Patient-to-Patient Hepatitis C Virus Transmissions Associated with Infection Control Breaches in a Hemodialysis Unit

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Abstract

Background: Three patients attending a hemodialysis unit were diagnosed with acute hepatitis C virus (HCV) infection. We investigated the scope and mode of transmission.

Methods: Patients and staff were tested to determine HCV infection status; all HCV-RNA-positive sera underwent quasispecies analysis to assess genetic relatedness. Staff practices were evaluated via interviews and observations. A cohort study was performed to assess risk factors for incident HCV infection.

Results: HCV infection was documented at time of hire or unit admission for 2 staff and 12 patients (prevalent case-patients). Seven (13%) of 52 HCV susceptible at admission to the unit subsequently acquired HCV infection (incident case-patients). Analysis of HCV quasispecies from the hyper variable region 1 identified 2 separate clusters each containing 3 incident case-patients and 1 prevalent case-patient. Incident case-patients received a higher median number of intravenous medications per dialysis session compared to susceptible patients (2.1 vs 1.8, p-value = 0.0606). Only one incident case-patient received dialysis on the same machine as their genetically related prevalent case-patient. Preparation of injection medications at the dialysis station on a mobile medication cart, and failures to clean environmental surfaces between patients were infection control breaches identified as likely modes of HCV transmission.

Conclusions: Epidemiologic and laboratory data revealed transmission of HCV among patients at the same dialysis unit. Transmission was most likely related to infection control breaches. Our findings reinforce the risk of patient-to-patient HCV transmission in hemodialysis units when staff fails to adhere to recommended infection control practices.

Keywords: Hemodialysis; HCV; Infection control; Outbreak; Prevention

In the United States the prevalence of hepatitis C virus (HCV) infection among patients undergoing hemodialysis (~8-10%) is approximately 5 times higher than the general population (1.6%) [1,2]. Due to implementation of routine screening of the blood supply and virtual elimination of HCV transmission via blood transfusion [3] and the overall declining incidence of acute HCV infection in the United States [4], intra-facility HCV transmission has been increasingly recognized as cause of incident HCV infection in hemodialysis patients [5-9].

During a 3-month period in 2006, 3 patients attending the same hemodialysis unit became jaundiced and were subsequently diagnosed with acute HCV infection. All 3 were documented to be HCV antibody (anti-HCV) negative on admission to the unit and had remained anti-HCV negative during routine screening performed annually. In response, the facility initiated monthly anti-HCV testing to identify additional newly infected patients and contacted public health officials for assistance identifying potential causes of HCV infection. To determine the magnitude, source and mode of transmission and implement necessary prevention measures a public health investigation was initiated by the Virginia Department of Health and the Centers for Disease Control and Prevention (CDC).

Materials and Methods

Case ascertainment

Medical records were reviewed to identify the HCV status of all patients attending the hemodialysis unit, those anti-HCV negative at the time of admission to the unit and in January 2006 (during routine annual screening) were tested monthly for anti-HCV between May and July by the facility. In June 2006, sera was collected from all current hemodialysis patients and staff and sent to the Division of Viral Hepatitis Laboratory at the CDC for testing by enzyme immunoassay (EIA) (ORTHO® HCV Version 3.0 EIA, Ortho-Clinical Diagnostics, Raritan, New Jersey) and HCV RNA testing by polymerase chain reaction (PCR) (AMPLICOR HCV Test, version 2.0, Roche Molecular Systems, Branchburg, New Jersey) with a lower limit of detection of ~50 copies/ml.

Definitions

The following case definitions were used to classify patients’ HCV-infection status. Patients with prevalent HCV infection (prevalent case-patients) were known to be anti-HCV positive upon first admission to the unit for treatment. Patients with incident HCV infection (incident case-patients) were known to be anti-HCV negative at time of admission to the unit and in January 2006 (during routine annual screening) and were documented to be anti-HCV positive at any time after this initial admission.

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case-patients) were known to be anti-HCV negative at the time admission to the unit but were subsequently found to be anti-HCV positive and/or HCV RNA positive. Patients were HCV susceptible if they were anti-HCV negative at the time of admission to the facility and remained anti-HCV negative and HCV RNA negative during all repeat tests performed through the end of the investigation. Patients were classified as having unknown HCV status if they were known to be anti-HCV negative at the time admission to the unit but were not tested as part of the investigation (e.g., deceased, transferred, or otherwise lost to follow-up).

