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Risk of exposure to cross-transmission of infections in a dialysis unit: structural analysis of a simulated epidemic model

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SUMMARY

Several studies show that cross-transmission of germs among patients under dialysis can occur as a consequence of processes in which the dialysis machine participates. The need of vascular access and lengthy periods of extracorporeal circulation increases the vulnerability to infection from nearby microorganisms. This study is intended to analyze the structural and dynamic features of the cross-transmission network generated by the propagation of germs which are capable of contaminating the hemodialyzers.

Methods: *The simulation was carried out in a Dialysis Unit equipped with 19 machines for 62 patients. One of these patients was randomly chosen and considered as a carrier of an infectious agent capable of being transmitted to other patients, by means of the shared use of the same dialysis machine. For 10 days, the patient-machine allocation couples were registered. Co-occurrence matrices were elaborated and processed with the program UCINET 6.1® for social network analysis. Graphs were designed to visualize the networks of contagion, the centrality measures were calculated and the dynamic performance of the network generated by the chaining of the successive exposures of machines and patients was studied.*

Results: *The simulation let us visualize a rapid expansion of the risk of contagion of patients and contamination of machines. In 10 days, 87,09% of patients could have been exposed to the infection, and 68,42% of the machines could have been contaminated. These figures supposes that 5,4 new patients and 1,3 new machines could be potentially exposed every day. Along the first 5 days, the daily rate of exposure for patients and machines remains relatively low (3 new exposed patients and 1,2 new exposed machines every day). But the speed with witch the risk of contagion spreads, increases drastically in the last 5 days (7,8 new exposed patients every day). The fact that each patient requires at least 3 weekly sessions of dialysis and that a different machine can be allocated to him in each session explains that the risk of exposure can spread in some few days to a lot of patients and machines. It can also explain the difficulties found by the researches in identifying the responsible source of the origin of the sero-conversion outbreaks studied by the moment.*

Conclusions: *If a germ can be transmitted from patient to patient by means of the incidental contamination of a dialysis machine, the appearance of an infected patient in a dialysis unit generates a risk of exposition that spreads quickly among other patients. Few days after an infected patient gets a dialysis session, it cannot be ruled out that most of the patients have been exposed to contagion and most of the machines exposed to contamination.*

Key words: *Dialysis. Transmission. Social Networks. Bibliometrics. Scientific Information.*

RESUMEN

El objeto de este trabajo es analizar la red de transmisión cruzada generada por la propagación de gérmenes capaces de contaminar las máquinas de diálisis.

***Métodos:* La simulación se llevó a cabo en una Unidad de Diálisis con 19 máquinas y 62 pacientes. Se eligió aleatoriamente a un paciente, que se consideró portador de un agente infeccioso susceptible de transmitirse a los demás pacientes, mediante el empleo compartido de una máquina de diálisis. Durante 10 días se registraron parejas de asignación paciente-máquina. Las matrices de co-ocurrencia se procesaron con el programa UCINET 6.1® de análisis de redes sociales. Se elaboraron grafos para visualizar las redes de contagio generadas por el encadenamiento de sucesivas exposiciones de máquinas y pacientes y se calcularon las principales medidas de centralidad.**

***Resultados:* La simulación permite visualizar una rápida expansión del riesgo de contagio. En 10 días, 87,09% de pacientes podría haberse expuesto a la infección, y 68,42% de máquinas podría haberse contaminado. El hecho de que cada paciente requiera 3 sesiones de diálisis semanales, y de que en cada sesión pueda asignársele una máquina diferente explica la rapidez de la expansión del riesgo a la exposición y la dificultad que encuentran los investigadores para identificar un foco al que atribuir los brotes de seroconversiones en unidades de diálisis estudiados hasta el momento.**

***Conclusiones:* Si un germen puede transmitirse de paciente a paciente a través de la contaminación incidental de una máquina de diálisis, la presencia de un paciente infectado en una Unidad de Diálisis genera un riesgo de exposición que se extiende con rapidez entre otros pacientes. Pocos días después de que se dialice un paciente infecta-**

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do, no podrá descartarse que la mayoría de pacientes se hayan expuesto al contagio, y que la mayoría de las máquinas se hayan expuesto a la contaminación.

Palabras clave: Niños. Diálisis. Transmisión. Redes Sociales. Bibliometría. Información científica.

INTRODUCTION

Industrial production of the first dialysis machines for commercial use was started in the 1950s, leading to the appearance of «dialysis units» designed to facilitate renal replacement therapy by periodic dialysis in groups of patients with chronic renal failure. Since then, prevention of cross-transmission of infections between patients by these machines has been a constant concern.

