Effectiveness and Safety of Generic Formulation of Meropenem (Penem®) for Treatment of Infections at Siriraj Hospital

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Objective: *generic meropenem (Penem®) has been available and was substituted for original meropenem in Siriraj Hospital, but its effectiveness and safety for treatment of infection in clinical setting are the main concern.*
Material and Method: *From July 2007 to July 2010, hospitalized patients aged 18 or older who received meropenem for at least 48 hours were identified retrospectively from the pharmacy database of Siriraj Hospital. 260 patients per group were required to demonstrate non-inferiority of generic meropenem (Penem®) versus original meropenem in term of overall favorable outcome.*
Results: *275 and 273 patients receiving original and generic meropenem were enrolled and analyzed. Overall favorable outcome and overall mortality were comparable between generic and original group (72.5% vs. 65.8%, p = 0.108; 38.6% vs. 39.3%, p = 0.918, respectively). No significant difference of adverse effect was found between two groups. The non-inferiority test indicated that the clinical outcome and overall mortality of the generic meropenem were non-inferior to the original meropenem (p < 0.001, p = 0.005, respectively). The independent factors associated with unfavorable outcome were previous use of an antibiotic, having respiratory tract infection, receiving lower dose and shorter duration of antibiotic. The independent factors associated with the overall mortality were underlying pulmonary disease, previous use of antibiotic, having respiratory tract or catheter related blood stream infection. Treatment with either generic or original meropenem did not relate to unfavorable outcome (p = 0.320) or overall mortality (p = 0.640).*
Conclusion: *Generic meropenem (Penem®) was not inferior to original meropenem for therapy of infections in the hospitalized patients at Siriraj Hospital.*

Keywords: *Meropenem, Original, Generic, Non-inferiority, Efficacy*

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Currently, generic medicines are increasingly used in clinical settings for several reasons. Among those common reasons are cost savings which lead to restriction of prescription policy and strict regulatory policy on the reimbursement of original medicines for price control[1]. Although generic medicine prescription or substitution may increase affordability for the public, especially in developing countries[2], its effectiveness and safety remains an issue of controversy[3-5]. Generally, approval of generic drugs requires only therapeutic equivalence which is assumed after demonstration of bioequivalence and pharmaceutical equivalence as innovator products[6]. However, most bioequivalence studies of generic product were evaluated in healthy subjects whose pharmacokinetics are quite different from the patients[7]. Therefore, effectiveness and safety of using generic drugs in clinical setting still remain topics of physician and public concern.

Meropenem, a broad spectrum antibiotic of carbapenem family, has been used for more than 10 years for treatment of a wide range of serious infection including complicated intra-abdomonal infection, complicated skin and skin structure infection and bacterial meningitis. Further, it was commonly prescribed for empirical therapy of severe bacterial infection in hospitalized patients[8]. After its patent has been expired, generic drugs from several pharmaceutical

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companies become available in the market. In Siriraj Hospital, a generic meropenem (Penem®), produced by M&H manufacturing Co. Ltd., has been substituted for the innovator product since October 2009. Its effectiveness and safety are crucial as it is used mostly for treatment of the seriously-ill patient.

The objective of the present study was to compare effectiveness and safety of generic meropenem (Penem®), with original products for treatment of infections in hospitalized patients at Siriraj Hospital.

Material and Method

Hospitalized patients aged 18 or older who received meropenem for at least 48 hours were identified retrospectively from the pharmacy database of Siriraj Hospital. The eligible patients were selected by systematic random sampling. Medical records of the chosen patients were reviewed to obtain demographic data, underlying conditions, indications of prescribing meropenem, type and site of infection, causative organism, previous and concurrent antibiotic use, microbiological and clinical outcomes and adverse events. Regarding hospital policy, after a generic meropenem became available in October 2008, it would be substituted for an innovator whenever meropenem was prescribed. Therefore, the eligible patients who received original meropenem were selected between July 2007 and October 2008 and those received generic meropenem (Penem®) were selected between October 2009 and July 2010.

