An Innovative Alternative Testing Strategy for the Prompt and Accurate Diagnosis of Syphilis in a High Prevalence Setting

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INTRODUCTION

Traditional serological syphilis testing includes screening with a nontreponemal assay that detects antibodies to lipoidal material released from host cells damaged by T. pallidum in the blood. Reactive specimens are confirmed with treponemal tests that detect antibodies specific to T. pallidum. It has been suggested that if this traditional algorithm be reversed so that screening begins with a treponemal test, such as an immunnoassay (IA). If reactive, the IA would be followed by a nontreponemal test for confirmation. This suggestion is due to the ability to automate the screening methodology thus increasing laboratory workflow, alleviating manual labor and potentially decreasing costs. In cases of discordance between the screening treponemal test and the confirmatory nontreponemal test, the CDC suggests that a second treponemal test (such as a TPPA) could be utilized to serve as a supplemental test. We evaluated the performance of this reverse sequence diagnostic algorithm relative to the traditional algorithm and developed a novel testing strategy for a high prevalence setting that would reduce turnaround time (TAT) of diagnosis to one day.

METHODS

Serum specimens were prospectively collected from July 3, 2012 to August 15, 2012 from two STD clinics in San Francisco. In total, 2,350 specimens were included in the study. The traditional diagnostic algorithm of VDRL (BD, Franklin Lakes, NJ) followed by TPPA (Fujirebio Diagnostics, Inc., Malvern, PA) was performed on all specimens and results were reported out according to standard protocols. Remnant serum from all 2,350 specimens were stripped of identifying information and blinded. Each specimen then received a TREP-SURE™ (TS-EIA) (Trinity Biotech, Jamestown, NY) and TPPA test. Results of all three testing methodologies were analyzed to determine early and active infection. Finally, the Syphilis Health Check rapid test (SHC-RT) (Trinity Biotech, Jamestown, NY) was performed on a subset of 249 specimens to evaluate its performance as a potential replacement for the TPPA.

The TS-EIA is an antibody sandwich assay that detects both IgM and IgG antibodies to T. pallidum in human serum or plasma. Results were provided in the form of qualitative and quantitative outputs. The signal-to-cutoff (S/CO) ratio (or index value) of each result was calculated by dividing the OD value by the mean of the cutoff calibrator controls. These index values determine the qualitative output (positive or negative) of each specimen tested and are proportional to the amount of antibody to T. pallidum found in each specimen.

Receiver operating characteristic (ROC) analyses were conducted to examine the relationship between the TS-EIA S/CO ratios and TPPA test results. This analysis was used to evaluate the optimal threshold cut-off point for the assay. The area under the ROC curve (AUCROC) was calculated to quantify the discrimination of the EIA in predicting TPPA results.

RESULTS

For the purposes of this study, the traditional syphilis algorithm of a VDRL screen followed by TPPA confirms was selected as the “gold standard” algorithm. 198 (8.4%) of 2,350 specimens were found reactive by VDRL, of which 189 were reactive on a TPPA, resulting in the detection of 189 infections has been included in this study. When the specimens were screened by the TS-EIA, 478 (20.3%) were positive, 186 (38.9%) of which confirmed reactive by VDRL (Figure 2). Of the 292 (61.1%) discordant EIA reactive and VDRL non-reactive specimens, only 249 (85.3%) were reactive by TPPA. Therefore, the reverse sequence algorithm, beginning with a treponemal EIA was able to detect 186 current and active syphils infections.

CONCLUSION

Screening with an EIA for syphilis infection in a high prevalence setting resulted in the detection of more serosapositive individuals than screening with VDRL, but did not result in the detection of more syphils cases. An algorithm that begins with an EIA screen may require additional tests for the resolution of discordant cases. When EIA reactive, VDRL non-reactive specimens are detected, the use of TPPA as a reflex test may not provide clear guidance regarding treatment. A possible solution to the limitations of a reverse algorithm may be to utilize the signal-to-cutoff ratio on the initial screening EIA to predict TPPA reactivity as it would eliminate, in a large number of cases, the need to perform the TPPA test. However, this may result in prolonged TAT due to the need to batch samples. The introduction of a rapid test such as the SHC-RT, could significantly reduce the TAT required to report a positive syphils diagnosis to as little as one day.

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