patients with 102 periods of increased incidence (PII) of CDI. Using PII patient sample ribotyping, which is defined as a method of identifying toxigenic isolates i.e. specific strains of CD within positive stool culture, confirmed 32% of these outbreaks to be the same CDI strain, and suggested that facilities should implement this isolate identification when greater than 10 patients are involved in PII of CDI. Overall results indicated at 40% reduction in the incidence of CDI in adult inpatients when PII causative strains were identified by using ribotyping isolation through improved infection control techniques for horizontal transmission and early identification of patients that may be involved in overall PII. In application to symptomology, PII’s in the studies facility were identified through symptoms experienced such as increased frequency/occurrence of liquid stools in multiple patients on different wards of facility. Limitations to this study include no documented amount of frequency or amount of stool experienced by patients, and only specified increased incidence in diarrhea in patients overall.
Abbett et al. (2009) defined symptom triggers for CDI as 6 or more loose stools over 24 hour periods in mild cases, defined as an afebrile patient with a white blood cell count less than 15000. Patients who experienced these symptoms were tested for CDI. Early identification though clear symptom triggers raised the index of suspicion for CDI, allowing a protocol for early identification and treatment to be successfully utilized. CDI rates decreased from an average of 1.10 cases per 1,000 patient days (95% confidence interval, 1.00-1.21) to 0.66 cases per 1,000 patient days (95% CI, 0.60-0.72), which equated to a 40% decrease in the rate of healthcare associated CDI post implementation.

**Diagnostic Testing Modalities**

The Healthcare Epidemiology of America (SHEA) and Infectious Disease Society of America (IDSA) (2010) cited diagnostics testing methods of choice for CDI as stool culture assay test, with reported sensitivity and specificity of >98% for both negative and positive predicted values, but note modality is not clinically practical due to slow turn-around time. In regards to glutamate dehydrogenase (GDH), suggested strategies are to employ a 2-step method that uses EIA assay detection of GDH as initial screening and then cytotoxicity assay or toxigenic culture to confirm GDH positive tests as GDH alone can lack sensitivity. Further of note is that results studies thus far appear to differ based on GDH kit used by the performing laboratory. GDH sensitivity is reported at 58%–68% and specificity at 94%–98%. Newer assay GDH-EIA tests show a sensitivity of 85%–95% and a specificity of 89%–99 and have a high negative predictive value. Polymerase chain reaction (PCR) testing is described as rapid, sensitive, and specific and may ultimately address concerns of clinical application of stool culture due to result turn
around without losing specificity and sensitivity, but data is lacking in regards to consistent results of equal sensitivity and specificity across different types of PCR’s, and data in regards to specific sensitivity and specificity percentages were not available at the time of publishing of 2010 guidelines, so no recommendation as to its use were made.

Aird et al. (2005) evaluated a two-step algorithm for detecting toxigenic Clostridium difficile utilizing enzyme immunoassay for glutamate dehydrogenase antigen (Ag-EIA), with reflex to a concurrent cell culture cytotoxicity neutralization assay (CCNA) for antigen positive specimens. Antigen negative results were greater than 99% predictive of CCNA negativity. Predictive value of a positive antigen result was 49%. This information does confirm this form of diagnostic testing is be best used for initial screening of CDI in a setting to rule out infection as opposed to in a patient whom has a high index of suspicion for active disease due to the low positive predictive value as suggested by ISDA and SHEA.

Chaugla et al. (2003) performed a study on 557 diarrhea stool samples from adult inpatients clinically suspected of CDI with cytotoxin B culture assay (CTA) C. difficile tox A/B II test, and the Triage Micro C. difficile Panel which detects toxin A and GDH simultaneously. Results of the CTA were compared with the C. difficile tox A/B II and the Triage Micro C. difficile panel, with results of the GDH being most sensitive but least specific, and the Tox A and Tox A/B less sensitive but highly specific. It was concluded that GDH would be the best screening test for CDI and stool culture most useful as a confirmatory test for GDH positive specimens.
Jessee (2010) reviewed the stool culture, GDH, and PCR use in CDI and concluded stool culture is the diagnostic method of choice. PCR detects and quantifies the CDI organism with rapid results, but is not able to identify toxin verses non-toxin forming strains. GDH is noted to have a high sensitivity and specificity but stool culture should follow any positive GDH results as specificity still lower in GHD than stool culture.