**Quasispecies analysis**

The HCV genotype for all HCV RNA positive specimens was determined from the sequence of a 300-nucleotide NS5B coding region. Genetic relatedness of the virus was assessed by analysis of HCV quasispecies (the population of related HCV variants that occur within infected individuals). The quasispecies were analyzed by sequencing a segment amplified from the E1-hypervariable region 1 (HVR1) of the HCV genome using methods previously described [10]. The HCV quasispecies obtained from patients and staff at the hemodialysis unit were compared to each other, and also to the quasispecies of selected sequences, with the same HCV genotype and > 95% nucleotide identity in the NS5B coding region, from HCV-infected individuals from the Third National Health and Nutrition Examination Survey (NHANES III) - a representative sample of the non-institutionalized civilian population of the United States [11].

**Epidemiologic Investigation and Cohort Study**

Hemodialysis treatment records, patient medical charts, and laboratory records including anti-HCV, hepatitis B virus (HBV) test results, and monthly liver enzyme test results for all patients who attended the dialysis unit were reviewed. Incident case-patients were interviewed by a public health official using a standardized questionnaire to elicit the presence of potential risk factors for HCV infection (e.g., history of illegal and injection drug use, sexual history, sexual or household contact with a person with HCV infection, and history of medical care received outside of the hemodialysis unit). To identify potential risk factors for incident HCV infection we performed a retrospective cohort study, including only incident case-patients and HCV susceptible patients dialyzed between November 1, 2005 and May 31st 2006 (the period during which incident case-patients were most likely exposed to HCV) [12]. Data collected included patient demographics, dialysis treatment characteristics, dialysis schedule, shift, station, and machine.

**Statistical Methods**

Patient demographic and dialysis–specific characteristics were compared using Fishers exact test for categorical variables and the nonparametric Kruskall-Wallis test for comparing the median of continuous variables. Potential dialysis-related risk factors, were compared using attack rates, defined as the number of incident HCV cases divided by the total number of patients with and without the risk factor assessed, and risk ratios (RR) and 95% confidence intervals (CI). All tests were 2-sided and p-values of < .05 were considered statistically significant. Statistical analysis was performed using SAS, version 9.2.

**Environmental and infection control assessment**

Inspections of the hemodialysis unit and observation of hemodialysis treatment and patient care practices was performed on multiple days and dialysis shifts. Infection control training manuals and facility policies, machine maintenance and cleaning schedules and dialyzer reprocessing logs were reviewed. Staff was interviewed about their routine dialysis and infection control practices at the facility.

**Results**

The dialysis unit was an outpatient community-based facility, with approximately 66 patients regularly attending each week, and treatment provided by 16 patient care staff. The unit had 17 dialysis stations, with one dedicated for the isolation of patients with HBV infection. All patients were routinely tested for anti-HCV upon admission to the unit and then annually, usually in January. All patients tested for anti-HCV in January 2006 were negative. HBV serologic testing at the unit followed CDC recommendations [13], and patients serum aspartate aminotransferase (AST) levels determined monthly. Monitoring of patient alanine aminotransferase (ALT) levels was not performed at this hemodialysis unit. Patients generally attend the unit 3 times each week on a Monday, Wednesday and Friday (MWF) schedule, or Tuesday, Thursday and Saturday (TTIS) schedule, during one of three daily shifts, morning (shift 1), mid-day (shift 2) or afternoon (shift 3). The median age of patients was 67 years (inter quartile range [IQR] 52 – 75 years), 42% were male and 55% had diabetes mellitus. The median length of time receiving hemodialysis was of 38 months (IQR 16 - 75 months).

**HCV infection status of patients and staff**

Based on past test results documented in patient charts and testing performed during the investigation, 2 patients had unknown HCV status (transferred to another unit prior to investigation), 12 patients were classified as having prevalent HCV infection (18%), 45 were HCV susceptible, and 7 had incident HCV infection. One patient had chronic HBV infection, and no new HBV infections were identified via review of routine testing. Among the 16 patient care staff tested for HCV in June 2006, 14 were anti-HCV and HCV RNA negative and 2 had HCV infection. Both had past diagnoses of chronic HCV infection prior to employment at the facility.

Three (43%) of 7 patients with incident HCV infection had symptoms consistent with acute HCV infection (i.e., jaundice and malaise), 2 required hospitalization one of whom died from an unrelated cause. Three patients were found to have incident HCV infection only during monthly HCV screening implemented by the facility, and the seventh patient was consistently anti-HCV negative but was found to be HCV RNA positive in June 2006 (Figure 1). Six of 7 incident case-patients had a serum AST levels increase greater than the upper limit of normal (>38 unit/L) between January - May 2006 (median peak AST: 99 units/L; range: 51 – 758 units/L), but only 3 had an increase >100 units/L. Via patient interview and chart review, no behavioral risk factors for HCV infection or other common exposure opportunities outside of the hemodialysis unit were identified for incident case-patients.

