Comparative performance of screening microdilution test in detection of ESBL phenotype in enterobacteriaceae clinical isolates.

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Background:

Venezuela has an increasing prevalence of ESBL, National surveillance program report an increase from 8% 2000 to 15% 2013, even although these represent a part of the whole universe of samples, looks undoubtedly that prevalence of ESBL is becoming a important problem for treatment and many of our micro labs are having difficulties or even lacking of phenotypic methods to confirm ESBL in a nationwide basis.

Objective:

To evaluate the predictive power of screening microdilution tests for detection of ESBL phenotype using MIC criteria of Ceftriaxone, Ceftazidime and Cefotaxime in clinical isolates of enterobacteriaceae.

Methodology:

Results of MIC microdilution test for Ceftriaxone, Ceftazidime and Cefotaxime (MIC ≥ 1 µg was considered as ESBL predictor) were compared to confirmation phenotypic criteria (using CLSI 2010 criteria: 3 fold increase comparing Ceftazidime´s MIC 0,25-128 µg/ml with Ceftazidime /Clavulanate 0,25-4 and 128-4 µg/ml) using 3 multivariate logistic regression models (one model for each antibiotic); as prediction of screening test in order to detect ESBL phenotype.

Dependent variable was considered as positive if phenotypic criteria was accepted or negative if not . (Dichotomous Dependent Variable).

Independent variables data were derived from 1832 Clinical isolates (one isolate per patient) of E.coli, K.pneumoniae and K.Oxitoca collected in Caracas, Venezuela from patients with intraabdominal or urinary tract infection for SMART project. (Merck initiated SMART project in 2002 to monitor the in vitro susceptibility of clinical aerobic and facultative gram-negative bacterial isolates from intra-abdominal infections (IAI) to selected antimicrobials. Collection of isolates from urinary tract infections (UTI) started in late 2009. This study is related to data collected in the period 2009-2014. Resistance patterns, patient age, year of sample collection (YOC), gender, location (3 sites: Hospital Universitario, Public university teaching Hospital 800 beds, Centro Medico de Caracas, Private Teaching Hospital 200 beds and Hospital de Clinicas Caracas, private Teaching Hospital of 300 beds) and sample type (Intraabdominal or urinary tract) . Each model was evaluated separately using forward stepwise multivariate logistic regression methodology, (final model was constructed with significant variables in univariate logistic regression) estimating sensitivity, specificity and ROC (Receiver Operating Characteristic). Sub analysis for E.coli and K.pneumoniae prediction model was also evaluated. General significance criteria were 0.05. STATA 11.0 was used as statistical package.

Results:

1. Every model (Ceftazidime, Ceftriaxone, Cefotaxime) shows a good capacity of prediction in terms of Sensibility and Specificity:
- **a.** Ceftazidime shows the best Sensibility (99%)
- **b.** Ceftriaxone shows the best Specificity (97%)
- **c.** Ceftazidime shows the best Sensibility/Specifity Relation (ROC 0.98)

2. Independently of other covariates included in the multivariate model (gender, age, YOC, location and type of sample) MIC ≥ to 1 µg was considered the best predictor related to phenotypic methods.

3. Separately evaluated Sub model results for E.coli and Klebsiella pneumoniae do not show significant differences.

Conclusions:

1. In setting were confirmation with secondary test for ESBL detection are not available or are expensive, MIC ≥ 1 of Ceftazidime is a good predictor of ESBL phenotype for enterobacteriaceae related to Intraabdominal or Urinary Tract Infection.

2. The Ceftazidime MIC´s can help generate information to guide therapy for the use of antibiotics in enterobacteriaceae 24 or 48 hours before having the results of phenotypic tests.

3. In limited resources scenarios or institutions Ceftazidime MIC´s can be useful for detection of ESBL isolates as an interim guidance.

Limitations of this study include:

- The number of SMART investigator sites varied each year; lack of clinical information to confirm nosocomial vs community-acquired isolates.
- Isolates were collected from 3 sites (Multispecialty teaching hospitals) in the same city (Capital City of Caracas), maybe that strategy can bias the type of sample with an overestimated prevalence of ESBL.
- Isolates were limited to IAI and UTI.

TABLE 1

General Characteristics of Patients / Isolates

		# (%)	% ESBL (Phenotype)
Isolates			
Organism	• E. coli	1415 (77.2)	26.1
	• Klebsiella pneumoniae	388 (21.1)	27.0
	• Klebsiella oxitoca	29 (1.5)	17.2
Body Location	• IAI (Intra abdominal Infec)	1163 (63.8)	27.0
	• ITU (Urinary Tract Infec)	658 (26.6)	24.9
	• Unknown	11 (0.6)	9.0
Year of Collection (YOC)	• 2009	HHI (12.2)	16.9
	• 2010	JKH (17.0)	27.2
	• 2011	JHK (17.5)	24.3
	• 2012	JIL (18.8)	28.0
	• 2013	JKM (17.1)	28.8
	• 2014	JKI (17.1)	28.9
Patients			
Age (Years, Mean (SD))		48,4 (23,6)	
Gender	• Female	1060 (58.9)	23.2
	• Male	739 (41.1)	30.8
Type of Hospital	• Private	1208 (65.94)	25.7
	• Public	624 (34.06)	27.0
Site	• Hospital Universitario	624 (34.0)	27.0
	• Centro Médico de Caracas	586 (30.8)	30.2
	• Hospital de Clínicas Caracas	643 (35.0)	20.7

TABLE 2

Model	Variable	OR	P	Sensitibity	Specifity	ROC
Ceftriaxone	• Ceftriaxone	377	0,001	91	97	94
	• Age	1,0	0,5			
	• Gender	1,0	0,8			
	• YOC	1,3	0,001			
Ceftazidime	• Cefatizidim	175	0,001	99	96	98
	• Age	6	0,15			
	• Gender	0,99	0,44			
	• YOC	1,2	0,01			
Cefotaxime	• Cefotaxime	170	0,00	92	96	95
	• Age	1,0	1,0,28			
	• Gender	1,0	0,3			
	• YOC	1,3	0,01			

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