Empiric antimicrobial use in the treatment of dialysis related infections in RIPAS Hospital

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ABSTRACT
Introduction: Haemodialysis catheter related infection has emerged as one of the many serious complications and remains a significant cause of morbidity and mortality. Patients who are immunocompromised and have history of bacteraemia are particularly at risk of getting catheter-related infection. The aim of this study is to assess the use of antimicrobial in the empirical treatment of continued ambulatory peritoneal dialysis (CAPD) peritonitis and dialysis line related infections in haemodialysis patients using the local published guidelines as the standard measure. Materials and Methods: Female patients undergoing renal replacement therapies who were admitted for CAPD peritonitis and dialysis line related infections in RIPAS Hospital between 15th March 2010 and 15th September 2010 were the subjects of this study. Data collection was performed in a prospective manner for six months. The patients were monitored continuously until discharged from the ward. Results: A total of 40 patients were included in the study. 95% (n=38) of the patients were started with either intravenous amoxicillin/clavulanic acid (55%, n=22) or ampicillin/subactam (40%, n=16). 70% (n=28) were also initiated with a second antimicrobial, a third generation cephalosporin, ceftazidime. 67.5% (n=27) of the patients were initiated with two antimicrobials whilst 30% (n=12) were on one antimicrobial. Of the 29 cases reviewed (72.5%), all patients were given least two weeks of antibiotic inclusive of oral antimicrobial that was given on discharge, the remaining of the 11 of the cases (27.5%) were unknown due to the loss of follow up. Conclusions: There is a need for review of the current published guidelines on the choice of antimicrobial for treatment of CAPD peritonitis, CAPD Tenckhoff catheter exit site infections, haemodialysis venous catheter related infections and haemodialysis AV fistula related infections.

Keywords: Antimicrobial, empiric therapy, dialysis, line related sepsis, peritonitis

INTRODUCTION
There are three different types of renal replacement therapy currently available; haemodialysis (HD), peritoneal dialysis (PD) and renal transplant. HD can either be undertaken in a hospital or at home and it is the most common mode of renal replacement therapy undertaken by end stage renal disease (ESRD) patients. PD is normally undertaken at patient’s home either using the technique of continuous ambulatory PD (CAPD) or auto-
mated PD (APD). Kidney transplants are normally from a living person, typically a related and are now rarely cadaveric. Statistic from the Department of Renal Medicine, Renal Ministry of Health Brunei Darussalam reported a total of 510 patients being on renal replacement therapy in 2009. Of this, 82% were on HD, 11.6% on PD and 6.5% had undergone renal transplant. Factors which can influence the choice of RRT include the suitability based on the patient’s lifestyle (e.g. patient who needs flexibility and freedom from rigid schedule of hospital haemodialysis may prefers PD over HD), availability of vascular access and patient’s ability to perform self care for dialysate exchange in PD.

Dialysis lines related infections are important cause of morbidity and mortality and increased health care cause. Although generally safe, foreign body vascular access such as a dialysis catheter is associated with complications such as infection. Infections related to dialysis lines have been reported to account for up to 20.5% of all recorded infections among patient undergoing going HD. Several factors have been found to increase to the risk for dialysis lines infection. Importantly, infections related to dialysis lines can be prevented or reduced through proper precautions and following good operating procedures.

To date, there is no published data on infections in patients with ESRD in Brunei Darussalam. This study assessed the choices of antimicrobials used for the empiric treatment of CAPD peritonitis and dialysis line related infections in RIPAS Hospital, a major referral centre in the country.

**MATERIALS AND METHODS**

**Patient Population:** Patients admitted to Ward 20 of RIPAS Hospital between 15th March 2010 and 15th September 2010 were the subjects of this study. This study only included female patients as the ward is a female medical wards where all female renal failure patients are admitted.

**Inclusion criteria:**
Patients undergoing renal replacement therapies who were admitted for CAPD peritonitis and dialysis line related infections were included in the study. The same patient may be included in the study more than once if there was a repeated admission within the six months period.

**Exclusion criteria:**
All patients admitted to ward 20 who are not under renal care or admitted for various medical conditions other than CAPD peritonitis and catheter related infections.
All renal patients who are not undergoing renal replacement therapy.

Data were analysed using the WordExcel programme and presented as absolute number and percentages.

**RESULTS**
A total of 40 patients were included in the study. The indications for empiric antimicrobial therapy are shown in Table 1. Temporary and HD venous catheter were the most common source of sepsis.