**Laboratory investigation and quasispecies analysis**

Six of 7 patients with incident HCV infection were tested for HCV-RNA and found to be positive with HCV genotype 1a; the seventh died and no serum was available for HCV RNA testing. Ten of 12 patients with prevalent HCV infection were HCV-RNA-positive; 7 were HCV genotype 1a, 2 were genotype 1b, and 1 genotype 2b. Both staff with chronic HCV infection were HCV-RNA-positive and HCV genotype 1a.

E1-HVR1 quasispecies analysis was performed on the 15 HCV-genotype 1a specimens (6 incident, 7 prevalent, 2 staff), and two highly related clusters were identified. For cluster A (3 incident and
were higher for patients dialyzed on the MWF schedule and on shifts 2

1 prevalent) the maximum HCV quasispecies sequence identity was
99.3% to 100%, and for cluster B (3 incident, 1 prevalent) the maximum
HCV quasispecies sequence identity was 97.3% to 100% (Figure 2). No

Cohort study

The retrospective cohort study included 7 incident case-patients and
45 HCV susceptible patients. Attack rates did not differ significantly by
age, gender, race, primary cause of renal failure, presence of diabetes,
or length or of time receiving dialysis (Table 1). The HCV attack rates
were higher for patients dialyzed on the MWF schedule and on shifts 2

and 3 (compared to shift 1), and were also higher for patients that that
more frequently (greater than the median value for the cohort) received
intravenous (IV) epoetin alfa, iron sucrose, paricalcitol and sodium
chloride during their dialysis sessions, however, these differences were
not statistically significant (Table 1). When the number of IV drugs
received per treatment session were combined, incident case-patients
received more IV drugs per dialysis session compared to susceptible
patients (2.1 vs 1.8, respectively; Wilcoxon rank sum, p=0.0606).

Evaluation of shared dialysis machines

To evaluate the potential for HCV transmission via the dialysis
machine, shared use of machines was assessed for the 6 incident case-
patients and 2 prevalent case-patients identified in each genetically
related cluster. In cluster A, all 3 incident case-patients were dialyzed
on the shift following directly after the prevalent case-patient. Two
prevalent case-patients were never dialyzed on the same machine after
the prevalent case-patient, and the third dialyzed on same machine
during only 4 dialysis sessions. In cluster B, all 3 incident case-patients
were dialyzed on the same shift as the prevalent case-patient and at
adjacent stations and were never dialyzed on the same machine.

Environmental and Infection Control Assessment

Interviews and observations of practices and the patient-care
environment were performed approximately 6 months after the first
patient was diagnosed with acute HCV infection. Staff hand hygiene,
glove, gown and face-shield use was appropriate. No opportunities for
HCV transmission were identified with respect to dialyzer reprocessing.
Disposable, single-use cloths soaked in a 1% bleach solution were
used to wipe down the dialysis station and machine between patients.
Although, technicians were observed wiping down machine and
station surfaces while the current patient remained in the station chair
waiting homeostasis. The contact time for bleach to disinfect surfaces
was limited to a few seconds.

During our observations, injectable medications were kept at
medication stations located at each end of the unit. However, they were
located directly next to and within splashing distance of the biohazard
bins for discarding used tubing, and plastic containers storing clean
supplies at the medication station were observed to have dried blood
splashes. No facility protocol was in place regarding routine cleaning
and disinfection for medication stations. Medication vials labeled as
single-use, specifically epoetin alpha, appeared to have been used as
multi-dose vials, as multiple puncture holes were observed in open
single-dose vials at the medication station. Interviews with staff
revealed that up until the month prior to the investigation, the facility
had routinely used a mobile medication cart to store and prepare
medications. The cart was transported between patients to each dialysis
station, where injection medications were prepare and administer to
patients.

Discussion

We identified patient-to-patient HCV transmission within a
hemodialysis unit, most likely attributable to failures to follow
recommended infection control practices. No HCV risk factors outside
the unit were indentified for incident case-patients, and incident case-
patients were found by quasispecies analysis to have the same virus as
two prevalent case-patients also attending the unit. Use of single dose
medication vials for multiple patients along with vial preparation at
the patient station, storage of clean supplies near biohazard disposal
areas, and failures to adequately clean and disinfect dialysis machines
and station between each patient are all plausible mechanisms of HCV
transmission that we identified. Each of these practices can facilitate cross-contamination and have previously been implicated in patient-to-patient HCV transmission in hemodialysis and other healthcare settings [6,7,9,14-16].