Bakker et al. (2011) analyzed 3 types of commercially available PCR’s to evaluate CDI and compared their efficacy against stool culture. 526 diarrhea samples were collected and results of both PCR and cytotoxigenic stool culture testing were compared for sensitivity, specificity, positive predicted value (PPV) and negative predicted value (NPV). Results indicated that all three PCR’s evaluated could be applied as a first screening test in an algorithm for diagnosing CDI but low PPVs hindered the use of PCR as stand-alone diagnostic testing modality. Suggestion was made that positive PCR should reflex to stool culture, but that delay of administration of antimicrobials in the presence of PCR positive tests while waiting for confirmatory stool culture should be avoided.

Treatment

The SHEA and ISDA (2010) recommended discontinuing antimicrobial agents as soon as possible, and cites Metronidazole (Flagyl) as the drug of choice for mild to moderate CDI. Vancomycin was cited as the drug of choice for severe CDI, and recurrent CDI. Also noted is to avoid antiperistaltic agents as they obscure symptoms and precipitate toxic megacolon.
Kelsey et al. (2011) conducted a systematic literature review of randomized controlled trials assessing antibiotic treatment of CDI associated diarrhea (CDAD) in adults. They examined 15 studies with 1152 participants and 9 different antibiotics used in CDI treatment. Vancomycin was found to be superior (41%) to placebo (4%) for initial symptomatic cure of CDAD, but studies did not find any statistically significant different in efficacy between Vancomycin, Metronidazole (Flagyl), Fusidic acid, Nitazoxanide or Rifaximin (Xifaxan). No new recommendation could be made in regards to treatment modalities of CDI due to the small number of patients within these studies, and the high risk of bias (12 out of 15 studies) related to dropouts.

Lo Vecchio and Zacur, 2012 noted that both Vancomycin and Metronitazolate (Flagyl) are associated with lack of response to treatment and recurrent disease of 20-30% in reference to a Canadian study performed to evaluate outcomes of reoccurrant CDI. Brazeau, Gagnon, Pepin, and Routhier (2006) report results of which in 463 patients diagnosed with a first CDI recurrence, 154 (33%) experienced a second recurrence. Neither drug of choice was proven as a direct causative factor to a first recurrence, however, it was suggested that both antimicrobials were causative factors in second recurrence as 51 patients (11%) developed at least 1 complication i.e. shock, need for colectomy, megacolon, perforation, or death within 30 days during the first recurrence. These complications were believed to be a result of decreased efficacy of Vancomycin and Metronitazole (Flagyl) in CDI predisposing patients to reinfection risk and complications CDI due to lack of efficacious antimicrobials administered for first recurrence. Efficacy decreases from 70% upon first episode to 35% with recurrent
episodes. Also noted was that Metronitazole (Flagyl) is not an FDA approved treatment for CDI.

Gerding, Hecht, Johnson, Patel, and Patel (2009) also noted emerging evidence that suggests that the use of Rifaximin (Xifaxan) in recurrent CDI post Vancomycin treatment is promising, where in a small study 4 out of 6 patients were successfully relieved of diarrhea symptoms post 400 mg administration three times daily. The study did not discuss if they were negative for CD by diagnostic testing modalities. Limitations of this study are very small sample size.

