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RETROSPECTIVE STUDY OF MICROORGANISMS ASSOCIATED WITH VASCULAR ACCESS INFECTIONS IN HEMODIALYSIS PATIENTS

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Abstract

Objective—To assess microorganisms associated with vascular access-associated infections (VAIs) in hemodialysis patients, with respect to possible origin from the mouth.

Study Design—A retrospective and comparative analysis of the microbes associated with VAI in hemodialysis patients treated during a 10-year period was performed using the Human Oral Microbiome Database (HOMD).

Results—Of 218 patient records identified, 65 patients collectively experienced 115 VAI episodes. The most common microorganisms involved were *Staphylococcus aureus* (49.6% of infections), *Staphylococcus epidermidis* (10.4%), *Serratia marcescens* (10.4%), *Pseudomonas aeruginosa* (9.6%), and *Enterococcus faecalis / fecum* (8.7%). None of these was found in 1% or more of HOMD clone libraries, indicating that they very rarely colonize the teeth or plaque.

Conclusions—Most VAIs were associated with microorganisms more likely to originate from other body sites than from the oral cavity. The risk of a VAI being caused by microorganisms originating from the oral cavity is very small.

Introduction

Renal disease is becoming increasingly recognized as a global health care crisis with a significant impact on the United States health care system. The United States has the second highest prevalence of end-stage renal disease in the world.[1] According to the U.S. Renal

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Data System, there were 598,311 persons with end-stage renal disease in the U.S. for the period from the 4th quarter of 2009 to the 4th quarter of 2010.[2] A large proportion of these patients receive hemodialysis. Data from the Dialysis Surveillance Network indicate that 3.2% of hemodialysis patients have a dialysis access-related infection each month.[3] Higher susceptibility to infection in this population is caused by their immunocompromised status, chronic systemic disease and illness, and repeated use of the vascular access site for hemodialysis.[3] These vascular access-related infections can lead to multiple morbidities ranging from local infection to sepsis with multi-organ failure, and death. A 10 year review of mortality rates in dialysis patients revealed that infection contributed to 24% of all deaths.[4]

Due to the morbidity and mortality associated with vascular access-associated infections (VAIs), the use of prophylactic antibiotics to prevent such infections is common prior to general surgical procedures.[5] This preventive practice has also been adopted with regards to dental procedures. Some nephrologists or dentists prescribe prophylactic antibiotics to prevent VAIs in hemodialysis patients undergoing dental treatment. However, a systematic review by Lockhart et al. found that there is no scientific evidence linking oral microorganisms to systemic infections in renal hemodialysis patients.[6] While some dental procedures can induce transient bacteremias,[6, 7] there is no evidence that these bacteremias cause VAIs. Further, guidelines from the American Heart Association indicate that antibiotic prophylaxis is not routinely recommended for dental procedures in patients with hemodialysis vascular access grafts.[8] Both publications indicated that additional research is needed on this issue. It is being increasingly recognized that such prophylactic use of antibiotics may serve minimal benefit and can result in potential significant harm. The risks of unnecessary antibiotic use include the development of resistant strains of bacteria; financial costs to the patient and/or society; and risk of adverse reactions such as rash, gastrointestinal upset, and possibly anaphylactic shock leading to death. Thus, the rationale for antibiotic prophylaxis for various medically complex patient populations undergoing invasive dental procedures is currently being challenged.[6]

A survey of infectious disease specialists, regarding the need for antimicrobial prophylaxis to prevent distant site infection, revealed differing opinions. Of 477 respondents questioned specifically about prophylaxis for patients on hemodialysis with dialysis catheters or shunts, less than 20% reported that they "always or usually" recommended such prophylaxis prior to invasive dental procedures. Moreover, approximately 45% of the respondents indicated that they "never" recommend prophylaxis for such patients.[9] Importantly, 90% of these infectious disease specialists indicated that additional research is needed to determine indications for antibiotic prophylaxis before dental procedures in various medically complex populations.[9] There is thus a pressing need for additional data on whether oral microorganisms can contribute to infections associated with vascular access in renal hemodialysis patients. In this study, we sought to determine the potential role of oral microorganisms in causing VAIs in hemodialysis patients, by identifying the microorganisms associated with such infections and determining whether they are normal inhabitants of the oral cavity.

