



TYGACIL-CLINICAL IMPORTANCE, MICROBIAL SPECTRUM AND ANTIMICROBIAL SUSCEPTIBILITY

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ABSTRACT

Tigecycline (TYGACIL) is an antibiotic belonging to the glycylcyclines. It is approved for use by the FDA on June 15, 2005. Tygacil is structurally related to minocyclines and tetracyclines. It is obtained by changes in the molecule, leading to a wider spectrum of action of Tygacil, including resistant Gram-positive bacteria (MRSA, MRSE, VRE).

Key words: Tygacil, antimicrobial susceptibility, antimicrobial spectrum, minimal- inhibitory concentration, broth microdilution test.

INTRODUCTION

TYGACIL as all glycylcycline antibiotics inhibits protein synthesis in bacterial cell at the stage of translation, by connecting a 30-S subunit of ribosomes and blocking entry of amino-acyl tRNA to ribosomes.

This prevents incorporation of amino acid residues and the extension of peptide chains. The decreased susceptibility of bacteria to TYGACIL is primarily due to increased transmission of antibiotic so-called. efflux pumps, especially in *P.aeruginosa* and *Proteus*, *Providencia*, *Morganella* group. (overexpression of ArcAB - efflux pump.)

Decreased susceptibility of *Acinetobacter baumannii* is due to overexpression of Ade ABC efflux pumps.

Threshold values of the Minimal Inhibitory Concentrations to TYGACIL (EUCAST) Minimum Inhibitory Concentration by the European Commission for the Study of Antimicrobial Susceptibility (EUCAST):

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Staphylococcus spp. S ≤ 0,5 mg / l R> 0,5 mg / l
Streptococcus spp. (Except *S.pneumoniae*) S ≤ 0,25R>0,5mg/l.

Enterococcus spp S ≤ 0,25 mg. / L R> 0,5 mg / l.
Enterobacteriaceae S ≤ 1 mg / l R> 2 mg / l

Anaerobes: *Clostridium*, *Bacteroides*-S->2 mg. /L
The indications for treatment are complicated intra-abdominal infections and complicated skin and soft tissue infections.

The microbial spectrum includes:

- Gram-positive aerobic species: *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Enterococcus spp.*, *Streptococcus anginosus* group (*S.anginosus*, *S.intermedius*, *S.constellatus*), *Streptococcus pyogenes*, *Streptococcus viridans* group.

-Gram-negative aerobic bacteria : *Citrobacter freundii*, *Citrobacter koseri*, *Escherichia coli*, *Escherichia coli*

-Anaerobes: *C.perfringens*, *Peptostreptococcus spp*, *Prevotella spp*

Here it is the microbial spectrum of species with acquired resistance among Gram-negative aerobic species: *Acinetobacter baumannii*, *Burkholderia cepacia*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus spp*, *Providencia spp*, *Serratia marcescens*,

Table 1.

MIC90 of tigecyclin and the tetracyclines <i>in vitro</i>				
Gram-positive	Tigecycline	Tetracycline	Doxycycline	Minocycline
<i>Staphylococcus aureus</i> , methicillin susceptible	0,12–0,5	1	0,5	0,12
<i>Staphylococcus aureus</i> , methicillin resistant	0,25–5	32	2	2
<i>Staphylococcus epidermidis</i> , methicillin susceptible	0,5	2	NA	0,5
<i>Staphylococcus epidermidis</i> , methicillin resistant	0,5	>8	NA	4
<i>Streptococcus pneumoniae</i> , penicillin sensitive	0,06–0,125	32	8	8
<i>Streptococcus pneumoniae</i> , penicillin intermediate	0,06	64	8	16
<i>Streptococcus pneumoniae</i> , penicillin resistant	0,06–0,125	64	8	16
<i>Streptococcus pyogenes</i>	0,06	4	0,5	0,25
<i>Enterococcus faecalis</i>	0,12–0,25	128	16	32
<i>Enterococcus faecium</i>	0,12–0,25	64	16	16

Table 2.

MIC90 of tigecyclin and the tetracyclines <i>in vitro</i>				
Gram-negative	Tigecycline	Tetracycline	Doxycycline	Minocycline
<i>Acinetobacter</i> spp.	2	>32	NA	1
<i>Burkholderia cepacia</i>	32	4	NA	2
<i>Citrobacter freundii</i>	0,5–2	8	NA	8
<i>Enterobacter aerogenes</i>	1	4	NA	2
<i>Enterobacter cloacae</i>	0,5–4	>8	NA	>8
<i>Escherichia coli</i>	0,5	>8	NA	8
<i>Klebsiella pneumoniae</i>	1–2	4	NA	4
<i>Moraxella catarrhalis</i>	0,12	0,25	NA	0,06
<i>Morganella morganii</i>	4–8	16	NA	4
<i>Proteus mirabilis</i>	8	32	NA	16
<i>Pseudomonas aeruginosa</i>	16	>32	NA	32
<i>Stenotrophomonas maltophilia</i>	2–4	32	NA	1
<i>Serratia marcescens</i>	2	>8	NA	8
<i>Haemophilus influenzae</i>	0,5–1	0,5	NA	8

Table 3.

