Short communication

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HCV viraemia in anti-HCV-negative haemodialysis patients: Do we need HCV RNA detection test?

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Abstract

Background: Hepatitis C virus (HCV) infection is still common among dialysis patients, but the natural history of HCV in this group is not completely understood. The KDIGO HCV guidelines of 2009 recommend that chronic haemodialysis patients be screened for HCV antibody upon admission to the dialysis clinic and every 6 months thereafter if susceptible to HCV infection. However, previous studies have shown the presence of HCV viraemia in anti-HCV-negative haemodialysis patients as up to 22%.

Objectives: To evaluate the presence of HCV viraemia, using HCV RNA detection, among anti-HCV-negative haemodialysis patients from a tertiary dialysis unit in Athens.

Methods: We enrolled 41 anti-HCV-negative haemodialysis patients diagnosed with third-generation enzyme immunoassay. HCV viraemia was evaluated using a sensitive (cut-off: 12 IU/mL) reverse transcriptase polymerase chain reaction (COBAS AmpliPrep/TaqMan system) for HCV RNA.

Results: None of the 41 anti-HCV-negative haemodialysis patients were shown to be viraemic.

Conclusions: Routine HCV RNA testing appears not to be necessary in anti-HCV-negative haemodialysis patients.

Keywords
HCV, anti-HCV, HCV RNA, haemodialysis

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Introduction

Hepatitis C virus (HCV) infection remains frequent among patients who undergo long-term haemodialysis both in developed and less developed countries. The systematic screening of blood products reduced the risk of transfusion-related HCV infection; however, these patients still continue to present a 'high-risk' group mainly due to nosocomial transmission through to health-care-related procedures.[1–4] Thus, a correlation between HCV infection and total spent time on dialysis has been reported.[5] Transmission of the virus via internal fluid pathways of the dialysis machine is, at most, a minor contributor to the nosocomial transmission of HCV among haemodialysis (HD) patients, and isolation of HCV-infected patients is not recommended.[2] The dialysis-related risk is estimated at 2% per year. There is a wide range in the prevalence of HCV infection among HD patients in different parts of the world, varying from 1% to 90%.[1] However, in southern Europe, the prevalence rate is around 10%.[2]

According to the KDIGO HCV guidelines of 2009, it is recommended that HD patients should be tested when they first start dialysis or when they transfer from anther

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Table 1. Clinical and demographic characteristics of 41 anti-HCV-negative HD patients.

Age (mean ± SD), years	54 ± 16
Sex: male, n/N (%)	31/41 (75.5)
Descent: Greek, n/N (%)	37/41 (90)
PDU, n/N (%)	0/41 (0)
ALT (mean ± SD), U/L	25.5 ± 6.7
Follow-up (mean ± SD), months	64.7 ± 85.5
Time in dialysis (mean ± SD), months	52.9 ± 70.3
Patients in dialysis before 1992, n/N (%)	2/41 (5)
History of transfusion before 1992, n/N (%)	5/41 (12)

HCV: hepatitis C virus; PDU: parenteral drug use; ALT: alanine aminotransferase; SD: standard deviation; HD: haemodialysis.

dialysis facility, while the recommendation for pre-dialysis patients with chronic kidney disease is weak.[2]

Currently, third-generation enzyme immunoassay (enzyme-linked immunosorbent assay-3 (ELISA-3)) is used as the preferable immunological assay and has been proven of high sensitivity also in HD patients. The detection of anti-HCV may be indicative of acute, chronic or even resolved infection. As a result, it is considered reasonable to perform initial screening for anti-HCV with ELISA-3 and repeat every 6–12 months in initially anti-HCV-negative HD patients.[2,5]

However, several studies claim that an unknown but substantial number of HD patients will be detected to be viraemic, despite the anti-HCV-negative result.[6] Especially in populations with known higher prevalence of infection, it was considered that HCV RNA is appropriate so as to avoid missing HCV infection, taking into consideration the disadvantage of a false-negative result in ELISA-3.[7–9]

The role of HCV infection as an independent and significant risk factor for death and/or liver disease–related fatal complications in HD patients has been documented by several studies.[10–12] However, the availability of direct-acting antiviral (DAA) agents to treat chronic HCV infection offers the opportunity for cure in most cases instead of the low efficacy and poor tolerability of interferon and ribavirin.[13] The antiviral therapy of HCV in HD patients is targeted both to slowing the progression of hepatitis C and avoiding the extrahepatic complications of HCV such as glomerulopathy.[5] Thus, the possible detection of a subgroup of HD patients presented with viraemia despite negative anti-HCV is very important.

