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Research Article

Audit on Antibiotics Regimen in Diabetic Foot Ulcers - Are We Following Guidelines?

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Introduction

Lower limb infections are the most common indication for hospital admission in patients with diabetes. Diabetic foot ulcers are common and can lead to chronic osteomyelitis if not treated well. In the most severe forms of infection, patients are known to develop necrotizing fasciitis and subsequent shock from cardiovascular collapse may ensue. Antibiotics are very important in the management of these infected ulcers in addition to adequate surgical debridement of the ulcers. The diabetic foot is highly susceptible to repeated ulceration, hence are more prone to more serious infection than other ulcers, and left untreated infection can lead to serious consequences such as amputation. This cycle can be broken only by aggressive treatment [1]. The proper use of antibiotics in the treatment of the diabetic foot is important. By following proper guidelines, we feel that most diabetic foot infection can be treated based on different types of bacteria cultured and the most appropriate antibiotics over a set period of time. This audit looks at the compliance the types of antibiotics used in the treatment of diabetic foot ulcers.

Methods

A retrospective study over 10 months on 30 selected patients who satisfy the criteria of an infected diabetic foot ulcer with the following data was analyzed. The data collected included age, gender, microorganism culture, type of antibiotics used, multidrug-resistant microorganism, white-blood cell count (WBC), and C-reactive protein (CRP).

We reviewed the antibiotics used during the clinical treatment course and compared them to the established published guideline on antibiotics for diabetic foot ulcers from the article "Antibiotics for Diabetic Foot Infections" written by Amaris Lim Shu Min and Aziz Nather, NUH. Two antibiotics regimens are recommended in the book, the first based on the 2015 International Working Group on the Diabetic Foot (IWGDF) guidelines on the diagnosis and management of diabetic foot infections, and the second based on the 2012 IDSA Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections [2]. In our study, data analysis was performed using basic statistical methods. We collected the demographic features of the patient including name, age and gender as shown in Table 1. To ensure that patient identification is anonymized and confidential, initials of their names are used. Then, we collected the information regarding the types of bacteria grown in the wound culture from the diabetic foot ulcer as shown in Table 2. Using the results of the wound cultures and the recommended antibiotics, we compare the final antibiotics medication used against the published guidelines. In table 3, we showed the types of antibiotics used in each patient and marked patients whose treatment adhered to the guideline as "Yes" and for those that did not as "No". In table 4, we showed the multidrug-resistant organism and their medications involved. In the supplementary documents, we provide more details of our data collected and present it in table 5,6,7,8,9. We further analyze patients whose cultures grew multi-organisms and we presented the types of bacteria in table 5. Furthermore, we calculate the number of patients in each antibiotic used and present it in Table 6. The levels of WBC count and CRP were presented as before treatment. We separated these results into different grading (normal, mild, moderate, severe, not related) and presented in Table 7, 8 or 9.

Results

Table 1: *Demographic features of the diabetic foot patients.*

Patient's	Name	Age	Gender
1.	SBS	62Y9M	Female
2.	CTH	51Y4M	Male
3.	LPK	63Y11M	Male
4.	PDS	43Y10M	Female
5.	RBW	52Y11M	Female
6.	MIBA	38Y2M	Male
7.	TKT	64Y7M	Male
8.	ARBS	67Y9M	Male

9.	LML	52Y11M	Female
10.	AABA	58Y2M	Male
11.	YMF	58Y2M	Female
12.	TBA	64Y7M	Female
13.	KBK	50Y3M	Female
14.	HBA	58Y4M	Female
15.	MKBA	56Y4M	Male
16.	KSSDS	33Y0M	Male
17.	NBO	57Y11M	Female
18.	MNFBMR	30Y0M	Male
19.	TKC	72Y7M	Female
20.	NHC	57Y2M	Male
21.	CKH	57Y9M	Male
22.	NHL	40Y8M	Female
23.	CSS	63Y9M	Male
24.	LTF	43Y7M	Male
25.	GBSJ	64Y6M	Male
26.	MBR	57Y3M	Female
27.	HSSPS	59Y2M	Male
28.	OKJ	72Y4M	Female
29.	BA	50Y11M	Male
30.	NIP	61Y0M	Male