Methods

This retrospective record review was conducted at the University of Connecticut Health Center (UCHC). Approval for the study was received from the UCHC Institutional Review Board and from Dialysis Clinic Inc. (DCI), which operates the UConn Dialysis Center in Farmington, CT. All research procedures were conducted in compliance with the Declaration of Helsinki. Electronic medical records were reviewed for all 218 patients

undergoing renal hemodialysis at the UCHC Dialysis Clinic between January 1, 1999 and February 27, 2009. Patients on peritoneal dialysis were not included.

A vascular access-associated infection (VAI) was defined as the occurrence of any of the following types of dialysis events, as defined by the Centers for Disease Control and Prevention.[10]

- Local access infection: Pus, redness, or swelling of the vascular access site; and access associated bacteremia was not present.
- Access-associated bacteremia: Blood culture positive with source identified as the vascular access site; or source was unknown (i.e. absence of any other documented infection).[10]

The following information was retrieved from the electronic medical records by a careful review of progress notes and other records: demographic data including date of birth, gender, and ethnicity/race; medical history information; mode of vascular access (arteriovenous (AV) graft, AV fistula, catheter, or a combination); dates of VAIs; and medical status at time of VAI. In addition, reports of microbial cultures (from blood and/or vascular access sites) were reviewed to identify the specific microorganism(s) associated with these infections. Microorganisms were identified by trained microbiology laboratory personnel using standard culture techniques and biochemical analyses in the John Dempsey Hospital clinical laboratory at the University of Connecticut Health Center.

To determine if microorganism(s) associated with VAIs could have originated from the oral cavity, the Human Oral Microbiome Database[11] was consulted. This is an NIH-supported comprehensive online database listing all known bacteria found in the human oral cavity by molecular cloning techniques. VAIs associated with bacteria were classified based on whether or not the associated microorganism(s) were found in the HOMD. For VAIs associated with yeast, this classification was based on literature documenting the presence of the associated yeast in the oral cavity.[12, 13]

Data were recorded in an Excel database and analyzed using descriptive statistics to assess the overall incidence of VAIs and nature of associated microorganisms. The proportions of VAIs associated with microorganisms found in the HOMD, across the different vascular access types, were compared using an Exact test because of small cell frequencies. A p value less than 0.05 was considered statistically significant.

Results

Incidence of VAIs and Subject Characteristics

Of the 218 renal hemodialysis patients for whom medical records were reviewed, 65 patients (29.8%) were found to have had at least one episode of a VAI. There were a total of 115 VAIs across these 65 patients. Therefore, a subsample of 65 patients and 115 VAIs was used for further analyses. In the 65 patients who experienced VAIs, the mean age was 65.6 years; 66 percent were male (n = 43) and 34 percent were female (n = 22). Ethnicity/race for the 65 patients was as follows: 40 patients were White; 13 were Black; 9 were Hispanic; 1 was Asian; and 2 were of unknown ethnicity/race. The most common co-morbidities in these patients were diabetes mellitus (34 patients), hypertension (49 patients), and coronary artery disease (17 patients), with many patients having multiple co-morbidities. Of the 115 VAIs, 50 (43.5%) occurred in patients with diabetes mellitus, 87 (75.7%) in patients with hypertension, and 35 (30.4%) in patients with coronary artery disease. Of the 65 patients, 37 (56.9%) received hemodialysis through a catheter; 16 (24.6%) through an AV fistula; 3 (4.6%) through an AV graft; 8 (12.3%) received hemodialysis through two different

vascular access types over the study period; and in 1 patient the involved access type(s) used was not able to be determined. Of the 8 patients who had 2 different access types over the study period, 7 patients received hemodialysis through a catheter and an AV fistula, and 1 patient received hemodialysis through a catheter and an AV graft.

