Journal of Microbiology and Infectious Diseases / JMID
2012; 2 (3): 109-112
doi: 10.5799/ahinjs.02.2012.03.0053

ORIGINAL ARTICLE

In-vitro activity of tigecycline against methicillin-resistant *Staphylococcus aureus* Isolated from wounds of burn patients in Tripoli-Libya

Abdulazziz Zorgani[1], Omar Elahmer[2], Hisham Ziglam[3], Khalifa Sifaw Ghenghesh[1]

[1] *Department of Microbiology and Immunology, Faculty of Medicine, Tripoli University, Tripoli-Libya*
[2] *National Centre for Diseases Control, Tripoli-Libya*
[3] *Centeral Hospital, Tripoli-Libya*

ABSTRACT

Objectives: Tigecycline is a new glycylcycline group antibiotic with broad-spectrum activity. In the present study we report on in vitro activity of tigecycline as well as the comparator antimicrobials linezolid and quinupristin/dalfopristin against methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA) strains isolated from burn wounds in Tripoli-Libya.

Materials and methods: Included in the study 155 MSSA and 144 MRSA isolates from wounds of burn patients and identified by PCR. The susceptibility of MSSA and MRSA isolates to tigecycline, linezolid and quinupristin/dalfopristin was determined by the disc diffusion technique.

Results: Of the MSSA and MRSA isolates examined, susceptibility to tigecycline was observed in 96.8% and 95.8%, to linezolid in 97.4% and 96.5% and to quinupristin/dalfopristin in 98.1% and 97.2%, respectively.

Conclusion: Tigecycline showed excellent in-vitro activity against MSSA and MRSA similar to the comparator drugs (i.e. linezolid and quinupristin/dalfopristin). However, tigecycline should be used to treat serious infections when no other option exists. *J Microbiol Infect Dis 2012; 2(3): 109-112*

Kew words: Tigecycline; methicillin-resistant *Staphylococcus aureus* (MRSA); wounds, burn patients, Libya.

Libya-Tripoli'de yanıklı hastaların yaralarından izole edilen methicillin-dirençli *Staphylococcus aureus* suşlarına karşı tigesiklinin invitro aktivitesi

ÖZET

Amaç: Tigesiklin geniş spektrum aktivitesi olan yeni bir antibiyotik grubudur. Bu çalışmada biz tigesiklinin ve karşılaştırma antibiyotikleri olarak da linezolid ve quinupristin/dalfospristinin, Libya-Tripoli'de yanık yaralarından izole edilen Metisilin-duyarlı *Staphylococcus aureus* (MSSA) ve Metisiline direncli *Staphylococcus aureus* (MRSA) suşlarına karşı invitro aktivitesini rapor ettik.

Gereç ve yöntem: Bu çalışmaya dahil edilen yanık yaralarından izole edilmiş 155 MRSA ve 144 MSSA suşu PCR ile tanımlandı. MSSA ve MRSA suşlarının tigesiklin linezolid ve quinupristin/dalfospristine duyarlılıkları disk difüzyon metodu ile belirlendi.

Bulgular: Çalışılan MSSA ve MRSA suşlarının, sırasıyla, tigesikline % 96,8 ve % 95,8, linezolide % 97,4 ve % 96,5 ve quinupristin/dalfopristine % 98,1 ve % 97,2 oranlarında duyarlı oldukları görüldü.

Sonuç: Tigesiklin MSSA ve MRSA suşlarına karşı karşılaştırma antibiyotikleriyle (linezolid ve quinupristin/dalfopristin) benzer şekilde mükemmel bir aktivite gösterdi. Ancak tigesiklin ciddi enfeksiyonlarda diğer seçenekler kullanılamadığı zaman kullanılmalıdır.

Anahtar kelimeler: Tigesiklin; metisilin-resistant *Staphylococcus aureus* (MRSA); yaralar, yanık hastaları, Libya.

