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Short Communication

The risk of HCV RNA contamination in serology screening instruments with a fixed needle for sample transfer

Elin Rondahl[a], Maria Gruber[a], Sandra Joelsson[a], Martin Sundqvist[b], Britt Åkerlind[a,c], Kristina Cardell[d], Magnus Lindh[e], Lena Serrander[a,d,*]

[a] Division Clinical Microbiology, Department of Clinical and Experimental Medicine, Linköping University, Sweden
[b] Division Clinical Microbiology, Örebro University, Sweden
[c] Division for Infection Control and Prevention, Östergötland County, Sweden
[d] Division of Infectious Diseases, Department of Clinical and Experimental Medicine, Linköping University, Sweden
[e] Department of Clinical Microbiology, Göteborg University, Sweden

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ABSTRACT

Background: Hepatitis C diagnostics involve antibody screening and confirmation of current infection by detection of HCV RNA positivity. In screening instruments with fixed pipetting needle, there is a risk of sample carry-over contamination.
Objectives: The aim of this study was to evaluate the risk of such contamination in a proposed clinical setting.
Study design: In the present study, known HCV RNA positive ($n = 149$) and negative ($n = 149$) samples were analysed by anti-HCV Abbott in an Architect instrument in an alternating fashion in order to test for contamination.
Results: In subsequent retesting of the previously HCV RNA-negative samples, six samples (4%) were positive by the Cobas Taqman assay with a maximum level of 33 IU/mL. The results show that there is a risk for transfer of HCV in the Architect instrument but they also show that the levels of HCV RNA observed are low.
Conclusions: We conclude that complementary HCV RNA testing on samples identified as anti-HCV positive by screening can be recommended because the complementary results are reliable in the majority of cases when either HCV RNA is negative or HCV RNA is positive with a level >1000 IU/mL. In a minority of cases, with low HCV RNA after anti-HCV antibody screening, cross-contamination should be suspected and a new sample requested for HCV RNA testing. This strategy would reduce the need for obtaining a new sample from the vast majority of patients with a newly discovered HCV antibody positivity.

1. Background

Hepatitis C is a blood-borne viral infection that is mainly transmitted by injection drug use, blood products or other nosocomial routes. Clinical symptoms are often lacking, but there is a long-term risk of developing cirrhosis or hepatocellular cancer if the infection is left untreated. The diagnosis involves screening for anti-HCV antibodies and the detection of HCV RNA [1–4].

Testing for HCV infection is performed in risk populations such as injection drug users, populations without risk prior to certain health procedures, and subjects for whom other tests indicate liver disorder. If anti-HCV antibodies are detected, further testing is required in order to establish if an active HCV infection is present, since antibody-status does not change even if patients have cleared the infection. Such complementary diagnostics comprise HCV core antigen testing by serology or the detection of HCV RNA by molecular methods. In our current setting, HCV RNA testing is recommended on a new, second blood sample and calling back the patient again for a second sample is not always successful. The rationale for this recommendation is the potential risk for false positive HCV RNA as a result of contamination from HCV positive samples in the serology screening instrument. This means that

Abbreviation: HCV, hepatitis C.

* Corresponding author at: Division of Infectious Diseases, Department of Clinical and Experimental Medicine, Linköping University, Sweden. Tel.: +46 709 14 29 45.
E-mail addresses: Elin.Rondahl@lio.se (E. Rondahl), Maria.Gruber@lio.se (M. Gruber), Sandra.Joelsson@lio.se (S. Joelsson), Martin.Sundqvist@orebroll.se (M. Sundqvist), Britt.Akerlind@lio.se (B. Åkerlind), Kristina.Cardell@lio.se (K. Cardell), magnus.lindh@microbio.gu.se (M. Lindh), Lena.Serrander@lio.se (L. Serrander).

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many patients are reported as possibly infected with HCV because of anti HCV antibodies being positive, but are never confirmed if truly infected or not. If more tests could be performed on the first sample it would save patient time and trouble as well as health care costs.