The aim of this study was to evaluate the presence of HCV viraemia using HCV RNA detection among anti-HCV-negative HD patients from a tertiary dialysis unit in Athens, Greece.

Materials and methods

We reviewed the records of all anti-HCV-negative HD patients attending one dialysis unit. All patients have been in this dialysis unit at least 6 months and have been confirmed as anti-HCV-negative using ELISA-3 (Ortho HCV 3.0 ELISA Test System; Ortho Clinical Diagnostics) at least 3–6 months before study initiation. All patients have never been treated for HCV, were HBsAg (−) and anti-HIV (−) and none of them experienced acute hepatitis or transaminase elevation of unknown origin at least 6 months before study initiation.

A serum sample from each patient was obtained before dialysis session in ethylenediaminetetraacetic acid (EDTA) tube for HCV RNA testing. HCV viraemia was evaluated using a sensitive (lower cut-off: 12 IU/mL) reverse transcriptase polymerase chain reaction (PCR; COBAS AmpliPrep/TaqMan system) for HCV RNA.

Results

In total, 41 anti-HCV-negative HD patients were included. Their mean age was 54 ± 16 years and 31/41 (75.5%) were men. The mean time in dialysis of our patients was 52.9 ± 0.3 months but only 2/41 (5%) patients were in dialysis before 1992. Parenteral drug use (PDU) was not reported by any patient, while other possible sources of infection such as transfusion of blood or blood products before 1992 have been recorded in 5 (12%) of them. The majority of our patients (90%) were Greeks, whereas the remaining 10% were immigrants mainly from Arabic countries (Table 1).

Finally, none of the 41 anti-HCV-negative HD patients who were screened for HCV RNA with a very sensitive reverse transcriptase PCR tested positive.

Discussion

The presence of HCV viraemia in anti-HCV-negative HD patients is controversial in literature.[7,8] Previous studies have reported anti-HCV negativity in 0%–22% of viraemic patients depending on the methods used for the detection of both the anti-HCV and the HCV RNA.[7] In general, first- or second-generation ELISA's have been used in some early studies which are not so sensitive and specific as ELISA-3 leading to false-negative anti-HCV results. However, HD patients, due to their inadequate antibodies production through immunosuppression, may experience prolonged viraemia before seroconversion to anti-HCV.[14,15] Finally,

HCV RNA presence in the absence of anti-HCV may be indicative of patients at early stage of the infection.

HD patients have generally lower viraemia levels compared to non-HD patients especially after dialysis session. Thus, we obtained our samples before HD session, and our result seems unlikely to be due to HD session itself.[16] Although we used ELISA-3 as screening test and a sensitive PCR method for viraemia confirmation, our results failed to confirm HCV viraemia in anti-HCV-negative HD patients. This finding is in accordance with results from a multicentric French survey published 7 years ago where only 2 of the 4357 anti-HCV-negative (0.05%) patients were viraemic with positive HCV RNA.[17]

As mentioned before, the dialysis-related risk is estimated at 2% per year and is much higher in patients who started dialysis before 1992 (the year of obligatory anti-HCV blood examination). Our study includes HD patients with a mean duration in dialysis of 52.9 ± 70.3 months which is higher than previously reported studies with documented viraemia in anti-HCV-negative HD patients.[7] Moreover, besides dialysis itself, our cohort did not include any other high-risk patients for HCV infection like PDU.

The small number of our patients and the design is the main limitation of our study. This study was conducted in an attempt to address the HCV RNA status in a small cohort of anti-HCV-negative HD patients who do not otherwise meet the criteria for HCV RNA testing. This small study provides evidence that routine HCV RNA detection in anti-HCV-negative HD patients who, according guidelines, are in close monitoring (screening every 6 months for anti-HCV and monthly alanine aminotransferase (ALT) levels) appears unnecessary, specially taking into account the cost of an HCV RNA analysis.

Aminotransferase monitoring and anti-HCV testing with ELISA-3 on a regular basis as is recommended are thought to be mandatory to avoid HCV transmission in HD patients.

Declaration of conflicting interests

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