Correspondence: Prof. Khalifa Sifaw Ghenghesh, MSc, PhD, DipBact Department of Microbiology and Immunology, Faculty of Medicine, Tripoli University, P.O. Box 80013, Tripoli, Libya Email: ghenghesh_micro@yahoo.com
Received: 09 June, 2012 Accepted: 24 September, 2012

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) are important causes of nosocomial as well as community-acquired infections.[1] Compared with methicillin-susceptible *S. aureus* (MSSA) MRSA infection has been associated with higher morbidity and mortality, resulting in high cost and poor clinical outcomes.[2,3] MRSA strains exhibit resistance to the β-lactams and other antimicrobials. Vancomycin, a glycopeptides, is the drug of choice for the treatment of MRSA infections. However, with the emergence of MRSA with reduced susceptibility to vancomycin, clinicians may need to consider the use of other drugs.[4] One of the few agents that are available at present for treatment of infections due to MRSA is tigecycline.

Tigecycline is a new glycylcycline broad-spectrum antibiotic that overcomes ribosomal protection and efflux pumps, two common mechanisms that are associated with tetracycline resistance. Tigecycline has a good in-vitro activity against multiresistant Gram-negative and Gram-positive (including MRSA) pathogens.[5,6] Recently, Bassetti et al. assessed the efficacy of tigecycline use in serious nosocomial infections.[7] They reported successful clinical response rates of 82% for intra-abdominal infections and 78% for complicated skin and soft tissue infections with an overall successful clinical response of 73%. They also reported 80% microbiological efficacy against MRSA associated with complicated intra-abdominal infections.

In Libya, reports on the susceptibility of MRSA and MSSA to tigecycline are lacking. The aim of the present study was to determine the in vitro activity of tigecycline as well as the comparator antimicrobials linezolid and quinupristin/dalfopristin against MRSA and MSSA strains isolated from burn wounds in Tripoli-Libya.

MATERIALS AND METHODS

Included in the study, non-duplicate *S. aureus* strains isolated from wounds of burn patients treated at the Burn Center of Tripoli (BCT) in the period January 2009 to June 2010 were evaluated. BCT is a 120 bed hospital that provides free medical care for burn patients with separate male, female and children Burn and Plastic Surgery Units and a Burn Intensive Care Unit (BICU).

Wound specimens were inoculated on to BBL CHROMagar MRSA (BD Diagnostic, Sparks, MD, USA), incubated at 37^0C for 48 h and MRSA was suspected if mauve-colored colonies were observed. Mauve-coloured colonies were subjected to coagulase testing by slide and tube methods. MRSA isolates detected by chromogenic medium and coagulase tests were confirmed by a real-time PCR technique using the BD GeneOhmTM MRSA assay (BD Diagnostics) following the manufacturer's instructions. The BD GeneOhm MRSA PCR assay has a sensitivity and specificity of 100% and 97%, respectively, compared to culture by use of BBL CHROMagar MRSA.[8]

Employing the disc diffusion method methicillin susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) isolates were tested for their susceptibility to tigecycline (15 µg), linezolid (30 µg), and quinupristin\dalfopristin (15 µg).[9] According to the US FDA criteria a tigecycline zone diameter of ≥ 19 mm is considered susceptible for *S. aureus*.[10] Antimicrobial disc used in the present study were obtained from BD Diagnostics. Quality control for antimicrobial susceptibility testing was performed with *S. aureus* ATCC 25923.

For statistical analysis, the Epi-2000 software (Centers for Disease Control and Prevention, Atlanta, GA, USA) was employed. P values were calculated using χ^2 test. $P < 0.05$ was considered statistically significant.

RESULTS

In the period of January 2009 to June 2010, 299 non-duplicate *S. aureus* strains were isolated from wounds of burn patients treated at the BCT. The patients aged between 2 months to 90 years (mean = 35 yrs.) and the male to female ratio of patients is 1.2:1. Of the 299 *S. aureus* examined 144 (48.2%) were identified as MRSA and 155 (51.8%) as MSSA by PCR. Susceptibility to tigecycline was observed in 96.8% and 95.8% of MSSA and MRSA isolates, respectively. Table 1 shows the susceptibility of MSSA and MRSA to tigecycline and comparator antimicrobials linezolid and quinupristin/dalfopristin.