Table 2: *Types of bacteria grow in patient's wound culture*

Patient's	Name	Microorganism culture
1.	SBS	MRSA
2.	CTH	Pseudomonas aeroginosa
3.	LPK	Streptococcus dysgalactiae & Staphylococcus aureus
4.	PDS	Enterobacter aerogenes & Staphylococcus aureus & Streptococcus agalactiae (Group B)
5.	RBW	Staphylococcus aureus & Staphylococcus dysgalactiae & Streptococcus agalactiae
6.	MIBA	Pseudomonas aeroginosa, Staphylococcus aureus
7.	TKT	Staphylococcus lugdunensis & Klebsiella pneumoniae
8.	ARBS	Klebsiella pneumoniae & Pseudomonas aeruginosa & MRSA & Enterococcus faecium

9.	LML	Staphylococcus aureus
10.	AABA	Morganella morganii & Bacteroides fragilis group & Streptococcus agalactiae(Group B) & Escherichia coli
11.	YMF	Staphylococcus aureus & Streptococcus agalactiae
12.	TBA	Enterobacter cloacae complex & Serratia marcescens & Escherichia coli
13.	KBK	Proteus mirabilis & Klebsiella pneumoniae
14.	HBA	Staphylococcus aureus & Streptococcus dysgalactiae
15.	MKBA	MRSA & Pseudomonas aeroginosa
16.	KSSDS	Staphylococcus aureus & Streptococcus dysgalactiae
17.	NBO	Staphylococcus aureus & Streptococcus agalactiae
18.	MNFB-MR	Pseudomonas aeroginosa, Staphylococcus aureus, Streptococcus dysgalactiae, Arcanobacterium haemolyticum
19.	TKC	Pseudomonas aeroginosa, Streptococcus agalactiae
20.	NHC	Streptococcus dysgalactiae & Peptostreptococcus species, Bacteroides fragilis group, Proteus mirabilis
21.	CKH	Streptococcus agalactiae & Peptostrreptococcus species, Pseudomonas aeruginosa, Actinomyces species
22.	NHL	Streptococcus agalactiae
23.	CSS	Citrobacter koseri, Staphylococcus aureus, Bacteroides fragilis group
24.	LTF	Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus agalactiae(Group B), Peptostreptococcus species, Bacteroides fragilis group
25.	GBSJ	Staphylococcus aureus
26.	MBR	Escherichia coli, Enterococcus raffinosus, Coagulase negative staphylococcus, Corynebacterium species
27.	HSSPS	Streptococcus dysgalactiae, Fusobacterium species
28.	OKJ	Coagulase negative staphylococcus
29.	BA	Pseudomonas aeruginosa
30.	NIP	Pseudomonas aeruginosa, Serratia marcescens

Table 3: *Types of antibiotics used in each patients and compare whether the treatment follow the guideline. There all total 21 patients that marked with "Yes" and 9 patients that marked with "No". Therefore, the percentage of patients following the protocol is about 70%.*