Characteristics of VAIs

Of the 115 episodes of VAI, 60 (52.2%) met the CDC definition of local access infection and 55 (47.8%) met the CDC definition of access-associated bacteremia. Of the 115 episodes of VAI, 63 (56%) episodes involved patients with a catheter; 22 (19%) episodes involved patients with an AV fistula; 20 (17%) episodes involved patients with both a catheter and a fistula; 5 (4%) episodes involved patients with a graft; and 4 (3%) episodes involved patients with both a catheter and a graft. The access type for one VAI episode was not able to be determined based on available records.

Microorganisms Associated with VAIs

Twenty-eight different microorganisms were identified in association with the 115 episodes of VAI across 65 patients. Of these 28 microorganisms, 25 (89.3%) were bacteria identified at the species level; 2 (6.9%) were yeast identified at the species level; and 1 (3.4%) was a bacterium identified at the genus level. *Staphylococcus aureus* (including *methicillin-resistant Staphylococcus aureus* (MRSA)) was the most common microorganism associated with VAIs, involved in 57 of the 115 (49.6%) episodes. Other prominent bacteria included *Serratia marcescens* (10.4%), *Staphylococcus epidermidis* (10.4%), Pseudomonas aeruginosa (9.6%), and Enterococcus faecalis / fecum (8.7%) (Tables 1 and 2). Of the 115 VAIs, 22 were associated with more than one microorganism (polymicrobial infections).

VAIs Associated with Infrequent Colonizers of the Teeth and Plaque

Of the 25 VAI-associated bacteria identified at the species level, 12 were found in the HOMD. All of these microorganisms were identified in very low clone numbers in the HOMD, ranging from 3 to 171, of a total of 34,879 total clones tested for the HOMD project. Ninety-six VAIs were associated with bacteria found in the HOMD and 4 VAIs were associated with yeast (*Candida albicans* or *Candida parapsilosis)* that have been isolated from the oral cavity.[12,13]*Staphylococcus aureus* (including MRSA) (involved in 57 VAIs) and *Staphylococcus epidermidis* (12 VAIs) were the most common of such microorganisms associated with VAIs. However, their prevalence in the HOMD clone libraries is extremely low (less than 0.05%). Since most samples for the HOMD project were derived from teeth and subgingival plaque, low prevalence in the HOMD clone libraries indicates that these microorganisms infrequently colonize the teeth and plaque.

Association of Infrequent Colonizers of Teeth/Plaque with VAIs, by Vascular Access Type

Of the 63 VAIs associated with a catheter alone, 54 (86%) were associated with at least one microorganism that can infrequently colonize the teeth and plaque, based on presence in the HOMD in low clone numbers. For fistulas alone, this number was 20 of 22 (91%) VAIs and for grafts alone, 5 of 5 (100%) VAIs. Of the patients who had 2 different access types over the study period, 16 of the 20 VAIs (80%) in patients with both a catheter and a fistula were associated with infrequent colonizers of teeth and plaque. In patients with both a catheter and a graft, all 4 VAIs were associated with infrequent colonizers of teeth and plaque. There was no significant difference among the different access types in the proportion of VAIs with involvement of infrequent colonizers of teeth and plaque ($p = 0.654$).

Lack of Involvement of the Most Common Colonizers of Teeth and Plaque in VAIs

To assess the involvement of the most common colonizers of teeth and plaque with VAIs, we examined the most common microorganisms in the HOMD, ordered according to the number of clones in which each microorganism was identified. A total of 16 specific microorganisms (Table 3) were found in 1% or more of the 34,879 total clones tested for the HOMD project. Thus, these were the microorganisms most commonly isolated from the oral cavity in the HOMD project. A comparison of these 16 bacteria with those found to be associated with VAIs (Table 1), found that none of these 16 bacteria were associated with VAIs.

Discussion

Infections associated with vascular access are a significant source of morbidity in hemodialysis patients. The results of this retrospective chart review indicated that almost one-third of the hemodialysis patients reviewed experienced at least one VAI, with many experiencing multiple infections.

In order to examine the potential contribution of the oral microflora to VAIs, we examined the microorganisms associated with the VAIs, with respect to whether they are normal inhabitants of the oral cavity. A large proportion of the VAIs were found to be associated with at least one microorganism that is present in the HOMD for bacteria. However, these microorganisms were found in the HOMD in very low clone numbers. The extremely sensitive molecular techniques, including amplification, used for the HOMD can result in the inclusion of microorganisms present in very small numbers, as well as at very low prevalence. It should be noted that prevalence in the HOMD clone libraries does not numerically equal prevalence in the general population. This is because the HOMD combined samples from several different studies, health states, and oral sites, in unequal proportions, and using different primer pairs.[14] All these variables can impact on the prevalence of a given microorganism in the HOMD clone libraries. However, in general, those microorganisms found in the HOMD at highest clone numbers are highly likely to be the most prevalent in the oral microbial population and vice versa. Further, most of the HOMD samples were derived from subgingival plaque and teeth. Since these sites are the major contributors to any bacteremia secondary to the most common invasive dental procedures (such as extractions), the HOMD actually better represents the microbiology of these sites than a sampling of all sites in the oral cavity. Thus, it is far more likely that these VAI-associated microorganisms originated from another body site. For example, the bacteria associated with the largest number of VAIs were *Staphylococcus aureus* and *Staphylococcus epidermidis*, which are much more likely to originate from the skin than from the mouth.[15-17] This is also supported by the very low prevalence of these microorganisms in the HOMD clone libraries.

To specifically assess the role of the most common colonizers of teeth and plaque in VAIs, we compared the bacteria most commonly found in the HOMD to those associated with VAIs in our study sample. This comparison showed that none of the most common colonizers of teeth and plaque was found to be associated with a VAI. Lockhart[18] identified microorganisms from blood cultures taken at 1 minute (53 microorganisms) and 3 minutes (65 microorganisms) after the initiation of a dental extraction. Thus, these microorganisms constituted a bacteremia induced by an invasive dental procedure. Only 1 specific microorganism thus identified (*Streptococcus salivarius*) was found to be associated with a single VAI in our study. Collectively, these data indicate that is exceedingly unlikely to find a VAI-associated microorganism colonizing the teeth and plaque.

Shariff et al.[19] examined microbial blood culture data involving a total of 72 VAIs in a group of 51 hemodialysis patients (32 patients via retrospective chart review and 19 patients prospectively). Most of the infections were found to be caused by *Staphylococci* and *Enterococci*, which is consistent with our findings. These were classified as "unlikely or rarely oral flora", based on the available literature. Therefore the authors concluded that oral microorganisms rarely, if ever, cause vascular access infections in hemodialysis patients. In the current study, we used a different method of classifying microorganisms, based on presence or absence in the Human Oral Microbiome Database. This database includes all bacteria that have been identified in the oral cavity by molecular cloning techniques. Despite the different methods of classifying microorganisms, results from both studies predominantly implicated microorganisms that are more likely to originate from sites other than the oral cavity.

A limitation of our study was that the medical records did not provide documentation on any dental procedures for the patients reviewed, and we did not have access to their dental records. This precluded investigation into any temporal relationships between invasive dental procedures and subsequent VAIs. Due to the retrospective nature of the study, we could not obtain oral cultures or information on the oral health status of the subjects. Thus, no evaluation of the relationship between oral status and VAIs was possible. Another limitation was that standard culture methods were used by the clinical laboratory for identification of microorganisms. Bahrani-Mougeot et al. demonstrated that DNA sequencing results in more accurate identification of bacteria than culture-based techniques.[20] However, the standard culture-based techniques are well-accepted and used in most hospitals for speciation and to base clinical treatment decisions on.

In conclusion, this study suggests that the true risk of a VAI caused by microorganisms originating from the oral cavity is very small. These findings support the AHA recommendation that antibiotic prophylaxis is not routinely needed for dental procedures in hemodialysis patients.