Aslam et al. (2005) performed an RCT of 207 patients with CDI at Houston Veterans Administration Medical Center from 2003 to 2004 and found 46 patients (22%) were resistant to first line recommendation of metronidazole and 58 patients (28%) who were initially responsive to Metronidazole (Flagyl) experienced symptom re-occurrence within 90 days. This suggests growing resistance rates to first line drugs in CDI.

Basu and Dinani (2010) performed an RCT of 25 patients with mild to moderate CDI who were unresponsive to Metronidazole (Flagyl). Subjects were given Rifaximin (Xifaxan) 400 mgs three times daily after discontinuation of Metronidazole (Flagyl) and 16 of 22 patients (73%) were CD negative by PCR at 14 days and upon follow up in 56 days. No explanation is given as to why 3 participants were not included in the results other than they did not meet inclusion criteria for Rifaximin (Xifaxan) treatment, and inclusion criteria was not discussed. Noted limitations for clinical use of this study include possible drug resistance and unexplained exclusion.
Bressler, Logan and Musher (2009) noted is a randomized trial of 50 patients whom showed that Nitazoxanide may be slightly more effective than Vancomycin in patients with mild to moderate and severe disease. This study was again small and has not yet been reproduced in order to make clinical practice suggestions based off findings. It is noted however that the high cost of the drug represents barriers for its defining role in CDI.

Grgurich et al. (2010) conducted a pharmaco-epidemiologic cohort study and secondary data analysis of 101,796 discharges from tertiary care centers over a 5-year period with primary interest of acid suppression therapy with Histamine 2 receptor antagonists and proton pump inhibitors were prescribed. Findings included the risk of nosocomial CDI increase from 0.3% (95% confidence interval) (CI) to 0.21%-0.31% in patients not receiving suppressive therapy, 0.6% (95% CI 0.49% -0.79%) in those receiving histamine 2 receptor antagonist therapy, and 0.9% (95% CI, 0.80%-0.98%) in those receiving daily proton pump inhibitor therapy, and 1.4% (1.15%-1.71%) in those receiving more frequent proton pump inhibitor therapy. Data suggests that increased risk of nosocomial CDI is associated with increased levels of pharmacologic acid suppression.

Voekler (2010) noted two randomized control studies of 200 patients were assessed by giving 2 monoclonal antibodies developed against CD toxins A and B against placebo. When given together as a single infusion to patients receiving Metronidazole (Flagyl) or Vancomycin, the antibodies reduced recurrence rates in patients with strain specific infections. This is of note as Kelsey et. al (2010) cites recurrence rates of CDI are cited to be as high as 6 to 25%
Leav, Lowy and Molrine (2010) reported in a double blind placebo controlled study of two fully human neutralizing monoclonal antibodies in which 200 patients (101 in the antibody group and 99 in the placebo group) were evaluated and the rate of recurrence of CDI resulted lower among patients treated with monoclonal antibodies (7% vs. 25%) with 95% confidence interval (P<0.001). The recurrence rates among CDI patients were 8% for the antibody group and 32% for the placebo group (P 0.06). In patients with more than one recurrent episode of CDI, recurrence rates were between 7% and 38% (P 0.006). The conclusion was therefore made that this study resulted in a 72% relative reduction in recurrence rated compared to placebo, but did not reduce the severity of infection, duration of diarrhea, or duration of hospitalization. Limitations and bias were not disclosed.

Lo Vecchio and Zacur (2012) reported the development of a biotherapy similar to a vaccine by Sanofi-Aventis which uses a naturally occurring strain of CD that does not produce disease causing toxins. Phase II RCT of CD toxoid vaccine are reportedly underway as sponsored by the manufacturer Sanofi-Aventis. Results of this clinical trial are still pending and further information is not available currently.