Table 1. Susceptibility of methicillin-susceptible (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) to tigecycline and comparator agents

Antimicrobial agent	No. (%) susceptible		
	MSSA (*n*=155)	MRSA (*n*=144)	Total (*n*=299)
Tigecycline	150 (96.8)	138 (95.8)	288 (96.3)
Linezolid	151 (97.4)	139 (96.5)	290 (97)
Quinupristin\ dalfopristin	152 (98.1)	140 (97.2)	292 (97.7)

DISCUSSION

MRSA and MSSA are important causes of infections in burn patients.[11-13] In accordance with other studies tigecycline in the present work showed excellent in vitro activity against MSSA and MRSA isolates (96.8%and 95.8%, respectively).[5,14] We observed no significant difference ($p > 0.05$) in the activity of tigecycline between MRSA and MSSA isolates. Other investigators reported similar findings.[15]

At present, tigecycline is licensed by the US FDA for the treatment of complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI), and community acquired pneumonia. However, in January 2010 the FDA issued a warning related to increased mortality with tigecycline in randomized controlled trials.[16] In addition, tigecycline is not effective against Pseudomonas aeruginosa, an important cause of infections in burn centers. Lately, Garcia-Cabrera et al. reported 12 (24%) cases of super infections (seven due to P. aeruginosa) in 51 patients treated with tigecycline for nosocomial infections due to multiresistant bacteria.[17] Five of patients with super infections died (42%), three due to super infections.

Recently, several review studies on tigecycline concluded that clinicians should use other antimicrobials in the treatment of severe cSSSI and cIAI and reserve tigecycline as a last-resort agent.[18,19] Of the MSSA and MRSA isolates examined 97.4% and 96.5% were susceptible to linezolid and 98.1% and 97.2% to quinupristin\dalfopristin, respectively. Although linezolid and quinupristin\dalfopristin showed better activity than tigecycline against MSSA and MRSA isolates the differences were not significant ($p > 0.05$). Also, no significant differences ($p>0.05$) were found in the activity of linezolid and quinupristin\dalfopristin between MRSA and MSSA isolates. Similar observations were reported by other investigators.[5,14.15]

A recent study from India reported that healthcare workers (HCWs) colonized with MRSA have been strongly associated with an increase in the isolation of the organism from wounds of patients in burns ward.[20] We found nearly 50% of *S. aureus* isolates were MRSA. A previous study, carried out in 2007, reported a prevalence rate of 54% for MRSA among *S. aureus* isolated from burn patients in BCT.[21] This indicates that MRSA is widely spread in BCT. Being a nosocomial pathogen HCWs in the BCT may play a role in the spread of MRSA among burn patients. Previously, we examined the rate of MRSA colonization among HCWs (including 196 doctors and 447 nurses) in six hospitals in Tripoli.[22] We found 25-50% (mean=37%) of HCWs were colonized with MRSA. With limited options available for the treatment of MRSA in burns patients infections control measures should be implemented urgently in the BCT with strong emphasis placed on the importance of hand washing among the HCWs.

In conclusion, tigecycline as well as linezolid and quinupristin/dalfopristin showed excellent activity against MSSA and MRSA isolated from wounds of burn patients in Tripoli. Clinicians in Libya should consider alternatives to tigecycline when treating patients with serious infections. However, tigecycline can be used to treat such infections when no other option exists. In addition, urgent implementation of infection control measures including a hand washing policy among HCWs in BCT is urgently needed.

Conflict of interest and funding

The authors declare no conflict of interest and not receiving funding or benefits from any source.

