SUSCEPTIBILITY TO TIGECYCLINE OF MULTiresistant BACTERIA AT IBN ROCHD UNIVERSITY HOSPITAL-CASABLANCA

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ABSTRACT

A descriptive prospective study was conducted between 2015 and 2017 at the Microbiology laboratory of the Casablanca University Hospital Center to study the Tigecycline susceptibility of isolated multi drug resistant bacteria (MDRB): Imipenem-resistant Acinetobacter baumannii (IRAB), ESBL+/- Carbapenemase -producing enterobacteria (ESBLE), Meticillin-resistant Staphylococcus aureus (MRSA) and Vancomycin-resistant Enterococci (VRE). Antibiotic sensitivity tests were performed by diffusion method and those for Tigecycline by E-test strips according to EUCAST / CA-SFM. Breakpoints of interpretation of Tigecycline sensitivity were according to the FDA. A total of 692 MDRB strains were studied. The Tigecycline resistance rate was 33.9% (25.3% I, 8.6% R). For IRAB, it was 46% (30.5% I, 15.5% R), for ESBLE 27.9% (100% I), for MRSA 10% (100% R) and no VRE was resistant to Tigecycline. However, as EUCAST has not determined breakpoints for the in vitro thresholds of A.baumannii concerning Tigecycline, conclusions should not be formally established as to its sensibility.

Keywords: Multi-resistant bacteria; Sensibility; Tigecycline.

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INTRODUCTION

According to the WHO, bacterial resistance is a major upsurge and represents a public health problem. Although the evaluation of older antimicrobial agents is important, there is a real need to develop new agents and to monitor the development and spread of bacterial resistance mechanisms [1]. Tigecycline is a glycycline derivative of tetracyclines which obtained its marketing authorization (MA) in France in 2006 [2]. Tigecycline is a molecule that is active on multi-resistant bacteria (MDRB). However, some authors have revealed the emergence of resistant strains to this antibiotic.

Therefore, the aim of this work was to study the Tigecycline susceptibility profile of isolated MDRB in the Microbiology laboratory of Ibn Rochd University Hospital in Casablanca.

PATIENTS AND METHODS

A prospective descriptive study has been conducted over 2 years (between September 2015 and August 2017). Data from the study were stored in the computerized database of the Microbiology laboratory of Ibn Rochd University Hospital-Casablanca.

The strains studied were: Imipenem-resistant Acinetobacter baumannii (IRAB), Extended-spectrum β-lactamase producing enterobacteria (ESBLE) +/- Carbapenemase, Meticillin-resistant Staphylococcus aureus (MRSA) and Vancomycin-resistant Enterococci (VRE). The strains were isolated from laboratory-derived diagnostic specimens for IRABs, EBLSEs and MRSA, and rectal carriage for VRE. Duplicates have been excluded. The isolates were identified according to standard bacteriological techniques. The identification of S. aureus was performed by an agglutination or coagulase test. API 20 E and API 20...
NE (Biomérieux, Marcy l’Etoile) were used to identify Gram-negative bacilli and API STREP (Biomérieux, Marcy l’Etoile) to identify Enterococci. The study of antibiotic susceptibility was carried out by diffusion method in agar and the study of the sensitivity to Tigecycline was carried out by E-test strips (Biomérieux, Marcy l’Etoile) according to the recommendations of EUCAST / CA-SFM.

Methicillin-resistant staphylococci were detected by the search for resistance to cefoxitin. Extended-spectrum beta-lactamase producing strains (ESBL) were detected by the synergy test between central amoxicillin + clavulanic acid disc and the cefotaxime and ceftazidime disks. The carbapenemase search was performed by the Hodge test.

E. coli strain ATCC 25922 was used as the reference strain. The interpretation breakpoints of Tigecycline were based on EUCAST 2015 recommendations. The interpretation criteria for MICs for A. baumannii were based on FDA recommendations [3, 4] according to the modalities:

- Sensible ≤ 2 mg / l
- Intermediate = 4 mg / l
- Resistant> 4 mg / l

RESULTS

A total of 692 MDRB strains were studied. Results were reported in Table I.