Gardiner, Rosenberg, and Zaharatos (2009) noted that there is also evidence that a DNA vaccine targeting CD toxin A given by electroporation has been effective in mice, but has not yet moved to human clinical trials for CDI. Mice receiving this DNA vaccine (TxA-RBD) by electroporation mounted strong antitoxin antibody responses with most mice reaching a 1:10,000 titer, a result significantly different from control group (p<0.05). Eight weeks post-vaccination, mice were challenged with 300ng of freshly reconstituted toxin A CD 100μl of sterile saline delivered via intra-peritoneal
syringe injection and examined twice daily for mortality up to 14 days post challenge. 100% of control mice died within 60 hours of toxin challenge, with most within 24 hours. Mice which had received TxA-RBD via electroporation demonstrated 100% survival.

Fang, Gao, Miller, Mubasher and Reifer (2010) noted that probiotic therapy is an alternative to recolonizing mucosa, increasing immunity, and restoring gastrointestinal flora equilibrium in patients with CDI. They reported a single RCT blinded study 255 adult inpatients in which 3 groups were made and administered 1 capsule or 2 capsules of Lactobacilli 50 billion CFU capsules and control group administered placebo. Results were reported as a 15.5% incidence of antibiotic associated diarrhea (ADD) in 2 capsule group, 28.2% ADD in 1 capsule group, and 44.1% ADD in placebo group. Symptom duration of ADD was also lower in each probiotic group and reported as 2.8 days in 2 capsule group and 4.1 days in 1 capsule group. Placebo symptom duration was 6.4 days. Similarly, 1.2% in 2 capsule groups had CDAD incidence and 9.4% had CDAD incidence for 1 capsule group. Each treatment group had a lower CDAD incidence vs. placebo (23.8%). Other varieties of probiotic strains also have also been shown to be effective but large RCT’s are lacking at this time.

**Discussion**

**Provider Recommendations**

CDI is major contributor to the morbidity and mortality of the adult inpatient population. Studies indicate it is surpassing more commonly known infections such as Methicillin Resistant Staph Aureus (Voekler, 2010). However, research and
recommendations for providers to access are not readily available, and at times contradictory. Guidelines for suggested clinical practice based on literature review findings are elaborated next.

The symptom management model specifies that though symptom experience, symptom management strategies, and associated outcomes, symptomology of disease processes can be proficiently managed and patient functionality retained, and morbidity and mortality improved.

Patient outcomes can be improved through the early identification of CDI symptoms. Although research is very limited, based on studies that were located it is reasonable for providers to utilize a criteria of two to three loose stools in a 24 hour timeframe to suspect potential CDI. There is no current research to indicate that volume of any stool episode is a criteria indication, however large volumes of liquid stool in one passing can be indicative of disease process, but this is not related to CDI alone.

Diagnostic testing modalities remain conflicted within the literature and no systematic review has been performed. The gold standard to determine active, toxic CDI remains stool culture, although use in acute clinical settings are limited due to turn around time of results. There is conflicting evidence in regards to utilizing GDH and PCR as stand-alone tests, and at this time both are best performed as a screening tool for rapid clinician results and properly correlated with stool culture follow up. There are no strong clinical studies that compare GDH and PCR to determine the most efficacious screening tool. Recommendations are that providers can reasonably utilize PCR for time sensitive testing but should be aware than some PCR’s cannot distinguish between active and colonized
CD, and appropriate correlation with clinical symptomology is crucial when initiating antimicrobial treatment. Currently PCR should continue to be confirmed by stool culture, and the decision to initiate treatment based on provider expert evaluation on a case by case assessment.

Pharmacological treatment involves the elimination of antiperistaltic agents and gastric acid suppressive agents, and appropriate antimicrobial therapy. Standard antimicrobial therapy suggested is Metronidazole (Flagyl) and Vancomycin as appropriate to severity of symptoms. Providers should accurately assess and prescribe these medications in congruence with corresponding disease severity. Compelling research has been performed in regards to use of medications such as Nitazoxanide and Rifaximin (Xifaxan), however there has not yet been enough RCT’s to incorporate these drugs into clinical practice guidelines for the provider. Current recommendations are judicious use of antimicrobials with attention to growing rates of CD resistance to both Metronitazole (Flagyl) and Vancomycin.

