



Phoenix is Overcalling the Resistance of Enterobacteriaceae to Temocillin.

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Abstract

Background: Temocillin (TMO) is a 6- α -methoxy-penicillin directed towards Gram negative bacteria. TMO has recently been introduced on Gram negative panels of the Phoenix® (PHX) in Belgium. Since then, increased occurrence of resistance to TMO has been observed with PHX but not with disc diffusion assay or Etest®. In this context, we have compared the susceptibility results generated by PHX with reference methods.

Methods: Enterobacteriaceae isolates declared resistant (R) by PHX were collected for 2 months and their MIC measured by Etest® (E) and broth microdilution (BM). A comparable number of isolates declared susceptible (S) by PHX were then collected for comparison. Categories were determined using the breakpoint by Fuchs et al. (1985 Eur J Clin Microbiol 4:30-33) as applied in the PHX. Quality controls were performed using *E. coli* ATCC 25922 and 35218.

Results: Isolates Confirmed phenotype by

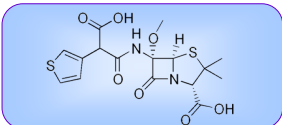
	PHX	E	BM
R (116)	17 (15%)	21 (18%)	
S (74)	73 (98%)	72 (97%)	

Agreement for S isolates was excellent. Conversely, less than 20% of R isolates were confirmed by either method. Surprisingly the MICs of the non-confirmed isolates were not all close to the breakpoint but distributed over a wide range (5 dilutions).

Conclusions: PHX is clearly overcalling the resistance among Enterobacteriaceae for TMO. This phenomenon seems not to be restricted to strains with borderline MIC. Isolates declared R by PHX should be reconfirmed by another method.

Background

Temocillin is a 6- α -methoxy penicillin directed towards Gram-negative bacteria. It has no useful activity against *Pseudomonas spp.* or *Acinetobacter spp.* but exhibits a remarkable stability against almost all types of β -lactamases including ESBL,^{1,2} AmpC,¹ and even carbapenemases.³



Temocillin has been recently introduced on the Gram-negative panel of the Phoenix® (Becton Dickinson & Co) in Belgium. Since then increased occurrences of resistance to temocillin have been reported by Phoenix users, while this did not happen so frequently when using other techniques to assess temocillin susceptibility (discs, E-tests, ...)

Objectives

- To reassess Phoenix® validity for testing Enterobacteriaceae susceptibility to temocillin
- To compare MIC distributions of isolates declared resistant and susceptible by Phoenix®

Results

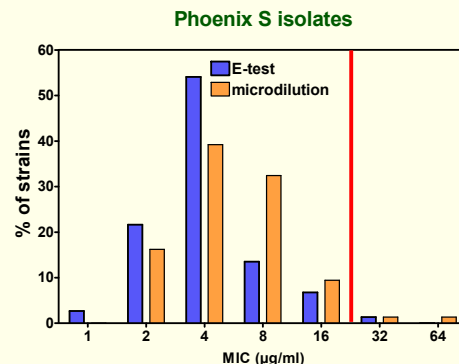
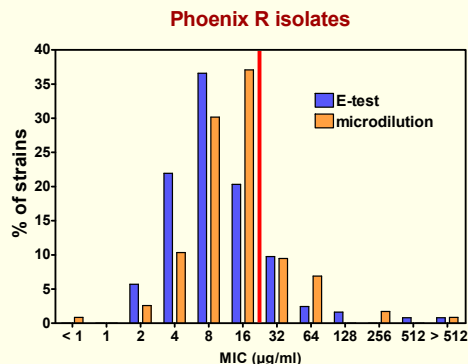
1. Species and Susceptibility to Temocillin

Species	R isolates ^a			S isolates ^b		
	Phoenix	E-test	microdilution	Phoenix	E-test	microdilution
<i>E. coli</i>	39	6 (15%)	6 (15%)	38	38 (100%)	38 (100%)
<i>E. aerogenes</i>	38	1 (2.5%)	3 (8%)	13	13 (100%)	12 (92%)
<i>E. cloacae</i>	18	3 (17%)	6 (33%)	9	9 (100%)	9 (100%)
<i>Serratia spp.</i>	12	5 (42%)	6 (50%)	3	3 (100%)	3 (100%)
others	9	2 (22%)	1 (4%)	11	10 (91%)	10 (91%)
TOTAL	116	17 (15%)	21 (18%)	74	73 (98%)	72 (97%)

^a number of isolates declared resistant by each method

^b number of isolates declared susceptible by each method

2. Comparison of MIC distributions for Temocillin



The red line corresponds to the breakpoint used in Belgium⁴ and applied by the Phoenix® system (i.e. susceptible $\leq 16 \mu\text{g/ml}$)

Materials & Methods

- Isolates declared resistant by the Phoenix system were collected during 2 months in each center
- Isolates declared susceptible were collected in a second phase for sake of comparison
- MIC was determined using Etest and broth microdilution
- Quality controls were performed using *E. coli* ATCC 25922 and ATCC 35218

Main observations and Conclusions

- Agreement for S isolates was excellent (more than 97%).
- Agreement for R isolates was rather poor (less than 20%).
- MICs of non-confirmed isolates were distributed over a 5 dilution range.
- Serratia spp.* made an exception with a better agreement. *Serratia* has always shown a lower susceptibility rate than the other Enterobacteriaceae towards temocillin which explains the higher number of isolates confirmed resistant.

- Phoenix is clearly overcalling the resistance of Enterobacteriaceae to temocillin.
- Isolates declared resistant by the Phoenix should be retested using another method.

Acknowledgements

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References

- Livemore, D. M., R. Hope, E. J. Fagan, M. Warner, N. Woodford, and N. Pötz. 2006. Activity of temocillin against prevalent ESBL- and AmpC-producing Enterobacteriaceae from south-east England. *J. Antimicrob. Chemother.* 57:1012-1014.
- Rodriguez-Villabos, H., V. Malvarde, J. Frankort, G. D. Mendonca, C. Nankoff, and M. J. Studenes. 2006. In vitro activity of temocillin against extended spectrum β -lactamase-producing *Escherichia coli*. *J. Antimicrob. Chemother.* 57:771-774.
- Docquier, J. D. M., L. Rocio, C. Magrani, F. Luzzati, A. Erdimian, A. Tonello, G. Antoncarra, and G. M. Rossolini. 2003. IMP-12, a new plasmid-encoded metallo-beta-lactamase from a *Pseudomonas* pulsed clinical isolate. *Antimicrob. Agents Chemother.* 47:1522-1528. *Journal Article, Name of Journal*
- Fuchs PC, Barry AL, Thomsberry C, Jones RN. Interpretive criteria for temocillin disk diffusion susceptibility testing. *Eur J Clin Microbiol.* 1985 Feb;4(1):30-3