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Impact of rapid diagnostic testing for chlamydia and gonorrhea on appropriate antimicrobial utilization in the emergency department☆,☆☆

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ABSTRACT

Prolonged turnaround time of *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) test results may delay time to notification and treatment of test-positive patients and result in unnecessary antimicrobial use in test-negative patients. This quasi-experimental study evaluated the impact of NG/CT rapid diagnostic testing (RDT) in an urban emergency department (ED) on treatment appropriateness, time to notification, and cost. Patients tested in December 2013–January 2014 (traditional group, $n = 200$) were compared with those in December 2014–January 2015 (RDT group, $n = 200$). There was a significant increase in treatment appropriateness in the RDT group, 72.5% versus 60% ($P = 0.008$) and time to results notification was significantly faster (median 17.4 versus 51.5 hours, $P = 0.010$). Availability of test result prior to discharge was associated with increased treatment appropriateness (odds ratio, 22.65 [95% confidence interval, 2.86–179.68]). The RDT would save approximately $37,000 annually. These results support the use of NG/CT RDT to expand antimicrobial stewardship efforts within the ED.

1. Introduction

N. gonorrhoeae (NG) and *C. trachomatis* (CT) are the 2 most common bacterial sexually transmitted infections (STI) which can result in serious complications if left untreated.(Centers for Disease Control and Prevention; Centers for Disease Control and Prevention, 2015a) In 2014, there were more than 350,000 cases of NG and 1.4 million cases of CT reported in the United States alone (Centers for Disease Control and Prevention). Nonculture methods, including nucleic acid amplification tests (NAAT), are widely available for the detection of genital NG/CT and are the preferred diagnostic tests recommended by the Centers for Disease Control and Prevention (CDC) (Centers for Disease Control and Prevention, 2014). With traditional NAAT, many health care facilities have a turnaround time between 1 and 4 days for results of NG/CT. This prolonged time to results impacts time to patient and partner notification as well as treatment for test-positive patients who do not receive empiric therapy. Meanwhile, excessive empiric antimicrobial use in test-negative patients may contribute to increasing rates of antimicrobial resistance (U.S. Department of Health and Human Services Centers for Disease Control and Prevention, 2014).

The emergence of widespread antimicrobial resistance is a threat to public health. The CDC considers drug-resistant NG as an immediate public health threat that requires urgent and aggressive action (U.S. Department of Health and Human Services Centers for Disease Control and Prevention, 2014). Since 1986, the CDC's Gonococcal Isolate Surveillance Project has monitored NG susceptibility to different antimicrobial therapies. Ceftriaxone and azithromycin, 2 of the last remaining antimicrobials with reliable coverage against NG, now demonstrate elevated MICs (Centers for Disease Control and Prevention National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention). While the percentage of NG isolates with decreased susceptibility to ceftriaxone peaked at 0.4% in 2011 and stabilized in 2013 at 0.05%, continued surveillance is warranted (Centers for Disease Control and Prevention National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention; Centers for Disease Control and Prevention, 2015b). The CDC Sexually Transmitted Diseases treatment guidelines recommend combination therapy for the treatment of NG to prevent the selective pressure for resistance to

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the remaining treatment options (Centers for Disease Control and Prevention, 2015b).

Antimicrobial stewardship programs have been developed within hospitals to promote optimal prescribing of antimicrobial agents in an effort to increase efficacy, improve patient safety, and reduce antimicrobial resistance (Dellit et al., 2007; Society for Healthcare Epidemiology of America et al., 2012). The development of rapid diagnostic tests (RDTs) can help to achieve these goals by providing timely detection of infectious organisms and allowing for targeted antibiotic therapy. The Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) advocate for the use of RDT to improve detection capabilities and to guide appropriate treatment as part of an antimicrobial stewardship program. SHEA and the IDSA also agree that investigations evaluating the development and cost-effectiveness of RDT are a priority. A RDT NAAT for the detection of genital NG/CT was approved in 2012. Independent analyses of the RDT have reported equivalent sensitivity and specificity as compared with traditional NAAT (Gaydos et al., 2013; Goldenberg et al., 2012; Tabrizi et al., 2013). A recently published open-label, randomized, controlled trial in emergency department (ED) patients found that use of the RDT for NG/CT resulted in decreased unnecessary antibiotic exposure in test-negative patients (May et al., 2016). Subjects randomized to the RDT arm were required to wait in the ED for 90 minutes following sample collection, increasing the likelihood that the patient would be present at the time the test results became available (May et al., 2016). This may not be feasible in a real-world setting. Additionally, the impact of the RDT on time to patient notification of test results or time to appropriate treatment was not evaluated.

