Original article

Morbimortality study of infection in patients undergoing different types of dialysis in a renal replacement therapy center

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Abstract

Introduction: Renal replacement therapy is the treatment of end-stage chronic kidney disease and can be performed through dialysis catheters, arteriovenous fistulas/grafts, and peritoneal dialysis. Patients are usually immunocompromised and exposed to invasive procedures, leading to high rates of infection and increased mortality.

Objectives: To compare the prevalence of infection and related deaths, as well as the sensitivity profile of the putative bacteria in patients treated with peritoneal dialysis, arteriovenous fistula hemodialysis and catheter hemodialysis.

Methods: This is a case-control study. Six hundred forty-four patients undergoing renal replacement therapy were selected. Patients were divided into three groups according to the modality of dialysis treatment: peritoneal dialysis (126 patients), arteriovenous fistula hemodialysis (326 patients), and catheter hemodialysis (192 patients).

Results: One hundred sixteen patients (18.01%) developed infection. There was a higher incidence of infection in the peritoneal dialysis group (44 patients; 34.92%; OR: 3.32; CI 95% = 2.13–5.17; p = 0.0001). In the catheter hemodialysis group, 48 patients (25%) had infection (OR: 1.88; CI 95%: 1.24–2.85; p = 0.0035). In the arteriovenous fistula hemodialysis group, 24 patients (7.36%) developed infection (OR: 0.19; CI 95%: 0.12–0.31; p = 0.0001). Five patients (4.31%) died due to infection (four in the peritoneal dialysis group and one in the catheter hemodialysis group). There were no deaths due to infection in the arteriovenous fistula hemodialysis group.

Conclusions: Peritoneal dialysis is the treatment with greater risk of infection and mortality, followed by catheter hemodialysis. The lowest risk of infection and mortality was observed in arteriovenous fistula hemodialysis group.
Introduction

Chronic kidney disease (CKD) has high prevalence and incidence worldwide, particularly in Brazil. Although the National Kidney Foundation (NKF) in 2002 has proposed staging CKD in order to slow the advance toward the functional failure of the kidneys, difficulties such as lack of early diagnosis, inadequate treatment in the early stages, delayed specialized monitoring, and the complexity of the disease lead many people to need renal replacement therapy (RRT). RRT can be implemented through hemodialysis (HD), peritoneal dialysis (PD), and renal transplantation. Each treatment has its own characteristics, advantages, disadvantages, and complications. Peritoneal dialysis allows the patient home treatment decreasing outpatient visits. Hemodialysis can be performed through a central catheter (CH) inserted in the internal jugular or subclavian vein or through an arteriovenous fistula (AVF) preferably in the upper limbs whose optimal functionality delay varies from one to three months. Nosocomial infection is one of the most serious complications and the second cause of death in dialysis patients. The risk factors that predispose to nosocomial infection in RRT may be influenced by patient characteristics, site of dialysis access, and disorders of the skin and mucous membranes; and comorbidities such as diabetes mellitus, anemia, cardiovascular disease, immunosuppression, and metabolic imbalances. Peritonitis is the most frequent infection in patients undergoing PD, and sepsis is the most frequent complication among patients on HD, especially when conducted through a central venous catheter. The kind of vascular access for HD has significant influence on patient survival. Catheters are associated with substantially greater risk of sepsisemia, hospitalization, and mortality compared to AVF. There are few studies in Brazil evaluating infection rates, the prevalent microorganisms and the susceptibility profile of bacterial infections associated with RRT. These data may be useful for empirical anti-infective therapy in these patients, as well as to better evaluate the choice of dialysis treatment aiming at preventing infections. The objective of the present study was to compare the prevalence of infection and related deaths, as well as the sensitivity profile of the putative bacteria in RRT treated patients.