Numerous studies have shown that a number of different infectious agents can be transmitted from patients to other patients during a dialysis session through mechanisms in which the machines act either directly or indirectly as a means of transmission. Among these germs, the most important are the viruses transmitted by human blood, particularly the hepatitis B (HBV) and hepatitis C (HCV) viruses.[1] Although certain risk factors, such as transfusions or transplants, may be responsible for virus infection in patients with chronic renal disease, a variety of evidence indicates that transmission can occur by physical contact with the external surfaces of the dialysis machine either directly or indirectly though staff hands.[2] Among the evidence supporting this possibility are the following:

- Virus transmission from patient to patient through dialysis machines contaminated with blood has been clearly demonstrated by molecular virology studies.[3]
- Cases of seroconversion against a virus with a common genotype have been reported in nephrological patients who shared the same dialysis machine.[4]
- Viral RNA particles were detected in ultrafiltrate fluid, to which they may have gained access from contaminated elements of the machine through microscopic breaks in the filter capillaries.[5,6]
- The prevalence of HCV and HBV in patients undergoing periodic hemodialysis is higher than in those who are maintained with peritoneal dialysis.[7]
- The risk of HCV seroconversion in patients with chronic renal disease increases with time on dialysis, and therefore with time in contact with the dialysis machine, at a predictable annual rate of 10% per year.[8]
- Physical isolation of HCV-infected patients reduces the rate of seroconversion among the rest of patients who share the same dialysis unit.[9]
- The incidence of HCV is higher in dialysis units with a higher prevalence.[10]
- Several epidemic outbreaks of viral hepatitis have been studied in dialysis units. In most outbreaks, the epidemic curve lasts for several months and suggests transmission between patients through fomites, possibly facilitated by manipulation of dialysis equipment items by healthcare staff. Some of the outbreaks originated from a single source of infection, which could not always be identified with certainty, but there is evidence that suggests that the monitors themselves may have played a role in the chain of transmission of the germs.[11]

Person-to-person transmission of germs can lead to the generation of complex networks of contagion. The simple calculations based on counting the number of cases (percentages, means, etc.) characterizing traditional methods of epidemiological analysis provide a very simplified vision of the characteristics of a network of contagion. Because of this, the methodology and statistical techniques derived form Graph Theory and Social Network Analysis are raising growing interest in the study of certain epidemiological processes, such as the spread of diseases from person to person.[12] This sophisticated analytical approach, applied to the field of biomedical sciences in relatively recent times, allows one to study in detail the structure and dynamic performance of networks of contagion (identification of clusters of cases with relatively strong links, analysis of subgroups and other complex substructures, determination of patients who comprise the core of the network and those at its edges, etc.).

The aim of this study was to analyze the structural features and dynamic performance of the cross-transmission network generated by the propagation among patients of a dialysis unit of a germ capable of contaminating a dialysis machine and then of infecting other patients dialyzed on the same machine.

MATERIALS AND METHODS

The study was carried out in the dialysis unit of a regional hospital (December 2007) equipped with 19 dialysis machines for 62 patients undergoing periodic dialysis three times a week in three daily shifts (morning, afternoon, and night). Approximately half of patients were dialyzed on Mondays, Wednesdays and Fridays, and the other half on Tuesdays, Thursdays and Saturdays. Changes in shifts were sometimes required to adapt to specific patient needs. At the time of the study, three of the patients were HBV-positive and four were HCV-positive. Two machines were reserved for exclusive use by these patients, and not shared by the seronegative patients.

To carry out the simulation, one of the patients in the periodic dialysis program was randomly chosen and considered as a carrier of an infectious agent capable of being transmitted to other patients by means of shared use of the same dialysis machine. For 10 consecutive days (excluding Sundays when no dialysis was performed), the machines allocated to each patient on successive shifts were recorded by an investigator external to the dialysis unit and this record was not known by the staff of the unit. During this period, the machines were allocated to the patients according to the usual procedure. Each patient is allocated a machine on which he or she is routinely dialyzed. However, this practice may be modified at certain times due to incidents related to functioning of the unit, care pressure, clinical needs, or patient convenience.

The information of a social network is contained in two basic elements: nodes (individuals or groups) and links, which define the relationship between the nodes. Social network analysis (SNA) analyzes the way individuals or groups are connected, defines the position they occupy in the network, groupings and overall structure, and the relationships of reciprocal influence. For the purposes of this study, the patients and machines will be considered the «nodes» of the network, and the «link» that connects them will be the physical contact patient – machine during a dialysis session.

A key tool in the methodology of social network analysis is «visualization» of the complex networks by graphical images that help us to understand the position of the nodes and their reciprocal relationships.[13] SNA facilitates formal representation of these relationships through standard graphical algorithms. In this way, the structure of a network of contagion can be displayed graphically and numerical indices measured that objectively define some of the network's properties and the relative position of the elements comprising it. The graph obtained from a network of contagion allows the relationships between infected individuals to be shown in an easily understandable way and provides a clear, visual impression of its structure, cohesive and isolated subgroups, etc.

In order to study a social network and construct a graphical representation that allows its visualization, the available data must be transformed into co-occurrence matrices. The nodes are defined (in this study, the patients and machines) in the first row and column of these matrices, and the possible co-occurrences are recorded (in this study, the occurrence of contact between patients and machines during a dialysis session) in the corresponding boxes of each pair of nodes. The computer programs designed to perform SNA transform the information contained in these matrices into graphical representations or graphs through the use of complex algorithms.