The purpose of this study was to determine if implementation of NG/CT RDT as the standard of care in the ED would improve treatment appropriateness by decreasing antimicrobial exposure in test-negative patients while increasing treatment rate in test-positive patients. We hypothesized that the implementation of the RDT would result in increased treatment appropriateness for NG/CT as well as improved time to patient notification and decreased cost of care.

2. Materials and methods

2.1. Study design and setting

This single-center, quasi-experimental study was conducted at an urban community teaching hospital with approximately 70,000 ED visits per year and more than 1500 NG/CT tests performed annually in the ED. Patients ≥15 years of age who were tested for NG/CT via the RDT (December 2014–January 2015) were compared to a historical control group tested using a traditional NAAT (December 2013–January 2014). Patients were excluded if they were tested at a satellite facility or admitted to the hospital following testing. Patients who left the ED prior to examination were excluded, as a provider was unable to evaluate the patient for empiric therapy. Patients diagnosed with pelvic inflammatory disease (PID) were also excluded, as treatment of PID may overlap with NG/CT treatment despite negative test results. Institutional review board approval with waiver of informed consent was obtained prior to study initiation.

2.2. Preintervention testing process

Traditional testing was performed using the Gen-Probe Aptima Combo 2 for NG/CT Assay (Hologic, Bedford, MA). Samples utilized by the ED included male urine or urethral samples and female endocervical samples. Once received by the microbiology laboratory, samples were placed in transport media and then couriered to an off-site laboratory for testing. The expected turnaround time from collection to results was 24–72 hours. Results were posted by the off-site laboratory 24 hours per day as they became available. A report of all results was reviewed once daily by ED staff.

2.3. RDT validation and intervention testing process

RDT was performed using the GeneXpert CT/NG assay (Cepheid, Sunnyvale, CA). The RDT was validated compared with the traditional testing method with sensitivity and specificity consistent with that reported by the manufacturer (Cepheid, 2015). A total of 53 patient specimens were collected and tested including male and female first-catch urine samples, patient-collected vaginal swabs, and provider-collected endocervical swabs. Additionally, a NG/CT verification panel was tested containing 17 samples: 4 strains of *C. trachomatis*, 2 strains of *N. gonorrhoeae*, 1 strain of *N. cinerea*, and 1 strain of *N. flavenscens*. The sensitivity for CT was 100% and specificity was 100%. The sensitivity for GC was 94% and specificity was 100%.

Samples utilized by the ED included urine specimens for males and females, self-collected vaginal swabs, and provider-collected endocervical swabs. Once received by the microbiology laboratory, samples were tested immediately using the RDT. The expected time from collection of specimen to results was approximately 120–180 minutes. Providers were responsible for assessing if results were available prior to patient discharge and decision to treat. Additionally, an electronic report was generated for review once daily by ED staff displaying all results from the previous 24 hours.

2.4. Selection of participants

A computer-generated report from the electronic medical record was used to retrospectively identify all patients tested for NG/CT during the study period. Data collected included patient characteristics, testing characteristics, antimicrobial therapy administered, initial treatment appropriateness, time to test results, time to patient notification of positive test results, time to appropriate treatment, and ED length of stay.

The traditional testing group consisted of 200 consecutive patients presenting to the ED between December 1, 2013 and January 31, 2014. Patients tested for NG/CT were considered for empiric treatment prior to discharge at provider discretion (Centers for Disease Control and Prevention, 2015b). Once test results returned, ED staff notified patients who tested positive for NG/CT of their results and provided counseling and education by telephone. Patients who did not receive empiric treatment were provided with treatment either by a telephone prescription or by request to return to the ED for parenteral antimicrobial administration. If a patient was unable to be contacted after 3 telephone attempts, a certified letter was mailed to the patient and patient information was forwarded to the county health department for follow-up.

The RDT was implemented for ED use in October 2014. The RDT group consisted of 200 consecutive patients presenting to the ED between December 1, 2014 and January 31, 2015. If results were available prior to discharge, patients with positive results were provided notification, counseling, and treatment for NG/CT while in the ED. Test-negative patients were notified and spared unnecessary antimicrobial administration. If patients were ready for discharge prior to the completion of RDT results, providers had the option to provide patients with empiric treatment and allow follow-up of results after discharge. Providers were not encouraged to delay patient discharge in order to await RDT results. ED staff would contact patients with positive results for notification, counseling, and treatment following the same process as the traditional test. In both groups, patients were also screened and treated for additional STIs (e.g., trichomonas) if indicated.

2.5. Outcomes

The primary end point of this study was to compare the percentage of patients who received appropriate treatment during their index ED visit using the traditional test versus the RDT for NG/CT. Appropriate treatment was defined as the combined end point of test-positive patients receiving antimicrobial therapy in concordance with the CDC