Preliminary Communication

Infective endocarditis in chronic haemodialysis: two treatment strategies

Juan Fernández-Cean, Asunción Alvarez, Sergio Burguez, Graciela Baldovinos, Patricia Larre-Borges and Mercedes Cha

Centro de Nefrología, Hospital de Clínicas, Universidad de la República, Montevideo, Uruguay

Abstract

Background. Infective endocarditis (IE) is more frequent in patients on chronic haemodialysis (CHD) than in the general population and vascular access is the more frequent identified port of its entry. According to experimental and clinical studies the vascular access may also interfere with the treatment of IE. To improve the treatment of IE in CHD, patients were temporarily switched to peritoneal dialysis (PD) after the removal of the vascular access. In this preliminary report the outcome of IE in those CHD patients switched to PD is compared with the outcome in IE patients who remained on CHD.

Methods. All cases of IE that occurred during a 5 year period were retrospectively analysed. The Duke criteria for IE were used for diagnosis. All patients underwent transeosophageal echocardiography. All patients were treated with the same schedule of antibiotic treatment. The vascular access of a patient was removed when it was judged to be the source of infection.

Results. Twenty-one patients were studied. Twelve patients had been temporarily switched to PD after the diagnosis of IE and nine patients had remained on CHD treatment. There were not statistically significant differences between the two groups with respect to demographic data, comorbid diseases and the frequency of Staphylococcus aureus as the causative germ. In-hospital mortality was 8.3% in patients switched to PD and 55.5% in patients maintained on HD (P: 0.03).

Conclusions. The data presented here suggest that the high mortality of IE in CHD patients may also be associated with the vascular access necessary for HD. If these results are confirmed by prospective studies with higher numbers of patients, PD could turn out to have a place in the treatment of IE in CHD patients.

Keywords: haemodialysis; infective endocarditis; peritoneal dialysis; vascular access

Introduction

Patients with end-stage renal disease (ESRD) are more susceptible to infections than the general population, and infections are the second most frequent cause of mortality in the ESRD population [1].

Bacteraemia is one of the most serious and life threatening infections in patients on chronic haemodialysis (CHD) [1–3]. The vascular access to the circulation is the primary source of bacteraemia in this group of patients [1,3] and the risk is higher when the vascular access is a polytetrafluoroethylene (PTFE) graft or an endovascular catheter [3]. In a French study, the incidence of bacteraemia was 0.93 episodes per 100 patient months in CHD patients [2]. In all CHD series, Staphylococcus aureus was the most frequent causative bacteria [2,3]. Marr [3] reported 1.2/100 patient-month episodes of S. aureus bacteraemia in CHD patients [3]. Bacteraemic episodes may be associated with metastatic complications such as osteomyelitis, abscess formation, septic arthritis and infective endocarditis (IE). Of the bacteraemic episodes in CHD patients, 6% in the EPIBACIDAL were complicated with a secondary septic focus [2]. Of these episodes, 2% were complicated with IE. The prevalence of IE was higher (12%) when only S. aureus bacteraemia was considered [3].

The annual incidence of IE in CHD patients is described rarely. In France it has been estimated at five to 13 cases per 10 000 dialysed patients [4].

The mortality rate of IE is higher in CHD patients than in the general population [4–7], ranging from 30 to 53%. This has been related to various factors: predominance of S. aureus, previous cardiac injury, predisposing heart condition or malnutrition [4,5].

In all of the published series of CHD-related IE [4–7], patients have remained on haemodialysis (HD) after the diagnosis of IE. In some cases HD was performed using the retained vascular access. In others, after the removal of the infected vascular access, HD was performed through a new endovascular catheter. Under either condition the outcome of IE could be...
affected. Among those patients that remain on HD with a new endovascular catheter, the intravascular prosthesis could become a harbour for the circulating bacteria or a new source of injury to the endocardium, making a cure more difficult to achieve [8]. If the original vascular access were maintained, it could persist as an endovascular nidus of infection [5]. With those hypotheses in mind, and in order to improve the outcome of IE in CHD, we temporarily switched patients to peritoneal dialysis (PD) until the infection was over.