The graphs are graphical representations that provide a «panoramic vision» of the networks and are an essential tools to show their structure and evolution. Dynamic graphs are used to visualize the changes in the structures over time. Multidimensional scaling (MDS) is a method for multivariate data analysis which can be used to display graphs of networks of contagion and to discover «hidden» structures in the data.[14] The nodes are displayed clustered in a mathematically predetermined formal structure which reflects the «strength» of their relationships. MDS can transform the data of a co-occurrence matrix (for example, patient-machine allocation couples) into a group of distances between nodes «embedded» in a multidimensional Euclidean space.

If we accept that a germ can be transmitted from patient to machine and vice versa by physical contact between the two, each dialysis session generates a «risk of exposure or transmission», expressed in this article as «potential exposure or transmission», «possible exposure or transmission», or simply «exposure or transmission». From the physical contact patient-machine (co-occurrence) emerges a relational structure that can help us to understand, manipulate and predict the successive chain of contagions that defines the epidemiological behavior of an infectious disease transmitted during a dialysis session.

We only considered the opportunities in which a potentially infected node (patient or machine) came in contact with another noninfected node, and therefore it was a one-way relationship or link. With the data collected during the 10 days of the study (patient-machine allocation couples), the corresponding co-occurrence directional matrices were elaborated. These matrices were processed with the program UCINET 6.1®,[15] considered the standard tool for social network analysis. Graphs were designed to visualize the network of patients and machines exposed every day to contagion by an infectious agent presumably capable of being transmitted through the dialysis machines. The main centrality measures were calculated and the dynamic performance of the network generated by the chaining of the successive exposures of machines and patients to cross-transmission was studied.

The distance between two points of a network is the length or number of links on the shortest (geodesic) path connecting them. Two points connected by a line are adjacent. In a network of contagion, a distance of 1 indicates a direct contagion (adjacency). The node degree or range in a network is numerical measure of the number of other nodes with which a direct or adjacency relationship has been established. In our case, degree counts the number of potential contagions in which each patient or machine is involved. The degree of mediation (betweenness) expresses the degree to which an actor can mediate between other actors in the network. An actor with a relatively low node degree may still play an important mediating role in a network. It estimates the intensity of the relationship (transmission) in the overall network. A high number of connections means a more important role of a patient or machine in the network of contagion.[16]

RESULTS

The simulation enabled us visualize a rapid expansion of the risk of contagion of patients and contamination of machines (fig. 1). In the 10 days of the study, 54 of 62 patients (87.09%) included in the dialysis program could have been exposed to cross-transmission of the infection, and 13 of 19 machines (68.42%) could have been contaminated with the infectious agent. These figures mean that, on average, 5.4 (SD = 2.7) new patients could be potentially exposed every day and 1.3 (SD = 0.95) new machines could be potentially contaminated every day.

In this simulated epidemic outbreak, two clearly differentiated phases can be observed (fig. 2). During the first 5 days, the daily rate of exposure for patients and machines remains relatively low, with an average of 2.8 (SD = 0.44) new exposed patients and 1.2 (SD = 1.2) new exposed machines every day. But the speed with which the risk of contagion spreads increases drastically in the last 5 days, with an average of 7.8 (SD = 0.83) new exposed patients every day, as the number of machines exposed to contamination increases.

It is worth noting that none of the HCV- or HBV-positive patients and none of machines dedicated to sole use by these patients were exposed in this simulated model, since they were physically excluded from the possibility of transmission by shared use of machines with other patients.

It should also be noted that not a single case of HBC, HCV, or HIV seroconversion has occurred in the dialysis unit under study in its 20 years of operation.