2. Objectives

The aim of this study was to investigate the risk for cross contamination in Architect instruments prior to analysing HCV RNA on the same sample, and to estimate if that risk justifies the request that a new sample be obtained for confirmation testing of patients who are positive for anti-HCV.

3. Study design

Antibody screening was performed on Architect instruments, models i2000 or i2000SR (Abbott Diagnostics, US) according to the manufacturer's instruction using the anti-HCV assay (Abbott Diagnostics, Germany). Nucleic acid extraction and HCV RNA quantification was performed on Cobas AmpliPrep/Cobas TaqMan48 Analyzer with Amplilink 3.2.2 software (Roche Diagnostics GmbH, Germany) using Cobas AmpliPrep/Cobas TaqMan HCV Test, v1 (Roche Diagnostics GmbH, Germany) according to manufacturer's instructions. This method reports samples as "No target detected" (Negative), <15 IU/mL (HCV RNA detected but below the linear range of quantification), or as a level between 15 and 69,000,000 IU/mL (positive reactions within the range of linear quantification).

Samples stored at −20 °C were selected on the basis of previously being tested for HCV RNA, but not for anti-HCV. Out of 298 samples, 149 had been HCV RNA negative, and 149 HCV RNA positive with mean HCV RNA level of 2,489,389, range 207–27,400,000 IU/mL.

Samples positive and negative for HCV RNA were placed in every other position in the Architect instrument and re-analysed for anti-HCV antibodies. This analysis was then followed by HCV RNA analysis of the previously HCV RNA negative samples ($n = 149$).

4. Results

After processing in the Architect instrument the rate of HCV RNA positivity in previously HCV RNA-negative samples had become 4.05% (6/149), with one sample showing 33.9 IU/mL and 5 samples containing levels <15 IUE/mL. These six samples had been analysed in the Architect instrument directly after samples that contained HCV RNA levels between 885,000 and 6,680,000 IU/mL had been analysed. Forty-eight initially HCV RNA-positive samples were reanalysed for HCV RNA and were shown to have lost 33% of the initial HCV RNA levels.

5. Conclusions

We conclude that carry-over contamination of HCV RNA may occur in the Architect instruments using fixed sampling needles, but we believe that the impact of this in the diagnostic setting would be very low. In the present study, cross contamination was observed in 4% of the negative samples that were analysed in Architect immediately after an HCV RNA positive sample had been analysed. In a typical diagnostic virology laboratory less than 5% of samples analysed in an Architect instrument are HCV RNA positive, indicating that approximately 0.2% of the samples would be contaminated by HCV RNA. The likelihood that such a contaminated sample would be analysed for HCV RNA is probably also low, and if this were the case, the level of detected HCV RNA would be very low. Still, it is important to be aware of this risk. Samples from patients who have not received any treatment usually show relatively high HCV RNA levels. Therefore, if a very low HCV RNA level is detected in a patient not being treated for hepatitis C, cross contamination has to be suspected and should be confirmed if the sample had originally been analysed in a serology instrument prior to HCV RNA testing. In such cases, testing of a new sample is required to either verify or rule out present infection. In patients treated for hepatitis C, detection of false, low HCV RNA levels would be of greater importance, because the results may influence the decision to continue or stop treatment. Therefore, HCV RNA quantification during treatment should not be performed on samples that have been used for serological testing. On the other hand, antibody testing on samples from patients being treated for HCV is not necessary and is rarely warranted since the serological status does not influence treatment strategy.

Our results support the position that samples that have been analysed in serology instruments should be recommended for HCV RNA testing, because both HCV RNA positive results with high levels (>1000 IU/mL) and HCV RNA negative results are reliable, and such results are present in the vast majority of samples. Low levels of HCV RNA (<1000) in samples previously analysed in a screening instrument with fixed needles should not be accepted and in such cases, a new sample should be requested. With this caveat, the approach of analysing HCV RNA on samples that have been analysed in a serology instrument is rational and reliable.

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Competing interests

None declared.

Ethical approval

The project has been given ethical approval from the Regional Ethical Review Boards; Linköping nr 2013/39-31.

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