To Treat or Not To Treat: Does a More Sensitive and Specific Testing Methodology Make the Treatment Decision More Clear?

Bakri Kulla, MD. Shivanjali Shankaran, MD. Hadiza I. Galadima, PhD. Matthew J Peworchik. Patrick Haggerty, M.D [1].

Internal Medicine, Infectious Disease, Eastern Virginia Medical School

Introduction

Clostridium difficile Infection (CDI) is a leading cause of infectious diarrhea in healthcare settings in the United States. Accurate testing methodology provides guidance to clinicians as to when to treat.

The accurate diagnosis of CDI is essential for optimum treatment, prevention and control of the disease. However, the optimal method for diagnosis of CDI remains difficult and challenging despite the variety of available tests. Our hospital made an effort to improve the accuracy of diagnosis of CDI by switching from stand-alone Toxin EIA testing (sensitivity of 60-89%) to performing a three-step algorithm testing that including GDH/Toxin A and B as a screen. If both GDH/Toxin are positive, it is reported as positive and if both negative then it is reported as negative. If only one is positive, it is indeterminate and the laboratory reflexes to performing the Nucleic Acid Amplification Test (NAAT) PCR (sensitivity of 88-100%).

Objective

Our study was designed to determine if more sensitive testing methodology implemented in 2013 reduced unnecessary treatment of hospital associated diarrhea (HAD).

It also aimed to determine the rates of treated individuals despite negative *C. difficile* testing before and after the more sensitive testing method was introduced.

The factors associated with patients being treated despite a negative *C. difficile* test were analyzed.

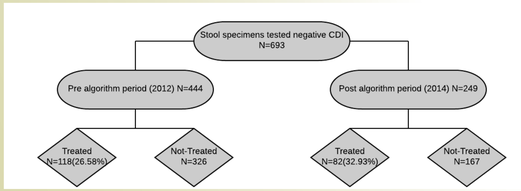

Figure 1: Study enrollment

Methods

Study Design: In a retrospective analysis, patients were identified who were tested for C. diff from January 2012 to December 2012 and then January 2014 to December 2014. This would be the year before and year after implementation of the new algorithm incorporating PCR testing for indeterminate samples. We identified patients with a negative C. diff test and performed a chart review on these patients.

Inclusion Criteria: Patients 18-89 years of age admitted to SNGH who underwent C. diff testing in 2012 and 2014 respectively.

Exclusion Criteria: Insufficient follow-up data within the patient's medical record.

Information on demographics and comorbid conditions was collected in all patients that were treated despite a negative test for CDI, to test the hypothesis that there is a change in the rates of treatment of patients with negative C. diff tests, the proportion of patients treated for C. diff before and after implementation of the new algorithm were compared using the Chi-square test.

Results

The distribution of the algorithm implementation in 2012 and 2014 between treated and not treated was not significant. The rate of treated symptomatic patients, despite negative C. diff testing was 26.58% (N=118/444) in 2012, and 32.93% (N = 82/249) in 2014. The results from the chi-square test for the change in the rates of treatment of patients between 2012 and 2014 showed a trend toward increasing treatment but this was not statistically significant (p = 0.0765). Table 1.

Table 1. pre and post Algorithm

	Treated N = 200 (28.86%)	Not Treated N = 493 (71.14%)	P-value	All subjects N = 693
Pre-algorithm (2012)	118 (26.58%)	326 (73.423%)	0.0765	444 (64.07%)
Post-algorithm (2014)	82 (32.93%)	167 (67.07%)		249 (35.93%)

The multiple logistic regression model showed that the main risk factors associated with patients being treated despite a negative C. diff test mainly include hypertension (p = 0.0143), organ transplant (p=0.0070), a prior diagnosis of C. diff (p = 0.0164), and a longer hospital stay (p = 0.0326).

The bivariate analysis of treatment status by patient demographics and characteristics revealed that the treated patients had significantly higher rate of hypertension (71.86% vs. 62.32%; P =0.0173), a prior diagnosis of C. diff (14.07% vs. 6.72%; P = 0.0021), organ transplant (19.70% vs. 9.59%; P = 0.0003), and a higher mean hospital length of stay (P = 0.0105). There was no statistical significant difference between treated and not treated in terms of age, sex, heart disease, diabetes, steroids usage, recent surgery, and other patient's characteristics as seen in Table 2.

Table 2. Patient demographics and clinical characteristics by treatment status

	Treated N = 200 (28.86%)	Not Treated N = 493 (71.14%)	P-value	All subjects N = 693
Demographics				
Age, mean (SD)	59.79 (14.90)	60.17 (16.54)	0.7798	60.06 (16.08)
Male	87 (43.72%)	253 (51.53%)	0.0631	340 (49.28%)
Female	112 (56.28%)	238 (48.47%)		350 (50.72%)
Co-morbid conditions				
Hypertension (Yes), N (%)	143 (71.86%)	306 (62.32%)	0.0173	449 (65.07%)
Heart disease (Yes), N (%)	113 (56.78%)	241 (49.08%)	0.0668	354 (51.3%)
ESRD (Yes), N (%)	52 (26.13%)	97 (19.76%)	0.0652	149 (21.59%)
Diabetes (Yes), N (%)	86 (43.22%)	181 (36.94%)	0.1253	267 (38.75%)
Immunosuppressive conditions, N (%)				
Organ Transplant (Yes), N (%)	39 (19.70%)	47 (9.59%)	0.0003	86 (12.5%)
Stem cell transplant (Yes), N (%)	1 (0.50%)	3 (0.61%)	0.8608	4 (0.58%)
Steroids (Yes), N (%)	79 (40.10%)	160 (32.65%)	0.0638	239 (34.79%)
Methotrexate (Yes), N (%)	3 (1.52%)	9 (1.85%)	0.7634	12 (1.75%)
Azathioprine (Yes), N (%)	7 (3.54%)	9 (1.85%)	0.185	16 (2.34%)
Other immunosuppressive condition				
AIDS	4 (33.33%)	9 (20.93%)	0.0447	13 (23.64%)
HIV	1 (8.33%)	11 (25.58%)		12 (21.82%)
Chemotherapy	1 (8.33%)	11 (25.58%)		12 (21.82%)
Prior Exposure				
Prior diagnosis of Cdiff (Yes), N (%)	28 (14.07%)	33 (6.72%)	0.0021	61 (8.84%)
Other Characteristics				
Recent surgery (Yes), N (%)	57 (28.64%)	155 (31.63%)	0.441	212 (30.77%)
Length of Stay, mean (SD)	21.27 (19.20)	16.27 (15.41)	0.0105	17.46 (16.49)

Conclusion

- ❑Despite the introduction of a new, more sensitive and specific testing algorithm, there was no overall decline in treatment of patients with a negative test.
- ❑We found that patients with an organ transplant and those with prior history of CDI were more likely to be treated post algorithm phase.
- ❑Education efforts while employed may need to be more intense and physicians directed when treatment outliers are identified.

This study has some limitations. First is the number of patients post algorithm phase was relatively low and may need more data to make the results conclusive. Second is retrospective analysis of a Quasi-experimental research design. Third is only a few infectious disease physicians were managing a large number of immunocompromised transplant patients and their bias may have skewed our results in the post algorithmic phase.

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Patrick Haggerty, Department of Internal Medicine, Division of Infectious Disease, Eastern Virginia Medical School, Norfolk, Virginia, USA, Tel: 757-446-8910; Fax: 757-446-7922; E-mail: HaggerPG@EVMS.edu

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