In this report we retrospectively compare the outcome of IE in CHD patients switched to PD with the outcome in those who remained on HD.

Subjects and methods

All CHD patients with the documented diagnosis of IE treated in the nephrology centre at the University Hospital between December 1995 and December 2000 were considered. The diagnosis of IE was based on the Duke criteria for IE [9], and only clinically certain cases were included. All patients had transthoracic (TTE) and transoesophageal echocardiography (TEE) performed by the same technician. Vascular access was removed when it was judged to be the source of infection. The choice of dialysis modality, after the diagnosis of IE, was made by the nephrologist in charge of the dialysis unit. The nephrologist’s decision was based on his or her particular expertise in each dialysis modality (HD or PD).

In patients switched to PD, double-cuff peritoneal catheters were placed by nephrologists using the guidewire split-sheath technique. Cycler-assisted PD was initiated immediately after the placement of the peritoneal catheter. In order to prevent leaks, patients remained in bed until day 15 after catheterization. In some cases, patients were allowed to walk a few hours a day, with abdomens dry. Patients who remained on HD and whose vascular accesses were removed were dialysed through an endovascular catheter. Endovascular catheters were inserted by attending nephrologists percutaneously in the internal jugular vein using sterile technique. Antibiotic treatment was based on the American Heart Association recommendations [10]. Data collected included: demographic information (age, gender, kidney disease); coexistent disease (diabetes mellitus, cancer); type of vascular access when IE was diagnosed [native arteriovenous fistula (AVF), PTFE graft or endovascular catheter]; clinical data [presence of murmur or new murmur on admission, fever, dyspnea, embolic episodes, infecting bacteria and whether the infecting portal was removed, intervals between the start of the symptoms and the confirmation of IE, antimicrobial therapy (drug used and duration), valve replacement, in-hospital mortality and cause of death].

Statistical analysis

Descriptive statistics were used to summarize the data. The Fisher test and the Student’s t-test were used for statistical comparisons.

Table 1. Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>HD n=9</th>
<th>DP n=12</th>
<th>P</th>
<th>All patients n=21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65±12</td>
<td>58±16</td>
<td>NS</td>
<td>61±14</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>4/5</td>
<td>7/5</td>
<td>NS</td>
<td>11/10</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
<td>0</td>
<td>NS</td>
<td>2</td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
<td>1</td>
<td>NS</td>
<td>3</td>
</tr>
<tr>
<td>Valvular disease</td>
<td>4</td>
<td>4</td>
<td>NS</td>
<td>8</td>
</tr>
<tr>
<td>Prosthetic valve</td>
<td>1</td>
<td>2</td>
<td>NS</td>
<td>3</td>
</tr>
<tr>
<td>Time on HD (months)</td>
<td>48±45</td>
<td>63±47</td>
<td>NS</td>
<td>56±46</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>3.2</td>
<td>3.1</td>
<td>NS</td>
<td>3.2</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>3</td>
<td>1</td>
<td>NS</td>
<td>4</td>
</tr>
<tr>
<td>Embolic phenomena</td>
<td>5</td>
<td>5</td>
<td>NS</td>
<td>10</td>
</tr>
<tr>
<td>Time to diagnosis (days)</td>
<td>18±19</td>
<td>22±20</td>
<td>NS</td>
<td>20±18</td>
</tr>
<tr>
<td>S.aureus</td>
<td>5</td>
<td>7</td>
<td>NS</td>
<td>12</td>
</tr>
<tr>
<td>Surgical treatment</td>
<td>2</td>
<td>1</td>
<td>NS</td>
<td>3</td>
</tr>
<tr>
<td>Number of death</td>
<td>5</td>
<td>1</td>
<td>P=0.03</td>
<td>6</td>
</tr>
</tbody>
</table>

