

**Stenotrophomonas maltophilia: an emerging pathogen in dialysis units**

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Infection is an important cause of morbidity and mortality among patients with end stage renal disease. *Stenotrophomonas maltophilia* is an unusual yet emerging pathogen in dialysis units. We performed a systematic PubMed/Medline and Scopus review of peer-reviewed English papers on *S. maltophilia* infections among patients undergoing chronic dialysis, with regard to vascular accesses, systemic infections and environment contaminations. Moreover, we suggest a treatment algorithm to preserve the patient and the permanent dialysis catheters.

**Introduction**

*Stenotrophomonas maltophilia* is an aerobic, non-fermentative, motile, Gram-negative bacterium, which was initially classified as *Pseudomonas maltophilia*. *S. maltophilia* was initially grouped in the genus *Xanthomonas* and then the genus *Stenotrophomonas* in 1993 (Palleroni & Bradbury, 1993). It propagates in moist environments (water, medical equipment, soil and sewage) and colonizes medical devices (Marshall et al., 1989; Passerini de Rossi et al., 2007).

*S. maltophilia* is becoming a relevant opportunistic pathogen, causing bacteraemia, pneumonia, and intra-abdominal and mucocutaneous infections; subjects at higher risk of *S. maltophilia* infection are debilitated, immunosuppressed and neutropenic patients (Looney et al., 2009; Brooke, 2012; Samonis et al., 2012). Dialysed patients are an ideal target for infections: they are immunosuppressed because of uraemia, old age, malnutrition, comorbidities and the increased use of artificial accesses such as prosthetic grafts, central venous or peritoneal catheters.

The treatment of *S. maltophilia* infections can become cumbersome because the pathogen harbours an intrinsic resistance to several classes of antibiotics, through beta-lactamase production, drug efflux pumps and decreased permeability, and this resistance might also emerge during the course of therapy (Garrison et al., 1996; Vila & Marco, 2002). Most *S. maltophilia* strains are in general resistant to extended-spectrum penicillin, third-generation cephalosporins and carbapenems (Pankuch et al., 1994; Vartivarian et al., 1994), but sensitive to the newest generation of quinolones, aminoglycosides and trimethoprim/sulfamethoxazole (Nicodemo & Paez, 2007; Samonis et al., 2012).

Here, we review the available literature about *S. maltophilia*-related infections in patients undergoing either extracorporeal or peritoneal dialysis.

**Methods**

We conducted a systematic PubMed/Medline and Scopus review of peer-reviewed papers on *S. maltophilia* infections among adult patients undergoing chronic dialysis. Search terms used were: ‘*Stenotrophomonas maltophilia*’ and ‘dialysis’. We found 24 and 17 articles in PubMed/Medline and Scopus respectively, but after a cross-matching and retrieving results specific for adult chronic dialysis patients and papers written in English, we were left with 17 papers (Table 1). Finally, we performed a summary of the literature with regard to the dialysis access outcome (Table 2).

**Results**

Only one study has been published on the role of *S. maltophilia* colonization in dialysis units. In a Greek multicentre study on the colonization of municipal water supplies, treated water and dialysate, *S. maltophilia* accounted for 13.5 % of isolates, just after *Pseudomonas* (22.7 %) and *Chryseobacterium* (14.9 %) (Arvanitidou et al., 2003). Earlier reports described *S. maltophilia* sepsis in 12 subjects, due to the use of reprocessed high-flux membranes with contaminated O-rings inside the dialysate; 4 out of 12 patients and 21 patients as described by Flaherty et al. (1993) and Roberts et al. (1994), respectively.

Manual or automated peritoneal dialysis is performed by introducing a dialysis solution into the abdominal cavity through a permanent tunneled catheter and most peritoneal dialysis literature on *S. maltophilia* addresses peritonitis and/or peritoneal catheter exit site infections. The
earliest reports recommended a prolonged antibiotic treatment and the removal of catheters (Berbari et al., 1993; Szeto et al., 1997; Taylor et al., 1999; Al-Hilali et al., 2000), perhaps due to the severity of the infection and also as is usual clinical practice. In more recent years, a tunneled catheter was removed in a woman with exit site infection due to <i>S. maltophilia</i> with multi-resistant antibacterial spectrum, a condition at high risk of peritonitis (Cheng et al., 2001). Nevertheless, as described by Taylor et al. (1999), three out of seven catheters were saved after a prolonged systemic therapy. More recently, a longer therapy with trimethoprim/sulfamethoxazole in combination with one or two additional agents (quinolones or aminoglycosides) has proved useful in preventing the removal of catheters (Baek et al., 2004; Tzanetou et al., 2004). In one study, four out of five catheters were maintained by treating peritonitis with a combination therapy of intraperitoneal ceftazidime plus endovenous trimethoprim and/or amikacin for a period of two weeks to two months (Baek et al., 2004). Another study reports the treatment of a <i>S. maltophilia</i> peritoneal infection through intraperitoneal instillation of ceftazidime and endovenous trimethoprim plus ticarcillin or amikacin for two to four weeks, saving three out of four catheters; the fourth catheter was removed because of fungal co-infection (Tzanetou et al., 2004). An additional study reports the successful treatment of <i>S. maltophilia</i> peritonitis in a female patient undergoing automated peritoneal dialysis with trimethoprim/sulfamethoxazole for 6 weeks and amikacin for 2 weeks (Machuca et al., 2005). Recently, a strategy to treat refractory <i>S. maltophilia</i>-related peritonitis has been proposed: the association of an antibiotic lock therapy, for example with a third-generation cephalosporin, after each peritoneal exchange in addition to the local instillation of antibiotics inside the peritoneum (Lee et al., 2009).

Few papers deal with <i>S. maltophilia</i>-related bacteraemia in dialysis patients with permanent central venous catheters. One paper reports treating a tunneled central venous catheter infection (due to <i>S. maltophilia</i>) with endovenous ciprofloxacin and the removal of the catheter (Ganadu et al., 1996). Another paper reports that the use of trimethoprim/sulfamethoxazole alone resolved the infection in two patients who experienced pancytopenia during therapy; however, in both cases catheters were removed (Korzets et al., 1997). In addition, one group reported successfully treating infected patients with a combination of trimethoprim/sulfamethoxazole and ciprofloxacin, and

### Table 1. Summary of the original articles published to date dealing with <i>Stenotrophomonas maltophilia</i> contamination or infection in patients with end stage renal disease

<table>
<thead>
<tr>
<th>Topic</th>
<th>No. of articles</th>
<th>No. of patients</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environment contamination</td>
<td>3</td>
<td>12</td>
<td>Flaherty et al. (1993); Roberts et al. (1994); Arvanitidou et al. (2003)</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>9</td>
<td>28</td>
<td>Berbari et al. (1993); Szeto et al. (1997); Taylor et al. (1999); Al-Hilali et al. (2000); Cheng et al. (2001); Baek et al. (2004); Machuca et al. (2005); Lee et al. (2009); Tzanetou et al. (2004)</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>4</td>
<td>5</td>
<td>Ganadu et al. (1996); Korzets et al. (1997); Kara et al. (2006); Shah &amp; Feinfeld (2000)</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>18</td>
<td>Wakino et al. (2009)</td>
</tr>
</tbody>
</table>

### Table 2. <i>Stenotrophomonas maltophilia</i>-related catheter infections with regard to catheter outcome

<table>
<thead>
<tr>
<th>Catheters</th>
<th>Total no. of patients (gender, age)</th>
<th>No. of catheters replaced</th>
<th>No. of catheters not replaced</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal dialysis</td>
<td>1 (M, 72y)</td>
<td>1</td>
<td>–</td>
<td>Berbari et al. (1993)</td>
</tr>
<tr>
<td></td>
<td>6 (NA)</td>
<td>6</td>
<td>–</td>
<td>Szeto et al. (1997)</td>
</tr>
<tr>
<td></td>
<td>7 (3M, 16–61y)</td>
<td>4</td>
<td>3</td>
<td>Taylor et al. (1999)</td>
</tr>
<tr>
<td></td>
<td>2 (NA)</td>
<td>2</td>
<td>–</td>
<td>Al-Hilali et al. (2000)</td>
</tr>
<tr>
<td></td>
<td>1 (M, 47y)</td>
<td>1</td>
<td>–</td>
<td>Cheng et al. (2001)</td>
</tr>
<tr>
<td></td>
<td>1 (F, 54y)</td>
<td>–</td>
<td>1</td>
<td>Machuca et al. (2005)</td>
</tr>
<tr>
<td></td>
<td>1 (NA)</td>
<td>–</td>
<td>1</td>
<td>Lee et al. (2009)</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>4 (2M, 40–64y)</td>
<td>1</td>
<td>3</td>
<td>Tzanetou et al. (2004)</td>
</tr>
<tr>
<td></td>
<td>1 (M, 72y)</td>
<td>1</td>
<td>–</td>
<td>Ganadu et al. (1996)</td>
</tr>
<tr>
<td></td>
<td>2 (F, 39y; M, 63y)</td>
<td>2</td>
<td>–</td>
<td>Korzets et al. (1997)</td>
</tr>
<tr>
<td></td>
<td>1 (F, 43y)</td>
<td>1</td>
<td>–</td>
<td>Kara et al. (2006)</td>
</tr>
<tr>
<td></td>
<td>1 (F, 37y)</td>
<td>–</td>
<td>1</td>
<td>Shah &amp; Feinfeld (2000)</td>
</tr>
</tbody>
</table>

M, Male; F, female; y, years; NA, not available.
removal of the catheter (Kara et al., 2006). Finally, a case of a S. maltophilia infection in a dialysed woman with a tunneled central venous catheter has been described by Shah & Feinfeld (2000): since a combination therapy of ceftazidime and ciprofloxacin failed to eradicate the infection, the addition of a long-term daily locked-in therapy with ceftazidime was able to save both the catheter and the patient.

To our knowledge there is only one study analysing S. maltophilia infections, not related to the dialysis vascular access, among uraemic subjects. As described by Wakino et al. (2009), 18 out of 199 (9%) bacteria from 120 dialysed patients, diagnosed with nosocomial pneumonia, were S. maltophilia. The pathogen was resistant to carbapenems, cephalosporins and ciprofloxacin, but sensitive to newer-generation quinolones. Two-thirds of patients died, confirming the higher mortality among the dialytic population.

Discussion

Among dialysed subjects, S. maltophilia-related infections could be challenging and life-threatening because of antibiotic resistance of the bacterium and the immuno-suppressed status of uraemic patients. In addition, it must be considered that S. maltophilia may not be the only pathogen involved in the infection, as S. maltophilia is frequently accompanied by Gram-positive bacteria, mainly Enterococcus faecalis (Wakino et al., 2009).

Finally we would like to use the available literature to give some suggestions in order to optimize the antibiotic therapy and preserve, whenever possible, the patient and the catheter.

1) When the infection is not accompanied by severe clinical symptoms or when the substitution of the catheter is not easily achievable (for instance, patients with multiple access failures and with previous central venous catheterizations or thrombosis): provide a long-course (2–4 weeks) intravenous administration of, at least, two antibiotics combined with the locked-in therapy. The catheter may remain in situ.

2) If the infection is mildly symptomatic a long course of antibiotic therapy, as in point one, can be pursued but if fever does not disappear in 48–72 h, replace the central venous catheter and continue systemic and local antibacterial therapy.

3) When the infection is accompanied by severe clinical symptoms or relapses in a few months: provide a long-term catheter and continue systemic and local antibacterial therapy.

According to the susceptibility of the bacterium, a prolonged combination therapy of endovenous aminoglycosides plus levofloxacin or ceftazidime or trimethoprim/sulfamethoxazole, and a locked-in instillation of gentamicin or ceftazidime, is safe, with an excellent outcome for both the patient and the catheter.

Conclusion

S. maltophilia is an emergent pathogen in dialysis units, causing infection in peritoneal and haemodialysis patients; since it is also a natural inhabitant in most environments inside and outside the hospital setting, it can induce infections in immunosuppressed subjects. The treatment of S. maltophilia-related infection could be cumbersome because of several bacterial and host characteristics. Antibiotic therapy, if well conducted, is able to cure the infection in most cases; in a few, it preserves patient safety and dialysis access patency.

References


