10-Years Hospital Experience in *Pseudomonas stutzeri* and Literature Review

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Abstract: *Pseudomonas stutzeri* is infrequently isolated from clinical material and rarely associated with invasive infections in human. During the past decade we have witnessed a significant increase in the number of *P. stutzeri* isolations from clinical material. Review of the hospital's experience revealed 93 isolations, the vast majority were from wounds and urine. Eighteen patients suffered from *Pseudomonas stutzeri* bacteremia. Ten patients died (10.8%) from whom only in two cases, death could be directly attributed to the infection. Despite the significant increase in *P. stutzeri* isolation from clinical material, it's still rarely associated with adverse clinical outcome and usually represents colonization rather than infection.

Keywords: Bacteremia, ear canal, *Pseudomonas stutzeri*, review, urinary tract infection, wound infection.

INTRODUCTION

Pseudomonas stutzeri is an aerobic, nonfermenting, active, gram-negative oxidase-positive bacteria. It is mostly a saprophyte found in soil, water, and rarely leads to serious community or nosocomial acquired infections [1]. Cases of *P. stutzeri* infection concern typically immunocompromised patients with underlying diseases or previous surgery [2]. The most common reported sites of clinical isolates are surgical wounds, blood, respiratory tract, and urine [3, 4]. Previous literature review showed that when *P. stutzeri* is isolated from clinical material it most likely represents colonization in hospitalized patients and uncommonly indicates pathogenicity [2]. During the past decade we have witnessed a significant increase of *P. stutzeri* isolations from clinical material in our medical center. The clinical significance of this increase remains unclear. The present study aimed to study the clinical significance of *P. stutzeri* isolations, type of antimicrobial therapy prescribed, antimicrobial susceptibility patterns, and determine the correlation between species isolation and clinical outcome. In addition, we have reviewed the literature on *P. stutzeri* infections.

MATERIALS AND METHODS

The microbiology computer records of Emek medical center, during 10 years period (2000-2010), were reviewed providing a list of all *P. stutzeri* isolations from clinical material. Infection was defined when *P. stutzeri* was isolated from a sterile site. The hospital medical charts for each isolate were reviewed and the following data were recorded: age, sex, site of isolation, the clinical setting, type of antimicrobial therapy (if prescribed), antibacterial susceptibility patterns of *P. stutzeri* isolates, number of blood culture sets obtained and number of sets that grow microorganisms, and outcome. Antimicrobial treatment failure was defined when the local or systemic clinical signs of infection persisted, with or without isolation of the pathogen from a sterile site, despite 3 days of antimicrobial therapy. We also retrieved an annual list of all *pseudomonas* spp. isolations during the study period.

Pseudomonas stutzeri isolates were identified initially by their typical wrinkled and dry colony morphology on MacConkey agar and subsequently through their metabolic profile as established till the year 2005 by the API non-Enterobacrteriaceae system (bioMérieux, France) and later on by Vitek II GN (Gram negative) card (bioMérieux, France). Antibiotic susceptibility testing was carried out using E Test (bioMérieux, France) and later on by employing the API Gram negative antimicrobial susceptibility testing (AST) card # NO98 (bioMérieux, France). The following antimicrobials were tested in the study: gentamicin, amikacin, ofloxacin, ciprofloxacin, amoxicillin-clavulanate, piperacillin, piperacillin-tazobactam, cephalothin, cefuroxime, ceftriaxone, cefotaxime, ceftazidime, cefepime, imipenem, meropenem, ertapenem, trimethoprim-sulfamethoxazole, nitrofurantoin, and polymyxin B.

The study was approved by the local ethics committee.

RESULTS

Ninety three *P. stutzeri* isolations from clinical material were identified during the study period (2000-2010). The mean age of the patients was 35 years (range 2 months-93 years). The sources of the clinical specimens included urine 31.2% (n=29), wounds 28% (n=26), blood 19% (n=18), ear canal 10.8% (n=10) and the rest from other sterile sites 10.8% (n=10) including synovial fluid (n=2), peritoneal fluid (n=4), conjunctiva (n=3), and cerebrospinal fluid (n=1).

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The number of isolations increased significantly from 2000 to 2010, the highest number of isolations was identified during 2010 (n=24). Stratifying the data according to the site of isolation (sterile or non-sterile) showed that nearly 74% of isolations from sterile sites (blood, synovial fluid, CSF, and peritoneal fluid) occurred during 2005-2010. This was in complete contrast to 3 isolations only from sterile sites during the 1990's at our medical center.