Results

Our cohort included 21 CHD patients with diagnosed IE. Of these patients 16 were transferred from out patients centres. The incidence rate ranged from 23 to 86 cases of IE per 10 000 CHD patients. General characteristics of the patients are presented in Table 1. Vascular accesses used when IE was diagnosed were: five native AVFs (23%), nine PTFE grafts (42%), seven endovascular catheters (33%). None of the patients had been active intravenous drug users, infected with the human immunodeficiency virus or on immunosuppressive medication.

All patients had high temperatures at the onset and 50% of them had chills during HD; four cases had presented dyspnea; eight had a new murmur; six had embolic episodes, neurologic (two episodes) and joint (four episodes); four patients manifested peripheral signs.

Staphylococcus aureus was the most common infecting organism (12 patients, 58%). Staphylococcus epidermidis was identified in two patients (9.5%) and Gram-negative bacteria in five (23%). In two patients blood cultures were negative (9.5%). TTE was positive in 10 cases (10/21) and TEE in all cases (21/21). Mitral valve was affected in nine patients (43%) and the aortic in six (28.5%). Two patients had both mitral and aortic valves involved (9.5%) and four had a right-sided IE (19%).

The infection was present in native valves in 18 cases and in prosthetic valves (aortic) in three. Eight patients had underlying valvular diseases (one with mitral valve prolapse, six with calcific valvular disease and one with rheumatic disease). The mean interval from the start of symptoms to echocardiographic diagnosis was 20±18 days (mean ± SD) and the mean duration of antibiotic treatment was 6.0±1.9 weeks.

The valvular complications found were: periannular abscesses (four patients), prosthetic valve dehiscence.
(two patients), rupture of the chordae tendineae (three patients) and new valvular regurgitation (14 patients). Three patients underwent cardiac valve replacement.

The vascular access sites were the most frequently identified portals of entry (20 cases, 96%): native AVF in four patients, PTFE graft in nine and endovascular catheter in seven. In one case IE was related to the contamination of the HD water. The four native AVF and the nine PTFE grafts judged to be infected were excised surgically. All endovascular catheters were removed (Figure 1). The case related to water contamination continued on HD using the native AVF.

After IE was diagnosed, 12 patients were temporarily switched to PD and nine patients were maintained on HD (Figure 1). There were no significant differences in demographic data, comorbid diseases, time on HD treatment and incidence of *S. aureus* as the causative germ, between either group (Table 1). There were no episodes of peritonitis during hospitalization, in patients temporarily switched to PD.

Six patients died. The global mortality was 28.6%; the mean interval between diagnosis and death was 40 ± 13 days (mean ± SD). The causes of death were cardiac failure (three patients) and uncontrolled sepsis (three patients). Among the 12 patients transferred to PD, only one died (mortality 8.3%); the time from diagnosis to death was 45 days and the cause of the death was cardiac failure. Among those who continued on HD, five died (mortality 55.5%), time to death was 39 ± 12 days and the causes of death were uncontrolled sepsis (three patients) and cardiac failure (two patients). The difference in mortality between HD- and PD-transferred patients was statistically significant (*P* = 0.03).

After discharge from the hospital, eight of the patients who had been switched to PD preferred to continue on continuous ambulatory PD.

### Discussion

To our knowledge, this is the first study to evaluate the relationship between dialysis modality and the outcome of IE in patients with ESRD who were previously on CHD. Mortality in patients switched to PD was lower than in those who stayed on HD. Global mortality (28.6%) was lower than in previous studies, but it was very high in patients who remained on HD after IE was diagnosed (55.5%). Although this was not a randomized study, patients that remained on HD were closely matched for factors related to IE outcome with those switched to PD (Table 1). Both groups were treated in the same medical centre and subjected to the same antibiotic schedule [10].