The study was conducted to demonstrate non-inferiority of generic meropenem (Penem®) in relation to overall favorable outcome including cure and improvement at the end of treatment. The authors assumed a favorable outcome of 70% with the original drug and non-inferiority margin of 10% for the generic drug. With a power of 80% and type I errors of 5% by using n Query Advisor 5.0, a sample size of 260 patients per each group was needed to show non-inferiority of generic meropenem. The authors firstly enrolled 300 patients in each group and later excluded 25 patient from original group and 27 patients from generic group for the following reasons: no evidence of infection (19 and 10 patients in original and generic group, respectively), received meropenem for less than 48 hours (6 and 17 patients in original and generic group, respectively). Thus, 275 patients were enrolled in original groups and 273 patients were enrolled in generic groups.

Mean, standard deviation, median and range were used to summarize continuous variables, whereas categorical variables were expressed as numbers and percentages. Chi-square test (Pearson's or Fisher's exact test) for categorical variables and Student's t-test or Mann-Whitney test for continuous variables were used as appropriate. Multiple logistic regression was performed to adjust for confounding factors and evaluate the factors which influenced favorable outcomes and mortality. The strength of association with unfavorable clinical outcome or overall mortality was measured using odds ratio and its 95% confidence interval. All statistical procedures were conducted on PASW statistics 18.0 (SPSS Inc., Chicago, IL, USA) and statistical software R version 2.12.0 (R Development Core Team, 2010). A p-value of 0.05 or less was considered statistically significant using two tailed or one tailed test as appropriate.

Results

The characteristics of patients who received original and generic meropenem are shown in Table 1. There was no difference between two groups in term of age and sex ratio. Around 95% of patients had co-morbidities of which heart disease (31.3% vs. 19%, $p = 0.001$) and hematologic malignancy (19.3% vs. 7%, $p < 0.001$) were found to be more common in the patients who received original product, whereas cancer was found to be more common in those received the generic product (23.4% vs. 12.4%, $p = 0.001$). In addition, prior exposure to other antibiotic before receiving meropenem is significantly more frequent in the patient who received original drug (72.0% vs. 52.4%, $p < 0.001$).

The infections of the patients are reported in Table 2. Approximately 87% of infections were health-care associated. There was no difference between two groups in terms of type and site of infection, except for infection of the central nervous system, which was found to be more common in the patients who received the original product (3.3% vs. 0.4%, $p = 0.020$). The most common pathogens were gram-negative bacteria including extended-spectrum- beta-lactamase (ESBL) producing *E. coli* and *K. pneumoniae*, *P. aeruginosa* and *A. baumannii*. The patients who received the original drug were infected with *A. baumannii* and MSSA more frequently than those received generic drug (14.9% vs. 4.8%, $p < 0.001$; 4.7% vs. 1.1%, $p = 0.023$, respectively). Regarding to susceptibility of organism to meropenem, *A. baumannii* in the original group were more susceptible than those in the generic group (30.8% vs. 0%, $p = 0.046$). Concurrent antibiotics, as shown in Table 3, were given more frequently in

Table 1. Characteristics of patients

	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	p-value
Age (yr)			0.169
Mean ± SD	65.2 ± 17.8	67.5 ± 16.5	
Median (min, max)	69 (16, 100)	72 (15, 99)	
Gender			0.860
Male	131 (47.6%)	127 (46.5%)	
Female	144 (52.4%)	146 (53.5%)	
Department			0.153
Medicine	182 (66.2%)	188 (68.9%)	
Surgery	80 (29.1%)	64 (23.4%)	
Other	13 (4.7%)	21 (7.7%)	
Underlying disease	262 (95.3%)	260 (95.2%)	1.000
DM	96 (34.9%)	90 (33.0%)	0.697
Heart disease	86 (31.3%)	52 (19.0%)	0.001**
Hematologic malignancy	53 (19.3%)	19 (7.0%)	< 0.001
Renal disease	46 (16.7%)	44 (16.1%)	0.938
Cancer	34 (12.4%)	64 (23.4%)	0.001
Pulmonary disease	24 (8.7%)	23 (8.4%)	1.000
Immunosuppressive agents	18 (6.5%)	20 (7.3%)	0.848
Liver disease	14 (5.1%)	26 (9.5%)	0.067
Previous use of antibiotic	198 (72.0%)	143 (52.4%)	< 0.001**

** significant at 0.01 level

patient who received original meropenem (42.5% vs. 33%, p = 0.026). Eighty-two to 90% of meropenem was prescribed as appropriate indication, shown in Table 4. An original meropenem was prescribed more appropriately than the generic drug (90.5% vs. 82.8%, p = 0.011). There was no difference between two groups in term of dosage and duration, as shown in Table 5.

