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Original Article

Impact of dialysis room and reuse strategies on the incidence of hepatitis C virus infection in haemodialysis units

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Abstract Background: Despite the advent of screening of blood products for anti-hepatitis C virus (HCV), the incidence of HCV infection among haemodialysis (HD) patients is alarmingly high and suggests transmission within the HD unit. To analyse trends in the prevalence and incidence of HCV infection, and evaluate the impact of dialysis room and reuse policies on the incidence of HCV infection, a hospital survey instrument was sent out to medical directors of all 71 HD units in Portugal in August 1994. Information for the years 1991, 1992 and 1993 was requested with respect to HCV infection, defined as positive anti-HCV test. Sixty-two of 71 units (87%) treating 4232 patients in 1993 responded. Overall, data from 5774 patient-years were available for analyses. Observations over multiple intervals were pooled into a single sample, and pooled logistic regression was used to evaluate the relationship between risk factors/strategies and incidence of HCV infection. By 1993, regular anti-HCV testing of patients and staff was practised by 98% and 82% of units, respectively. There was a significant decline in the incidence of HCV infection from 9.9% in 1991 to 5.7% in 1992 and 5.1% in 1993. The incidence was directly related to the prevalence in the dialysis unit. Units with a prevalence of less than 19% had an annual incidence of 2.5% compared to a 35.3% incidence in units with a prevalence greater than 60%. There was a wide variation in the incidence of HCV infection in HD units across the country, with geographical location, unit ownership and socioeconomic factors playing a significant role. The incidence was lowest among units that: (i) were located in the northern regions of the country; (ii) were private hospital-based units; and (iii) used dedicated machines or separate rooms for anti-HCV-positive patients. The incidence among units that reprocessed dialysers (6.1%) was not significantly different from that among units that did not reprocess dialysers (7.4%). However, among units that did reprocess dialysers, the incidence of HCV infection was lowest in: (i) units that used separate rooms for reprocessing dialysers from anti-HCV-positive patients or did not reprocess these dialysers; and (ii) units that used Renalin as the sterilant. These results suggest the transmission of HCV infection in HD units and that use of dedicated machines and isolation of anti-HCV-positive patients and their dialysers may reduce the incidence of HCV infection.

Key words: Hepatitis C; haemodialysis; reuse; dialysis complications

Introduction

Hepatitis C virus (HCV) is the leading cause of liver disease in patients on dialysis and renal transplant recipients [1–4]. HCV is parenterally transmitted and patients with chronic renal failure are at risk of acquiring infection from blood transfusions or organ transplantation [5,6]. The widespread use of recombinant human erythropoietin therapy in dialysis patients, resulting in decreased transfusion needs, and ban on use of blood products and organs from donors with antibody to HCV (anti-HCV), have reduced the risk of acquiring HCV infection in patients with chronic renal failure [3,7].

The above notwithstanding, 5 years after the advent of anti-HCV testing, the prevalence and incidence of HCV infection among haemodialysis (HD) patients remains alarmingly high [4]. This strongly suggests the transmission of HCV infection within HD units, and has kindled debate on HD unit strategies such as patient isolation, dedicated machines and a ban on reuse, to reduce the risk of acquiring HCV infection in the HD unit [2]. Indeed, these measures have been associated with a decrease in the incidence of hepatitis B virus (HBV) infection in HD units [1]. However, unlike HBV, HCV circulates in low titres in infected serum and is rapidly degraded at room temperature [8], there currently is no vaccine available and superinfections can occur [9]. Further, anti-HCV tests cannot distinguish between current or past infection, and negative tests do not exclude current infection [6].

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Although testing for HCV RNA by polymerase chain reaction (PCR) can detect infection in some patients with a negative anti-HCV test [6], it is not approved for clinical use. Consequently, the rationale for isolating anti-HCV-positive patients has been questioned.

The need for strategies to reduce the incidence of HCV infection in HD patients is especially urgent in countries like Portugal where the prevalence of HCV infection in HD units is alarmingly high [10]. Therefore, in 1994, we developed a hospital survey instrument to study HD unit policies regarding the testing of staff and patients for anti-HCV, to evaluate trends in the prevalence and incidence of HCV infection in HD units, to identify risk factors associated with a high incidence of HCV infection, and to identify HD room and dialyser reprocessing strategies associated with a low incidence of HCV infection. We surveyed all HD units in Portugal for the period 1991–1993, after the institution of anti-HCV testing of blood products.