<table>
<thead>
<tr>
<th>Strains</th>
<th>Number</th>
<th>IRAB: Imipenem-resistant Acinetobacter baumannii; ESBLE: Extended spectrum beta-lactamases</th>
</tr>
</thead>
<tbody>
<tr>
<td>K. pneumoniae</td>
<td>146</td>
<td>(21%)</td>
</tr>
<tr>
<td>E. Coli</td>
<td>53</td>
<td>(7%)</td>
</tr>
<tr>
<td>E. Cloacae</td>
<td>41</td>
<td>(6%)</td>
</tr>
<tr>
<td>MRSA</td>
<td>50</td>
<td>(7%)</td>
</tr>
<tr>
<td>VRE</td>
<td>49</td>
<td>(7%)</td>
</tr>
<tr>
<td>Total</td>
<td>692</td>
<td></td>
</tr>
</tbody>
</table>

The MICs found for Tigecycline for IRAB, ESBLE and MRSA ranged from 0.5 to 8 mg /l (Fig.1).

**Fig.1 In vitro activities of Tigecycline against the different MDR strains**
The Tigecycline resistance rate was 33.9% (25.3% I, 8.6% R). The IRAB resistance rate was 46% (31% I and 15% R). The sensitivity of ESBLE, MRSA and ERV were 72%, 90%, and 100% respectively.

DISCUSSION

The results of this study highlight the interesting activity of this antibiotic against MDR bacteria with a total sensitivity of 66%. These results were broadly comparable to those in the literature (Table II).

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>IRAB</td>
<td>54% MIC≤2</td>
<td>-</td>
<td>47% MIC≤2</td>
<td>-</td>
<td>40% MIC≤2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MIC90=8mg/l</td>
<td>MIC90=2mg/l</td>
<td>MIC90=8mg/l</td>
<td>MIC90=1mg/l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K.pneumoniae</td>
<td>86.7%</td>
<td>76.7%</td>
<td>97%</td>
<td>80.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESBL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.coli ESBL</td>
<td>72%</td>
<td>100%</td>
<td>98%</td>
<td>100%</td>
<td>98.9%</td>
<td></td>
</tr>
<tr>
<td>E.cloacae</td>
<td>96.1%</td>
<td>75.6%</td>
<td>92%</td>
<td>92.6%</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>ESBL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>90%</td>
<td>100%</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>VRE</td>
<td>100%</td>
<td>100%</td>
<td>-</td>
<td>100%</td>
<td>99.5%</td>
<td></td>
</tr>
</tbody>
</table>

IRAB: Imipenem resistant A.baumannii, ESBL: Extended-spectrum β-lactamase, MRSA: Meticillin resistant S.aureus, VRE: Vancomycin resistant enterococcus

Breakpoints of interpretation concerning A.baumannii are subject to controversy. Indeed, sensitivity thresholds vary from 0.5 to 2 mg / l according to some studies [6, 9]. Some authors have defined the MIC90 as the lowest concentration capable of inhibiting 90% of strains of the species studied in order to overcome the disagreement over the interpretation thresholds to A.baumannii. Our MIC50 and MIC90 (2 and 8 mg / l respectively) were higher than those described by some authors [5, 7] and comparable to others [6, 9]. These high MICs can be explained by the dissemination of resistant clones.

Tigecycline thus, represents a potential alternative in the therapeutic management of MDR infections. However, as EUCAST did not determine breakpoints for the in vitro sensitivity thresholds of Tigecycline in A.baumannii, conclusions should not be formally established regarding its sensitivity.

Some limitations to the use of tigecycline persist, including its documented inefficiency in urinary sites, its ineffectiveness against certain enterobacteria that are naturally resistant (Morganella spp, Proteus sp, and Providencia spp) and against P.aeruginosa as well as in children under 8 years old. [11] A rationalization of its prescription is thus essential, it should be limited to the infections labeled with MDRB in order to avoid the emergence of resistant mutants.

CONCLUSION

The MDR bacteria resistance rate for Tigecycline remains relatively low in our context and shows that it may be a therapeutic alternative. However, there is still no consensus on sensitivity thresholds of A.baumannii to Tigecycline. It is imperative to institute a rigorous MDR surveillance policy and to insist on the rationalization of the prescription of antibiotics including Tigecycline in order to avoid the spread of resistant strains.

ABBREVIATIONS:

IRAB: Imipenem resistant A.baumannii, ESBL: Extended-spectrum β-lactamase, MRSA: Meticillin resistant S.aureus, VRE: Vancomycin resistant enterococcus, EUCAST: European committee on antimicrobial susceptibility testing, CA-SFM: comité de l’antibiogramme - société française de microbiologie, FDA: Food and drug administration, MIC: minimum inhibitory concentration

CONFLICTS OF INTEREST: None
REFERENCES:


