~~Chapter 242~~271

Viral infections in patients on dialysis

~~Infections in Dialysis~~

Laura Labriola, Michel Jadoul, and Eric Goffin

Introduction

Viral hepatitis has been recognized from the early days of haemodialysis (HD) as an extremely frequent complication. The manipulation of large quantities of blood during HD indeed favours dissemination in the HD environment and nosocomial transmission of blood-borne viruses. The most infective one is the hepatitis B virus (HBV), followed in descending order by the hepatitis C virus (HCV) and the human immunodeficiency virus (HIV), as illustrated by the risk of viral transmission after accidental needle-stick puncture with a contaminated needle: around 30% for HBV, 2% for HCV, and 0.3% for HIV. This gradient parallels the respective serum viral loads (Edey ~~et al.~~ et al., 2010)

~~A.~~ Hepatitis B

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Epidemiology

Since the mid ~~seventies~~ 1970s (when hygienic precautions started to improve) and the ~~eighties~~ 1980s (when anti-HBV vaccination became available), the frequency of HBV infection in HD has decreased dramatically in most countries. Still, HBV infection remains more frequent in HD patients than in the general population worldwide, with prevalence figures of 0 ~~–~~ 6.6% in W~~w~~estern countries but up to 15% in some emerging countries (Edey et al., 2010) and incidence rates of 0.0078 events per patient-year in W~~w~~estern countries (Burdick et al., 2003).

Prevention

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The infectivity of HBV is high. Thus, in addition to adequate screening of blood donors, the prevention of transmission of HBV within HD units requires the isolation of potentially infective HBV carriers in a separate ward, in addition to hygienic precautions (required for all blood-borne pathogens) and the vaccination of all susceptible patients.

~~a)~~ Isolation

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To be effective, isolation of infective patients should be prompt. Regular testing of non-immune HD patients is thus advised. The US ~~Centre for Disease Control (CDC~~Centers for Disease Control and Prevention ~~, Atlanta, Georgia)~~ currently still recommends monthly testing for the hepatitis B surface antigen (HBsAg); this should, however, probably be tailored to the local prevalence of HBV carriers, especially in (very) low-prevalence countries such as Northern European countries where frequent testing may detect more false positives than true positives. More importantly, patients should be tested when returning from a high-prevalence country (e.g. after a holidays) (Bhattacharya ~~et al.~~ et al., 2009)

~~b)~~ Hygienic precautions

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These are discussed ~~below~~ in the 'Prevention' section ~~in the~~of HCV ~~section~~.

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~~c)~~ Vaccination

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Ideally, CKD patients likely to ever reach ~~ESRD~~ end-stage renal disease should be vaccinated as soon as possible, prior to starting HD. In those referred late, a full vaccination course should be offered soon after the start of HD ~~start~~. This will provide immunity in 50–60% of patients only. More immunogenic vaccines are currently under investigation. Awaiting their availability, double-dose vaccination or additional

intramuscular injections of a standard vaccine have been shown to somewhat increase ~~somewhat~~ the seroprotection rate. Finally the intradermal route ~~improves~~ modestly improves response rates in non-responders but the available vaccines are usually not licensed for intradermal administration (~~Labriola and Jadoul 2010,~~ Edey ~~et al.~~ et al., 2010; Labriola and Jadoul, 2010). In addition to lower response rates, HD patients also have lower peak ~~titers~~titres of anti-HBs, declining with time, and thus shorter duration of protection. Booster doses are recommended in those whose ~~titer~~titre falls below 10–100 IU/~~l~~L.

Diagnosis

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Unlike in the general population, acute ~~hepatitis B virus~~HBV infection is frequently mildly symptomatic or asymptomatic in HD patients. Systematic screening for HBsAg and hepatitis B core antigen (anti-HBc) is thus required. In addition, the level of aminotransferases is markedly lower in HD patients than in the general population. Peak alanine aminotransferase (ALT) level may thus be as low as 50–100 IU/~~l~~L in acute HBV infection. Such an ALT level, if unexplained, should prompt immediate serological testing for HBV (and HCV) in an HD patient. Chronic HBV infection is more frequent in HD patients than in the general population, most likely as a result of impaired immunity. Finally, occult HBV infection (negative HBsAg ~~antigen~~ but positive anti-HBc and HBV-DNA) has recently been reported but has relatively little relevance in terms of nosocomial transmission. Most such patients indeed have very low HBV-DNA levels (~~below~~ ≤ 50 copies/m~~l~~L) (Aghakhani ~~et al.~~ et al., 2010).