Methods

This is a case–control study. The study sample consisted of 644 patients treated in the RRT outpatient center at Santa Casa de Misericordia de Ponta Grossa Hospital during a 29-month period. Patients on RRT who developed nosocomial infection (116 patients) were considered as cases. Patients who did not develop infection (528 patients) were considered as controls. Nosocomial infections were considered when the Commission of Hospital Infection Control (CHIC) identified the case as such, based on clinical features, complementary blood tests, and culture results of biological material. Unconfirmed cases of infection by the CHIC were excluded. The patients were divided into three groups according to the type of dialysis treatment: PD (116 patients), CH (192 patients), and arteriovenous fistula hemodialysis (AVH) (326 patients). The study was approved by the local ethics committee.

Statistical analysis

To compare categorical variables, two-tailed Fisher’s exact test with Bonferroni correction for multiple comparisons was used. To evaluate the effect size Odds Ratio (OR) was calculated with 95% confidence interval (CI) and its transformation in probability (p). The samples were properly tested for normality by Anderson–Darling test. The presence of outliers was checked by the Grubbs test. The statistical power of the sample was computed in each comparison. Results are presented as mean ± standard deviation (SD). Analyses, including descriptive statistics, were performed using EPI INFO program. p < 0.05 was considered statistically significant.

Results

Of the 644 patients who underwent dialysis during the study period, 116 (18.1%) developed some infection (63 male; 57.22 ± 12.76 years). One hundred fifty-six infections were reported. Seventy-one (45.51%) infections (56.14 ± 11.22 years) were in patients on PD, 60 (38.46%) infections (59.82 ± 13.33 years) in patients on CH, and 25 (16.2%) infections in patients on AVH (53.8 ± 14.7 years) (Table 1).

Comparison between groups

Of the 126 patients undergoing PD, 44 (34.92%) had at least one infection during the study period, which was significantly higher than that in the other two groups (OR: 3.32; CI 95%: 2.13–5.17; p = 0.0001). CH also showed up as a risk factor for the development of infection with 48 (25%) of the 192 infected patients (OR: 1.8824; CI 95%: 1.24–2.85; p = 0.0035). The lowest incidence of infection was observed in AVH group: 24 (7.36%) of 326 patients (OR: 0.19; CI95%: 0.12–0.35; p = 0.0001). For all comparisons made, the statistical power was greater than 99%, with a consequent error – beta less than 1% (Table 2).

Individual comparison between groups

Comparing the groups individually, AVH turned out to be the safest method with less infections, resulting in lower incidence of morbidity when compared with CH (OR: 0.23; CI 95%: 0.14–0.40; p = 0.0001) and PD (OR: 0.14; CI 95%: 0.08–0.25; p = 0.0001). There was no statistically significant difference between the incidence of infections in the PD group and the CH group (OR: 0.62; CI 95%: 0.38–1.01; p = 0.0593). The statistical power to detect these differences was 100% in both cases, therefore no beta error (Table 3).

Deaths

Of patients infected (116), five died due to infection, with an overall mortality rate of 4.31%. There were four deaths (9.09%)
in PD group and one (8.2%) in CH group. No death was observed in AVH group.

Sites of infection and bacterial etiology

Microbiological tests were carried out in 151 (96.78%) patients, with infections turning out positive in 126 (80.76%). CH group was the group with the highest positivity rate (93.33%; 56/58 cultures), followed by the PD group (81.28%; 59/71 cultures) and the AVH group (52%; 13/22 cultures). The biological samples used for culture were peritoneal fluid in 46.47% of infections of PD group, blood culture in 72.41% of infections of CH group and 40.9% of infections of AVH group. Other samples used for culture were catheter secretion, dialysate fluid, cardiac valve secretion, sputum, and urine (Table 4). The most common infection in the PD group was peritonitis in 55 (77.46%) patients. In CH group, bloodstream infection was the most frequent infection occurring in 44 (73.33%) patients. Vascular access was the commonest site of infection in AVH group occurring in 12 (48%) patients (Table 5). Staphylococcus aureus was the most commonly recovered bacteria present in 44 (32.59%) cases (24 in PD group, 16 in CH group, and 4 in AVH group). Coagulase-negative Staphylococcus spp. (SNPC) was recovered from 47 (34.81%) cases (13 in PD group, 29 in CH group, and 5 in AVH group). Escherichia coli was isolated in 18 (13.33%) cases (10 in PD group, 6 in CH group, and 2 in AVH group). Other less frequent bacteria are shown in Table 6.