The use of monoclonal antibodies has shown significantly high prevention rates, but studies are limited and long term side effects not yet know. Preventative measures such as probiotic prophylaxis and toxoid vaccination are not efficacious in treatment of CDI but are significant players in the role of prevention of CDI in the at-risk hospitalized patient. Suggestion to providers for clinical practice at this time is the incorporation of Lactobacillus administration in an at-risk hospitalized patient. Future recommendations may include vaccination with CD toxoid upon admission of the at-risk patient, however completion of clinical trials are needed to further assess this.
Recommendations for Future Research

As discussed previously, there were very few articles related to the initial symptoms experienced in CDI. All of the articles noted liquid stool however; only one study delineated the amount and timeframe from symptom onset in the assessment of CDI. More research is needed to support and delineate a clear symptom criteria in regards to CD associated diarrhea for providers to utilize appropriately when initiating a diagnostic work up for CDI. Currently there is one retrospective study (WIRB #1132601) in process of being conducted that defines symptomatic diarrhea associated with CDI as a) 3 or more liquid stools in 24 hour timeframe, b) single episode of liquid stool greater than 500 milliliters, c) liquid stool requiring use of rectal tube collection device as identified by primary nurse in the intensive care setting (Ghannam & Sloot 2012). This and future studies could potentially delineate clear stool symptom leading to testing triggers for providers to utilize to uphold evidence based practice suggestion of early identification and intervention to improve morbidity and mortality (SHEA & IDSA, 2010).

Next, there remains much controversy over the testing modality of choice in CDI. It is widely accepted that the gold standard is cell toxicity culture, but that modality is not clinically useful in acute diagnosis and prompt initiation of treatment. Additional RCT’s need to assess both the two step GDH with reflex to stool culture, and the PCR method as both stand alone and as screening for culture reflex, to obtain an evidence based recommendation that can be utilized appropriately in clinical practice. Current recommendations remain that the gold standard of testing is stool culture. PCR is noted
as a valuable tool to identify any form (active or non active) CD to insure proper
infection control techniques are initiated, but there is discrepancy over the initiation of
antimicrobial therapy based on PCR positive alone. Consideration of activating a non
active strain of CD with improper initiation of antibiotics based on PCR positive is of
concern and is an additional area of needed research.

The systematic review of antibiotic use in CD associated disease (CDAD) could
not conclude that the use of currently recommended antibiotics employed in CDI
treatment are appropriately efficacious. Studies further suggest that current
recommendations may precipitate complications as their efficacy further decreases with
repeated use in recurrence, regardless of regimes employed. Furthermore Kelsey et al.
(2010) noted that stopping current antimicrobial treatment to use Metronidazole (Flagyl)
or Vancomycin in CDI may lead to increased resistance development of systemic
pathogens, therefore appropriate choice of initial agents is crucial for effective cure and
reduced risk resistant microbe development. Additional studies are needed to readdress
emerging antimicrobials and compare to current recommended treatments to confirm the
most effective pharmacologic intervention.

Further assessment of monoclonal antibody use in prevention of reoccurrence,
and use of biotherapies in prevention reoccurrence, and toxoid vaccine to provide
immunity to toxic strains of CDI should be evaluated. Both primary prevention and
reoccurrence prevention would be key to symptom management and improved patient
outcomes, and should be a primary focus of research.
Conclusion

CDI is challenging to identify, efficiently diagnose, and effectively treat. Primary prevention is key to decreasing patient symptomology, morbidity and mortality, improving outcomes, and overall health satisfaction. Treatment of CDI is best performed with clear understanding of symptom experience, symptom management strategies, and patient centered outcomes. Utilization of these strategies will aid the provider in providing perception focused, timely, efficacious care to adults within the hospital setting suffering from CDI.
Figure 1. Symptom Management Model (Lee & Miaskowski, 2011).
References


