IN-DEPTH REVIEW

Hepatitis C virus: an important occupational hazard?

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Infection with Hepatitis C virus (HCV) is estimated to affect 3% of the world’s population and is an important cause of liver disease. It is most commonly transmitted by percutaneous exposure. Although current evidence does not suggest an increased prevalence of HCV infection among healthcare workers, transmission of infection following occupational exposure has been demonstrated. An average transmission rate of 1.8%, following percutaneous injury, has been reported. The risk of transmission is higher from patients with viraemia, as measured by a positive polymerase chain reaction for HCV RNA. After exposure to HCV, healthcare workers should be actively followed up, initially using a test to detect viral RNA. This may facilitate earlier diagnosis and treatment. Recent reports in the UK, of transmission of infection to patients from HCV infected healthcare workers, have prompted a review of the appropriateness of HCV infected individuals undertaking exposure prone procedures.

Key words: Employment; epidemiology; hepatitis C virus; management; occupational exposure.

INTRODUCTION

The discovery of hepatitis C virus (HCV) in 1989 marked a major step forward in combating the spread of one of the major causes of viral hepatitis and highlighted its association with hepatocellular carcinoma. Identification was followed by confirmation of its aetiological role in non-A non-B hepatitis in general, and post-transfusion hepatitis in particular.

CHARACTERISTICS OF HEPATITIS C VIRUS

HCV is a positive stranded RNA virus of around 9500 nucleotides. Its gene coding is similar to that of the flaviviridae family with greatest homology shared with members of the pestivirus group. The virus has six main genotypes numbered 1 to 6. Genotypes have different geographic prevalence rates with types 1a, 1b, 2a, 2b and 3a found most commonly in the United States and western Europe while type 4 is commonest in the Middle East.

CLINICAL HISTORY

Only 20–30% of people infected with HCV develop acute symptoms. These are usually mild and may include jaundice, with fluctuating alanine aminotransferase concentrations. HCV has not been associated with fulminant hepatitis. The incubation period for acute infection may range from 2 weeks to 6 months but is usually around 6–8 weeks. A high proportion of those infected with HCV (60–70%) develop chronic infection. Of these, 20% will eventually develop serious long-term complications, including cirrhosis and hepatocellular carcinoma, usually in the second or third decade after infection.

Follow-up studies have identified some risk factors for the development of cirrhosis and hepatocellular carcinoma. These include age of onset (over 40 years at time of infection), male sex and alcohol misuse. High viral load correlates with increased liver injury and patients with co-infection with other blood-borne viruses also have more rapid disease progression. Disease severity has also been associated with viral genotype.

PREVALENCE OF HEPATITIS C

The prevalence of HCV infection has been estimated at less than 0.1% in the UK blood donor population, 1.8% in the general population in the USA and 3% worldwide, although higher rates are recorded in Africa.
Prevalence studies have been undertaken in healthcare workers. Zuckerman and colleagues studied a large cohort of clinical healthcare workers in the USA and found a HCV seroprevalence of 0.28%. Average seroprevalence rates of 1% among hospital based healthcare workers in the USA have been reported. A small study in Austria found a prevalence of 2% among 294 healthcare workers. The prevalence of HCV among US dentists has been investigated in a series of studies between 1984 and 1992. These studies screened almost 3000 dentists and oral surgeons. The percentage testing positive for antibodies to HCV ranged from 0 to 2%. In Taiwan, Kuo and colleagues found only three cases of HCV infection among 481 (0.65%) dentists. This seroprevalence rate is similar to that in local blood donors and pregnant woman. There is no evidence from these studies to suggest a substantial excess of HCV infection among clinical staff in the UK or elsewhere.

**ROUTES AND RISK OF TRANSMISSION**

Although the principal routes of transmission of HCV have been established, in 10–20% of cases no mode of transmission can be determined. The commonest means of transmission is by percutaneous exposure—transfusion of blood or blood products before routine screening of donors, or needle sharing amongst injecting drug mis-users. Almost all patients with haemophilia in the UK, treated before 1987, have HCV infection. Rates of HCV infection among dialysis patients vary between countries; Alter suggested an average of 20% but rates appear lower in the UK. Tattoos have also been linked to HCV acquisition.

Vertical transmission is not common but does occur with increased frequency where the mother is an HIV carrier and may be more likely when the mother has a high HCV load. The risk of transmission through sexual contact is small but may depend on a number of factors including viral load in a sexual partner and sexual promiscuity. A history of sexually transmitted disease is an independent risk factor for hepatitis C infection. Other risk factors include heavy alcohol intake and low socio-economic class. Hepatitis C is now the commonest blood-borne virus involved in reported occupational exposures in England and Wales (Dr M. Ramsay, PHLS, personal communication) and elsewhere. A number of studies have investigated the risk of transmission following occupational percutaneous injury. These have varied from no cases in a Spanish series of 81 healthcare workers who were followed up for 12 months following exposure to HCV, to 10% in a Japanese series reported by Mitsui and colleagues. Other studies have reported rates between 0.6% and 6.0%. A review of available studies suggested an average transmission rate of 1.8%. In the study by Mitsui and colleagues all the index cases were positive for HCV RNA, suggesting active viraemia is important to transmission of infection. Dore and colleagues undertook a meta-analysis of published studies which examined the transmission of hepatitis C from source cases where information existed on both HCV antibody status and the presence of viraemia as measured by polymerase chain reaction for HCV RNA. The authors reported rates of transmission from PCR positive patients of 6.2% for perinatal exposure, 6.1% after needlestick exposure, 78% after solid organ or bone marrow transplantation and 83% after transfusion of blood components. No definite cases of transmission in 874 people exposed to PCR negative sources were recorded.

These rates of transmission are higher than those estimated for HIV but less than the previously recorded rates for transmission of hepatitis B from index cases that are both surface antigen and core antigen positive.

There is little information on risks from mucocutaneous exposure but there is a case report of hepatitis C virus sero-conversion after an eye splash and a case report of simultaneous HIV and HCV transmission by the same route.

In a study by Puro and colleagues 646 occupational exposures to HCV were followed up. Transmission of infection occurred in four cases (0.6%). In all four cases the source of exposure was a hollow-bore needle. Other sharps injuries were not associated with infection.

Two series noted that co-infection with HIV enhanced the likelihood of HCV transmission. This greater risk has also been observed in cases of vertical transmission from mother to infant.

**RISK TO PATIENTS**

There are a limited number of published reports of transmission of HCV from healthcare worker to patient. In two prospective studies which investigated the effectiveness of screening blood donors for antibodies to HCV, Esteban and colleagues identified five patients who had developed HCV post-operatively but unrelated to blood transfusion. The cardiac surgeon involved in the patients' care was infected with HCV and genotyping closely linked the surgeon with these patients. The surgeon involved reported approximately 20 percutaneous injuries per 100 procedures, identifying the tying of wires during closure of the sternum as the main cause. This had previously been associated with the transmission of hepatitis B virus. In the UK there are two reports of transmission of HCV from surgeon to patient. Infection of a large number of patients by an anaesthetist in Spain has been reported. He was an i.v. drug misuser and was suspected of administering part of a dose of opioid analgesia to himself before using the same syringe to inject his patients.

**DIAGNOSIS OF HEPATITIS C VIRUS AND SEROLOGICAL MARKERS**

Antibody screening is still the initial test of choice in diagnosing HCV infection and is usually undertaken using third generation enzyme immunoassays (EIA) to
detect antibodies reactive to both core and non-structural recombinant HCV antigens. Reactivity in these assays is further characterized by supplementary recombinant immunoblot assays (RIBA) where antibodies to individual HCV recombinant antigens can be identified. The main purpose of the RIBA assay is to confirm the specificity of the screening EIA by sifting out false positive tests. For the serological investigation of healthcare personnel RIBA tests should always be performed on EIA reactive sera. It must be stressed that while both EIA or RIBA tests confirm exposure to HCV, neither identify persistent infection.

In the occupational health setting the definitive diagnostic test for HCV is one which identifies the presence or absence of the virus in a patient’s blood. This can be achieved by either nucleic acid amplification assays (polymerase chain reaction (PCR)) or signal amplification assays (branched-DNA (bDNA)). Cost, and for PCR, reproducibility, restrict these assays to: (1) identifying persistent infection in antibody positive individuals; (2) monitoring the response to antiviral treatment; and (3) the investigation of patients with poor humoral antibody responses, e.g. patients post-transplant or on chronic haemodialysis.

TREATMENT OF HCV INFECTION

Deciding who to treat is still a difficult area. Treatment is not routinely indicated for patients with persistently normal aminotransferase or decompensated cirrhosis and is mainly aimed at those who would benefit most, in particular those most likely to progress to cirrhosis (persistently abnormal aminotransferase levels, detectable HCV viraemia and inflamed hepatic histology). Interferon-α has been the mainstay of treatment for HCV infection and is now being used to better effect in combination with ribavirin. Patients most likely to clear the virus following treatment are those infected with a non-1 genotype, with a low viral titre and with minimal liver inflammation. It has been suggested that early treatment of acute hepatitis increases the likelihood of clearing the infection. Although treatment is aimed at clearing HCV carriage and preventing the development of cirrhosis, patients with cirrhosis can also improve with therapy by both viral clearance and improvements in liver histology. Currently a wide range of options for treating HCV infection are under investigation. These include polymerase and protease inhibitors, whose mechanisms of action have proved useful in the management of HIV.