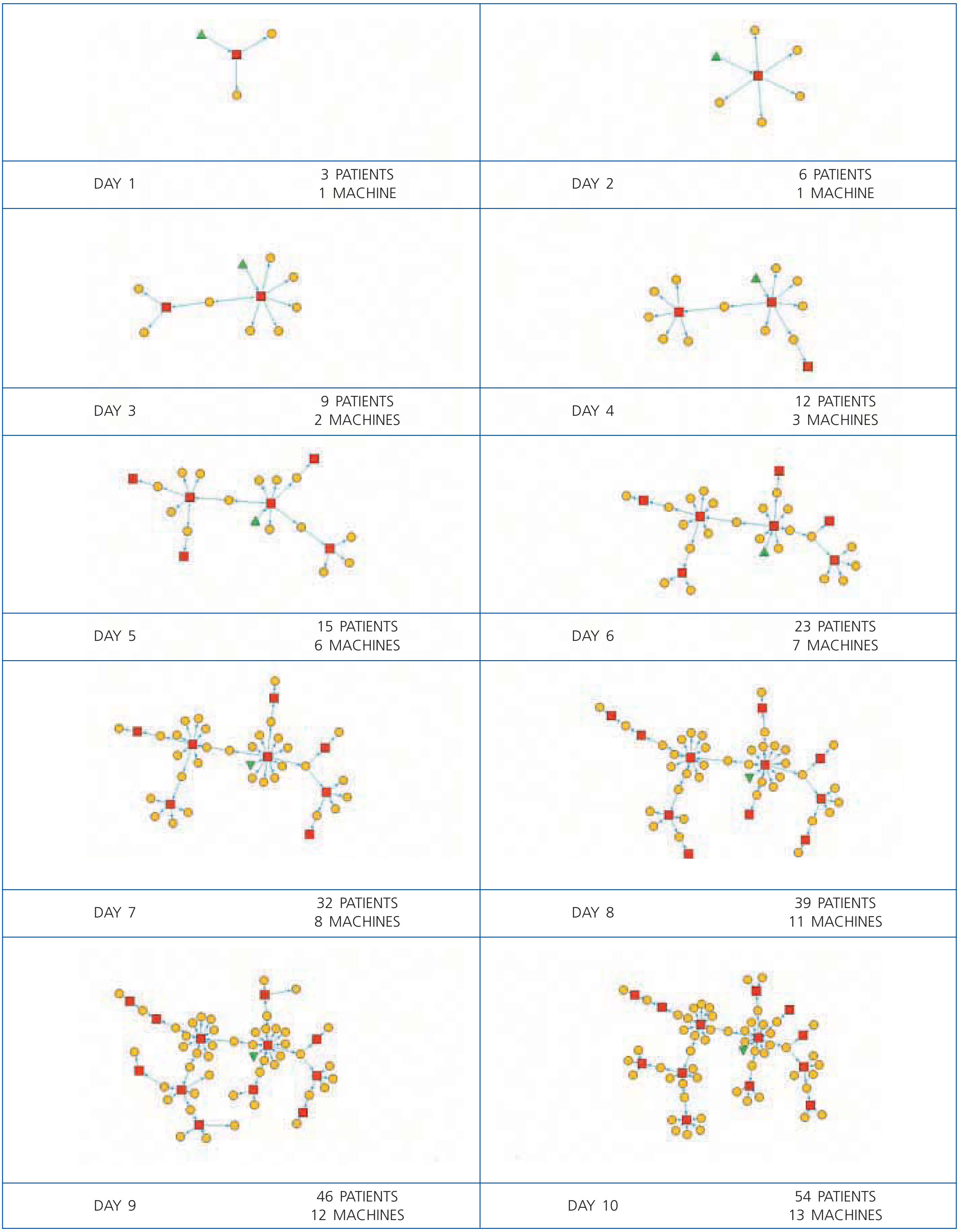

Figure 1. Daily change in exposure of patients (yellow circles) and contamination of dialysis machines (red squares). The initially infected patient is represented with a green triangle.

DISCUSSION

Renal patients requiring periodic hemodialysis have depressed immunity and increased susceptibility to infections. The inevitable need for vascular access and lengthy periods of extracorporeal circulation during dialysis through a circuit with points permeable to viruses and bacteria increases even further the vulnerability of renal patients to infection from nearby microorganisms.[17]

The epidemiology of infections by viruses and other germs transmitted by human blood in patients undergoing intermittent dialysis is not completely known. In spite of the numerous investigations and epidemiological studies conducted, it is not known exactly how a virus such as HCV is transmitted to dialysis patients, and controversy persists on the effectiveness of the measures proposed for its prevention.

It is reasonable to assume that any of the surfaces of a dialysis machine can be contaminated with an infectious agent as a result of a splash of blood or any other organic fluid, or by simple contact with contaminated objects or carrier persons. Some viruses, such as HBV and HCV, show relatively high stability at room temperature on contaminated surfaces. On the other hand, frequent successive manipulations of the components of the machine and vulnerable points of the extracorporeal line (venipuncture site, arteriovenous fistula, dialysis system connections, blood sample collection points, etc.) may act as a mechanism of transfer of microorganisms between machine and patient, and vice versa.[18] Such an eventuality is possible even when the most rigorous hygiene measures are strictly complied with, but it can be considered as highly probably when these precautions fail to be implemented. Physical proximity of infected and noninfected patients could conceivably enhance cross-transmission of germs through object-mediated environmental mechanisms in which the dialysis machines themselves may play a role.

Various clinical guidelines establish recommendations to prevent transmission of viral diseases in dialysis units: Kidney International Disease Improving Global Outcomes[19] (KDIGO-2008), Centers for Disease Control[20] (CDC-2001), European Best Practice Guidelines[21] (EBPG-2002) and Spanish Society of Nephrology[22] (SEN-2006), among others. These recommendations can be summarized into three categories:

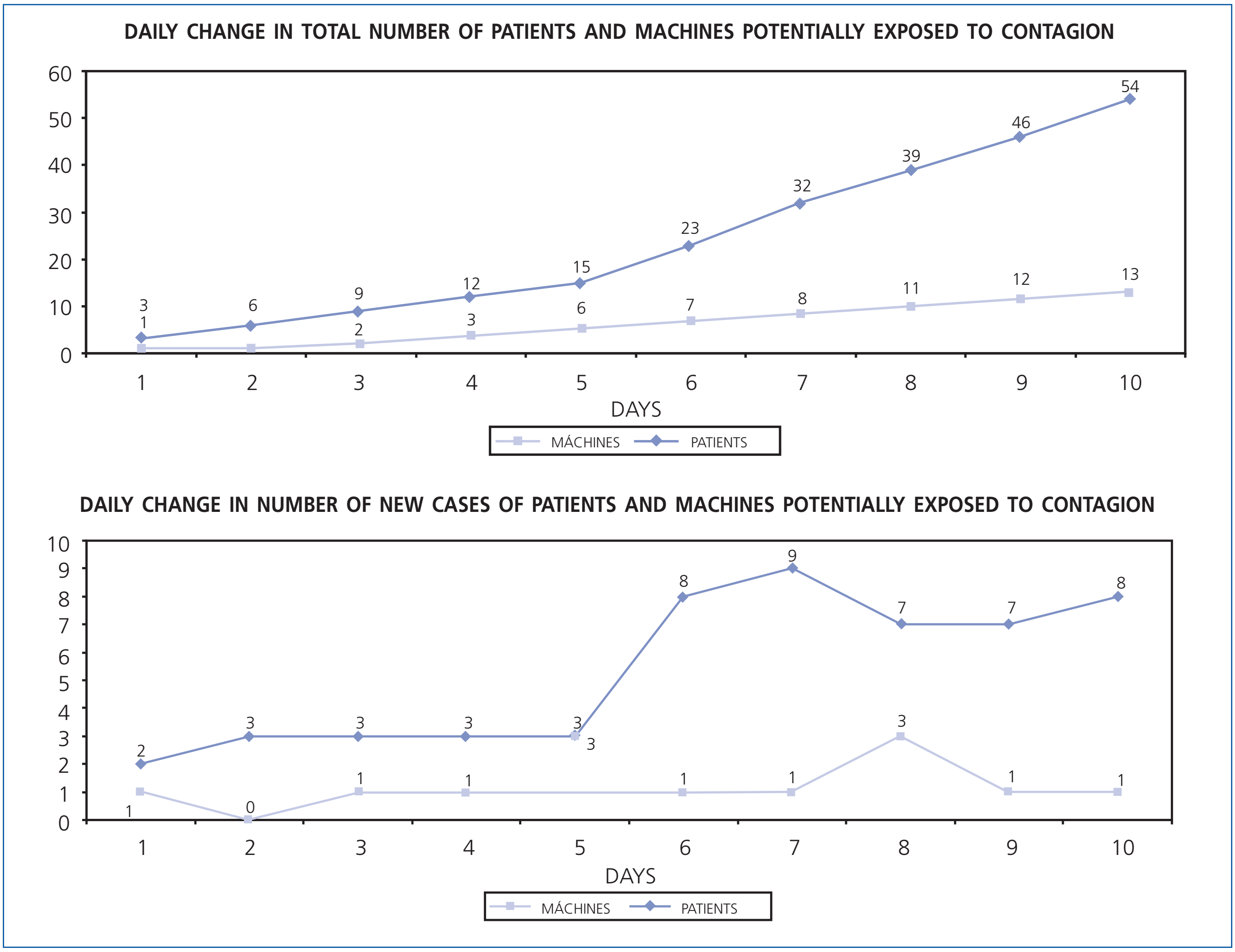

Figure 2. Daily change in the number of patients and machines (total cases and new cases) potentially exposed to contagion.