The outcomes of meropenem therapy are shown in Table 6. There was no significant difference in term of an overall favorable outcome (65.8 % vs. 72.5%, p = 0.108) and adverse effects between the original and the generic groups. Even though infection related death was found more common in generic group and death related to other causes was found to be more common in the original group, no significant difference was found in overall mortality (39.3% vs. 38.6%, p = 0.918). Table 7 showed the non-inferiority test of main outcome between original and generic meropenem. The generic meropenem was non-inferior to original meropenem in relation to overall favorable outcome (p < 0.001) and overall mortality (p = 0.005). Regarding overall favorable outcome, although the lower bound of the 95% confidence interval of difference (-14.3%) was lower than 10%, in favor to generic meropenem, the upper bound was within non-inferiority margin (1.0%).

The independent factors associated with clinical outcomes and mortality are shown in Table 8 and Table 9. By using a multiple logistic regression, treatment with either generic or original meropenem did not relate to unfavorable outcome (adjusted OR = 1.23, 95% CI: 0.82, 1.84, p = 0.320) or overall mortality (adjusted OR = 1.10, 95% CI: 0.75, 1.60, p = 0.640). The unfavorable outcome was independently associated with previous use of antibiotic (adjusted OR = 1.60, 95% CI: 1.06, 2.42, p = 0.027), having respiratory tract infection (adjusted OR = 2.43, 95% CI: 1.65, 3.58, p < 0.001), receiving lower dose antibiotic (adjusted OR = 1.24, 95% CI: 1.02, 1.51, p = 0.031) and shorter duration of antibiotic (adjusted OR = 1.03, 95% CI: 1.00, 1.07, p = 0.067). The overall mortality was associated with underlying pulmonary disease (adjusted OR = 2.28, 95% CI: 1.20, 4.30, p = 0.011), previous use of antibiotic (adjusted OR = 1.43, 95% CI: 0.97, 2.11, p = 0.069), having respiratory tract infection (adjusted OR = 2.18, 95% CI: 1.51, 3.15, p < 0.001) or catheter related blood stream infection (adjusted OR = 4.99, 95% CI: 1.25, 19.89, p = 0.023). Less mortality was found in patients who received a greater dose of meropenem (adjusted OR = 0.83, 95% CI: 0.69, 0.99, p = 0.042).

Table 2. Infections in the patients who received meropenem

	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	p-value
Type of infection			
Community-acquired	28 (10.2%)	40 (14.7%)	0.145
Health-care associated	247 (89.8%)	233 (85.3%)	
Site of infection			
Respiratory	124 (45.1%)	110 (40.3%)	0.294
Genitourinary	59 (21.5%)	59 (21.6%)	1.000
Intra-abdominal	32 (11.6%)	46 (16.8%)	0.104
Wound/soft tissue	20 (7.3%)	11 (4.0%)	0.145
CNS	9 (3.3%)	1 (0.4%)	0.020*
Primary bacteremia	2 (0.7%)	4 (1.5%)	0.449
Others	5 (1.8%)	0 (0%)	0.061
Evidence of infection			< 0.001**
Microbiological documented	191 (69.5%)	143 (52.4%)	
Clinical documented	84 (30.5%)	130 (47.6%)	
Common causative organism			
E.coli (ESBL- ve)	19 (6.9%)	15 (5.5%)	0.611
E.coli (ESBL+ ve)	40 (14.5%)	39 (14.3%)	1.000
K.pneumoniae (ESBL- ve)	22 (8.0%)	11 (4.0%)	0.076
K.pneumoniae (ESBL+ ve)	34 (12.4%)	22 (8.1%)	0.128
Pseudomonas aeruginosa	36 (13.1%)	31 (11.4%)	0.624
Acinetobacter baumannii	41 (14.9%)	13 (4.8%)	< 0.001**
MSSA	13 (4.7%)	3 (1.1%)	0.023*
MRSA	10 (3.6%)	4 (1.5%)	0.180
Enterococcus spp.	10 (3.6%)	5 (1.8%)	0.302
Isolated susceptible to meropenem			
E.coli (ESBL+ ve)	36/36 (100%)	39/39(100%)	1.000
K.pneumoniae (ESBL+ ve)	34/34 (100%)	21/21 (100%)	1.000
Pseudomonas aeruginosa	29/36 (80.6%)	22/30 (73.3%)	0.688
Acinetobacter baumannii	12/39 (30.8%)	0/11 (0%)	0.046

