Incidence and Potential Risk Factors for Seroconversion to Hepatitis C Positivity in Patients on Maintenance Hemodialysis in Sub-Saharan Africa

Gloria E. Ashuntantang, Richard Njouom, Andre-Pascal Kengne, Antoine N. Ngemhe, Francois F. Kaze, Henry N. Luma, Oudou Njoya

Abstract

PURPOSE
Maintenance hemodialysis (HD) is a high risk milieu for nosocomial Hepatitis C virus (HCV) infection. We evaluated the rate and potential risk factors of seroconversion to anti-HCV positivity in maintenance HD patients in a tertiary hospital in Cameroon.

METHODOLOGY
This was a retrospective cohort study involving 40 patients on HD for at least 3 months with a negative baseline HCV serology tested with a third-generation ELISA (Monolisa anti-HCV plus version 2, Biorad) who were retested by the same test during March and April 2010. Relevant clinical patient data were recorded. The Fischer and Student tests or equivalents were used to determine the rate of seroconversion to anti-HCV positivity and the potential risk factors.

RESULTS
The mean age was 48±13yrs, median duration on dialysis of 17 months (IQR12-25.7), median number of blood units transfused of 5 (IQR 3-18.5). Ten of the 40 patients developed anti-HCV antibodies on dialysis (cumulative seroconversion rate 25%). A longer duration on dialysis (14 vs. 27 months, p=0.003) and a higher number of blood units received (19.5 vs. 5 units, p=0.001) where significantly associated with seroconversion.

CONCLUSION
The seroconversion rate to anti-HCV positivity in this study is alarming. Longer dialysis on duration, higher frequency of blood transfusions and perhaps non-adherence to universal infection control measures were potential risk factors of this nosocomial transmission.

KEY WORDS:
Hemodialysis, hepatitis C antibodies, seroconversion, risk factors.

Résumé

OBJECTIFS
L'hémodialyse (HD) chronique est un milieu à haut risque pour la transmission du virus de l’Hépatite virale C (VHC). Nous avons évalué le taux et les facteurs de risque potentiels de séroconversion au VHC chez les hémodialysés chroniques dans un hôpital tertiaire du Cameroun.

MÉTHODES
Il s’agissait d’une étude de cohorte rétrospective incluant 40 patients en HD depuis au moins 3 mois, ayant une sérologie initiale négative au VHC par un test ELISA de troisième génération (Monolisa anti-HCV plus version 2, Biorad) qui étaient à nouveau testées par le même test de mars à Avril 2010. Les données cliniques importantes des patients étaient enregistrées. Les tests de Fischer et Student ou équivalents ont été utilisés pour déterminer le taux de séroconversion ainsi que les facteurs potentiels de risques.

RÉSULTATS
L’âge moyen était de 48±13ans, la durée médiane en dialyse de 17 mois (IQR12-25.7) et le nombre médian d’unités de sang transfusées de 5 (IQR 3-18.5). Dix des 40 patients ont développé des anticorps anti-VHC en dialyse (taux cumulé de séroconversion de 25%). L’ancienneté en dialyse (14 vs. 27 mois, p=0,003) et le nombre élevé d’unités de sang reçues (19,5 vs. 5 unités, p=0,001) étaient significativement associés à la séroconversion au VHC.

CONCLUSION
Le taux de séroconversion au VHC dans cette étude est alarmant. Une longue durée en dialyse, la fréquence élevée des transfusions sanguines et peut-être la non-observance des mesures universelles d’hygiène étaient les facteurs de risque potentiels de cette transmission nosocomiale.

MOTS CLÉS
Hémodialyse, anticorps virus hépatite virale C, séroconversion, facteurs de risque.
INTRODUCTION

Hepatitis C virus infection (HCV) is highly prevalent in patients undergoing maintenance hemodialysis where it adversely affects patient survival [1-4]. The reported prevalence of HCV varies from 1.9% to 80% in the hemodialysis population, with low rates reported in Western Europe and very high rates in Eastern Europe and Sub-Saharan Africa [5-7]. While some patients enter the dialysis program with hepatitis C positivity, the majority acquire the infection while on this therapy [8-11]. Reported seroconversion rates to HCV positivity vary from 0-42% depending on facility, country or continent [5, 6, 12-16]. Identified risk factors for seroconversion include: a long duration on dialysis, blood transfusions, a high facility prevalence of HCV, facility practices and the non-adherence to universal infection control precautions [7, 9-11, 15, 17-32]. Most of these risk factors are suggestive of a patient-to-patient transmission route through the contaminated hands of staff and objects. [11,28-30,33,34] The decline in incidence rates observed in the HD population in some countries is attributable to improved blood safety measures, the availability of erythropoietin[5-7,10,23], the implementation of universal infection control measures[18,23,35] and in some cases the isolation of anti-HCV positive patients [15,24,25,32].

Enabling factors for HCV transmission abound in the HD environment in Sub-Saharan Africa. Like other resource-limited settings, blood donor screening for HCV is inconsistent despite the high population prevalence of HCV antibodies [36, 37]. Furthermore, blood transfusion remains the main therapy for uremic anemia, [13, 31, 38, 39] while patient overcrowding in the scarce hemodialysis facilities [40] and shortage of healthcare personnel in quantity and quality [40] renders the respect of universal infection control measures elusive.

Yet very little information exists on the seroconversion to HCV positivity in patients on maintenance hemodialysis in high endemic regions of Sub-Saharan Africa. This study was therefore designed to determine the incidence and identify potential risk factors of seroconversion to HCV positivity in patients on maintenance hemodialysis in a single center within a high endemic Sub-Saharan African country.

MATERIAL AND METHODS

This was a retrospective cohort study involving 40 patients on maintenance HD for at least 3 months with a negative baseline HCV serology tested with a third-generation ELISA at the virology laboratory of Centre Pasteur du Cameroun. The study period was March-April 2010. After an informed and written consent, relevant socio-demographic and medical data was recorded on a pre-tested questionnaire. This included duration on dialysis and number of blood transfusions received while on dialysis. A sample of 10 ml of blood was then collected from the patients and taken to the virology laboratory of the Centre Pasteur du Cameroun where serum was obtained. The presence of anti-HCV antibodies was checked using a commercial third-generation ELISA (Monolisa anti-HCV plus version 2, Biorad, Marnes-La-Coquette, France). The reactivity or non-reactivity of a sample was determined as previously described. [41] Briefly, a ratio (R) of Optical Densities (OD) for each sample was calculated by dividing its OD with the cut off value. A sample was scored as positive if its R ratio was equal or above 6, whereas all samples with R less than 6 were scored as negative. Ethical clearance was obtained from the Hospital ethical committee.

Statistical Analysis

Data analysis used SPSS v.17.0 (SPSS Inc., Chicago, USA) for Windows®. Results are reported as count (percentages), mean and standard deviation (SD) or median and 25th – 75th percentiles. Group comparisons used the Fisher exact test for categorical variables, and Student t test and Mann-Whitney U test for quantitative variables. A p-value<0.05 was used to characterize statistically significant results.

Study Setting

The setting is a public hemodialysis facility situated in a tertiary hospital. Created in November 2002, the center has 12 Fresenius ® 4008S HD generators (Fresenius Medical Care Homburg, Germany). It serves both acute and chronic patients undergoing maintenance hemodialysis at the time of the study. The center did not practice any isolation policy for patients with Hepatitis B and C positive patients. At the time of the study, the center had 2 nephrologists and 14 nursing staff. The nursing staff was made up of 10 state-registered nurses (SRN) and 2 assistant nurses (AS). Six of the state registered nurses were on their first job and had worked in the center for less than one year. Only three of the nurses had received at least 3 months or more of formal training in hemodialysis. Nurses worked in teams and shifts following a monthly roster. A team was usually made up of 2 SRNs and one AS. There were 2 shifts: a daytime (6a.m – 5pm), and a night-time (5p.m- midnight) one. The team usually worked 2 consecutive daytime, followed by 2 consecutive nighttime shifts, then takes off 2 days. Recombinant erythropoietin in prefilled syringes of 2000IU was available for those who could need it.
afford but heparin in multi-dose vials was shared amongst patients. Screening of blood donors for HCV antibodies was routine practice since 1996 at the hospital blood bank. However patients could obtain blood from other blood banks in the city.

RESULTS
A total of 40 patients were included in the study, with 28 (70%) being men. They had a mean age of 48 years (standard deviation 13). This mean age was borderline higher for men than women (50.5 vs. 42.1 years, p=0.06), (Table 1). Participants had been on dialysis for a median duration of 17 months (25-75th percentile: 12-25.7) which was not appreciably different between men and women (p=0.16). During this period, they received a median number of 5 units of blood (25-75th percentiles: 3-18.5), again with no significant difference between men and women (p=0.046).

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There was a significant positive correlation between the duration on dialysis and the number of units of blood transfusion received (Spearman correlation coefficient 0.46, p=0.003; Figure 1). While on dialysis, 10 patients (cumulative incidence rate 25%) seroconverted to hepatitis C positivity (Figure 2). This seroconversion rate was non-significantly higher in women than in men (42% vs. 18%, p=0.13, Figure 2). Compared with participants who remained seronegative for hepatitis C, those who acquired a positive status had similar age (47.3 vs. 50 years, p=0.58). However, they had a much longer median duration on dialysis (14 vs. 27 months, p=0.003); during which time they also received more units of blood (19.5 vs. 5 units, p<0.001, Table 1). The small number precluded further investigations through multivariable regressions analysis.

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DISCUSSION

This study evaluated the incidence of seroconversion and its potential risk factors in a retrospective cohort of anti-HCV negative participants at initiation of maintenance HD in a Sub-Saharan African facility. The cumulative incidence of seroconversion was 25% within a median dialysis duration of 17 months. A long duration on dialysis and a high number of blood units received for transfusion were potential risk factors for seroconversion identified. However, only long dialysis duration was independently associated with seroconversion to HCV positivity in this study. Data on seroconversion to HCV positivity in the maintenance hemodialysis population is scarce in Sub-Saharan Africa. El Amin reported a seroconversion rate of 17.1% within a mean dialysis duration of 33.7 months in Sudan. [13] Similar high seroconversion rates have been found in recent years in the high endemic countries of North Africa, Middle East, and Asia [39, 31,42]. Khodir et al reported a seroconversion rate of 11% in 2011 in HD facilities in an Egyptian region. [42] These rates are quite high compared to the trends in most western countries during the same period where rates of less than 1% have been reported in several countries. [5,6,10,18,14] A long duration on dialysis, [5-8,10,13,17,27,32] blood transfusions, [9,20,28,31,42] a high facility prevalence of HCV, [7,19,21,24] facility practices, [5,12,22,24,30,32] and the non-adherence to universal infection control precautions. [7,11,18,21,29,30,31,33,35,43] have been reported as risk factors for seroconversion in several studies. The positive association between a long dialysis duration and seroconversion to HCV positivity as was seen in the present study reinforces the role played by the hemodialysis environment in this nosocomial infection. Indeed, the risk of seroconversion has been shown to increase by 10% for each year spent on HD [44].

The effect of blood transfusion could not be independently evaluated in this study due to the small numbers and the positive correlation between the number of blood units transfused and the duration on dialysis. It is obvious that those who stay longer on dialysis are more likely to receive more blood transfusions. It is worth noting however, that no case of seroconversion was observed in the 7 participants who had never received blood transfusions. Blood transfusion contrary to earlier reports no longer plays a major role in the incidence of HCV in chronically hemodialysed populations in Europe, USA, some parts of Africa and Asia. [5,6,9,10,13-15] This change in epidemiology has occurred in regions with low general population prevalence, improved blood safety and especially where access to recombinant erythropoietin has rendered blood transfusions obsolete in treating uremic anemia. In this study, the mean number of blood units received per participant was 12, within a median dialysis duration of 17 months, compared to a mean of 1.3 units reported in Belgium over a similar dialysis duration [18]. The post-transfusional risk of infection has been reported as being very low in western countries.[45] Blood transfusion however continues to be a major risk factor for HD acquired HCV infection in regions with high general population prevalence such as Egypt and Pakistan. [31, 39,42] Khodir found blood transfusion to be significantly associated with HCV seroconversion in 2011 among patients undergoing long-term HD in a region in Egypt [42]. It is therefore plausible that blood transfusions will continue to play an important role in regions with high population prevalence, inconsistent blood screening for HCV, and where blood transfusion remains the main therapy for uremic anemia. The high population prevalence of HCV [36], coupled with inconsistent blood donor screening for HCV antibodies in the recent past [37] reported in Cameroon, makes blood transfusion a possible risk factor in this study.

Other factors not addressed in this study such as facility prevalence and the adherence to infection control strategies may have contributed to the high incidence of seroconversion in this study. The general population prevalence of anti-HCV in Cameroon is 12.8%, [36] and the prevalence of anti-HCV antibodies among patients undergoing hemodialysis in Cameroon was 48% in 2003 using a third generation ELISA test [46]. The increased risk of seroconversion in facilities with a high prevalence of HCV has been reported by several authors [5,7,19-21] While some authors have advocated isolation of anti-HCV positive patients in facilities with a high prevalence [12,15,24,26]; current guidelines do not recommend any isolation policy.[47,26] Dedicating material and geographical space for some patients in a resource-limited setting is a difficult puzzle to solve. The study setting was very conducive for the non-respect of recommendations for infection control. The use of multi-dose heparin vials [8], the high number of dialysis shifts per day, [22,29] understaffing [21,30] and a high proportion of inexperienced staff, [5] as seen in this study have been shown to promote non-adherence to infection control measures. Arenas et al found a patient-to-nurse ratio of 3 and above to be an independent factor affecting hand washing before and after an activity; while a high number of dialysis shifts per day was associated with lower rates of glove use and fewer glove changes between patients in hemodialysis [22]. Several studies have shown a spectacular decline in seroconversion rates with implementation of standard...
precautions of infection control in HD.[18,35] A multicentric Belgian study reported a decline in incidence rate from 1.41% to 0% over a 54 months period through the implementation of universal precautions alone [18].

Some limits of this study must be mentioned. Firstly, the use of anti-HCV screening can overestimate HCV infection in the HD population [31, 39, 47, 48]. HCV RNA was only found in the sera of 84.1% of anti-HCV positive patients in one study. [39] However, cases of occult HCV infection where HCV RNA is negative in serum but positive in mononuclear cells have been described. [49] The additional use of optical density ratios as was done in this study highly increases the specificity of the third generation ELISA.[41]. False negative anti-HCV antibodies have also been described in a negligible proportion with third generation ELISA tests, [31,39,48] so the seroconversion rate in the present study is representative.

In conclusion, the rate of seroconversion to anti-HCV positivity is very high in this study. A longer duration on hemodialysis was found to be associated with seroconversion. Blood transfusion could not be shown to be an independent risk factor because of the small numbers. Although not directly evaluated, it is plausible that non-adherence to universal precautions and the high facility prevalence of HCV are the main contributors to this nosocomial infection. This study provides a clue for preventive strategies for HCV in this population. A reduction in staff workload and patient overcrowding as well as an audit of staff knowledge and adherence to infection control recommendations is necessary. The role of blood transfusion in seroconversion to HCV positivity in this setting needs further evaluation in more powered studies.

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