Effect of Antibiotic Administration Prior to Bone Sample Obtainment on Bone Culture Yields in Diabetic Foot Osteomyelitis

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Introduction

- Bone sample collection is considered a cornerstone of the process of diagnosing diabetic foot osteomyelitis[1]
- Histological data and microbiological data are essential for establishing a diagnosis as well to help guide antibiotic therapy and potentially avoid unnecessary antibiotic usage[1,2]
- Guidelines recommend obtaining bone samples once patients are off systemic antibiotics for two weeks, however data to define optimal timing of bone sample collection specifically in the setting of diabetic foot osteomyelitis is currently lacking[1]

Methods

Study Objectives:

- Determine if receipt of antibiotics prior to bone sample collection affects whether an organism is identified on bone culture
- Determine whether there are any clinical variables predictive of microbiological yield

Study Design and Setting:

- This is a single-site, retrospective observational study
- A list of patients with any iteration of "diabetic foot infection" and "osteomyelitis" in their problem list (both active and resolved problems were queried) within the date range of April 1 2015 through April 30 2018 were screened for inclusion
- Patients were excluded from the study if they were documented to have necrotizing fasciitis or if they left the hospital against medical advice (AMA)

Statistics:

- Outcomes will be compared using student's t-test, Wilcoxon-rank sum, or Chi-square tests as appropriate
- Logistic regression will be used to determine if any clinical variables were predictive of microbiological growth on cultures

Inclusion Criteria:

- At least 18 years old and diagnosed with diabetes
- Diagnosed with diabetic foot osteomyelitis based on clinical criteria
- Had an evaluable bone sample
- Received at least one dose of antibiotic outside of pre-operative antibiotics during hospitalization

Clinical criteria used to diagnose diabetic foot osteomyelitis:

- Presence of imaging demonstrating osteomyelitis, documentation of wound probing to bone, or visible bone in wound
- AND an elevated erythrocyte sedimentation rate (ESR) or elevated C-reactive protein (CRP) drawn during the admission

Evaluable bone sample definition:

- Bone sample with evidence of microbiological growth or histological evidence of osteomyelitis
- Sampling error was considered to have occurred when bone samples had neither microbiological growth nor histological evidence of osteomyelitis – these were excluded

Results

480 encounters screened for inclusion → 115 encounters included

365 encounters excluded:
- N = 266 admitted for condition other than diabetic foot osteomyelitis
- N = 58 did not meet diagnostic criteria
- N = 13 no bone sample available
- N = 15 with unevaluable bone sample
  - N = 8 with cultures not ordered
  - N = 2 with pathology not ordered
  - N = 5 with sampling error
- N = 3 did not receive antibiotics
- N = 4 diagnosed with necrotizing fasciitis
- N = 6 left AMA

Demographics:

	Abx given prior (n = 78)	Abx given post (n=37)
Age, years (mean ± SD)	52.7 ± 8.4	53 ± 8.5
Male	58 (74.4)	33 (89)
LOS, days (mean ± SD)	8.4 ± 6.0	7.4 ± 3.2
Osteomyelitis on imaging	67 (85.9)	36 (97.3)
Wound probing to bone	46 (58.9)	23 (62.2)
Visible bone in wound	9 (11.5)	4 (10.8)
ESR elevated	74 (94.7)	36 (97.3)
ESR (median [IQR])	94 (67 – 121.5)	89 (77 – 124)
CRP elevated	66 (84.6)	35 (94.6)
CRP (median [IQR])	138.3 (45.3 – 202.1)	53.3 (29.9 – 99.8)
Peripheral vascular disease	14 (17.9)	6 (16.2)
ESRD on hemodialysis	5 (6.4)	3 (8.1)
HIV with CD4 <200 or < 14%	0	0
Immunosuppressive therapy within 3 months of admission		
Chemotherapy	0	0
Monoclonal antibodies	1 (1.3)	1 (2.7)
TNF-inhibitor	0	0
Steroids[a]	0	0
Transplant anti-rejection therapy	0	0

Values are n (%) unless otherwise stated
Abbreviations: Abx = antibiotics; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; LOS = length of stay; ESRD = end-stage renal disease; HIV = human immunodeficiency virus; TNF = tumor necrosis factor
[a]dose equivalents of at least 20 mg per day of prednisone for at least 3 weeks

Microbiology Data:

	Abx given prior (n = 78)	Abx given post (n = 37)	P value
Growth on culture	61 (78.2)	28 (75.7)	0.762
No abx prior to admission	60 (76.9)	28 (75.7)	
Growth on culture	50/60 (83.3)	23/28 (82.1%)	0.890