Name	Antibiotics used	Follow Guideline
SBS	Clindamycin, Mupirocin	No
CTH	Cloxacillin & Ciprofloxacin	No
LPK	Bactrim (Trimethoprim, Sulfamethoxazole)	No
PDS	Ciprofloxacin & Clindamycin	Yes
RBW	Tetracycline	No
MIBA	Augmentin (amoxicillin & clavulanate), Piptazo(piperacillin/tazobactam)	Yes
TKT	Augmentin (amoxicillin & clavulanate)	Yes
ARBS	Vancomycin IV, Piptazo(piperacillin/tazobactam)	Yes
LML	Cefazolin	No
AABA	Ceftriaxone IV	Yes
YMF	Augmentin (amoxicillin & clavulanate)	Yes
TBA	Co-trimoxazole (sulphamethoxazole & trimethoprim)	No
KBK	Co-trimoxazole (sulphamethoxazole & trimethoprim)	No
HBA	Augmentin (amoxicillin & clavulanate)	Yes
MKBA	Mupirocin, Vancomycin IV	Yes
KSSDS	Augmentin (amoxicillin & clavulanate) & Clindamycin	Yes
NBO	Augmentin (amoxicillin & clavulanate)	Yes
MNFBMR	Augmentin (amoxicillin & clavulanate)	Yes
TKC	Ciprofloxacin & Augmentin (amoxicillin & clavulanate)	Yes
NHC	Augmentin(amoxicillin & clavulanate), Amoxycillin	Yes
CKH	Ciprofloxacin, Piptazo	Yes
NHL	Augmentin (amoxicillin & clavulanate)	Yes
CSS	Co-trimoxazole (sulphamethoxazole & trimethoprim)	Yes
LTF	Augmentin (amoxicillin & clavulanate), Ciprofloxacin	Yes
GBSJ	Levofloxacin	Yes
MBR	Metronidazole, Co-trimoxazole(sulphamethoxazole & trimethoprim)	No
HSSPS	Augmentin (amoxicillin & clavulanate)	Yes
OKJ	Cloxacillin	No
BA	Augmentin (amoxicillin & clavulanate), Tazocin(Piperacillin/Tazobactam)	Yes
NIP	Piperacillin-tazobactam	Yes

Table 4: *Multidrug resistant organisms and the medications involved. There were 10 out of the total of 30 patients that bacteria cultures showed multidrug resistant. The percentage of multidrug resistant, % MDR was 33.33%.*

Name	Multidrug resistant organism
SBS	MRSA (Penicillin G & Cloxacillin)
CTH	X
LPK	X
PDS	X
RBW	X
MIBA	X
TKT	x
ARBS	MRSA (Penicillin G, Cloxacillin, Clindamycin), Enterococcus faecium (Ampicillin, Doxycycline), Klebsiella pneumoniae (Ampicillin & Ciprofloxacin)
LML	X
AABA	Morganella morganii(Ampicillin, Augmentin, Ciprofloxacin, Cotimoxazole)
YMF	X
TBA	Enterobacter cloacae complex (Ampicillin, Augmentin)
KBK	X
HBA	X
MKBA	MRSA (Penicillin G, Cloxacillin, Clindamycin)
KSSDS	Staphylococcus auureus(Penicillin G, Co-trimxazole, Clindamycin)
NBO	X
MNFBMR	X
TKC	X
NHC	X
CKH	X
NHL	X
CSS	X
LTF	Staphylococcus auureus(Penicillin G, Co-trimxazole)
GBSJ	X
MBR	Escherichia coli(Ampicillin, Augmentin(amoxicilin, clavulanate), Ceftriaxone, Ceftazidime, Ciprofloxacin; Coagulase negative staphylococcus(Penicillin G, Cloxacillin, Clindamycin)
HSSPS	X
OKJ	Coagulase negative staphylococcus(Penicillin G, Cloxacillin)
BA	X
NIP	Serratia mercescens(Ampicillin, Augmentin)

Table 5: *Types of the bacteria and their frequency (number of cases).*

Bacteria cultured	Frequency
Arcanobacterium haemolyticum	1
Actinomyces species	1
Bacteroides fragilis group	4
Coagulase negative staphylococcus	2
Corynebacterium species	1
Citrobacter koseri	1
Enterobacter aerogenes	1
Enterococcus faecium	1
Enterobacter cloacae complex	1
Escherichia coli	3
Enterococcus raffinosus	1
Fusobacterium species	1
Klebsiella pneumoniae	3
MRSA	3
Morganella morganii	1
Pseudomonas aeroginosa	10
Peptostreptococcus species	3
Proteus mirabilis	2
Streptococcus dysgalactiae	7
Staphylococcus aureus	13
Streptococcus agalactiae (Group B)	9
Staphylococcus lugdunensis	1
Serratia marcescens	2
Total:	**72**

Table 6: *Showed different types of antibiotics and the total number of patients using it.*

