Microbiology Diagnostics and Antibiotic Treatment in Diabetic Foot Infection in a Teaching Hospital

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Introduction

Deep tissue and bone samples are advised in patients with diabetic foot infections to rationalise antibiotic regimens. We studied the yield of microbiological testing, whether culture results influenced final antibiotic choice and whether the empirical choice was appropriate.

Methods

- All diabetic patients who had a deep foot tissue sample between January 2012 and December 2013 at our Centre were identified from the microbiology laboratory database (Telepath).
- Using the Infectious Diseases Society of America (IDSA) and International Working Group on the Diabetic Foot (PEDIS) classifications, each patient's presenting condition was graded 1 (no infection) to 4 (severe infection)[1].
- Osteomyelitis (OM) was treated as a discrete diagnostic entity.
- Information was collected on the microbiology gram stain, culture and susceptibility results.
- Further information was collected from the hospital patient information and communication system (PICS) on the antibiotics prescribed at the time of collection and at the time the final report of the culture result was received.
- The antibiotics prescribed were compared to our local prescribing guidelines. *Table 1*

Table 1

Infection severity	1st choice antibiotic	2nd choice	MRSA positive
Mild (2)	Flucloxacillin 1g QDS PO	Clindamycin 450mg QDS PO	Vancomycin 1g BD IV or Doxycycline 200mg Stat, 100mg BD PO
Moderate (3)	Co-amoxiclav 625mg TDS PO or 1.2g TDS IV	Clindamycin 300-450mg QDS PO or 300-600mg QDS IV and Ciprofloxacin 500mg BD PO or 400mg BD IV	As 2nd choice or Vancomycin 1g BD IV and Rifampicin 600mg BD PO and Ciprofloxacin 500mg BD PO or 400mg BD IV or Replace Rifampicin with Sodium fusidate 500mg TDS PO
Severe (4)	Meropenem 1g TDS IV	Clindamycin 600 mg IV and Ciprofloxacin 400 mg IV	Meropenem 1g TDS IV and Vancomycin 1g BD IV and Rifampicin 600mg BD PO
Osteomyelitis (OM)	If stable, delay antibiotics until surgical or radiological sampling otherwise…		
	Flucloxacillin 2g QDS IV and Ciprofloxacin 750mg BD PO and Metronidazole 400mg TDS PO	Clindamycin 450mg QDS PO or 600mg QDS IV and Ciprofloxacin 750mg BD PO	Vancomycin 1g BD IV and Ciprofloxacin 750mg BD PO and Metronidazole 400mg TDS PO

Results

Demographics

- One hundred and eighteen samples from 74 patients were examined.
- For 6 patients (8 samples) we were unable to obtain antibiotic prescribing information. These patients were only included in the analysis of the culture results.
- Mean age of patients was 62 years (range 27-88 years).
- 77% of patients were male.
- 69% of the samples were taken within an operating theatre and the remainder in an outpatient clinic setting or on the ward.
- 71% of samples were bone samples, with the rest represented by soft tissue samples.

Gram stain

- In 50% of samples an organism was seen (not including no predominant organism). *Table 2*
- 45.8% (n=54) of gram stains were in agreement with the final culture result.
- Overall sensitivity and specificity of the gram stain compared to culture was poor (76% and 73%, respectively), specificity was particularly poor (35%) for gram positive cocci and sensitivity was particularly poor (24%) for gram negative rods. *Table 3*

Table 2

Gram stain result	N (%)
No organisms seen	46 (39.0)
No predominant organism	13 (11.0)
Gram positive cocci	45 (38.1)
Gram negative rods	10 (8.5)
Gram positive rods	4 (3.4)

Table 3

Gram Stain result	Sensitivity (%)	Specificity (%)
Gram positive cocci	86	35
Gram positive rods	50	96
Gram negative rods	24	97
Overall	76	73

Culture results

- 95 (80.5%) of samples had a positive culture with a median of 2 organisms per sample (range 0-5). *Graph 1*
- Excluding anaerobic growth and 1 candida species , at least 1 gram positive organism was isolated in 59 (50.0%) samples and gram negatives in 47 (39.8%).
- In 22 (18.6%) samples there was no growth.
- 24 (20.3%) grew both gram positive and gram negative organisms.
- The organism most commonly isolated was *Escherichia coli* (n=13, 9.8%), followed closely by coagulase negative Staphylococcus (n=12, 9.0%).
- Methicillin Resistant *Staphylococcus aureus* (MRSA) was isolated in 7 patients (9.5%), this was a new diagnosis in 3 of the patients.
- Vancomycin Resistant Enterococci (VRE) were isolated in 2 patients (2.7%), a new diagnosis in both.
- There was no significant difference between the organisms isolated in the different ulcer grades (p = 0.206). *Graph 2*
- Despite a clinical diagnosis of OM, 7 samples failed to grow any organisms.
- Polymicrobial growth was identified in all grades of ulcer. *Graph 3*
- When the isolates from the samples received in the lab on the same day of sampling were compared to those received the following day there was no significant difference (p = 0.258). *Table 4*

Table 4

Received in the lab same day	Gram -ve (%)	Gram +ve (%)	Mixed anaerobes (%)	No growth (%)	Total
Yes	37 (29.4)	55 (43.7)	16 (12.7)	18 (14.3)	126
No	22 (36.7)	21 (35.0)	12 (20.0)	5 (8.3)	60

Antibiotic use

- Antibiotic prescribing information was only available for 68 patients (110 samples).
- At the time the sample was taken, 70% of the patients were already on antibiotics, but in only 33.6% was the antibiotic decision appropriate.
- After the final culture report was received, 85.5% of patients were on an appropriate antibiotic regimen. This meant 63.6% of patients had a change of antibiotic regime in relation to the final report. *Graph 4*
- The most common antibiotic choices are shown in *Tables 5 & 6.*