Subjects and methods

Hospital survey instrument

A questionnaire was sent out to medical directors of all 71 HD units in Portugal in August 1994. Information for the years 1991, 1992 and 1993 was requested with respect to HCV infection, defined as positive anti-HCV test. The data collected included the following.

(1) Demographic information such as ownership of the unit (private free-standing, private hospital-based or public hospital-based), geographical zone (north, central, south or islands), location (big cities or others), and date the dialysis unit began functioning.

(2) Patient and staff testing policies with respect to HCV—whether testing is routinely performed and if so the frequency of testing.

(3) Prevalence and seroconversion rate for each year among patients on dialysis at the start of the year, patients admitted to the unit during the year and patients who left the units during the year. The incidence of HCV was defined as the proportion of anti-HCV-negative patients who seroconverted.

(4) Dialysis room strategies used to prevent the transmission of HCV infection, and date of implementation. Five mutually exclusive dialysis room strategies were considered: no policy, fixed machines/stations for all patients in the unit, dedicated machines/stations for anti-HCV-positive patients, a separate area for anti-HCV-positive patients and a separate room for anti-HCV-positive patients.

(5) Whether dialysers are reprocessed and if so the date when reprocessing was begun.

(6) Information on reprocessing, including manual or automatic, and sterilant used (formalin or Renalin).

(7) For units that reprocessed dialysers, the reprocessing strategies for dialysers from anti-HCV-positive patients, and date of implementation. Five mutually exclusive reprocessing strategies were considered: no policy, dialysers from anti-HCV-positive patients reprocessed last, separate equipment for dialysers from anti-HCV-positive patients, a separate room for dialysers from anti-HCV-positive patients or ban on reuse of dialysers from anti-HCV-positive patients.

Statistics

We employed a HD unit-based model for describing the range of prevalence and incidence rates across HD units for each of the 3 years. We used a patient-based model for analyses of trends in incidence and factors influencing these trends. Observations over multiple intervals were pooled into a single sample. Pooled logistic regression was used to evaluate the relationship between risk factors/strategies and incidence of HCV infection. This methodology is similar to a time-dependent covariate Cox regression analysis. Univariate analyses were performed. The odds ratio (OR) and 95% confidence interval of the OR were calculated. Analyses were run in SAS/Stat (SAS Institute Inc., Cary, NC) and Splus for DOS (Statistical Services Inc., Seattle, WA).

Results

Sixty-two of 71 units (87%) treating 4232 patients in 1993 responded. Overall, data from 5774 patient-years were available for analyses (1378 for 1991, 1775 for 1992 and 2623 for 1993). By 1993, regular anti-HCV testing of patients was practised by 98% of units at an interval of 6 months (22%), 3 months (33%), 2 months (2%) or 1 month (43%). Also, by 1993, regular anti-HCV testing of dialysis unit staff was practised by 82% of units at an interval of 1 year (43%), 6 months (52%) or 3 months (5%).

Trends in the incidence and prevalence of HCV infection

Using the HD unit-based analyses, the mean (range) for prevalence of anti-HCV in HD units for the years 1991, 1992 and 1993 was 22.2% (0–62%), 28.3% (0–76.9%) and 28.8% (0–75.5%), respectively. The mean (range) for incidence of anti-HCV in HD units for the years 1991, 1992 and 1993 was 11.2% (0–61.9%), 7.2% (0–39.6%) and 6.5% (0–57.8%), respectively.

All results reported hereafter are from the patient-based analyses. As shown in Fig. 1, there was a significant decline in the incidence of HCV infection from

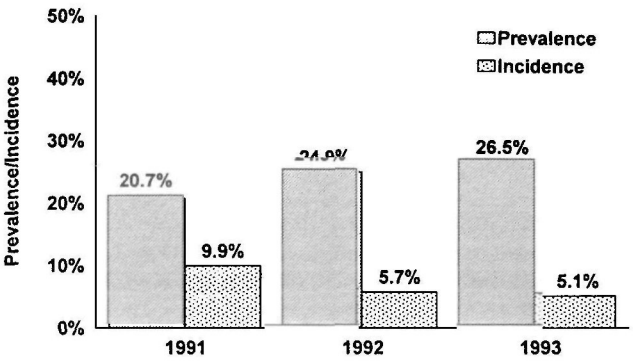

Fig. 1. Trends in the incidence and prevalence of HCV infection. With the incidence in 1991 as the reference, the odds ratio for incidence in 1992 was 0.56 ($P<0.001$) and for 1993 was 0.49 ($P<0.001$). The number of patients in the analysis was 1376, 1775 and 2623 for the years 1991, 1992 and 1993, respectively.

9.9% in 1991 to 5.7% in 1992 and 5.1% in 1993. With the incidence in 1991 as the reference, the odds ratio for incidence in 1992 was 0.56 (0.42–0.73, $P<0.001$) and for 1993 was 0.49 (0.38–0.62, $P<0.001$). During the same period, the prevalence remained essentially unchanged or higher at 20.7% in 1991, 24.9% in 1992 and 26.5% in 1993. The annual incidence of HCV infection was directly related to the prevalence in the dialysis unit (Fig. 2). Units with a prevalence of less than 19% had an annual incidence of 2.5% compared to a 35.3% incidence in units with a prevalence greater than 60%. The OR of acquiring HCV infection was 1.05, 1.25 and 1.56, respectively, for 1%, 5% and 10% increase in the prevalence in the HD unit.

Relationship between demographics and incidence of HCV infection

There was an asymmetric geographic distribution in the incidence. The northern region had the lowest incidence rates (0.5%) followed by the islands (2.0%), south (7.4%) and central regions (14.3%). Using the north as the reference group, the OR for incidence was 4.4 (1.34–14.61, $P=0.02$) for the islands, 17.6 (7.82–39.68, $P<0.001$) for the south, and 36.7 (16.05–84.12, $P<0.001$) for the central regions of the country. There was no significant difference in incidence between small cities' (7.0%) and big cities' units (6.1%). The incidence of HCV infection was lowest among private hospital-based units (2.9%) followed by public hospital-based units (4.4%) and private free-standing units (7.4%). Using private hospital-based units as the reference group, the OR for incidence rates was 1.55 (0.90–2.69, $P=0.12$) for public hospital-based units and 2.71 (1.71–4.29, $P<0.001$) for private free-standing units.

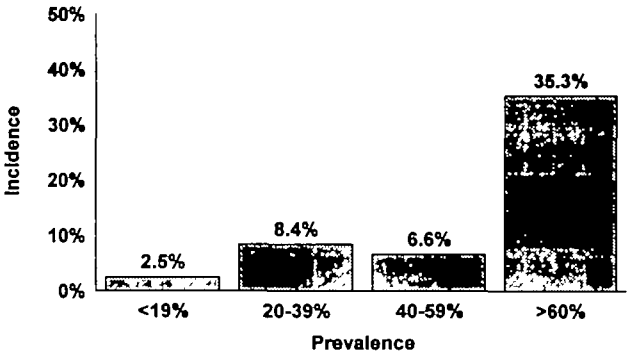

Fig. 2. Relationship between incidence and prevalence of HCV infection in HD units. The odds ratio of acquiring HCV infection was 1.05, 1.25 and 1.56 for 1%, 5% and 10% increase in the prevalence in the HD unit, respectively. The number of patients in the analysis was 2471, 2320, 816 and 167, respectively, for units with anti-HCV prevalences of <19%, 20–39%, 40–59% and >60%.

Impact of dialysis room strategies on the incidence of HCV infection (Table 1)

By 1993, 71% of patients were treated in HD units that had at least one dialysis room strategy in place to reduce the transmission of HCV infection. Compared to units without specific dialysis room measures to prevent the transmission of HCV infection, units with dedicated machines/stations or separate rooms for anti-HCV-positive patients had a significantly lower incidence of HCV infection; units with a separate area for anti-HCV-positive patients had incidence rates that were not significantly lower; and units with dedicated machines/stations for all patients (whether anti-HCV positive or not) had a significantly higher incidence of HCV infection.

Impact of reprocessing policies on the incidence of HCV infection (Tables 2 and 3)

The majority of dialysis units in Portugal reprocess haemodialysers. As shown in Table 2, the incidence of HCV infection in patients treated in units that reprocessed dialysers (6.1%) was not significantly different from that among patients treated in units that did not (7.4%). The analyses in Table 3 are restricted to units that did reprocess dialysers. By 1993, 72% of patients were treated in HD units that had at least one reprocessing room strategy in place to reduce the transmission of HCV infection. In units that reprocessed dialysers, compared to units that did not follow any specific precautions in reprocessing dialysers from anti-HCV-positive patients, units that used a separate room to reprocess dialysers from anti-HCV-positive patients

Table 2. Impact of reprocessing of dialysers on the incidence of HCV infection in haemodialysis units

Dialysers reprocessed	Patient-years	Incidence	Odds ratio (95% CI)	*P*
No	1267	7.4%	1	—
Yes	4507	6.1%	0.82 (0.64–1.04)	0.1

Table 1. Impact of dialysis room strategies on the incidence of HCV infection in haemodialysis units

Policy for HCV-positive patients	Patient-years	Incidence	Odds ratio (95% CI)	*P*
No policy	2131	6.7%	1	—
Dedicated machines/station for all patients	1435	9.4%	1.46 (1.14–1.86)	0.003
Dedicated machines/stations	584	1.5%	0.22 (0.11–0.43)	<0.001
Separate area	964	6.6%	1.00 (0.73–1.35)	0.98
Separate room	661	3.2%	0.46 (0.29–0.73)	0.001

Table 3. Impact of dialyser reprocessing strategies on the incidence of HCV infection in haemodialysis units

Policy for HCV-positive dialysers	Patient-years	Incidence	Odds ratio (95% CI)	*P*
No policy	2235	6.9%	1	—
Reprocessed last	423	10.2%	1.53 (1.07–2.18)	0.02
Separate equipment	1001	7.1%	1.03 (0.77–1.38)	0.86
Separate room	495	0.4%	0.06 (0.01–0.22)	<0.001
Not reprocessed	354	2.0%	0.27 (0.13–0.59)	<0.001

and those that did not reprocess dialysers from anti-HCV-positive patients had significantly lower incidence rates; units that used separate equipment for reprocessing dialysers from anti-HCV-positive patients had incidence rates that were not significantly lower; and units that reprocessed dialysers from anti-HCV-positive patients last had a significantly higher incidence of HCV infection.

The incidence of HCV infection in units that reprocessed dialysers manually (6.0%) was not significantly different ($P=0.42$) from that in units that used automated reprocessing (5.4%). However, the incidence in units that used Renalin as the germicide (4.2%) was significantly lower ($P=0.002$) than that in units that used formaldehyde (6.7%). Compared to units that used formaldehyde, the OR for incidence in units that used Renalin was 0.62 (0.46–0.84).

Discussion

The results of this study demonstrate that, by 1993, the majority of dialysis patients and staff in Portugal were regularly tested for anti-HCV. Between 1991 and 1993 there was a steady decline in the incidence of HCV infection in HD units in Portugal. Nonetheless, the prevalence and incidence of HCV infection among HD patients in 1993 remains alarmingly high. The incidence was higher in HD units with a high background prevalence of infection. There was a wide variation in the incidence of HCV infection in HD units across the country, with geographical location, unit ownership and socioeconomic factors playing a significant role. The incidence was lowest among units that: (i) were located in the northern regions of the country; (ii) were private hospital-based units; and (iii) used dedicated machines or separate rooms for anti-HCV-positive patients. Although the incidence among units that reprocessed dialysers was not significantly different from that among units that did not reprocess dialysers, among units that did reprocess dialysers, the incidence of HCV infection was lowest in (i) units that used separate rooms for reprocessing dialysers from anti-HCV-positive patients or did not reprocess these dialysers; and (ii) units that used Renalin as the sterilant. These results suggest the transmission of HCV infection in HD units, and that use of dedicated machines and isolation of anti-HCV-positive patients and their dialysers may reduce the incidence of HCV infection.

The incidence of HCV infection among HD units in Portugal has steadily declined from 11.2% in 1991 to 7.2% in 1992 and 6.5% in 1993, and among HD patients from 9.1% in 1991 to 5.7% in 1992 and 5.1% in 1993. The large initial decrease in incidence from 1991 to 1992 coincided with the introduction of anti-HCV screening of blood products by the more sensitive second-generation ELISA, and the availability of erythropoietin to all dialysis patients in Portugal. The subsequent smaller but consistent decline in incidence probably reflects a better appreciation by the HD unit staff of the risk of transmission within dialysis units, the need for regular testing of staff and patients, and measures taken by several HD units to limit the transmission of HCV infection. Indeed, by 1993, 98% of patients and 82% of staff were regularly tested for anti-HCV, 71% of patients were dialysed in units that had at least one dialysis room strategy in place to reduce the transmission of HCV infection, and 72% of patients were dialysed in units that had at least one reprocessing room strategy in place to reduce the transmission of HCV infection.

There was a wide variation in the prevalence (0–75.5%) and incidence (0–57.8%) of HCV infection among different HD units across Portugal. Large variation in prevalence and incidence rates between countries and even within countries is not unusual. The European Dialysis and Transplant Association survey for 1993 also revealed a large variation in the prevalence of HCV infection among member countries, ranging from 1% in Finland to 44% in Egypt [4]. Even within countries, the prevalence varies from region to region and unit to unit [11]. Clearly, the thoroughness of screening of blood products for anti-HCV, the meticulousness with which individual HD units adhere to 'universal precautions' and dialysis unit hygiene, the thoroughness with which dialysis and reprocessing equipment are cleaned, and implementation of additional precautionary measures to retard the transmission of HCV infection within the unit, all play an important role in these differences.

The results of this study suggest the transmission of HCV within HD units. First, despite the screening of blood and blood products for anti-HCV, the incidence of HCV infection in HD patients remains high. Second, the incidence of HCV directly correlated with the prevalence of infection in the units. Third, patients treated in units that implemented strategies that used dedicated machines or isolated anti-HCV-positive patients and their dialysers had the lowest incidence

of HCV infection. This adds to several epidemiological and genetic studies and case observations in dialysis patients that have provided evidence in support of nosocomial mode of transmission of HCV in dialysis units. First, home dialysis and peritoneal dialysis, both of which provide an isolated environment and limit patient-to-patient contact, have been associated with a lower prevalence of anti-HCV as compared to in-centre HD [2]. Second, outbreaks of HCV infection in HD units have occurred as a result of multiple breaks in infection control policies [12]. Third, the use of dedicated machines and isolated rooms has been shown to be associated with a lower incidence of anti-HCV [13,14]. Finally, studies using genotype analysis of HCV strains have shown relative homogeneity of HCV variants in patients in single dialysis units compared to the heterogeneity in anti-HCV-positive patients in the non-dialysis population [15,16].

Among the different dialysis room strategies considered, the lowest incidence of HCV infection was observed in units that had a separate room for anti-HCV-positive patients, suggesting that the treatment of anti-HCV-positive patients in separate rooms with dedicated machines and staff could reduce the transmission of HCV in HD units. This observation supports the results of a prospective multicentre study in Belgium which found that all seroconversions for HCV occurred exclusively in units where anti-HCV-positive patients were dialysed and not in units without anti-HCV-positive patients [17]. Further, these authors observed a higher seroconversion rate among patients dialysed at a station adjacent to an anti-HCV-positive patient [17]. Likewise, other investigators have also found that anti-HCV-positive HD patients were clustered in a group of patients who had never been transfused but who had been dialysed in the same ward and in the same session [18]. Although isolation of anti-HCV-positive patients and their dialysers is intuitively a rational strategy, there are several limitations to this strategy. First, a negative anti-HCV test does not unequivocally exclude HCV infection, especially in HD patients [2]. Although testing for HCV RNA by PCR could solve this problem, PCR is time consuming, requires a specialized laboratory and is also fraught with false positive and false negative results [2]. Second, infection with a given strain does not protect against infection with another strain or even the same strain and dialysis patients have been known to be infected with more than one strain of the virus [9]. Consequently, use of dedicated machines and isolation of anti-HCV-positive patients with different strains of the virus could lead to superinfections. Third, several groups of investigators have reported an absence or low rate of seroconversion in units where strict 'universal precautions' were rigorously implemented along with strict sterilization of HD machines and the environment [19–21]. Finally, the economical consequences of patient isolation would further burden the already strained dialysis budget in most countries. At the present time, the Centre for Disease Control and Prevention (CDC) does not recommend either dedicated machines or isolation for anti-HCV-positive patients [22].

The incidence of HCV infection among patients from HD units that did not reprocess dialysers was not significantly different from that among patients from units that reprocessed dialysers. These results are similar to those reported by Jadoul and colleagues who prospectively studied patients from 15 HD units in Belgium and did not find higher incidence of HCV infection among patients treated in units that reprocessed dialysers [17]. However, in our study, among units that did reprocess dialysers, the lowest incidence was observed among patients in units that used separate rooms to reprocess dialysers from anti-HCV-positive patients or had a ban on reprocessing of anti-HCV-positive dialysers. These data suggest that contamination in the reprocessing room may be another vector for the transmission of HCV in HD units. Nonetheless, the CDC does not recommend a ban on reuse of dialysers from anti-HCV-positive patients [22].

