Evaluation of LIAISON® C. difficile glutamate dehydrogenase and LIAISON® C. difficile toxin A and B in Copan FecalSwab™ samples in a three-step algorithm for the diagnosis of Clostridium difficile infection

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Summary

The presumptive laboratory diagnosis of Clostridium difficile infection is achieved by the means of the detection of a common antigen (glutamate dehydrogenase, GDH) in stool, then confirming the positives either by the detection of toxins A and B or by a molecular test for the detection of pathogenicity locus, encoding for the two toxins and for the binary toxin. A fully automated chemiluminescence system for the GDH antigen (LIAISON® C. difficile GDH) and for the detection of toxins A and B (LIAISON® C. difficile Toxin A and B) (DiaSorin, Gerenzano, Italy) allows for the performance of these tests on large numbers of samples in a short time, ensuring the traceability of the data.

Objective

The first phase of the study evaluated the use of LIAISON® C. difficile GDH test on stool samples collected using Copan FecalSwab™ (Copan Italia, Brescia, Italy), comparing them with the results obtained using stool samples collected with no transport medium.

In the second phase, using only samples collected using Copan FecalSwab™, we compared the current routine two-step algorithm (GDH + molecular), with a three-step diagnostic algorithm (GDH + Toxins A and B + molecular), assuming the molecular test being performed only on GDH-positive but negative for toxins samples.

Materials and Methods

LIAISON® C. difficile GDH is a chemiluminescent immunoassay (CLIA) intended for use as a screening assay to detect Clostridium difficile antigen, glutamate dehydrogenase, in human feces from persons suspected of having C. difficile disease.

LIAISON® C. difficile Toxin A & B is a chemiluminescent immunosassay (CLIA) intended for the qualitative determination of Clostridium difficile toxins A and B in human feces with suspected CDAD.

EUROCLONE C. difficile GDH is a rapid chromatographic immunosassay for the qualitative determination of glutamate dehydrogenase (GDH) in human feces from people with suspected CDAD.

Xpert® C. difficile (Cepheid Inc., Sunnyvale, CA, USA) is a qualitative in-vitro diagnostic test for the rapid identification and differentiation of Toxin B, and Binary Toxin from appropriate stool specimens collected from patients suspected of having C. difficile infection (CDI). The test utilizes automated real-time polymerase chain reaction (PCR) to detect Toxin producing C. difficile, which is associated with CDI.

Results

In the first phase were tested 100 samples: 11 were positive and 89 negative by both methods (100% agreement) (Figure 1A).

Eleven GDH positive samples for both methods were tested with LIAISON® C. difficile Toxin A & B. 3 were positive and 6 were negative for both methods, while 2 were discordant (positive for LIAISON® C. difficile Toxin A&B IFU and negative for LIAISON Toxin A&B Copan fecalSwab™) (Figure 1B).

These results of the first phase confirming that the LIAISON® C. difficile GDH and Toxin A&B tests can be performed with stool samples collected in Copan FecalSwab™.

In the second phase 200 samples analyzed by routine laboratory immunochromatographic method for the detection of GDH were re-tested with the test LIAISON® GDH. 157 samples were negative with both methods; whereas 39 samples were GDH positive for both methods, and 4 were GDH weakly positive with LIAISON® and negative for the routine method. (being the four negative samples for the routine method not analyzed by the molecular method and consequently discarded) (Figure 1C).

The 39 GDH positive samples were evaluated using either the LIAISON® C. difficile Toxin A & B and routine molecular method...
GeneXpert® C. difficile test, Cepheid). 18 samples were positive and 10 negative by either method, whereas 11 samples were discordant (negative LIAISON® Toxin A & B and positive for the molecular test) (Figure 1D).

Conclusions

The LIAISON® test is a reliable method for detecting C. difficile toxins. The use of a molecular test allows for an increase in sensitivity but is significantly more expensive. Using a three-steps algorithm and performing the molecular test only if the test LIAISON® Toxin A & B was negative, only 21 samples would have been tested by the molecular method (11 discordant + 10 toxins A and B negative), rather than 39, with a 46.2% reduction of molecular tests.

Finally, the three-step algorithm makes it possible to achieve the same results of well the two-step algorithm (GDH + molecular), however with significant time- and cost-savings by optimizing the workflow, thanks to the complete automation of the LIAISON® system.