Sensitivity profile of etiologic agents

The sensitivity profiles of the main isolated bacteria are shown in Table 7. Among the most important findings, 5 (11.4%)
Table 4 – Microbiological culture results from patients on different types of dialysis.

<table>
<thead>
<tr>
<th>Culture</th>
<th>PD</th>
<th>CH</th>
<th>AVH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Positive</td>
<td>57</td>
<td>81.28</td>
<td>56</td>
<td>93.33</td>
</tr>
<tr>
<td>Negative</td>
<td>14</td>
<td>19.71</td>
<td>2</td>
<td>3.33</td>
</tr>
<tr>
<td>Not done</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3.33</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>45.51</td>
<td>60</td>
<td>38.46</td>
</tr>
</tbody>
</table>

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

Table 5 – Site of infection in patients on different types of dialysis.

<table>
<thead>
<tr>
<th>Site</th>
<th>PD</th>
<th>CH</th>
<th>AVH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Peritonitis</td>
<td>55</td>
<td>77.46</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blood stream (BS)</td>
<td>3</td>
<td>4.22</td>
<td>44</td>
<td>73.33</td>
</tr>
<tr>
<td>Related to vascular access/catheter</td>
<td>12</td>
<td>16.90</td>
<td>14</td>
<td>23.33</td>
</tr>
<tr>
<td>Urinary tract infection (UTI)</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3.33</td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Peritonitis + BS + UTI</td>
<td>1</td>
<td>1.40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>45.51</td>
<td>60</td>
<td>38.46</td>
</tr>
</tbody>
</table>

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

Table 6 – Etiology of infections from patients on different types of dialysis.

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>PD</th>
<th>CH</th>
<th>AVH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>24</td>
<td>40.67</td>
<td>16</td>
<td>25.39</td>
</tr>
<tr>
<td>SNPC</td>
<td>13</td>
<td>22.03</td>
<td>29</td>
<td>46.03</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>1</td>
<td>1.69</td>
<td>1</td>
<td>1.58</td>
</tr>
<tr>
<td>Streptococcus sp.</td>
<td>1</td>
<td>1.69</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>10</td>
<td>16.94</td>
<td>6</td>
<td>9.52</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>3</td>
<td>5.08</td>
<td>2</td>
<td>3.17</td>
</tr>
<tr>
<td>Serratia spp.</td>
<td>2</td>
<td>3.38</td>
<td>3</td>
<td>4.76</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3.17</td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1.58</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>3</td>
<td>5.08</td>
<td>3</td>
<td>4.76</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>2</td>
<td>3.38</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>43.70</td>
<td>63</td>
<td>46.66</td>
</tr>
<tr>
<td>Polymicrobial infection</td>
<td>2</td>
<td>3.50</td>
<td>6</td>
<td>10.71</td>
</tr>
<tr>
<td>Monomicrobial infection</td>
<td>55</td>
<td>96.49</td>
<td>50</td>
<td>89.28</td>
</tr>
</tbody>
</table>

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

Methicillin-resistant S. aureus (MRSA) isolates, all observed in PD group, and 7 (15.2%) methicillin-resistant SNPC infections (6 in CH group) stand out. There was no reported resistance to neither vancomycin nor rifampicin. One (5.5%) E. coli isolate from PD group was extended-spectrum β-lactamase producer (ESBL) and multidrug resistant to antimicrobials. Multidrug resistant Klebsiella pneumoniae was recovered from two isolates (40%), one from PD group and another from CH group. Isolates of Serratia spp. (5) were susceptible to most antimicrobials tested. Resistant Pseudomonas aeruginosa was observed in only one isolate (16.7%) from CH group. Carbapenem resistance was not detected. The remaining isolates were susceptible to most antibiotics tested. Overall, multidrug resistant bacterial infections were recovered from 16 (10.26%) patients: 9 (56.25%) from CH group and 7 (43.75%) from PD group, representing 14.28% and 11.86% infections, respectively, with no statistical difference (OR: 1.23; 95% CI: 0.42–3.5; p = 0.7914; statistical power of 100%). No multidrug resistant isolate was recovered from AVH group.