Although epidemiological studies clearly suggest the transmission of HCV infection in HD units, the exact modes are as yet unclear. Breakdown in standard infection control practices such as sharing of a multidose heparin vial between patients and failure to change gloves between patients while performing HD treatments have been associated with outbreaks of HCV infection [23,24]. Rigorous infection-control measures, cleaning and disinfection of all instruments and environmental surfaces that are routinely touched, and ban on sharing of articles among patients resulted in a decline in the incidence of HCV infection in these units [13,19–21]. Theoretically, the passage of HCV through intact dialyser membranes seems improbable as the viral particles have much higher estimated size (35 nm [25]) than the pores of even the permeable dialysis membrane. However, any alteration in pore size or disruption of the membrane integrity, associated with the process of filter assembly, the dialysis session itself, or with dialyser reuse, could hypothetically permit the passage of the virus into the dialysate compartment. Two recent studies have reported that neither low-flux (cuprophan) nor high-flux (cellulose-diacetate, polysulfone and polyacrilonitrile) dialysers permit contamination of the dialysis ultrafiltrate with HCV [26,27]. In contrast, others have detected HCV RNA by PCR in the dialysate of apparently intact polyacrylonitrile membranes, but not cuprophan membranes [28]. It is important to emphasize that a positive PCR may only imply the presence of viral particles and not of the infective virus itself, a situation which probably does not always lead to transmission of the infection. On the other hand, negative PCR does not absolutely rule out the presence of HCV in the dialysis ultrafiltrate as passage of minimal amounts of HCV, below the detection threshold of the PCR assay, may have occurred through the dialysis membrane. However, such a low viral load in the dialysis ultrafiltrate may represent a negligible risk of dissemination of HCV infection.

Despite the strong evidence in this study demonstrat-

ing that specific dialysis room and reprocessing room strategies are associated with a low incidence of HCV infection, these results are based on a retrospective hospital survey instrument. Hence, a clear cause and effect relationship cannot be established. It is indeed possible that units with strict dialysis and reprocessing room strategies and a low incidence of HCV infection could be those that were most cognizant of the risks of transmission of HCV infection. Consequently, these units may have been the most diligent in practising 'universal precautions' and cleansing of dialysis and reprocessing equipment. Nonetheless, the 28.8% prevalence and 6.5% incidence in the HD unit-based model or 26.5% prevalence and 5.1% incidence in the patient-based model in 1993 is alarmingly high. Hence, prospective studies are required to confirm the efficacy of the interventions described in this report. Meanwhile, strict adherence to 'universal precautions' is strongly recommended.

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References

1. Tokars J, Alter MJ, Favero MS *et al.* National surveillance of hemodialysis associated diseases in the United States, 1992. *ASAIO J* 1994; 40: 1020–1031
2. Natov SN, Pereira BJG. Hepatitis C infection in patients on dialysis. *Semin Dial* 1994; 7: 360–368
3. Pereira BJG. Hepatitis C infection and post-transplantation liver disease [Review]. *Nephrol Dial Transplant* 1995; 10: 58–67
4. Valderrábano F, Jones EHP, Mallick NP. Report on management of renal failure in Europe, XXIV, 1993. *Nephrol Dial Transplant* 1995; 10(suppl 5): 1–25
5. Esteban JI, Esteban R, Viladomiu L *et al.* Hepatitis C virus antibodies among risk groups in Spain. *Lancet* 1989; ii: 294–296
6. Pereira BJG, Milford EL, Kirkman RL *et al.* Prevalence of HCV RNA in hepatitis C antibody positive cadaver organ donors and their recipients. *N Engl J Med* 1992; 327: 910–915
7. Donahue JG, Muñoz A, Ness PM *et al.* The declining risk of post-transfusion hepatitis C virus infection. *N Engl J Med* 1992; 327: 369–373
8. Yoshizawa H, Otoh Y, Iwakiri K, Tanaka A, Tachibana T. Non-A, non-B (type 1) hepatitis agent capable of inducing tubular structures in the hepatocyte cytoplasm of chimpanzees: inactivation by formalin and heat. *Gastroenterology* 1982; 82: 502–506
9. Farci P, Alter HJ, Govindarajan S *et al* Lack of protective immunity against reinfection with hepatitis C virus. *Science* 1992; 258: 135–140
10. Carrera F, Silva JG, Oliveira C, Frazao JM, Pires C. Persistence of antibodies to hepatitis C virus in a chronic hemodialysis population. *Nephron* 1994; 68: 38–40
11. Huraib S, Al-Rashed R, Aldrees A, Aljefry M, Arif M, Al-Faleh FA. High prevalence of and risk factors for hepatitis C in haemodialysis patients in Saudi Arabia: a need for new dialysis strategies. *Nephrol Dial Transplant* 1995; 10: 470–474
12. Niu MT, Alter MJ, Kristensen C, Margolis HS. Outbreak of hemodialysis-associated non-A, non-B hepatitis and correlation with antibody for hepatitis C virus. *Am J Kidney Dis* 1992; 19: 345–352
13. Garcia-Valdescasas J, Bernal MC, Cerezo S, Garcia F, Pereira BJG. Strategies to reduce the transmission of HCV infection in hemodialysis (HD) units [abstract]. *J Am Soc Nephrol* 1993; 4: 347
14. Vagelli G, Calabrese G, Guaschino R, Gonella M. Effect of HCV+ patients isolation on HCV infection incidence in a dialysis unit. *Nephrol Dial Transplant* 1992; 7: 1070
15. Sampietro M, Badalamenti S, Salvadori S *et al.* High prevalence of a rare hepatitis C virus in patients treated in the same hemodialysis unit: evidence for nosocomial transmission of HCV. *Kidney Int* 1995; 47: 911–917
16. Stuyver L, Caleys H, Wyseur A *et al.* Hepatitis C virus in a hemodialysis unit: molecular evidence for nososcomial transmission. *Kidney Int* 1996; 889–895
17. Jadoul M, Cornu C, Van Ypersele de Strihou C, the UCL Collaborative Group. Incidence and risk factors for hepatitis C seroconversion in hemodialysis: a prospective study. *Kidney Int* 1993; 44: 1322–1326
18. Da Porto A, Adami A, Susanna F *et al.* Hepatitis C virus in dialysis units: a multicenter study. *Nephron* 1992; 61: 309–310
19. Gilli P, Soffritti S, Vitali EDP, Bedani PL. Prevention of hepatitis C virus in dialysis units. *Nephron* 1995; 70: 301–306
20. Fabrizi F, Lunghi G, Guarnori I *et al.* Incidence of seroconversion for hepatitis C virus in chronic haemodialysis patients: a prospective study. *Nephrol Dial Transplant* 1994; 9: 1611–1615
21. Zeuzem S, Scheuermann EH, Waschk D *et al.* Phylogenetic analysis of hepatitis C virus isolates from hemodialysis patients. *Kidney Int* 1996; 49: 896–902
22. Moyer LA, Alter MJ. Hepatitis C virus in the hemodialysis setting: a review with recommendations for control. *Semin Dial* 1994; 7: 124–127
23. Gilli P, Moretti M, Soffritti S *et al.* Non-A, non-B hepatitis and anti-HCV antibodies in dialysis patients. *Int J Artif Organs* 1990; 13: 737–741
24. Okuda K, Hayashi H, Yokozeki K *et al.* Mode of nosocomial HCV infection among chronic hemodialysis patients and its prevention. *Hepatology* 1994; 19: 293
25. Yuasa T, Ishikawa G, Manabe S, Sekiguchi S, Takeuchi K, Miyamura T. The particle size of hepatitis C virus estimated by filtration through microporous regenerated cellulose fibre. *J Gen Virol* 1991; 72: 2021–2024
26. Caramelo C, Navas S, Alberola ML *et al.* Evidence against transmission of hepatitis C virus through hemodialysis ultrafiltrate and peritoneal fluid. *Nephron* 1994; 66: 470–473
27. Hubmann R, Zazgornik J, Gabriel C *et al.* Hepatitis C virus-does it penetrate the haemodialysis membrane? PCR analysis of haemodialysis ultrafiltrate and whole blood. *Nephrol Dial Transplant* 1995; 10: 541–542
28. Lombardi M, Cerrai T, Dattolo P *et al.* Is the dialysis membrane a safe barrier against HCV infection? *Nephrol Dial Transplant* 1995; 10: 578–579

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