MIC90 of tigecyclin and the tetracyclines *in vitro*

Anaerobes	Tigecycline	Tetracycline	Doxycycline	Minocycline
<i>Bacteroides fragilis</i>	2 -4	32	8	8
<i>Clostridium difficile</i>	0,125-0,5	0,125	0,125	0,032
<i>Clostridium perfringens</i>	0,25-0,5	8	0,125	0,125
<i>Peptostreptococcus spp.</i>	0,125-0,25	16	4	8
Other	Tigecycline	Tetracycline	Doxycycline	Minocycline
<i>Chlamydia pneumoniae</i>	0,125	NA	0,25	NA
<i>Legionella pneumoniae</i>	NA	1-8	4	4
<i>Mycoplasma pneumoniae</i>	0,25	1	1,6	1

* Data from references 3 and 4. MICs are presented in µg/mL.
MIC90 indicates minimum inhibitory concentration of 90% of isolates; NA,

MATERIALS AND METHODS

There were examined a total of 330 clinical strains: 200 - Gram (-) neg. bacteria, 130 - gram (+) positive bacteria. The strains were isolated from wound secretions, urines, materials from the respiratory system. The aim of this study is to determine the susceptibility

of the strains (MIC) by Broth microdilution method - the method of serial dilutions in liquid medium.

RESULTS

The results of our study are shown in the next tables: Table 4, Table 5, Table 6, Table 7

Table 4. Susceptibility of clinical isolates of Gram (+) and Gram (-) bacteria to TYGACIL

Susceptibility of clinical isolates Gram positive and Gram negative bacteria to TYGACILs

Microorganism	Number strains	Susceptible		Resistant	
		Number	%	Number	%
<i>E. coli</i>	50	50	100	0	0
<i>K. pneumoniae</i>	48	47	97.92	1	2.08
<i>K. oxytoca</i>	7	7	100	0	0
<i>Enterobacter spp., Serratia spp.</i>	66	61	92.42	5	7.58
<i>Acinetobacter baumannii</i>	29	28	96.55	1	3.45
<i>S. aureus</i>	50	45	90	5	10
<i>S. agalactiae</i>	20	4	20	16	80
<i>S. pneumoniae</i>	30	1	3.33	29	96.66
<i>Enterococcus spp.</i>	30	21	70	9	30
	330	264		66	

Table 5. Sensitivity / MIC / bacterial isolates from the family Enterobacteriaceae for Tygacil**Susceptibility /MIC/ of bacterial isolates from family Enterobacteriaceae to Tygacil**

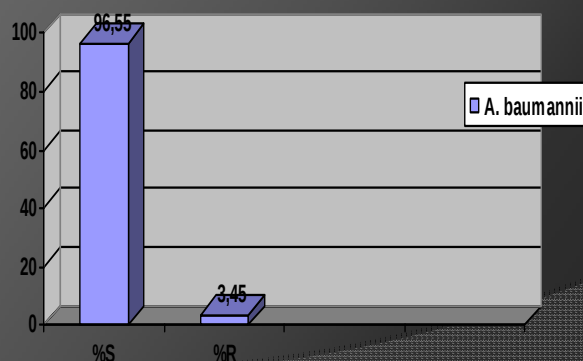
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Enterobacter spp., Serratia spp.	66	61	92.42	5	7.58

Table 6. Susceptibility of Gram / + / bacteria to Tygacil**Susceptibility (MIC) of Gram /+/ bacteria to Tygacil**

Microorganism	Number strains	Susceptible		Resistant	
		Number	%	Number	%
S. aureus	50	45	90	5	10
S. agalactiae	20	4	20	16	80
S. pneumoniae	30	1	3.33	29	96.66
Enterococcus spp.	30	21	70	9	30

Table 7. Susceptibility of *Acinetobacter baumannii* to Tygacil**Susceptibility of *Acinetobacter baumannii* to Tygacil**

Microorganism	Number strains	Susceptible		Resistant	
		Number	%	Number	%
<i>Acinetobacter baumannii</i>	29	28	96.55	1	3.45

**CONCLUSIONS**

TYGACIL is another treatment option for severe infections by bacteria with multiple resistance!

REFERENCES

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