Ten patients died, all of whom were elderly with a mean age of 80.7 years and suffered from chronic comorbidities [chronic kidney disease (n=3), cancer (n=3), cirrhosis (n=2), and previous cerebro-vascular accident with pressure sores (n=2)]. The isolation sites among the patients who died included blood (n=4), deep pressure sores (n=3), and urine (n=3). Eighteen patients suffered from *P. stutzeri* bacteremia, the vast majority of them suffered from chronic comorbidities (83%) with a mortality rate of 22% (n=4) (Table **1**). Seventeen patients (94%) received empirical antimicrobial therapy, from which only in 8 patients (44%) the therapy was anti-pseudomonal (Table **2**).

Twenty nine patients had *P. stutzeri* isolated from the urinary tract (Table **1**), 65% suffered from chronic comorbiditeis, the mortality rate in this group was ~10%. Fifteen patients (52%) received empirical antimicrobial therapy (Table **2**). Only 58% of the patients (n=17) complained of symptoms suggestive of urinary tract

Table 1. Clinical Characteristics and Isolation Sites of Patients with *Pseudomonas stutzeri* Infection (or Colonization)

	Site of Isolation				
	Blood	**Urine**	**Wounds**	**Ear Canal**	**Other**
No. of isolates	18	29	26	10	10
Age range (mean)	4-94 (39.3)	11-98 (56.8)	4-93 (33.4)	6-65 (28.3)	2-65 (24.3)
No. of patients with underlying chronic diseases	15 (83)	19 (65)	9 (34)	1(10)	2 (20)
Chronic kidney disease (%)	8 (44)	4 (14)	3 (11)	1(10)	0
Diabetes mellitus (%)	6 (33)	10 (34)	2 (7)	0	1 (10)
Cancer (%)	2 (11)	4 (14)	0	0	0
Congestive heart failure (%)	3 (16)	5 (17)	1(4)	0	0
Death (%)	4 (22.2%)	3 (10.3)	3 (11.5)	0	0

Table 2. Types of Antimicrobial Therapy Prescribed for Patients Infected (or Colonized) with *Pseudomonas stutzeri*

	Site of Isolation				
	Blood	**Urine**	**Wounds**	**Ear Canal**	**Other**
No. of isolates	18	29	26	10	10
Antimicrobial therapy §	17	15	18	10	9
Ceftriaxone	4 (1)				
Cefuroxime (intravenous)	2		1(1)		
Cephalothin	1		1		
Amoxicillin+clavulanic acid	3 (1)		3 (2)	5*	1*
Ciprofloxacin				4	
Trimethoprim-sulfamethoxazole		5 (3)			
Nitrofurantoin		2			
Cefuroxime (oral)		8			
Gentamicin & Ciprofloxacin	1				
Cefamezine & Gentamicin	2 (1)				2
Gentamicin	1				
Ampicillin & Gentamicin	1				
Piperacillin & Gentamicin				1	4
Ceftriaxone & Ofloxacin	1				
Cefuroxime & Ciprofloxacin	1(1)				
Fusidic acid (topical cream)			7		
Gentamicin (topical)			6		2

Numbers in parentheses indicates no. of patients who died.
§Empirical antimicrobial therapy.
*Cases where antimicrobial therapy was eventually switched to anti-pseudomonal therapy.

infection, the rest (42%) were asymptomatic and were not treated and none required therapy afterwards. Of those who were treated, nearly 66% received an empirical antimicrobial therapy that was eventually inappropriate (cefuroxime and nitrofurantoin) (Table **2**). Three patients died in this group, all of whom received an empirical antimicrobial treatment active against *P. stutzeri*, their death was attributed to cardiovascular (n=2) and pulmonary causes (n=1). None of the patients in the whole group suffered from adverse outcomes directly related to the infection or lack of therapy.

In 26 cases *P. stutzeri* was isolated from superficial wounds, pressure sores, and post-operative wounds (Table **1**), the mean age of the patients in this group was 33.4 (range 4-93). A third of the patients suffered from chronic comorbidities. Only in six cases a local anti-pseudomonal therapy was prescribed, none of the patients developed an invasive infection that required parenteral therapy. Three patients died (11.5%), two of whom due to massive stroke (n=1) and one due to nosocomial pneumonia (n=1). Ten patients had *P. stutzeri* isolated from the ear canal (Table **1**), only five received empirical anti-pseudomonal therapy (3 received parenteral therapy and two received topical treatment), the other five received amoxicillin (n=3) and cefuroxime(n=2). In 10 cases *P. stutzeri* was isolated from other sites including synovial fluid (n=2), peritoneal fluid (n=4), cerebrospinal fluid (n=1), and conjunctiva (n=3). In 8 cases (80%) an empirical anti-pseudomonal therapy was prescribed. No death was reported in this group.