*,** significant at 0.05, 0.01 level respectively

Table 3. Concurrent antibiotics

	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	p-value
No	158 (57.5%)	183 (67.0%)	0.026*
Yes	117 (42.5%)	90 (33.0%)	
Glycopepeptide	64 (22.3%)	54 (19.8%)	0.373
Colistin	17 (6.2%)	17 (6.2%)	1.000
Aminoglycoside	13 (4.7%)	5 (1.8%)	0.097
Quinolone	14 (5.1%)	9 (3.3%)	0.404
Beta-lactam	1 (0.4%)	0 (0%)	1.000

* Significant at 0.05 level

Discussion

Although most characteristics of the patients in original and generic meropenem were comparable, there were some differences related to underlying diseases, proportion of common organism, previous and concurrent antibiotic use. However, overall favorable outcome, overall mortality and adverse effect were comparable between two groups. Multiple

Table 4. Indications of Meropenem

Indication	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	p-value
No	26 (9.5%)	47 (17.2%)	0.011*
Yes	249 (90.5%)	226 (82.8%)	
Confirmed or suspected infection due to *P.aeruginosa*	105 (42.2%)	103 (45.6%)	0.513
Severe infection due to ESBL-producing pathogens	61 (24.5%)	54 (23.9%)	0.963
Empirical therapy for hospital-acquired infection not respond to cephalosporin, aminoglycoside, fluroquinolone, beta-lactam+ beta-lactam inhibitor	44 (17.7%)	41 (18.1%)	0.989
Infection due to pathogen resistant to cephalosporin, aminoglycoside, fluroquinolone, beta-lactam+ beta-lactam inhibitor	24 (9.6%)	19 (8.4%)	0.759
Empirical therapy for febrile neutropenia	14 (5.6%)	8 (3.5%)	0.390
Infection due to pathogen susceptible to other antibiotic but the patient unable to receive such antibiotics	1 (0.4%)	1 (0.4%)	1.000

*Significant at 0.05 level

Table 5. Dosage and duration of Meropenem

	All patients	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	p-value
Dosage of Meropenem (gram per day)				0.863
Mean $\pm$ SD	2.2 $\pm$ 1.1	2.2 $\pm$ 1.0	2.2 $\pm$ 1.1	
Median (min, max)	2.0 (0.5, 6.0)	2.0 (0.5, 6.0)	2.0 (0.5, 6.0)	
Duration of Meropenem (day)				0.889
Mean $\pm$ SD	9.1 $\pm$ 6.6	9.4 $\pm$ 7.4	8.8 $\pm$ 5.7	
Median (min, max)	7.0 (2.0, 58.0)	7.0 (2.0, 58.0)	7.0 (2.0, 34.0)	

independent factors associated with unfavorable outcome or mortality were previous or concurrent use of other antibiotic, having respiratory tract or catheter related infection, underlying pulmonary disease, receiving inadequate dose or shorter duration of meropenem. From non-inferiority test, generic meropenem was not inferior to original drug in term of favorable outcome and overall mortality. Additionally, treatment with either generic or original did not affect clinical outcomes or overall mortality.

Because of the increasing cost of pharmaceutical expenditures, generic drugs become more widely used for their cost saving. To contain the costs, some countries or institutions stimulate generic use through generic substitution: the delivery of a generic drug by the pharmacist when a branded drug is indicated on the GP prescription[1]. Generally, therapeutic equivalence of generic drug was based solely on biopharmaceutical equivalence which is mostly conducted in healthy subjects[7] or by *in vitro* microbiological assay[9]. Such similarities may not always imply therapeutic equivalence. Vesca O et al found agonistic-antagonistic actions of three generic of vancomycins caused from inhibitory and stimulatory principles in formulations which lead to their lower bactericidal efficacy in mice[10]. Mastoraki E et al also reported a higher incidence of postoperative infection following CABG surgery in adult patients receiving generic cefuroxime instead of original cefuroxime as antimicrobial prophylaxis[11]. Therefore, prescribing generic meropenem for ill or severe patients in clinical practice needs to be evaluated carefully.