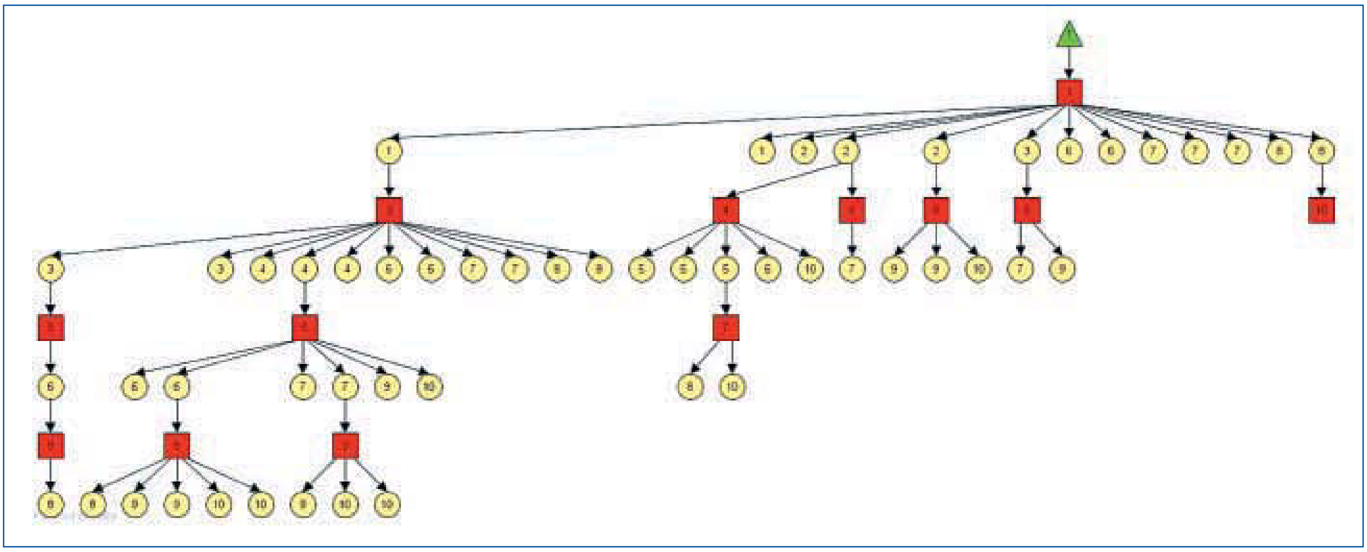

Figure 3. Hierarchical graphical algorithm of the network of contagion. The red squares represent the dialysis machines and the yellow circles represent patients. The green triangle represents the initially infected patient. The written inside each node indicates the day on which each patient or machine was exposed for the first time to contagion.

1. There is wide consensus on the recommendation to isolate HBV-infected patients and to allocate them dedicated monitors and staff.
2. There is wide consensus on the recommendation not to isolate HIV-infected patients and not to allocate them dedicated monitors and staff.
3. The KDIGO and CDC guidelines do not recommend to isolate HCV-infected patients or to allocate them dedicated monitors or staff. The EBPG guideline recommends to isolate HCV-infected patients in units with a higher prevalence of HCV infection. The SEN guideline recommends grouping HCV-infected patients considered «infectious» (PCR positive) in a clearly delineated area of the unit with staff dedicated exclusively to them during the session, but without the need for using dedicated monitors.

Patients undergoing hemodialysis account for a considerable workload for nursing staff during each session, which lasts approximately 4 hours. Manipulation of contaminated objects (including dialysis machines) and infected patients by nursing staff may have a role in nosocomial transmission of infections among these patients. It has been shown that there is a relationship between understaffing in dialysis units and virus transmission between dialyzed patients.[23] The SEN recommends a minimum staff of 1 nurse per 4-5 stations and 1 assistant per 8-10 stations,[24] which agrees with the recommendations of other European countries. The risk of infection after accidental exposure is estimated at 1% for HCV, 2-40% for HBV, and 0.2-0.5% for HIV.[25]

The fact that each patient requires at least 3 weekly sessions of dialysis and that a different machine can be allocated to each patient in each session explains how the risk of exposure can spread rapidly in just a few days to many patients and machines. This circumstance can also explain the difficulties found by the investigators in identifying a single initial source (patient or machine) responsible for the seroconversion outbreaks in the dialysis units studied up to now. In Figure 3 it can be seen that a few days after the first transmission occurred, a germ was able to «jump» several times between machines and patients and infect patients who had had no relationship (did not share a machine) with those initially infected. It can also be seen that the initially infected machines are responsible for a larger proportion of potential direct contagions of patients. The 2 (15.38%) initially infected machines were able to transmit the infection directly to 24 patients (44.44%).

Transmission was carried out more efficiently «from machine to patient», since each machine is used daily with several patients every day. A single machine can transmit the infection to many patients, but in most cases an infected patient contaminates a single machine (transmission «from patient to machine»). Therefore, the machines (square nodes) are the ones that achieve a higher «degree centrality» index in the network of propagation of the infection, as can be seen in Figure 4. However, the patients can show a high «mediation» (betweenness) index, as can be seen in this figure (red arrow). In other words, although a patient contaminates a single machine, this transmission can be an essential link in the chain of transmission for many other patients to be infected. Or, put in other words, if we had prevented transmission of the infection to a single patient (marked with the red arrow), the final number of machines and patients infected would have been drastically reduced.

Dialysis machines are usually a vehicle of horizontal and not vertical transmission of the infection during the session.

While the vaccine against HBV has considerably reduced its prevalence in patients undergoing dialysis, there is still no effective vaccine against other parenterally transmitted viruses such as HCV, CMV, and HIV.[26] For now, the only way to

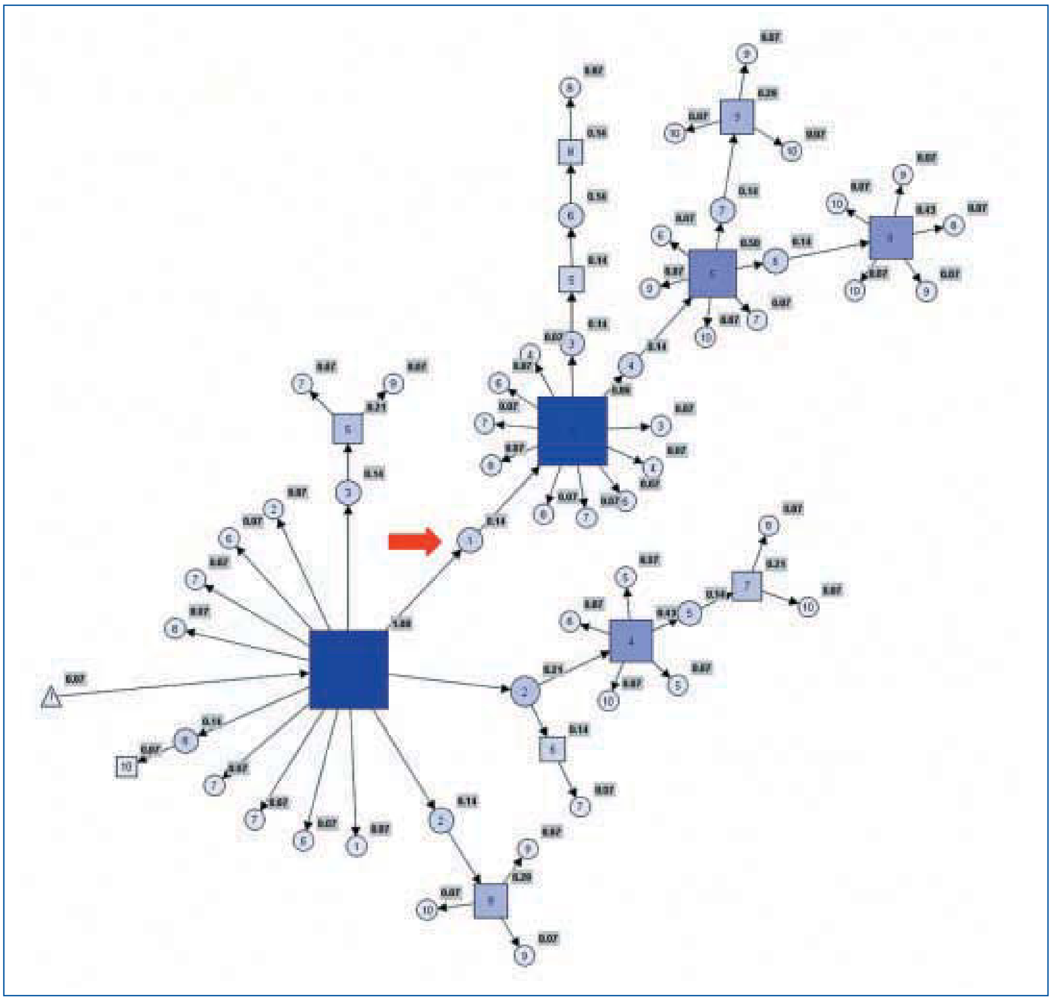

Figure 4. Potential network of transmission generated by propagation of exposure between patients and dialysis machines. The numerical value accompanying each node indicated its degree centrality. The size of the nodes is proportional to this value. The more central nodes are represented in a darker color.

prevent horizontal transmission of these viruses is by the application of strict hygienic measures and physical isolation to prevent contact between healthy patients and contaminated objects or persons.

The geographical mobility that dialysis patients now enjoy, and the consequent transfer of patients between units, has a multiplying effect on this phenomenon of epidemic expansion of the risk of transmission, which may reach national or even international proportions. In a recent cohort study initiated after detecting a case of HBV reactivation in a patient undergoing dialysis in Ireland, 306 potentially infected patients were identified in 17 dialysis centers (14 of them in Ireland and the other 3 in different European countries).[27] Several researchers have currently shown interest in the high prevalence in patients undergoing hemodialysis of other viruses transmitted by the parenteral route (HGV, TTV,…), whose clinical significance is not well known.

Finally, experience recommends that we maintain constant surveillance against any new epidemiological threat that may arise in the future. The constant growth in the number of patients undergoing dialysis, the increase in their age and comorbidity, the expansion of dialysis units in developing countries, the geographical mobility of renal patients (who even travel to exotic and tropical regions), the permanent threat of the emergence of new infective viruses or mutations that alter the capacity of transmission of known viruses, are factors that may modify in the future the role of dialysis machines in cross-transmission of infections among renal patients.

CONCLUSIONS

If the hypothesis is accepted that a germ can be transmitted from patient to patient by means of the incidental contamination of a dialysis machine they share, the appearance of an infected patient in a dialysis unit generates a risk of exposure that spreads quickly among other patients. In other words, a few days after an infected patient gets a dialysis session, it cannot be ruled out that most of the patients have been exposed to contagion and most of the machines exposed to contamination.

The practice of allocating different machines to the same patient in successive sessions has a key role in the propagation of the risk of contamination to all machines in the unit and cross-transmission of the germ to all patients dialyzed in this unit.