![Fig. 1. Diagram of vascular access and dialysis therapy modality before and after diagnosis, and death from infective endocarditis. IE, infective endocarditis; AVF, arterio-venous fistula; HD, haemodialysis; EC, endovascular catheter; PD, peritoneal dialysis; PTFE, polytetrafluoroethylene.](https://academic.oup.com/ndt/article-abstract/17/12/2226/1821363)
In all other studies of IE in CHD, patients remained on HD after diagnosis. Cross and Steigbigel [7] reported 53% mortality in 34 patients studied. Hanslik et al. [4], in a French retrospective national survey of IE in dialysis patients, found a 43% mortality in 30 reported cases. Mortality was 30% in a cohort of 20 cases reported by Robinson et al. [5].

The preliminary results presented here suggest that not only is HD a risk factor for developing IE [4,8] but also that it might interfere with treatment of IE. If HD continues to be performed using the previous vascular access, it could act as a persistent nidus. This hypothesis is proposed by Robinson et al. [5] to explain the high mortality in his series of patients who continued with the PTFE graft access after IE was diagnosed. In our cohort, vascular accesses were removed after IE was diagnosed in all but in one case. That patient continued HD through a native AVF, because HD water was considered the source of infection and he died during hospitalization. We can suppose that the native AVF was also colonized and that this was a factor which interfered with antibiotic treatment.

In all other published IE series, when the causative vascular access was removed, patients continued on HD treatment via a new endovascular catheter. Eight patients in our series were treated in this way. A new substitute catheter could contribute to maintaining an infection. Although antibiotics were administered immediately after IE was diagnosed, bacteria may not have been totally eliminated, because antibiotics do not instantaneously kill or inhibit bacteria [11]. These circulating bacteria may therefore sequester in any foreign material old or newly installed. It has been very well demonstrated in experimental IE that foreign bodies may promote infection, contributing to sequestration of bacteria in areas inaccessible to antibiotics and host defences [8,12–14]. Host-derived proteins are deposited on catheter surfaces as little as 24 h after insertion, and circulating bacteria, particularly S. aureus, adhere firmly to such proteins. Once associated with a foreign surface, microorganisms exhibit increased resistance to antimicrobials [15].

These events confirmed by clinical and experimental studies, could explain the high mortality of IE in CHD patients and the worse outcome in those in the present series who continued HD.

In PD a vascular access is eliminated. It has been stated that septicemia occurs frequently in PD as well as in CHD [1]. Nevertheless, in the Powe series bacteremia was less frequent in PD than in CHD patients with endovascular catheters. Besides, there are no published series on IE in PD patients. PD, therefore, does not appear to add new risk factors to patients with IE but does eliminate those HD-related factors that may interfere with the antibiotic treatment.

It has been stressed that patients with a previous episode of IE have higher risks of developing a new episode in the future [8,11]. If these patients continue on CHD, particularly with PTFE graft or endovascular catheter, the risk of developing IE may increase. These are additional and compelling reasons to maintain these patients on PD, even after the IE has been cured.

According to these arguments we consider that HD, as all renal replacement procedures that need a vascular access to the circulation, is the worst option in the aftermath of a diagnosis of IE in CHD patients.

This preliminary study has important limitations: it is a retrospective, non-randomized study and the number of patients is small. In spite of those limitations our results are clinically relevant and suggest a promising strategy to improve the poor results of treating IE in CHD patients.

In conclusion, to our knowledge this is the first study to consider the relationship between dialysis modality and the outcome of IE in CHD patients. Our findings suggest that the high mortality of IE in CHD patients may be partly due to the maintenance of an infected vascular access for haemodialysis. The removal of the access and temporary transfer of PD may be the preferred option for such patients. However, our findings need to be confirmed by a prospective, randomized and controlled study before definite conclusions can be reached about the place of PD in the treatment of IE in CHD patients.

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References


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