Due to concurrent treatment of hemodialysis patients in a shared area, the risk for blood contamination of the physical environment, equipment (e.g., healthcare hands, gloves, needles and syringes), and medication vials is high [12]. To reduce the risk of bacterial and viral contamination of medication vials, CDC recommends vials and injection equipment are stored and prepared in a clean environment away from the immediate patient treatment area, that medications packaged as single-use be dedicated to single patient use, and that medications packaged as multidose be assigned to single patients [7].

Table 1: Risk for hepatitis C virus infection among cohort of 7 incident case-patients and 45 HCV susceptible patients according to selected patient and hemodialysis treatment risk factors, November 2005 to May 2006.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Exposed Incident Cases</th>
<th>Exposed Total patients</th>
<th>Exposed Attack rate %</th>
<th>Unexposed Incident Cases</th>
<th>Unexposed Total patients</th>
<th>Unexposed Attack rate %</th>
<th>Risk Ratio (95% CI); p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 68 years</td>
<td>3</td>
<td>24</td>
<td>12.5</td>
<td>4</td>
<td>28</td>
<td>14.3</td>
<td>0.875 (0.217 – 3.527); &gt;0.999</td>
</tr>
<tr>
<td>Male gender</td>
<td>4</td>
<td>17</td>
<td>23.5</td>
<td>3</td>
<td>35</td>
<td>8.8</td>
<td>2.745 (0.691 – 10.910); 0.295</td>
</tr>
<tr>
<td>Race: White</td>
<td>4</td>
<td>15</td>
<td>26.7</td>
<td>3</td>
<td>38</td>
<td>7.9</td>
<td>3.378 (0.856 – 13.320); 0.179</td>
</tr>
<tr>
<td>Cause of renal failure: Hypertension</td>
<td>4</td>
<td>35</td>
<td>11.4</td>
<td>3</td>
<td>17</td>
<td>17.6</td>
<td>0.648 (0.163 – 2.575); 0.827</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2</td>
<td>28</td>
<td>7.1</td>
<td>5</td>
<td>22</td>
<td>22.7</td>
<td>0.314 (0.067 – 1.469); 0.245</td>
</tr>
<tr>
<td>Dialysis &gt;34 months</td>
<td>3</td>
<td>25</td>
<td>12</td>
<td>4</td>
<td>27</td>
<td>14.8</td>
<td>0.810 (0.201 – 0.267); &gt;0.999</td>
</tr>
<tr>
<td>Dialyzed on MWF schedule</td>
<td>6</td>
<td>30</td>
<td>20.0</td>
<td>1</td>
<td>22</td>
<td>4.3</td>
<td>4.400 (0.570 – 33.980); 0.226</td>
</tr>
<tr>
<td>Dialyzed on 1st shift</td>
<td>1</td>
<td>25</td>
<td>4.0</td>
<td>6</td>
<td>27</td>
<td>22.2</td>
<td>0.180 (0.023 – 1.392); 0.124</td>
</tr>
<tr>
<td>Received epogen alpha</td>
<td>4</td>
<td>26</td>
<td>15.4</td>
<td>3</td>
<td>26</td>
<td>11.5</td>
<td>1.333 (0.331 – 5.378); &gt;0.999</td>
</tr>
<tr>
<td>Received paricalcitol</td>
<td>5</td>
<td>27</td>
<td>18.5</td>
<td>2</td>
<td>25</td>
<td>8.0</td>
<td>2.315 (0.493 – 10.870); 0.486</td>
</tr>
<tr>
<td>Received iron sucrose</td>
<td>3</td>
<td>26</td>
<td>15.4</td>
<td>3</td>
<td>26</td>
<td>11.5</td>
<td>1.333 (0.331 – 5.378); &gt;0.999</td>
</tr>
<tr>
<td>Received sodium chloride</td>
<td>4</td>
<td>26</td>
<td>15.4</td>
<td>3</td>
<td>26</td>
<td>11.5</td>
<td>1.333 (0.331 – 5.378); &gt;0.999</td>
</tr>
</tbody>
</table>

CI: Confidence Interval
MWF: Monday, Wednesday, and Friday
Attack Rate: Number incident cases / number total patients x 100
1: Two-sided Fisher exact p-value
2: Cohort median
3: Received greater than cohort median value

Our findings suggest that apparent failures to follow existing infection control recommendations resulted in patient-to-patient HCV transmission, most likely through contamination of shared medication vials or of environmental surfaces and not via shared use of the same dialysis machine. Additionally, this investigation highlights the value of routine HCV screening programs to identify new HCV infections and alert staff to potential HCV transmission among patients.
remain the cornerstone of preventing HCV transmission among hemodialysis patients.

Acknowledgements & Disclosures

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References