REFERENCES

1. Barril G. Transmisión de la hepatitis C en unidades de diálisis. *Nefrología* 1998; 18 (Supl. 1): 46-52.
2. Jadoul M. Transmission routes of HCV infection in dialysis. *Nephrol Dial Transplant* 1996; 21: 288-91.
3. Stuyver L, Claeis H, Wyseur A et al. Hepatitis C virus in hemodialysis unit: molecular evidence of nosocomial transmission. *Kidney Int* 1996; 49: 889-95.
4. Barril G, Castro M, Rincón B, Sánchez Tomero JA, Bernis C et al. Epidemiología del virus C. *Nefrología* 1993; 5: 435-9.
5. Hubmann R, Zazgornick J, Gabriel C, Garbeis B, Blauhut B. Hepatitit C virus —does it penetrate the haemodialysis membrane? PCR analysis of haemodialysis ultrafiltrate and whole blood. *Nephrol Dial Transplant* 1995; 10: 541-2.
6. Valtuille R, Fernández JL, Berrido J, Moretto H, Del Pino N, Rendo P, Lef L. Evidences of hepatitis C virus pasaje across diálisis membrana. *JASN* 1996; 7: 1467.
7. Cendoroglo M, Draibe SA, Silva AE, Ferraz ML, Granato C, Pereira CA et al. Incidence of and risk factors for hepatitis B virus and hepatitis B virus infection among haemodialysis and CAPD patients: evidence for environmental transmission. *Nephrol Dial Transplant* 1995; 10: 240-6.
8. Hardy NM, Sandroni S, Danielson S, Wilson WI. Antibody to hepatitis C virus increases with time of dialysis. *Cli Neprol* 1992; 38: 44-8.
9. Okuda K, Hayashi H, Yokozeki K, Kobayashi S, Ire Y. Mode of hepatitis C infection not associated with blood transfusion among chronic haemodialysis patients. *J Hepatol* 1995; 23 (1): 28-31.
10. Pujol FH, Ponce JG, Lema MS, Capriles F, Devesa M, Sirit F et al. High incidence of hepatitis C infection in haemodialisys patients in units with high prevalence. *J Clin Microbiol* 1996; 34 (7): 1933-6.
11. Castell J, Gutiérrez G. Brote de 18 casos de hepatitis C en una unidad de hemodiálisis. *Gac Sanit* 2005; 19 (3): 214-20.
12. Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. *N Engl J Med* 2007; 357: 370-9.
13. Sanz L. Análisis de Redes Sociales: o como representar las estructuras sociales subyacentes. *Apuntes de Ciencia y Tecnología* 2003; 7: 21-9.
14. Leydesdorff L. Various Method for the Mapping the Science. *Scientometrics* 1987; 11: 295-324.
15. Borgatti SP, Everett MG, Freeman LC. Ucinet 6 for Windows: Software for Social Network Analysis. Harvard: Analytic Technologies, 2002.
16. Villanueva S, De Granda Orive, Aleixandre-Benavent R, García Río F, Valderrama-Zurián JC, Alonso Arroyo A. Análisis de la red de colaboración científica sobre tabaquismo entre centros sanitarios españoles a través del Science Citation Index (1999-2003). *Arch Bronconeumol* 2007; 43 (7): 378-85.
17. Jadoul M, Cornu C, Van Ypersele C. Incidence and risk factors for hepatitis C seroconversion in hemodialysis: a prospective study. The UCL collaborative group. *Kidney Int* 1993; 44: 1322-6.
18. Caramelo C, De Sequera P, López MD, Ortiz A. Hand-borne mechanisms of dissemination of hepatitis C virus in dialysis units: basis for new addenda to the present preventive strategies. *Clin Nephrol* 1999; 51: 59-60.
19. KDIGO Clinical Practice Guidelines for the Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in Chronic Kidney Disease. Guideline 3: Preventing HCV transmission in hemodialysis units. *Kidney Int* 2008; 73 (Supl. 109): 46-52.
20. Centers for Desease Control and Prevention. Recommendations for Preventing Transmission of Infections Among Chronic Hemodialysis Patients. *MMWR* 2001; 50: 18-30.
21. European Best Practice Guidelines for Haemodialysis (Part 1). *Nephrol Dial Transplant* 2002; 17 (Supl. 7): 79-80.
22. Otero A, Conde J, Martín de Francisco AL, Gonzáles Parra E. Guías de Centros de Hemodiálisis (SEN). Introducción. *Nefrología* 2006; 26 (Supl.) 8: 1-4.
23. Petrosillo N, Gilli P, Serrano D et al. Prevalence of infected patients and understaffing have a role in hepatitis C virus transmisión in diálisis. *Am J Kidney Dis* 2001; 37: 1004-10.
24. Alcalde G, Martín de Francisco AL, Fernández A, Conde JL. Dotación de personal para centros de hemodiálisis ambulatoria. *Nefrología* 2006; 26 (Supl. 8): 11-4.
25. Geberding JL. Incidence and prevalence of human immunodeficiency virus, hepatitis B virus, hepatitis C virus and cytomegalovirus among health care personal at risk for blood exposure: final report from a longitudinal study. *J Infect Dis* 1994; 170: 1410-7.
26. Franco A, Serrano R, Gimeno A, De Juan J, Merino E, Jiménez del Cerro L y Olivares. Estudio de carga viral y antigenemia como valores predictivos de recidiva de infección CMV en el trasplante renal. *Nefrología* 2007; 27 (2): 202-6.
27. Thornton L, Fitzpatrick F, De la Harpe D, Brennan A, Murphy N, Connell J et al. Hepatitis B reactivation en an Irish dialysis unit, 2005. Euro Surveill 2007; 12 (4). Disponible en http://www.eurosurveillance.org/em/v12n04/1204-224.asp