CURRENT GUIDELINES ON MANAGING OCCUPATIONAL EXPOSURE TO HCV

In the US authoritative guidance has recommended that healthcare institutions include the following procedures in their policies for managing percutaneous or mucocutaneous exposure to blood.

- For the source, baseline testing for antibody to HCV (anti-HCV).
- For the person exposed to an anti-HCV positive source, baseline and follow-up (e.g. 6 months) testing for anti-HCV andaminotransferase activity.
- Confirmation by supplemental anti-HCV testing of all anti-HCV results reported as repeatedly reactive by enzyme immunoassay (EIA).

This authoritative guidance included a recommendation against offering post-exposure prophylaxis with immunoglobulin or antiviral agents. Available evidence does not suggest that either is effective.

The evidence that early treatment of acute HCV infection may improve rates of viral clearance has prompted a debate about more active post-exposure management. A test for viral RNA (RT-PCR) is likely to provide evidence of infection earlier than an antibody test using an EIA. Typically the average interval between exposure and seroconversion by EIA is 8–10 weeks but may be as long as 6 months. An argument can therefore be made for modifying the above guidance to include a PCR test and EIA monthly for the first 3 months and an EIA at 6 months. Emission of transmission of infection should lead to prompt referral to an appropriate clinical specialist.

Where the source of contamination is unknown it could be argued that post-exposure screening as for an anti-HCV positive source is indicated. In the UK the Advisory Group on Hepatitis has considered these issues and has recently published further guidance. Post-exposure counselling of healthcare workers should include discussion of the risks of transmission of infection and advice on the potential risks to subsequent household and clinical contacts. There is no indication for restricting the professional practice of healthcare workers following exposure to HCV.

FITNESS TO PRACTICE

In the UK, guidelines restricting the working practices of healthcare workers infected with blood-borne viruses are issued by the four UK health departments. In the case of hepatitis viruses this guidance is based on the recommendations of the Advisory Group on Hepatitis. In 1995 this group recommended that HCV infected healthcare workers shown to have been associated with transmission of infection to a patient during the performance of exposure prone procedures, should cease to perform such procedures. A definition of exposure prone procedure is given elsewhere. This restriction was not extended to HCV infected healthcare workers not associated with transmission of infection to patients. The Advisory Group on Hepatitis keep the subject under review, and the department is currently considering whether there is a need to issue guidance on the management of healthcare workers infected with hepatitis C (Dr H. Nicholas, personal communication).

There are grounds for reconsidering the current position in the UK. It could be argued that the sub-
clinical nature of HCV infection reduces the likelihood that infected healthcare workers will be identified as a source of transmission and therefore all those known to be infected with HCV should be excluded from exposure prone procedures. Recent reports in the UK, of transmission of infection to patients during surgery, raise concerns that transmission may be more common than previously believed. The lack of case reports elsewhere in the world suggest that transmission from healthcare worker to patient is not being identified or reported in higher prevalence areas.

A more restrictive approach would however present problems. It would raise questions about the need for mass screening of healthcare workers, as is already undertaken for Hepatitis B. This would be costly and without an available vaccine such screening would need to be repeated periodically. Such an approach may not therefore be effective in excluding recently infected healthcare workers from undertaking exposure prone procedures. HIV infected healthcare workers are excluded from undertaking exposure prone procedures, but there is no direct screening in the UK. Instead the responsibility is placed on the individual to report infection or suspected infection with HIV. This might be a more reasonable interim arrangement for HCV infected healthcare workers, until there is a better estimate of the true risk to patients. The sub-clinical nature of HCV infection may however reduce the effectiveness of this approach.

Arguably, consideration of an individual healthcare worker’s suitability for undertaking exposure prone procedures could be based on the results of an accredited PCR test. An antibody positive person with a repeatedly negative PCR could reasonably be considered as not viraemic and therefore of low or no infectivity.

Other guidance from the Department of Health on universal precautions for the prevention of transmission of blood-borne viruses has been published and in the absence of more proscriptive guidelines, should form the basis of advice to any HCV infected healthcare worker.

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REFERENCES

A. B. Stevens and P. V. Coyle: Hepatitis C virus: an important occupational hazard? 381


