Activity of Fusidic Acid Tested Against Contemporary Staphylococcus aureus Collected from United States Hospitals

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Abstract

Background: Fusidic acid (FA) is an established anti-staphylococcal agent used primarily in Europe in Australia and Canada for at least three decades. FA is under clinical development for treatment of acute bacteremia skin and skin-infections (ASSB) in the USA. In 2008-2009, we investigated susceptibility to FA in isolates collected from S. aureus in 51 USA sites. This is the largest collection of clinical S. aureus isolates tested against FA.

Methods: S. aureus (7,340) were collected from 51 institutions distributed within USA (laboratories: 2008-2009). Clinical, epidemiological, and resistance data were extracted through BioMérieux Clinical and Laboratory Data System (CLDSS) for 5,826 (2008) and 1,502 (2009) isolates. FA susceptibility was determined using the Etest (bioMérieux, Hazelwood, MO) or 16S rRNA sequencing, protocols. Only one isolate per patient from documented cases was included in the reaction to detect strains with identical 16S rRNA sequences.

Results: Ninety-five percent FA susceptibility were those found in M100-S20-U and quality control according to the Clinical and Laboratory Standards Institute (CLSI: 2010). 90.6% FA susceptibility were those found in M100-S20-U and quality control according to the Clinical and Laboratory Standards Institute (CLSI: 2010).

Conclusions: Fusidic acid exhibits potent activity against nearly all S. aureus (0.4% non-susceptible) similar to parenteral-only agents (glycopeptides and vancomycin). Fusidic acid is an agent that can be developed into a new class of agents.

Introduction

Fusidic acid (FA) was first isolated in 1962 from Fusidium coccineum, a genus of the Basidiomycota. It is a naturally derived agent with a 20-membered macrolactone ring. Resistance to FA is clinically considered to be caused by mutations in fusA, fusB, and fusC, with differences in resistance patterns and mechanisms of resistance described in clinical strains. These mobile genes, named fusidic acid resistance mechanisms have also been described in clinical strains. These mobile genes, named fusidic acid resistance mechanisms have also been described in clinical strains.

Fusidic acid has been used in Europe and Australia since the 1960s and China since 1980. However, the compound has been licensed by the United States (USA) and Food and Drug Administration (FDA) for it is not currently available for prescription in the USA. The introduction of fusidic acid into this country may now be viewed as timely because it provides an additional antistaphylococcal agent with low toxicity and a unique mechanism of action that is distinct from that of other classes of antibacterials (including methicillin-resistant Staphylococcus aureus [MRSA]). Furthermore, the extensive foreign experience with fusidic acid in the treatment of severe staphylococcal infections over the past four decades provides a wealth of information about optimal use, particularly with regards to the implementation of dosage/therapy strategies to delay or avoid the development of resistance.

In this work, we evaluated the activity of fusidic acid against S. aureus isolated in USA medical centers during 2008 and 2009. Isolates were categorized according to different resistance patterns and mechanisms of resistance evaluated for these strains showing elevated fusidic acid MIC results (0.12µg/mL).

Materials and Methods

Resistant strains. A total of 7,340 S. aureus strains collected during 2008 and 2009 in 51 USA hospitals, located in the nine Census Regions were analyzed as part of the SENTRY Antimicrobial Surveillance Program. These isolates were collected from respiratory, skin and soft tissue-infections, skin and skin-infections (ASSB), according to defined protocols.

Fusidic acid susceptibility. Isolates per patient from documented infections were included. Species identification was confirmed using biochemical tests, the Vitek System (bioMérieux, Hazelwood, MO) or 16S rRNA sequencing, when necessary.

Fusidic acid susceptibility testing. Isolates were suspended in 200 µl sterile distilled water to a density equivalent to 0.5 McFarland for inoculation into a 90 mm dish containing 10 ml of Mueller Hinton Broth (Difco, Sparks, MD) supplemented with 0.5% NaCl (Difco). After a 15 min incubation at 37°C, 0.1 ml of the inoculum was transferred into a 90 mm dish containing 10 ml of Mueller Hinton Broth (Difco) supplemented with 0.5% NaCl (Difco) and incubated at 37°C for 24 h. The central agar was then flooded with 2 ml of a 0.9 µM stock solution of FA (CEM-102).

The FA plates were incubated at 37°C for 24 h. The zone of inhibition was recorded.

Results

Fusidic acid was compared with other 203 agents (intrinsic of CEM-102). Isolates were amplified and sequenced using Enterobacter H-K-01 Master Mix (AEGene, Eugene, OR), PCR primers (5% and 2%) that were used to identify fusidic acid resistance mechanisms.

Table 1. Antimicrobial activity of fusidic acid and comparator agents against S. aureus isolated in the United States (2008-2009).

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Year</th>
<th>no. isolates</th>
<th>no. sites</th>
<th>%S / %R</th>
<th>no. isolates</th>
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<tr>
<td>FA</td>
<td>2008</td>
<td>3306</td>
<td>289</td>
<td>99.6 / 0.4</td>
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<td>2009</td>
<td>4034</td>
<td>363</td>
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FA susceptibility testing was performed by standard CLSI methods (CLSI: 2010) or 16S rRNA sequencing, protocols. Only one isolate per patient from documented cases was included in the reaction to detect strains with identical 16S rRNA sequences. This test was the only test evaluated for the activity of FA against other agents with similar clinical activity.

Table 2. Resistance mechanisms to fusidic acid isolated in the United States (2008-2009).

<table>
<thead>
<tr>
<th>Resistance mechanism</th>
<th>Year</th>
<th>no. isolates</th>
<th>no. sites</th>
<th>%S / %R</th>
<th>no. isolates</th>
<th>no. sites</th>
<th>%S / %R</th>
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<td>Fusidic acid resistance</td>
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Conclusions

Fusidic acid (FA) is an established anti-staphylococcal agent used primarily in Europe.

FA susceptibility testing was performed by standard CLSI methods (CLSI: 2010) or 16S rRNA sequencing, protocols. Only one isolate per patient from documented cases was included in the reaction to detect strains with identical 16S rRNA sequences.

References


2. Castanheira M, Watters AA, Bell JM, Turnidge JD, Jones RN (2010). Fusidic acid susceptibility testing of staphylococcal isolates from the United States: results from the CLSI external quality assessment program. JID 2010 201:Suppl D1, D152-D156.