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References

[1]. Vecihi Batuman, M. Pradeep Arora, M., editor. [cited 2012 Apr 13] [Internet] Chronic Kidney Disease. FACP, FASNupdated 2012 March 28Available from: http://emedicine.medscape.com/article/238798-overview#a0156

[2]. USRDS. Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases [Internet]; US Renal Data System; Bethesda (MD): 2011. Available from: http://www.usrds.org/qtr/default.aspx [cited 2011 November 25]

[3]. Tokars J, Miller E, Stein G. New national surveillance system for hemodialysis-associated infections: initial results. Am J Infect Control. 2002; 30:288–95. [PubMed: 12163863]

[4]. Berman S. Infections in patients with end-stage renal disease. An overview. Infect Dis Clin North Am. 2001; 15:709–20. vii.

[5]. Zibari G, Gadallah M, Landreneau M, McMillan R, Bridges R, Costley K, et al. Preoperative vancomycin prophylaxis decreases incidence of postoperative hemodialysis vascular access infections. Am J Kidney Dis. 1997; 30:343–8. [PubMed: 9292561]

[6]. Lockhart P, Loven B, Brennan M, Fox P. The evidence base for the efficacy of antibiotic prophylaxis in dental practice. J Am Dent Assoc. 2007; 138:458–74. [PubMed: 17403736]

[7]. Lockhart P, Durack D. Oral microflora as a cause of endocarditis and other distant site infections. Infect Dis Clin North Am. 1999; 13:833–50. vi. [PubMed: 10579111]

[8]. Baddour LM, Bettmann MA, Bolger AF, Epstein AE, Ferrieri P, Gerber MA, et al. Nonvalvular cardiovascular device-related infections. Circulation. 2003; 108:2015–31. [PubMed: 14568887]

[9]. Lockhart P, Brennan M, Fox P, Norton H, Jernigan D, Strausbaugh L. Decision-making on the use of antimicrobial prophylaxis for dental procedures: a survey of infectious disease consultants and review. Clin Infect Dis. 2002; 34:1621–6. [PubMed: 12032898]

[10]. Centers for Disease Control and Prevention. [cited 2011 Dec 20] Dialysis Events. [Internet]. Available from: http://www.cdc.gov/nhsn/psc_da_de.html

[11]. Chen T, Yu W-Han, Izard J, Baranova OV, Lakshmanan A, Dewhirst FE. The Human Oral Microbiome Database: a web accessible resource for investigating oral microbe taxonomic and genomic information 2010. Database, Vol. 2010 Article ID baq013, doi: 10.1093/database/baq013]. Available from: http://www.HOMD.org.

[12]. Ghannoum M, Jurevic R, Mukherjee P, Cui F, Masoumeh Sikaroodi M. Characterization of the oral fungal microbiome (mycobiome) in healthy individuals. PLoS Pathogens. 2010; 6:1–8.

[13]. Yang YL, Leaw SN, Wang AH, Chen HT, Cheng WT, Lo HJ. Characterization of yeasts colonizing in healthy individuals. Med Mycol. 2011; 49:103–6. [PubMed: 20491531]

[14]. Dewhirst FE, Chen T, Izard J, Paster BJ, Tanner AC, Yu WH, et al. The Human Oral Microbiome. J Bacteriol. 2010; 192:5002–17. [PubMed: 20656903]

[15]. Sychev D, Maya ID, Allon M. Clinical management of dialysis catheter-related bacteremia with concurrent exit-site infection. Semin Dial. 2011; 24:239–41. [PubMed: 21517993]

[16]. Minga T, Flannagan K, Allon M. Clinical consequences of infected arteriovenous grafts in hemodialysis patients. Am J Kidney Dis. 2001; 38:975–8. [PubMed: 11684549]

[17]. Chiller K, Slekin B, Murakawa G. Skin microflora and bacterial infections of the skin. J Investig Dermatol Symp Proc. 2001; 6:170–4.

