In Vitro Activity of Fusidic Acid (CEM-102) Against Resistant Strains of Staphylococcus aureus

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Abstract

Background: CEM-102 (fusidic acid) is being developed for the treatment of acute bacterial skin and skin structure infections (ABSSSI). The activity of a variety of resistant strains of Staphylococcus aureus was investigated.

Methods: In the in vitro activity of CEM-102 was compared with that of telithromycin, azithromycin, levofloxacin, linezolid and doxycycline against a total of 272 resistant S. aureus by agar dilution procedures (CLSI, M7-A7, M100-S16). The tested strains included S. aureus MRSA (meCA genotype; 176 isolates), macrolide-resistant (ermA, B, C genotype or MLSB-resistant; 58) and ciprofloxacin-resistant (gyrA and parC genotype; 38).

Results: Against S. aureus MRSA (meCA), CEM-102 (MIC90 0.25 mg/L) and telithromycin (MIC90 0.06 mg/L) were more active than doxycycline (MIC90 1 mg/L), linezolid (MIC90 2 mg/L), levofloxacin (MIC90 16 mg/L), azithromycin (MIC90 >32 mg/L) and erythromycin (MIC90 >32 mg/L). CEM-102 (MIC90 0.25 mg/L) was significantly superior to linezolid (MIC90 2 mg/L), levofloxacin (MIC90 4 mg/L), telithromycin (MIC90 4 mg/L), azithromycin (MIC90 >32 mg/L) and erythromycin (MIC90 >32 mg/L) against macrolide-resistant S. aureus (ermA, B, C genotype or MLSB-resistant). Against ciprofloxacin-resistant S. aureus (gyrA and parC genotype), CEM-102 (MIC90 0.25 mg/L) and telithromycin (MIC90 0.06 mg/L) were more active than doxycycline (MIC90 1 mg/L), linezolid (MIC90 2 mg/L), azithromycin (MIC90 16 mg/L), levofloxacin (MIC90 >32 mg/L), and erythromycin (MIC90 >32 mg/L). CEM-102 was significantly superior (p<0.05) to antimicrobial agents tested, such as levofloxacin, linezolid and doxycycline against a variety of S. aureus strains isolated from patients.

Materials and Methods

Strains

- A variety of recently isolated (1995-2008) S. aureus strains represented clinical isolates, mostly from upper or lower respiratory tract infections, blood cultures or wound cultures.
- S. aureus strains were represented both CA- and HA-MRSA isolates.
- Multiple cultures from the same patient or source were excluded unless a change in organism or antibiogram was noted.
- Organisms were identified by standard methods as described by Murray et al (1).

In this study, we determined the minimum inhibitory concentration (MIC90 and MIC50) of CEM-102, telithromycin, azithromycin, erythromycin, levofloxacin, linezolid and doxycycline against a variety of S. aureus strains isolated from patients.

Determination of MICs

- MICs were determined using the CLSI agar dilution method (2, 3) with replicate plating of the organisms onto a series of agar plates of increasing concentrations from 0.004 mg/L to 64 mg/L.
- Mueller-Hinton agar was used as the testing medium for the S. aureus strains.
- Staphylococcus aureus ATCC 29213 and Escherichia coli ATCC 25922 were included as controls.

Determination of genotypes mecA; ermA, B, C; mefE; gyrA and parC

- Genomic DNA was isolated as described by Smith et al (4).
- Multiplex PCR was performed with primers specific for mecA, ermA, ermB, ermA and mefE as described by Sutcliffe et al (5).
- Multiplex PCR was performed with primers specific for gyrA and parC as described by Gonzalez et al (6).

Discussion

- CEM-102 showed significant activity (MIC90 0.25 mg/L) against categorized S. aureus strains, including strains that were resistant to β-lactams, macrolides or quinolones.
- Activity of CEM-102 was significantly superior (p<0.05) to the macrolides tested, azithromycin and erythromycin, and was much more potent than linezolid and doxycycline.
- Activity of CEM-102 against S. aureus was also significantly superior to levofloxacin, the quinolone tested.
- Against mecA-positive MRSA (meCA genotype) S. aureus the activity of CEM-102 (MIC90 0.25 mg/L) was greater than doxycycline (MIC90 2 mg/L), linezolid (MIC90 2 mg/L), levofloxacin (MIC90 16 mg/L).
- Against macrolide-resistant (ermA, B, C genotype) S. aureus strains, CEM-102 (MIC90 0.06 mg/L) was the most active agent tested (telithromycin, azithromycin and erythromycin (MIC90 4 mg/L)).

Conclusions

- CEM-102 shows broad spectrum antimicrobial activity against the most usual strains of S. aureus isolated from upper or lower respiratory tract, blood culture or wound infections.
- CEM-102 is active against mecA and ciprofloxacin-resistant S. aureus.
- CEM-102 is active against resistant S. aureus strains represented by both CA- and HA-MRSA isolates.

References

2. Performance standards for antimicrobial susceptibility testing: 18th Informational Supplement; M100-S18, Clinical and Laboratory Standards Institute (CLSI), Wayne, PA, January 2008.