Types of antibiotics	Number of patients using this antibiotic
Augmentin (amoxicillin & clavulanate)	14
Amoxycillin	1
Bactrim (Trimethoprim, Sulfamethoxazole)	1
Co-trimoxazole (sulphamethoxazole & trimethoprim)	4

Clindamycin	3
Cloxacillin	2
Ciprofloxacin	5
Cefazolin	1
Ceftriaxone IV	1
Levofloxacin	1
Mupirocin	2
Metronidazole	1
Tazocin/Piptazo(Piperacillin-tazobactam)	5
Tetracycline	1
Vancomycin IV	2

Table 7: *showed value of WBC and CRP in each patient.*

Name	WBC (*10^9/L)	CRP (H mg/L)
SBS	8.21	159
CTH	12.2	150
LPK	17.86	153
PDS	7.7	44
RBW	12.52	X
MIBA	14.2	169
TKT	11.53	X
ARBS	21.02	130
LML	6.11	25
AABA	9.7	54
YMF	15.09	85
TBA	15.23	114
KBK	24.65	188
HBA	13.7	249
MKBA	10.39	361
KSSDS	8.26	161
NBO	11.55	32
MNFBMR	14.58	38
TKC	6.69	46
NHC	18.71	263
CKH	13.22	102

NHL	19.71	203
CSS	20.4	214
LTF	12.42	259
GBSJ	14.44	66
MBR	11.46	102
HSSPS	8.48	128
OKJ	9.43	73
BA	5.99	57
NIP	7.66	232

Table 8: *showed grading of CRP and their frequency*

CRP	Range(*10^9/L)	Frequency
normal	0-10	0
mild	11-50	5
moderate	51-100	5
severe	>100	18
no related data	X	2
	Total:	**30**

Table 9: *showed grading of WBC and their frequency*

WBC	Range(*10^9/L)	Frequency
normal	3.84-10.01	10
mild	10.02-15.00	12
moderate	15.01-20.00	5
severe	>20.00	3
	Total:	**30**

Discussion

Diabetes mellitus is a common health problem in the world, causing a huge burden for individuals, families, and communities. Diabetes mellitus is the second most significant cause of disease in Singapore after ischaemic heart disease [3]. We should know that the major driving factors of the global type II diabetes epidemic include overweight and obesity, sedentary lifestyle and increased consumption of unhealthy diets containing high levels of red meat and processed meat, refined grains and sugar-sweetened beverages [4]. Nowadays, we should take more concern about the possible complication of diabetes. Among patients with type II diabetes, cardiovascular complications are the leading cause of morbidity and mortality, and kidney complications are highly prevalent in patients in Asia with diabetes mellitus [4]. Also, diabetes often affects

the circulation of the vascular, especially blood circulation of the foot, causing diabetic foot. There is a high association of foot complications in people with Type II diabetes [5]. It has been estimated that of patients with foot complications, approximately 25-44% are due to neuropathy, 10% are due to ischaemia and 45-60% are neuro-ischaemic, a combination of both. Infection is often the final complication leading to presentation. Neuropathy affects sensory, motor and autonomic nerves, each of which has deleterious consequences for the foot. Sensory neuropathy results in loss of protective sensation, allowing injury to go unnoticed. Peripheral artery disease (PAD) due to atherosclerosis is four times more common in patients with diabetes and around half of patients with a diabetic foot ulcer have co-existing PAD [6]. Diabetic foot complications continue to remain a major medical and public health issue as we face patients in increased numbers, age, and comorbidities. Diabetic foot complications are major sequelae of diabetes that often end in end-stage complications including lower-extremity amputations, shortened lifespan and the commensurate increased burden of social care [7]. So there is a strong need to increase the awareness about foot care knowledge, early screening, and identification and management of foot complications especially in people with type II diabetes. Although the treatment of diabetes foot is important, we cannot simply use any types of antibiotics. We need to use the correct one following the guideline. Misuse of antibiotics might cause many adverse effects. One of the studies in the USA showed that acute kidney injury (AKI) were more likely to have recurrent ulcerations, recurrent infections, and recurrent hospitalizations during follow-up. Besides, acute kidney injury occurred frequently in their patient population but the association with antibiotic exposure was uncertain [8]. Therefore, this reminds us of the importance of the correct decision in choosing antibiotics for the treatment of the diabetic foot. Many patients with diabetes mellitus who have the peripheral vascular disease are asymptomatic until they develop tissue loss. In the context of tissue loss, increasing ischemia elevates the risk of limb loss and, therefore, healing usually requires revascularization. Offloading, debridement, antibiotics, optimal glycemic control and a multidisciplinary team are fundamental to the effective treatment of diabetic foot complications [9]. The infected foot in a patient with diabetes is a surgical emergency. In addition to antibiotics, debridement and surgical drainage of infection should be considered within the first 24 hours. Once the foot is made safe, revascularization should be undertaken in those with significant arterial disease [6]. However, in our audit study, we only focused on antibiotic treatment.

