In Vitro Activity of Colistin and Tigecycline Against Extended-Spectrum-Beta-Lactamase (ESBL)-Producing *Escherichia coli* and *Klebsiella pneumoniae* Isolated from Patients in Siriraj Hospital

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INTRODUCTION

The prevalence of extended-spectrum-beta-lactamase (ESBL)-producing organisms and their antimicrobial resistance patterns may vary between geographic areas. The prevalence of ESBL-producing *E. coli* and *K. pneumoniae* causing infections,
especially hospital-acquired infections, in Thailand has been increasing. The prevalence of ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from the patients of Siriraj Hospital in 2003 was 56.9 percent and 33.3 percent, respectively. ESBL-producing *E. coli* and *K. pneumoniae* are usually more resistant to antibiotics than ESBL-non-producing strains. They are usually resistant to most beta-lactams including penicillins and cephalosporins. The choice of antibiotic therapy for ESBL-producing *E. coli* and *K. pneumoniae* is, therefore, limited. The most effective antibiotic for severe infections caused by such organisms is a carbapenem, and as a result, any new agents effective against ESBL-producing *E. coli* and *K. pneumoniae* are sought after.

Colistin has been shown to be active and effective against multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* including those isolated from Thai patients. Tigecycline is a glycylcycline antibiotic that shows promising activity against a wide range of organisms. The objective of the study was to determine an in vitro activity of colistin and tigecycline against ESBL-producing *E. coli* and *K. pneumoniae* isolated from the patients hospitalized at Siriraj Hospital from 2004 to 2005.

**MATERIALS AND METHODS**

The studied organisms were 113 and 92 strains of ESBL-producing *E. coli* and *K. pneumoniae* isolated from different patients hospitalized at Siriraj Hospital from 2004 to 2005. The method for detection of ESBL-producers was the double-disk diffusion as recommended by the Clinical and Laboratory Standards Institute (CLSI). The susceptibility of colistin was determined by the disk diffusion test, using a 10-µg colistin sulfate disk, and the minimal inhibitory concentration (MIC) was determined by the E-test method for 50 isolates of ESBL-producing *E. coli* and 50 isolates of ESBL-producing *K. pneumoniae*. A quality control was performed by testing the susceptibility of *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853. The MIC of tigecycline was determined by the E-test method for 62 and 42 isolates of ESBL-producing *E. coli* and *K. pneumoniae*, respectively. Quality control was performed by testing the susceptibility of *E. coli* ATCC 25922. The methodology for susceptibility testing was done by direct colony suspension as recommended by the CLSI. The test isolate was grown overnight on blood agar at 35°C, and colonies were picked to suspend in sterile normal saline equivalent to a 0.5 McFarland standard. The suspension was used to inoculate on Mueller-Hinton agar, and the E-test strip was placed according to the manufacturer’s recommendation. The agar plates were incubated at 35°C for 18 hours before the inhibition zone and the MIC results were read.

**RESULTS**

The inhibition zones of colistin against *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were both 12 mm, and their MICs were both 0.25 mg/L. The MIC of tigecycline against *E. coli* ATCC 25922 was 0.12 mg/L. All aforementioned values were within reference limits. An in vitro activity of colistin revealed that 1) all isolates had an inhibition zone of ≥11 mm, 2) the MIC$_{50}$ and MIC$_{90}$ of colistin against ESBL-producing *E. coli* were 0.5 mg/L and 1 mg/L, respectively, and 3) the MIC$_{50}$ and MIC$_{90}$ of colistin against ESBL-producing *K. pneumoniae* were 0.5 mg/L and 0.5 mg/L, respectively. An in vitro activity of tigecycline revealed that 1) the MIC$_{50}$ and MIC$_{90}$ of tigecycline against ESBL-producing *E.coli* were 0.5 mg/L and 1 mg/L,
respectively and 2) the MIC\textsubscript{50} and MIC\textsubscript{90} of tigecycline against ESBL-producing \textit{K. pneumoniae} were 1.5 mg/L and 2 mg/L, respectively.

**DISCUSSION**

The susceptibility breakpoints of colistin against Gram-negative bacilli are the inhibition zone of \(\geq 11\) mm, and the MIC of \(\leq 2\) mg/L, whereas the susceptibility breakpoint of tigecycline against Enterobacteriaceae is the MIC of \(\leq 2\) mg/L. Therefore, nearly all strains of ESBL-producing \textit{E. coli} and \textit{K. pneumoniae} isolated from the patients hospitalized at Siriraj Hospital from 2004 to 2005 were susceptible to colistin and tigecycline. Our observations on susceptibility of ESBL-producing \textit{E. coli} and \textit{K. pneumoniae} to colistin and tigecycline were similar to several reports from other countries.\textsuperscript{6-8} However, clinical studies on efficacy of colistin and tigecycline for infections caused by ESBL-producing \textit{E. coli} or \textit{K. pneumoniae} are needed before they can be recommended in clinical practice. In addition, there are two different bases between colistin used in an in vitro susceptibility (colistin sulfate) and in clinical indications (sodium colistimethate). Even though sodium colistimethate, after intravenous administration, will dissociate into colistin sulfate, conclusion from most studies between correlation of in vitro susceptibility and clinical outcome cannot be drawn. Colistin and tigecycline may prove to be important antibiotics for treatment of ESBL-producing \textit{E. coli} and \textit{K. pneumoniae} infections in Thailand in the near future once more clinical information on colistin and tigecycline therapy of such infections becomes available.

**CONCLUSION**

Colistin and tigecycline are found to be active against ESBL-producing \textit{E. coli} and \textit{K. pneumoniae} isolated from Thai patients. Both antibiotics have a potential for being alternative therapy for infections caused by ESBL-producing \textit{K. pneumoniae} and \textit{E. coli} in the near future.

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**References**


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