Table 5

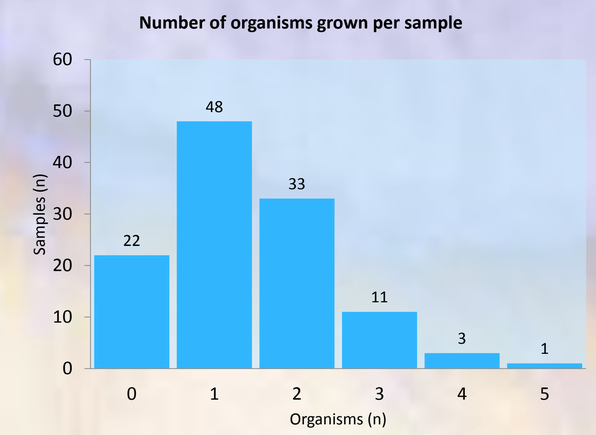
Most common empirical antibiotics			
Monotherapy	n (%)	Combined therapy	n (%)
Co-amoxiclav	13 (15.5)	Ciprofloxacin/ Metronidazole/ Flucloxacillin*	6 (7.1)
Flucloxacillin	10 (11.9)	Ciprofloxacin/ Clindamycin*	4 (4.8)
Piperacillin-tazobactam	7 (8.3)		
Clindamycin	7 (8.3)		

Table 6

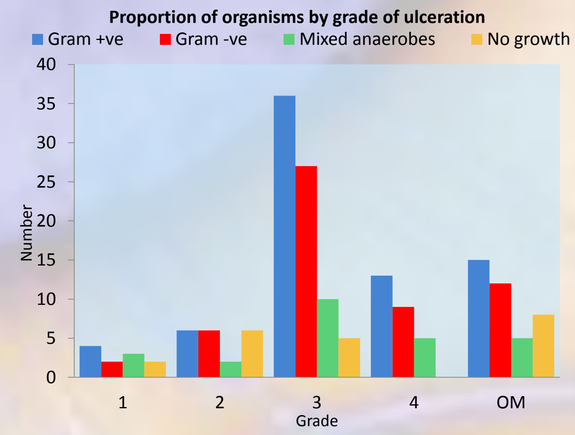
Most common antibiotics guided by report			
Monotherapy	n (%)	Combined therapy	n (%)
Co-amoxiclav	12 (13.6)	Ciprofloxacin/ Metronidazole/ Flucloxacillin*	6 (7.10)
Flucloxacillin	11 (12.5)	Benzylpenicillin/ Flucloxacillin	5 (5.7)
Clindamycin	8 (9.1)	Ciprofloxacin/ Clindamycin*	4 (4.8)

*Combined therapy guided by local prescribing guidelines or Microbiologist advice.

Graph 1

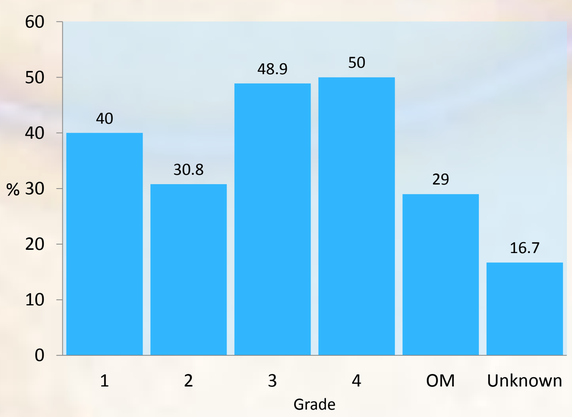


Graph 2

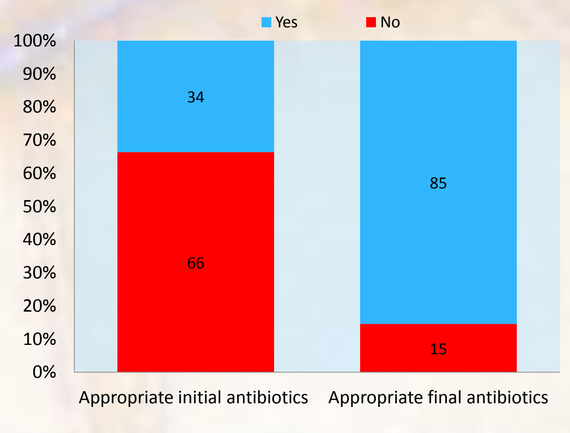


N=112, 6 samples unable to extract grade of ulcer retrospectively

Graph 3



Graph 4



Discussion

- Microbiological testing often reveals polymicrobial growth in diabetic foot infections, even at lower grades of infection, confirming the role of tissue sampling in guiding therapeutic choices.
- Culture yield may not be affected if there is a delay in processing.
- There is considerable adjustment of antibiotic regimens in response to culture results supporting that the results are clinically relevant and acted upon.
- Microscopy may not be useful in guiding therapeutic choices given the poor correlation with the final culture results.
- Despite available local and international guidance, diabetic patients are still started occasionally on inappropriate empirical antibiotics for their foot infection. In many cases, this was represented by the use of a single agent with mainly gram positive coverage (such as flucloxacillin) for grade 4 infections or OM. This may be due to clinicians erroneously considering the treatment of a diabetic foot infection to be the same as that for cellulitis in a non-diabetic patient.

Conclusion

The results confirm the polymicrobial nature of diabetic foot infection and highlight the major role played by the microbiological testing in improving the quality of antimicrobial prescribing in this group of patients.

Reference
1) Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;**54**(12):e132-73.

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Background image courtesy of Wellcome Images, www.wellcomeimages.org