

Role of Ampicillin-Sulbactam: A District Hospital's Experience in Treating Diabetic Foot Ulcers

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Abstract: Ampicillin-sulbactam combination is the most frequently prescribed antibiotic in diabetic foot ulcers. We conducted a retrospective study to evaluate the antibiotic sensitivity of bacteria isolated to this antibiotic. In 33 patients with diabetic foot ulcer (September 2008-March 2009), 67% were culture positive in which *Citrobacter spp* accounted for 36% of these isolates. The rest isolated included *Pseudomonas aeruginosa* (22%), *Proteus spp* (18%), *Acinetobacter spp* (9%), *Klebsiella pneumoniae* (5%), *Escherichia coli* (5%) and *Staphylococcus aureus* (5%). These isolates were more likely to be ampicillin-resistant (n=18) than were ampicillin-sensitive isolates (n=4). Ampicillin resistance has raised our concern about current practice of prescribing ampicillin/ sulbactam as monotherapy for majority of our patients with such ulcers.

Key words: Diabetic foot ulcers, Ampicillin-sulbactam, District hospital

Diabetic foot is a well recognised complication of poorly controlled diabetes mellitus. More than 50% of our orthopaedic unit admissions were those of diabetic foot ulcers. Increasing prevalence of diabetic foot ulcers was attributed to poorly controlled sugar levels. Owing to its broad coverage nature (aerobic gram-positive and gram-negative bacteria and anaerobic organisms), ampicillin/sulbactam has been widely used since its introduction in 1986. However, resistance to such antibiotic has been reported recently in several case-control studies.^{1,2} This cross-sectional retrospective study was conducted to examine antibiotic sensitivity of bacteria isolated in diabetic foot ulcers and to compare with the type of antibiotic prescribed.

Retrospective data was obtained from case notes of patients with diabetic foot ulcers admitted to our hospital between September 2008 and March 2009. Diabetic foot ulcers were classified according to Meggit-Wagner classification.³ The outcomes of swab culture and the corresponding antibiotics were noted and tabulated, comparing those treated with ampicillin/sulbactam and non-ampicillin/sulbactam regimens.

Out of 33 patients (26 males and 7 females) studied, no growth was noted among 11 patients. The rest, 67% (n=22), were culture-positive cases. *Citrobacter spp* was reported among 8 of them. 22% had *Pseudomonas aeruginosa* isolated. Another 27% were identified to be *Proteus spp* (18%) and *Acinetobacter spp* (9%) respectively. *Klebsiella pneumoniae*, *Escherichia coli* and *Staphylococcus aureus* constituted 15% (5% each) of overall culture-positive subjects. (Figure 1)

Figure 1: Swab culture outcomes of 33 patients

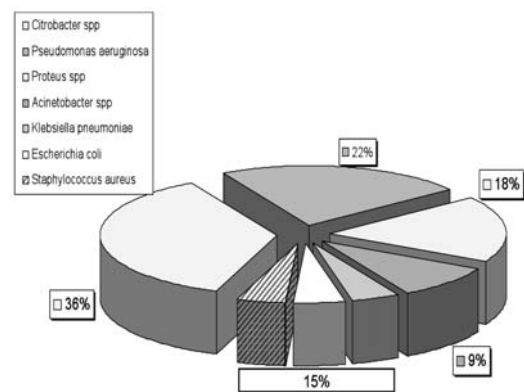


Table I showed 83% (n=15) were resistant to ampicillin in the ampicillin-sulbactam group (n=18). Only 17% of those resistant to ampicillin were prescribed non-ampicillin/sulbactam antibiotics. On the other hand, only 4 out of 22 culture-positive isolates were found to be sensitive to ampicillin. The odds ratio for difference between ampicillin/sulbactam group versus non-ampicillin/sulbactam group in terms of ampicillin resistance favoured neither group (1.667, 95% confidence interval 0.13 to 22.00).

Table 1: Ampicillin-resistant vs ampicillin-sensitive (Swab culture results) in patients prescribed either ampicillin/sulbactam or non-ampicillin/sulbactam regimens.