In our study, we found that there were 70% of patients who were treated using the protocol written by the guideline mentioned above (Table 3). A total of 15 types of antibiotics were used, and the most commonly used antibiotic was Augmentin (Table 6). In our study, there were 17 male and 13 female patients with a mean age of 55 years and 6 months, ranging from 30 years old to 72 years and 7 months old(Table 1). A total of 23 types of microorganisms were cultured and 33.33% of the patients' wound grew multidrug-resistant microorganisms (Table 2 & Table 4). Studies at Istanbul University showed that among patients who were re-hospitalized, methicillin-resistant Staphylococcus infections was detected as the most common agent, and Klebsiella spp. infections were found to be significantly associated with fatality [10]. Therefore, it is important to identify the types of multidrug-resistant organism in the infected diabetic foot. Besides, many studies have cited that diabetic foot infection is polymicrobial, with aerobic gram-positive cocci and the most common causative organisms are staphylococci [11]. In our study, we obtained the same result as others and it showed that the most common microorganisms are Staphylococcus aureus (18%) and Pseudomonas aeruginosa (13.8%) (Table 5). There were 3 cases of MRSA treated with Vancomycin and Muciprocin or Clindamycin and Muciprocin. 56.7% of patients were treated with only one antibiotic whereas 43.33% of

patients were treated with two antibiotics. The percentage of only one microorganism cultured was 23.3%, with two microorganisms cultured were 40%, with three microorganisms cultured were 13.3%, with four microorganisms cultured were 20% whereas those with five microorganisms cultured were only 3.3% (Table 2). From table 8, we noted that most of the patients n=18, 60%) in our study had their CRP value >100 and graded as severe. From table 9, we noted that most of the patients (n=12, 40%) in our study had their WBC value in the range of 10.02-15.00 (*10^9/L) and graded as mild. To assess the severity of inflammation associated with DFI, we often measure the values of specific inflammatory markers like white blood count (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and neutrophil-to-lymphocyte ratio (NLR). Another study in the USA calls into question the utility of measuring and trending CRP, ESR, and NLR in patients with a diabetic foot infection. Instead, a cheaper and more accessible marker, WBC count, is more useful in assessing the severity of the diabetic foot at follow up [12]. The key to management of diabetic foot wounds is prevention, and our main efforts should be put into education. Education should mainly be directed at patients and caregivers, but also professionals (general practitioners, allied health professionals and nurses) so that they can effectively educate patients and caregivers. Patient education includes care of diabetes mellitus, care of the foot and use of appropriate footwear. Patients also tend to have poor foot hygiene. Annual foot screening for diagnosed diabetics plays an important role [3].

Conclusion

After reassessing our hospital protocol and current practice, we are confident to say that we have adhered closely to our established guideline. We would encourage other hospitals and treating physicians to diabetic patients to keep abreast with the latest published and evidence based treatment using antibiotics for diabetic foot ulcers. Diabetic foot ulcers are chronic conditions and we have presented based on our experience the likely and varied multiorganisms that cause these infected wounds and the recommended antibiotics. We also feel the need for a larger multicenter study with a more heterogenous group of patients from different ethnic and geographical backgrounds. This would help to strengthen the data and evidence for a more robust guideline in the future.

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