REFERENCES

1. Eady EA, Cove JH. Staphylococcal resistance revisited: community-acquired methicillin resistant *Staphylococcus aureus*: an emerging problem for the management of skin and soft tissue infections. Curr Opin Infect Dis 2003; 16:103-124.
2. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. Clin Infect Dis 2003; 36:53-59.
3. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length

of stay, and hospital charges. Infect Control Hosp Epidemiol 2005; 26:166-174.
4. Boyce JM, Cookson B, Christiansen K, et al. Meticillin-resistant *Staphylococcus aureus*. Lancet Infect Dis 2005; 5:653-663.
5. Betriu C, Rodríguez-Aviala I, Gómeza M, et al. the Spanish Tigecycline Group. Antimicrobial activity of tigecycline against clinical isolates from Spanish medical centers. Second multicenter study. Diagn Microbiol Infect Dis 2006; 56:437-444.
6. Verkade EJM, Verhulst CJMM, Huijsdens XW, Kluytmans JA. In vitro activity of tigecycline against methicillin-resistant *Staphylococcus aureus*, including livestock-associated strains. Eur J Clin Microbiol Infect Dis 2010; 29:503-507.
7. Bassetti M, Nicolini L, Repetto E, Righi E, Del Bono V, Viscoli C. Tigecycline use in serious nosocomial infections: a drug use evaluation. BMC Infect Dis 2010; 10:287. http://www.biomedcentral.com/1471-2334/10/287.
8. Snyder JW, Munier GK, Johnson CL. Comparison of the BD GeneOhm methicillin-resistant *Staphylococcus aureus* (MRSA) PCR assay to culture by use of BBL CHROMagar MRSA for detection of MRSA in nasal surveillance cultures from intensive care unit patients. J Clin Microbiol 2010; 48: 1305-1309.
9. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial disk diffusion susceptibility tests 19th ed. CLSI document M100-S19; 2009.
10. Food and Drug Administration (FDA), Tygacil®. http://www.accessdata.fda.gov/ drugsatfda_docs/label/2009/021821s016lbl.pdf (accessed 29th November 2011).
11. Appelgren P, Björnhagen V, Bragderyd K, Jonsson CE, Ransjö U. A prospective study of infections in burn patients. Burns 2002; 28:39-46.
12. Keen EF 3rd, Robinson BJ, Hospenthal DR, et al. Prevalence of multidrug-resistant organisms recovered at a military burn center. Burns 2010; 36:819-825.
13. Murray C, Hospenthal DR. Burn wound infections. Medscape http://emedicine.medscape.com/article/213595-overview (accessed 3rd December 2011).
14. Dowzicky MJ, Chmelarova E. Global in vitro activity of tigecycline and linezolid against Gram-positive organisms collected between 2004 and 2009. Int J Antimicrob Agents 2011; 37:562-566.
15. Wang H, Liu Y, Sun H, Xu Y, Xie X, Chen M. In vitro activity of ceftobiprole, linezolid, tigecycline, and 23 other antimicrobial agents against *Staphylococcus aureus* isolates in China. Diagn Microbiol Infect Dis 2008; 62:226-229.
16. FDA. FDA Drug Safety Communication: Increased risk of death with Tygacil (tigecycline) compared to other antibiotics used to treat similar infections. http://www.fda.gov/Drugs/DrugSafety/ucm224370.htm (accessed 3rd December 2011).
17. Garcia-Cabrera E, Jimenez-Mejias ME, Gil Navarro MV, et al. Hospitale Universitarios Virgen del Rocio Super infection during treatment of nosocomial infections with tigecycline. Eur J Clin Microbiol Infect Dis 2010; 29:867-871.
18. Slover CS, Rodvold KA, Danziger LH. Tigecycline: A novel broad-spectrum antimicrobial. Ann Pharmacother 2007; 41:965-972.
19. Yahav D, Lador A, Paul M, Leibovici L. Efficacy and safety of tigecycline: a systematic review and meta-analysis. J Antimicrob Chemother 2011; 66:1963-1971.
20. Duggal S, Kaur N, Hans C. An investigation of MRSA from the burns ward: the importance of hand hygiene. J Clin Diag Res 2011; 5:476-479.
21. Zorgani A, Shawerf O, Tawil K, El-Turki E, Ghenghesh KS. Inducible clindamycin resistance among staphylococci isolated from burn patients. Libyan J Med 2009; AOP: 090128.
22. Zorgani A, Elahmer O, Franka E, Grera A, Abudher A, Ghenghesh KS. Detection of methicillin-resistant *Staphylococcus aureus* among healthcare workers in Libyan hospitals. J Hosp Infect 2009; 73:91-92.