Treatment

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Treating HBV infection is rarely required in HD patients, except in those with HBV replication (high ~~titers~~titres of HBV DNA), either candidates for kidney transplantation or with little comorbidity and thus a long life- expectancy. The available strategies should then be discussed with a consultant hepatologist, usually after a liver biopsy (Edey et al 2010).

~~B.~~ Hepatitis C

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Epidemiology

The incidence and prevalence of HCV infection in HD patients have decreased substantially since the identification of HCV in the late ~~eighties~~1980s. Current prevalence rates are ~~below~~ < 10% in most countries (Fissell ~~et al.~~ et al., 2004~~,~~; Jadoul ~~et al.~~et al., 2004~~,~~; Johnson et al., ~~2008~~2009). Still, incidence rates remain high (> 1%), although improving, in several emerging countries (Johnson et al., ~~2008~~2009)

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Prevention

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The Kidney Disease: Improving Global Outcomes (KDIGO) workgroup (KDIGO ~~HCV guidelines~~, 2008) has reviewed the available evidence regarding the prevention of nosocomial transmission of HCV in HD. The cornerstone remains a careful, actual~~,~~ implementation of basic hygienic precautions. These are summarized in Boxtable 242271.1.4. The KDIGO workgroup further concluded that there was no evidence supporting ~~n~~either isolation by room~~,~~ ~~n~~or by machine of HCV carriers. These strategies should thus not be used as alternatives to the actual implementation of careful hygienic precautions. Admittedly, in many countries, the actual implementation of hygienic precautions remains suboptimal so that isolation has been used extensively. Units opting for isolation of HCV-positive ~~(+)~~ patients in an attempt to reduce a persistently high

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incidence of HCV infection should, however, realize that this equals ~~to~~ accepting the suboptimal implementation of hygienic precautions. Additional reasons against an isolation strategy include the need of four~~4~~ different wards for B+ C–, B–C+, B–C–, and B+C+ patients and the diagnostic window between infection and positivity of serological tests, expected to limit the efficiency of an isolation strategy (Jadoul, 1995).

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Diagnosis

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Screening for ~~hepatitis C virus (~~HCV~~)~~ infection usually relies on ~~3rd~~ third-generation immunoenzymatic assays. There is, however, a serological window (around 5 months) between contamination by HCV and the development of detectable anti-HCV antibodies in HD patients. In high-prevalence settings, the use of nucleic acid testing (polymerase chain reaction for the detection of HCV-RNA or similar tests) may thus be more appropriate, at least for initial testing. A recent systematic review (KDIGO, 2008) concluded that third-~~3rd~~ generation immunoenzymatic assays have a sensitivity of 75% and a specificity of 95% for the presence of HCV-RNA. In the absence of isolation policy, performing such serological tests at HD start and then twice a year, as well when patients return from another HD unit, is adequate. ~~Like~~ As for acute HBV infection, it should be realized that any ~~, even mild,~~ increase in transaminase levels, even mild, may point to acute hepatitis and should prompt additional testing for HCV (and/or HBV as appropriate).

Treatment

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The treatment of chronic HCV infection in the general population is changing rapidly with many new drugs available. In HD patients, the KDIGO guidelines (KDIGO, 2008)

concluded that the treatment should not be started before 3 months after the diagnosis of infection as spontaneous remission is observed in up to 20% of cases. Beyond that delay, the current standard regimen in HD patients is pegylated interferon together with low-dose ribavirin, with weekly monitoring of haemoglobin level. This treatment should only be performed, usually after a liver biopsy, under careful supervision by clinicians with substantial experience in the field. Those likely to benefit among HD patients are, ~~like~~ as for HBV treatment, potential candidates for kidney transplantation or with little comorbidity and thus a good life expectancy on HD. Tolerance is usually worse than in the general population but response rates tend to be good in those able to tolerate (KDIGO, 2008; Deltenre ~~et al.~~ et al., 2011) and these responses are usually sustained after a kidney transplantation (Gordon ~~et al.~~ et al., 2011).

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Table Box 242271.14

Key points for the prevention of nosocomial transmission of blood-borne viruses

- Wear gloves, to be changed between patients/stations
- Hand hygiene (hydroalcoholic solution) before contact with patient and after gloves withdrawal
- Prepare injectable drugs in clean area
- Do not return unused material from contaminated to clean area
- Clean/disinfect surfaces of HD environment including surface of machine before next session
- Dedicate small items (tourniquet, tape, etc.,...) to a single patient (if not, disinfect between patients).