Discussion

As previously reported, PD patients had higher rate of infection compared to CH and AVH patients. Likewise, a high mortality rate (9.9%) of infected patients was observed in PD
Table 7 – Sensitivity profile of the main isolated bacteria.

| Antimicrobial | S. aureus | | | SNPC | | | E. coli | | | K. pneumoniae | | | P. aeruginosa | | |
|---------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|               | n | s | % | n | s | % | n | s | % | n | s | % | n | s | % |
| Azithromycin  | 44 | 32 | 72.72 | 46 | 19 | 41.30 | 18 | 3 | 16.66 | 5 | 0 | 0 | 18 | 1 | 5.55 |
| Ampicillin (Amp) | | | | | | | | | | | | | | | |
| Amp/Sublactam  | 18 | 11 | 61.11 | 5 | 2 | 40 | 18 | 12 | 66.66 | 5 | 2 | 40 | 18 | 12 | 66.66 | 5 | 2 | 40 |
| Cefazolin     | | | | | | | | | | | | | | | |
| Cefalotin     | 44 | 39 | 88.63 | 46 | 38 | 82.60 | 18 | 14 | 77.77 | 5 | 3 | 60 | 6 | 5 | 83.33 |
| Ceftazidime   | | | | | | | | | | | | | | | |
| SMT + TMT     | 44 | 40 | 90.90 | 46 | 31 | 67.39 | 18 | 12 | 66.66 | 5 | 3 | 60 | 6 | 5 | 83.33 |
| Gentamycin    | 44 | 39 | 88.63 | 46 | 31 | 67.39 | 18 | 10 | 55.55 | 5 | 4 | 80 | 6 | 5 | 83.33 |
| Ciprofloxacin | 44 | 39 | 88.63 | 46 | 34 | 73.91 | 18 | 16 | 88.88 | 5 | 3 | 60 | 6 | 5 | 83.33 |
| Amikacin      | | | | | | | | | | | | | | | |
| Ceftiraxone   | 18 | 17 | 94.44 | 5 | 4 | 80 | 18 | 18 | 100 | 5 | 5 | 100 | 6 | 6 | 100 |
| Meropenem     | | | | | | | | | | | | | | | |
| Penicilllin   | 44 | 8 | 18.18 | 46 | 5 | 10.86 | 16 | 16 | 100 | 5 | 4 | 80 | 6 | 5 | 83.33 |
| Oxacillin     | 44 | 39 | 88.63 | 46 | 39 | 84.76 | 16 | 16 | 100 | 5 | 4 | 80 | 6 | 5 | 83.33 |
| Vancomycin    | 44 | 44 | 100 | 46 | 100 | | | | | | | | | |
| Cefepime      | | | | | | | | | | | | | | | |
| Aztreonam     | 16 | 16 | 100 | 5 | 4 | 80 | 6 | 5 | 83.33 |
| Erythromycin  | 44 | 32 | 7272 | 46 | 33 | 71.73 | 16 | 16 | 100 | 5 | 4 | 80 | 6 | 5 | 83.33 |
| Clindamycin   | 44 | 37 | 84.09 | 46 | 32 | 69.56 | | | | | | | | | |
| Chloramphenicol | 44 | 40 | 90.90 | 46 | 44 | 95.65 | | | | | | | | | |
| PIP + TZB     | 44 | 44 | 100 | 46 | 100 | | | | | | | | | |
| Rifampin      | | | | | | | | | | | | | | | |
| Tobramycin    | | | | | | | | | | | | | | | |

Conclusions

The present study provides evidence that the type of vascular access in RRT is an important predisposing factor for infection which, in turn, increases comorbidity and hospital costs. The AVF for hemodialysis is the safest access for RRT. These results emphasize the need for early referral program for patients with CKD regarding the indication and maturation of the dialysis method. This policy decreases morbidity, mortality, and
hospital costs. More studies are needed, especially those that are prospective and adequately powered.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

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References