The most common antimicrobials used were intravenous (IV) ceftazidime,
amoxicillin-clavulanic acid and ampicillin-sulbactam (Table 2). One patient each was given vancomycin, cloxacillin and imipenem respectively.

The number of antimicrobial started empirically ranged from one to three (Table 3).

**CAPD Peritonitis (n=2):** Both patients were initiated on two antimicrobials (amoxicillin/clavulanic acid and ceftazidime). In the first patient, both antimicrobials were given through the intraperitoneal (IP) route for a total of 12 days, and this were stopped when the PD culture revealed *Trichosporon Asahii*. The catheter was changed and a dose of IP vancomycin 1gm was also given. This patient was also treated for a chest infection (ciprofloxacin for two days before ceftriaxone 1g OD was added). The antibiotic was given for 13 days and later changed to oral ciprofloxacin for another two weeks. The duration of antimicrobial treatment for the second patient was unknown.

**CAPD Tenckhoff Catheter Exit Site Infections (n=2):** One patient was given amoxicillin-clavulanic acid (1.2gm BD) for three days and this was changed to ceftazidime (2gm) given post HD when the swab culture isolated *Pseudomonas* species. This patient was treated started with oral ciprofloxacin 250mg BD for two weeks for line sepsis. Overall, the patient was on antimicrobial throughout the admission (29 days). One patient was initiated with two antimicrobials (ampicillin/sulbactam 1.5gm twice daily (BD) and ceftazidime). However, further detail was not available.

**Haemodialysis AV Fistula related Infections (n=3):** Two patients were initiated on only one antimicrobial. The third patient was initiated with two antimicrobial (ampicillin/sulbactam 1.5gm BD and ceftazidime 1gm OD). *Staphylococcus aureus* (*S. aureus*) sensitive to both ampicillin/sulbactam and amoxicillin/clavulanic acid was isolated in two patients. Including discharged medications, the total duration of treatment were three weeks.

### Table 1: Type of infections.

<table>
<thead>
<tr>
<th>Types of infections</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD Peritonitis</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>CAPD Tenckhoff catheter exit site infections</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Haemodialysis venous catheter related infections</td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td>Haemodialysis AV fistula related infections</td>
<td>3 (7.5%)</td>
</tr>
<tr>
<td>Temporarily dialysis lines infections</td>
<td>22 (55%)</td>
</tr>
<tr>
<td>Total</td>
<td>40 (100%)</td>
</tr>
</tbody>
</table>

### Table 2: Initial choices of antimicrobial prescribed.

<table>
<thead>
<tr>
<th>Choices of antimicrobial</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous (IV) ceftazidime</td>
<td>28 (70%)</td>
</tr>
<tr>
<td>IV amoxicillin/clavulanic acid</td>
<td>22 (55%)</td>
</tr>
<tr>
<td>IV ampicillin/sulbactam</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>IV vancomycin</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>IV cloxacillin</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>IV imipenem</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Total*</td>
<td>69 (100%)</td>
</tr>
</tbody>
</table>
The remaining patient received IV amoxicillin/clavulanic acid 600mg TDS for three days and converted to oral therapy for another five days upon discharged.

**Haemodialysis Venous Catheter related infections (Permcat) (n=11):** 10 patients (90.9%) were initiated with two antimicrobials. Culture results were available for seven patients (63.6%); *S. aureus* (n=4) and *Coagulase negative S. aureus* (n=3). Only one showed sensitivity to amoxicillin/clavulanic acid. One case was changed to vancomycin. One patient was positive with both *Coagulase negative S. aureus* and *Chryseobacterium Indologenes*, and the antimicrobials were replaced with ciprofloxacin which was effective against both organisms. All the antimicrobials were adjusted according to culture results. There were two deaths recorded.

**Temporarily dialysis lines related infection (n=22):** 13 patients (59.1%) were initiated with two antimicrobials. One patient (4.5%) was started on three antimicrobials simultaneously (amoxicillin/clavulanic acid and ampicillin/sulbactam, in addition to ceftazidime). One of the beta lactamase was stopped after pharmacist intervention.

The remaining eight patients (36.4%) were started on one antimicrobial (amoxicillin/clavulanic acid n=5, imipenem n=1, vancomycin n=1 and cloxacillin n=1). *S. aureus* sensitive to cloxacillin was isolated from the patient who was empirically started on cloxacillin. One patient each was empirically started on imipenem and vancomycin respectively due to history of repeated line sepsis and previous Methicillin resistant *S. aureus* (MRSA) infection. MRSA was isolated in the latter patient.