Conclusion

The present study showed non-inferiority of generic meropenem (Penem®) compared with its

Table 6. Outcomes of Meropenem therapy

	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	p-value
Clinical outcome			0.027*
Favorable outcome (Cure + Improve)	181 (65.8%)	198 (72.5%)	0.108
Infection worse	31 (11.3%)	12 (4.4%)	0.005
Die of infection	60 (21.8%)	60 (22.0%)	1.000
Others	3 (1.1%)	3 (1.1%)	1.000
Microbiological outcome			< 0.001**
Eradicate	66 (24.0%)	72 (26.4%)	0.588
Persist	35 (12.7%)	8 (2.9%)	< 0.001**
New organism	38 (13.8%)	23 (8.4%)	0.061
Undetermined	136 (49.5%)	170 (62.3%)	0.003**
Length of hospital stay (day)			0.087
Mean $\pm$ SD	40.2 $\pm$ 41.4	34.9 $\pm$ 32.0	
Median (min, max)	30.0 (3.0, 334.0)	25.0 (3.0, 266.0)	
Discharge status			< 0.001**
Alive	164 (59.6%)	167 (61.2%)	0.779
Die of infection	63 (22.9%)	89 (32.6%)	0.015*
Die of other causes	43 (15.6%)	16 (5.9%)	0.008**
Against advice	5 (1.8%)	1 (0.4%)	0.222
Adverse effects			
Antibiotic allergy	2 (0.7%)	0 (0%)	0.482
Antibiotic-associated diarrhea	26 (9.5%)	27 (9.9%)	0.978
Overall mortality			
n	270	273	0.918
	106 (39.3%)	105 (38.6%)	

*, ** significant at 0.05, 0.01 level respectively

Table 7. Main outcomes of Meropenem therapy

Factor	Original Meropenem (n = 275)	Generic Meropenem (n = 273)	Difference (95% CI)	Chi-square test (p-value)	Non-inferiority test (p-value)
Clinical outcome					
(Cure + Improve)	181 (65.8%)	198 (72.5%)	-6.7% (-14.3, 1.0)	0.108	< 0.001**
Infection worse	31 (11.3%)	12 (4.4%)	6.9% (2.4, 11.6)	0.005**	< 0.001**
Die of infection	60 (21.8%)	60 (22.0%)	0% (-6.9, 6.9)	1.000	0.003**
Others	3 (1.1%)	3 (1.1%)	0% (-2.2, 2.2)	1.000	< 0.001**
Overall mortality					
n	270	273			
	106 (39.3%)	105 (38.6%)	0.8% (-7.4, 8.9)	0.918	0.005**

**Significant at 0.01 level

innovators in overall favorable outcome and overall mortality. No version of meropenem was associated to unfavorable outcome or overall mortality. There were limitations of the study in relation to different timing of the present study and the study design since the study was not designed as a randomized control trial. Nevertheless, there is enough evidence to conclude that generic meropenem (Penem®) was not inferior to original meropenem for therapy of infections in the hospitalized patients at Siriraj Hospital.

Table 8. The association between potential factors and unfavorable clinical outcome in infected patients

Factor	Crude OR (95% CI)	p-value	Adjusted[a] OR (95% CI)	p-value
Previous use of antibiotic	1.62 (1.10, 2.38)	0.015*	1.60 (1.06, 2.42)	0.027*
Duration of Meropenem, day	1.05 (1.01, 1.08)	0.006**	1.03 (1.00, 1.07)	0.067
Respiratory tract infection	2.38 (1.64, 3.45)	< 0.001**	2.43 (1.65, 3.58)	< 0.001**
Length of hospital stay (day)	1.01 (1.00, 1.02)	0.004**	1.01 (1.00, 1.02)	0.005**
Dosage of Meropenem (gram/day)	1.22 (1.02, 1.46)	0.026*	1.24 (1.02, 1.51)	0.031*
Received generic meropenem[b]	1.37 (0.95, 1.97)	0.09	1.23 (0.82, 1.84)	0.320