The antibiotic susceptibility patterns of isolates reviewed in the current study are shown in Table **3**.

Table 3. Antibiotic Susceptibility Patterns of *Pseudomonas stutzeri* Isolates

Antibacterial Drug	No. of Isolates Tested	% of Isolates Susceptible
Gentamicin	86	99%
Ofloxacin	81	99%
Amikacin	48	98%
Imipenem	40	98%
Ciprofloxacin	65	97%
Meropenem	39	97%
Ceftazidime	58	95%
Piperacillin	54	93%
Polymyxin-B	39	92%
Trimethoprim-sulfamethoxazole	32	91%
Piperacillin&Tazobactam	11	91%
Ertapenem	4	75%
Cefepime	7	71%
Ceftriaxone	5	60%
Amoxicillin-clavulanic acid	8	50%
Cefotaxime	4	50%
Nitrofurantoin	11	27%
Cefuroxime	7	14%
Cephalothin	8	12.5%

During the study period there were 9971 isolations of *Pseudomonas aeruginosa* and *Pseudomonas* spp. from clinical samples with mild and steady increase over the past decade. *P. stutzeri* had comprised only ~ 0.9 % of all *Pseudomonas* isolations.

DISCUSSION

Review of the hospital records during the past decade showed that despite the gradual increase in *P. stutzeri* isolations, the microorganism is still infrequently isolated, representing nearly 1% of all *Pseudomonas* isolations, and when it is isolated it frequently represents colonization rather than infection without significant pathogenicity. Ten patients died all of whom suffered from multiple and chronic comorbidities. Excluding two cases, death could directly be attributed to other, and rather significant, comorbidities than to the presence of *P. stutzeri* in the clinical material.

The antibiotic susceptibility patterns of the isolations are consistent with prior studies showing that the microorganism is almost invariably susceptible to aminoglycosides, quinolones, carbapenems (excluding ertapenem) antipseudomonal penicillins, polymyxin, and trimethoprim-sulfamethoxazole [2, 3, 5, 6]. Excluding ceftazidime, third and fourth generation cephalosporins are not optimal therapies for *P. stutzeri* infections with a coverage rate ranging from 50-70%. *P. stutzeri* isolates were generally more sensitive than *Pseudomonas aeruginosa* strains (data not shown; NB) consistent with previous observations [7].

Literature review revealed that reported cases of *P. stutzeri* infections are primarily sporadic with very few outbreaks that were attributed to contamination of intravenous fluids [8], water system used for hemodialysis [9], or soap used to prepare skin for intravenous insertions [10], all of which occurred during the 1970's and 1980's. To our knowledge, no other outbreaks of *P. stutzeri* infections had occurred since then. Community-acquired infections caused by *P. stutzeri* have included pneumonia with empyema [11, 12] and without empyema [13, 14] including one case in a previously healthy child [15]. *P. stutzeri* has also been associated with septicemia [9, 16-20] and bacteremia [21], as well as endocarditis on a prosthetic mitral valve [22], and a case of endocarditis with relapse after several years [23]. Meningitis due to *P. stutzeri* has also been described [24-26]. Bone and joint infections included vertebral osteomyelitis in a previously healthy young man [27], infection of an open fracture of the femur [28], hip joint infection [29], and a case of prosthetic knee infection [30]. Pediatric cases include calcaneal osteomyelitis in a healthy 12-year-old boy who sustained a nail puncture through his sneaker [31], and a child with knee arthritis following knife puncture wound [32]. Other reports include continuous ambulatory peritoneal dialysis (CAPD)- *P. stutzeri* associated peritonitis [33], conjunctivitis [34] and corneal infections [35]. Cases of nosocomial transmission of *P. stutzeri* include secondary bacteremia caused by contamination of a dialysate, in hemodialysis patients [9]; endophthalmitis after cataract surgery [36]; orbital abscess after eye surgery [37]; and brain abscess after subdural grid implantation before surgery for refractory epilepsy [38].

In summary, the isolation of *P. stutzeri* from clinical material rarely indicates pathogenicity. Obviously, isolation of *P. stutzeri* from sterile sites should be given serious consideration prior to formalizing the cause of the infection and

administer appropriate antimicrobial therapy. In contrast, isolation of *P. stutzeri* from non-sterile sites rarely indicates pathogenicity and therapy should be guided by the clinical symptoms and signs.

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CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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