Values are n (%) or n/N (%)
Abx = antibiotics

78 patients received antibiotics prior to bone sample obtainment; time between first dose of antibiotic and bone sample collection compared:
- 2 ± 1.4 days in those without growth on cultures
- 1.6 ± 2.3 days in those with growth on cultures (p = 0.0942)

Bone Sample Characteristics:

	Abx given prior (n = 78)	Abx given post (n = 37)
Bedside biopsy	5 (6.4)	6 (16.2)
OR open biopsy	73 (93.6)	31 (83.8)
Osteomyelitis identified		
Acute	64 (82.1)	25 (67.6)
Chronic	5 (6.4)	3 (8.1)
Acute-on-chronic	2 (2.6)	5 (13.5)
None	7 (8.9)	4 (10.8)
Time from ED admission to sample obtainment (days, mean ± SD)	1.8 ± 2.1	1.1 ± 1
Time from first dose abx to bone biopsy (days, mean ± SD)	1.7 ± 2.1	n/a

Values are n (%) unless otherwise specified
Abx = antibiotics; OR = operating room; ED = emergency department

Microbiological Growth identified:

	Abx given prior (n = 61)	Abx given post (n = 28)
Polymicrobial growth	40 (65.6)	15 (53.6)
MRSA identified	10 (16.4)	5 (17.9)
***Pseudomonas* identified**	1 (1.6)	2 (7.1)
Anaerobes identified	23 (37.7)	7 (25.0)
Gram positive identified	53 (86.8)	26 (92.3)
Gram negative identified	14 (22.9)	7 (25.0)

Values are n (%)
Abx = antibiotics; MRSA = methicillin-resistant *Staphylococcus aureus*

Antibiotic Usage:

	Abx given prior (n = 78)	Abx given post (n = 37)	P value
Anti-MRSA agent, n (%)	78 (100)	35 (94.6)	
DOT anti-MRSA agent	4.4 (2.6 – 6.4)	3.7 (2 - 5.8)	0.257
Anti-*Pseudomonas* agent, n (%)	75 (96.2)	33 (89.2)	
DOT anti-pseudomonal agent	4 (2.5 – 6.2)	2 (1.9 – 4.3)	0.067

Values are median (IQR) unless otherwise stated
Abx = antibiotics; MRSA = methicillin-resistant *Staphylococcus aureus;* DOT = days of therapy

Regression Analysis:

Logistic regression analysis performed to see if any of the following variables were predictive of microbiological growth on cultures:
- Peripheral vascular disease
- End-stage renal disease
- Beside vs open biopsy
- Type of osteomyelitis identified
- Receipt of antibiotics prior to admission
- Use of anti-MRSA agent
- Use of anti-*Pseudomonas* agent

None of the variables showed any association with microbiological yield.

Discussion

- Current data examining if pre-treatment with antibiotics affect bone culture results has yielded mixed results[3-7], with much of the literature focusing on vertebral osteomyelitis[3-7,10,13]; few studies focus on non-vertebral osteomyelitis[8,9,11,12]
- Recent meta-analysis suggests vertebral osteomyelitis and non-vertebral osteomyelitis are dissimilar enough that it may not be appropriate to extrapolate findings on effect of pre-treatment with antibiotics on culture yields from vertebral osteomyelitis to non-vertebral osteomyelitis[14]
- To our knowledge, this is the first study to focus on diabetic foot osteomyelitis and the effect of pre-biopsy antibiotics on culture yield
- This study suggests that up to 2 days of antibiotic administration for treatment of diabetic foot osteomyelitis does not affect culture yield. Of the variables examined via logistic regression, none were found to be predictive of microbiological growth on cultures.
- A major limitation of this study is that it is a single-center study – practice differences within other institutions may account for differences seen in the literature
- For example, within our cohort – average time from admission to bone biopsy obtainment was between 1.1 to 1.8 days; Marschall et al[4] report a median of 3 days from admission to bone biopsy.
- Antibiotic exposure prior to bone biopsy may also differ between institutions – within our cohort, mean days of antibiotic exposure prior to biopsy was only 1.7 days; Kim et al[3] report median of 8 days antibiotic exposure within group who did not have growth on cultures and median of 4 days in those who did have growth on culture
- Another limitation to this study is its retrospective nature, which makes it difficult to control for all aspects of patient care that may affect culture yields
- In conclusion, our study suggests that receipt of up to two days of antibiotics prior to bone biopsy is unlikely to affect culture yields; larger prospective studies are needed to better define the duration of antibiotic therapy at which a difference in bone culture yields can be expected

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