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	RESULTS OF SWAB CULTURE:	
	AMPICILLIN-RESISTANT	AMPICILLIN-SENSITIVE
Patients prescribed ampicillin-sulbactam	15	3
Patients prescribed non-ampicillin/sulbactam regimens (i.e. cefuroxime, sulperazone, imipenem)	3	1

Figures denotes number of cases

Discussion

In our hospital, we tend to treat diabetic foot ulcers with a single broad-spectrum agent, ampicillin-sulbactam. As indicated in the present study, 82% of culture-positive subjects (18 patients) were prescribed such antibiotic. This was based on the good clinical success in diabetic foot infections demonstrated in previous studies.^{4,6} Almost all organisms (95%) isolated were of Gram-negative bacilli. Only one of the swab culture turned out to be Gram-positive cocci (*Staphylococcus aureus*). This monomicrobial Gram-negative nature of the growth isolated is consistent with the findings in several similar studies.⁷⁻⁹ Vast majority of the subjects in this study were found to be resistant to ampicillin. Furthermore, the organisms isolated were of Enterobacteriaceae (eg. *Citrobacter spp*, *Proteus spp*, *Klebsiella pneumoniae*, *Escherichia coli*), capable of producing extended-spectrum beta-lactamase. This could pose serious a major challenge to the widespread prescription of ampicillin-sulbactam in our hospital for treating diabetic patients with lower limb infection. On the other hand, ampicillin-sulbactam is well recognized to be ineffective against *Pseudomonas aeruginosa* (22% in this current study). However, the study here is solely based on the initial empirical antibiotics given prior to the culture results. Although such study has the advantage of relatively quick data collection and analysis and is useful at identifying associations, several weaknesses have been identified.

First of all, the sampling bias that has involved only the subjects from Kuala Pilah Hospital. The outcome of this study may therefore not reflect the real scenarios in other district hospitals throughout Malaysia. Secondly, the small sample size (n=33) could render the result of the study less representative of the general population. Thirdly, other managements do play a crucial role in managing diabetic foot ulcers, including diabetic control, debridement, and dressing. For instance, nephropathic patients as a result of poor diabetic control have been linked to 3-fold increased risk of amputations.⁹ Apart from that, the organism isolated in such study may not be the true pathogens contributing to the lower-limb problems in patients with diabetes. Deep tissue culture following debridement is thus deemed necessary for recognizing the culprit pathogens and for instituting the accurate antibiotics.¹⁰

In conclusion, the routine use of ampicillin-sulbactam for treating diabetic foot ulcers in our hospital does pose a challenge based on the findings of ampicillin resistance and the type of organisms isolated. However, the relatively small sample size and the nature of the current study (cross-sectional retrospective) do limit the conclusive statement derivation of introducing alternative antimicrobial agents for ameliorating such condition. Further large-scale prospective studies are required to validate the findings.

Acknowledgement

We would like to give a special thanks to Professor Teng Cheong Lieng (Department of Family Medicine, International Medical University) in reviewing this article and the invaluable comments given. No sources of funding were used in the formulation of current research.

REFERENCES

1. Carmeli, Y., Castro, J., Eliopoulos, G.M., Samore, M.H. Clinical isolation and resistance patterns of and superinfection with 10 nosocomial pathogens after treatment with ceftriaxone versus ampicillin-sulbactam. *Antimicrobial Agents and Chemotherapy* 2001; 45: 275-9.

2. Kaye, K.S., Harris, A.D., Gold, H, Carmeli, Y. Risk factors for recovery of ampicillin-sulbactam-resistant *Escherichia coli* in hospitalized patients. *Antimicrobial Agents and Chemotherapy* 2000; 44: 1004-9.
3. Wagner, F.W. The dysvascular foot: A system for diagnosis and treatment. *Foot Ankle* 1981; 2: 64-122.
4. Grayson, M.L., Gibbons, G.W., Habershaw, G.M., Freeman, D.V., Pomposelli, F.B. Rosenblum, B.I. et al. Use of ampicillin/sulbactam versus imipenem/cilastatin in the treatment of limb-threatening foot infections in diabetic patients. *Clinical Infectious Diseases* 1994; 18: 683-93.
5. Chow, I, Lemos, E.V., Einarson, T.R. Management and prevention of diabetic foot ulcers and infections: a health economic review. *Pharmacoeconomics* 2008; 26: 1019-35.
6. Lode, H.M. Rational antibiotic therapy and the position of ampicillin/sulbactam. *International Journal of Antimicrobial Agents* 2008; 32: 10-28.
7. Raja, N.S. Microbiology of diabetic foot infections in a teaching hospital in Malaysia: a retrospective study of 194 cases. *The Journal of Microbiology, Immunology and Infection* 2007; 40: 39-44.
8. Oni A.A., Ogunkunle M.O., Oke, A.A., Bakare, R.A. Pattern of Gram-negative rods bacteraemia in diabetic patients in Ibadan, Nigeria. *African J of Medicine and Medical Sciences* 2000; 29: 207-10.
9. Rathur, H.M., Boulton, A.J. The diabetic foot. *Clinics in Dermatology* 2007; 25: 109-20.
10. Gentry, L.O. Diagnosis and management of diabetic foot ulcer. *Journal of Antimicrobial Chemotherapy* 1993; 32 (Suppl A): 77-89.