Among the five patients initiated with amoxicillin/clavulanic acid, all had positive blood cultures; *S. aureus* (n=3), *Coagulase negative S. aureus* (n=1) and MRSA (n=1). One patient with *S. aureus* sepsis also had *Eschericeria coli* (*E. coli*) isolated in the sputum. Cellulitis of the hand was the source of *S. aureus* sepsis in one patient and this was treated with IV amoxicillin/clavulanic acid (four days) followed by oral flucloxacillin (500mg four times daily, QDS) for three weeks post discharge. For the patient with Coagulase negative *S. aureus*, the antimicrobial was changed to IV vancomycin given post HD (a dose of clindamycin before converting to vancomycin). The patient with MRSA was given IV vancomycin 1gm post HD until discharge. The patient with dual organisms was switched to ampicillin/sulbactam as both organisms were sensitive to this antimicrobial.

**DISCUSSION**

Sepsis is an important cause of morbidity and mortality for patient with end stage renal failure. Infections for those undergoing dialysis are usually dialysis lines related, and from frequent instrumentations. In a seven years follow up longitudinal study by Powe *et al.*, 11.7% of 4,005 patients on HD and 9.4% of...
913 patients on PD had at least one episode of documented septicaemia. Among the HD patients, low albumin, temporary vascular access and dialyser reuse were associated with an increased risk of septicaemia. The risk was higher in patients with temporary catheter compared to those with arteriovenous fistula. Berman at al. reviewed 433 HD patients treated in a single hospital-based dialysis programme with over a 9 year period and 424,700 days of dialysis recorded a total of 2,412 episodes of bacterial or fungal infections. This translated to an infection rate of 5.7 episodes per 1000 days of dialysis. Infection associated with HD vascular access devices accounted for 20.5% of the total episodes. The authors concluded that patients with ESRD have an enormous burden of infection, especially patient with concomitant disease of diabetes mellitus. This situation is also true including Brunei Darussalam with infection being one of the top causes of death in renal failure patients.

From the culture results of our study, S. aureus is the most common pathogen in majority of the cases (63.6%). This is not unexpected given the frequent AVF cannulations and manipulations of the dialysis lines in patients who are already immune compromised from the renal failure and other comorbid conditions. The other isolated organisms were MRSA (13.6%), Coagulase negative S. aureus (9.1%), Streptococcus (4.5%), Enterobacter sakazakii (4.5%) and Pseudomonas aeruginosa (4.5%) and Chryseobacterium indologenes. Unfortunately, results were not available in 9.1% (2 cases) either due to loss of follow-up or results were not available during the study period. Despite this, our findings are comparable to what have been reported in the literatures.

In our study, the duration of antimicrobial therapies were not less than two weeks, and most patients were converted to oral antimicrobial upon discharged for a minimum of two weeks. However, some patient had longer duration due to concomitant infections. In our setting, repeat cultures are usually done after the completion of a course of antimicrobials to ensure complete eradication of the infection. The duration of treatment was also based on patient’s medical conditions and their response to the antimicrobials. The antimicrobials chosen, typically broad spectrum beta lactamase (amoxicillin-clavulanic acid or ampicillin/sulbactam) and a third generation cephalosporin (ceftazidime) generally covered most the suspected infection and organisms. Several patients were started on other antimicrobials due to previous known recent infections or suspected organisms. Once culture results were available, the treatment were adjusted according to culture sensitivity. Therefore, the choices of antimicrobials in our setting were generally appropriate despite third generation cephalosporin not included as the first line of empiric treatment in the National Antibiotic guideline for this particular group of patient.

A limitation of this study was that the data collection was only collected from a female medical ward in RIPAS Hospital. The prescribing pattern for similar indications in the male medical wards or renal unit is not truly reflected in this study. However, given that the team of doctors looking after these patients both male and female work closely and supervised by the same consultants, it is likely that the practise did not defer much.
Whether the spectrum of infections and the organisms responsible causing the infection is the same for female and male patients undergoing dialysis is not fully known and requires further study.

In conclusion, this study showed that the choice of antimicrobial used for the empirical treatment of dialysis lines related infection appropriately covered the suspected organisms. However, there were some differences to what have been outlined in the National Antibiotic Guideline. A review of the guideline may be required. Judicious and appropriate use of antimicrobial is essential in order to reduce the selective pressure which favours the emergence of antimicrobial resistance.

REFERENCES
3: Department of Renal Medicine, Ministry of Health. Statistic from the Renal Department, Brunei Darussalam 2009.