[18]. Lockhart PB. An analysis of bacteremias during dental extractions. A double-blind, placebo-controlled study of chlorhexidine. Arch Intern Med. 1996; 156:513–20.

[19]. Shariff G, Brennan M, Louise Kent M, Fox P, Weinrib D, Burgess P, et al. Relationship between oral bacteria and hemodialysis access infection. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004; 98:418–22. [PubMed: 15472656]

[20]. Bahrani-Mougeot FK, Paster BJ, Coleman S, Ashar J, Knost S, Sautter RL, et al. Identification of oral bacteria in blood cultures by conventional versus molecular methods. Oral Surg Oral Med Oral Path Oral Radiol Endod. 2008; 105:720–4. [PubMed: 18485308]

Statement of Clinical Relevance

These findings suggest that oral microorganisms are rarely involved in causing infections associated with vascular access in hemodialysis patients. These data support the American Heart Association recommendation that antibiotic prophylaxis is not routinely needed for dental procedures in such patients.

Table 1

Vascular Access Infection (VAI) - associated microorganisms that are found in the Human Oral Microbiome Database (HOMD)

	Total Number of VAIs Associated with Each Microorganism	Number of VAIs associated with each microorganism by type of access device			
		Catheter	Graft	Fistula	Access Device Unknown
Bacteria identified at the species level					
Acinetobacter baumannii	2	1	0	0	0
Burkholderia cepacia	1	1	0	0	0
Enterococcus faecalis / fecum	10	6	1	3	0
Escherichia coli	5	4	0	1	0
Klebsiella pneumoniae	6	3	1	2	0
Pseudomonas aeruginosa	11	9	2	0	0
Staphylococcus aureus	31	22	3	5	1
Methicillin-resistant Staphylococcus aureus	26	13	1	12	0
Staphylococcus epidermidis	12	8	0	4	0
Staphylococcus warneri	1	0	0	0	0
Stenotrophomonas maltophilia	2	0	0	2	0
Streptococcus agalactiae	1	0	0	1	0
Streptococcus salivarius	1	0	0	1	0
Yeasts identified at the species level					
Candida albicans	2	2	0	0	0
Candida parapsilosis	2	2	0	0	0
Bacteria identified at the genus level					
Streptococcus alpha haemolytic	1	1	0	0	0

Table 2

Vascular Access Infection (VAI) - associated microorganisms that are NOT found in the Human Oral Microbiome Database (HOMD)

Name of Microorganism	Total Number of VAIs Associated with Each Microorganism	Number of VAIs associated with each microorganism by type of access device			
		Catheter	Graft	Fistula	Unknown Access Device
Bacteria identified at the species level					
Acinetobacter haemolyticus	1	1	0	0	0
Bacteroides fragilis	1	1	0	0	0
Enterobacter asburiae	1	1	0	0	0
Enterobacter aerogenes	2	2	0	0	0
Enterobacter cloacae	3	3	0	0	0
Escherichia vulneris	1	1	0	0	0
Morganella morganii	1	1	0	0	0
Pasteurella multocida	1	1	0	0	0
Providencia stuartii	2	2	0	0	0
Serratia marcescens	12	10	0	2	0
Staphylococcus auricularis	1	1	0	0	0
Staphylococcus hominis subsp. hominis	3	0	0	3	0
Staphylococcus saccharolyticus	1	1	0	0	0

Table 3

Most common specific microorganisms present in the HOMD (defined as those species found in 1% or more of clones tested for the HOMD project).

Rank in the HOMD	Microorganism
1	Veillonella parvula
2	Streptococcus mitis
3	Streptococcus mutans
4	Streptococcus sanguinis
5	Veillonella dispar
6	Streptococcus anginosus
7	Gemella morbillorum
8	Gemella haemolysans
9	Granulicatella adiacens
10	Streptococcus gordonii
11	Fusobacterium nucleatum subsp. vincentii
12	Dialister invisus
13	Streptococcus mitis bv. 2
14	Streptococcus parasanguinis II
15	Campylobacter gracilis
16	Selenomonas noxia