OR = Odds ratio
[a] adjusted for underlying heart disease, underlying hematologic malignancy, underlying cancer
[b] original meropenem is the reference group of received meropenem
*,** significant at 0.05, 0.01 level respectively

Table 9. The association between potential factors and overall mortality in infected patients

Factor	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Underlying pulmonary disease	2.51 (1.37, 4.63)	0.003**	2.28 (1.20, 4.30)	0.011*
Previous use of antibiotic	1.44 (1.00, 2.06)	0.050	1.43 (0.97, 2.11)	0.069
Respiratory tract infection	2.22 (1.56, 3.16)	< 0.001**	2.18 (1.51, 3.15)	< 0.001*
Dosage of Meropenem (gram/day)	0.81 (0.69, 0.96)	0.017*	0.83 (0.69, 0.99)	*
Catheter related blood stream infection (CRBSI)	4.31 (1.13, 16.43)	0.032*	4.99 (1.25, 19.89)	0.042*
Received generic meropenem[b]	1.03 (0.73, 1.45)	0.875	1.10 (0.75, 1.60)	0.023* 0.640

OR = Odds ratio
[a]adjusted for underlying heart disease, underlying hematologic malignancy, underlying cancer
[b]original meropenem is the reference group of received meropenem
*, ** significant at 0.05, 0.01 level respectively

Potential conflict of interest

None.

References

1. Pechlivanoglou P, van der Veen WJ, Bos JH, Postma MJ. Analyzing generic and branded substitution patterns in the Netherlands using prescription data. BMC Health Serv Res 2011; 11: 89.
2. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet 2009; 373: 240-9.
3. Silva E, Diaz JA, Arias MJ, Hernandez AP, de la Torre A. Comparative in vitro study of the antimicrobial activities of different commercial antibiotic products for intravenous administration. BMC Clin Pharmacol 2010; 10: 3.
4. Snyman JR, Schoeman HS, Grobusch MP, Henning M, Rabie W, Hira M, et al. Generic versus non-generic formulation of extended-release clarithromycin in patients with community-acquired respiratory tract infections: a prospective, randomized, comparative, investigator-blind, multicentre study. Clin Drug Investig 2009; 29: 265-74.
5. Zuluaga AF, Agudelo M, Cardeno JJ, Rodriguez CA, Vesga O. Determination of therapeutic equivalence of generic products of gentamicin in the neutropenic mouse thigh infection model. PLoS One 2010; 5: e10744.
6. FDA U.S. Food and Drug Administration. Greater access to generic drugs [Internet]. 2011 [cited 2011 Dec 6]. Available from: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143545.htm
7. Boonleang J, Panrat K, Tantana C, Krittathanmakul S, Jintapakorn W. Bioavailability and

pharmacokinetic comparison between generic and branded azithromycin capsule: a randomized, double-blind, 2-way crossover in healthy male Thai volunteers. Clin Ther 2007; 29: 703-10.
8. Wiseman LR, Wagstaff AJ, Brogden RN, Bryson HM. Meropenem. A review of its antibacterial activity, pharmacokinetic properties and clinical efficacy. Drugs 1995; 50: 73-101.
9. Rodriguez CA, Agudelo M, Catano JC, Zuluaga AF, Vesga O. Potential therapeutic failure of generic vancomycin in a liver transplant patient with MRSA peritonitis and bacteremia. J Infect 2009; 59: 277-80.
10. Vesga O, Agudelo M, Salazar BE, Rodriguez CA, Zuluaga AF. Generic vancomycin products fail in vivo despite being pharmaceutical equivalents of the innovator. Antimicrob Agents Chemother 2010; 54: 3271-9.
11. Mastoraki E, Michalopoulos A, Kriaras I, Mouchtouri E, Falagas ME, Karatza D, et al. Incidence of postoperative infections in patients undergoing coronary artery bypass grafting surgery receiving antimicrobial prophylaxis with original and generic cefuroxime. J Infect 2008; 56: 35-9.

ประสิทธิผลและความปลอดภัยของยาสามัญ meropenem (Penem®) ในการรักษาโรคติดเชื้อในโรงพยาบาลศิริราช

ณสิกาญจน์ อังคเศกวินัย, พีระวงษ์ วีรารักษ์, ศศิมา ทองสาย, วิษณุ ธรรมลิขิตกุล

วัตถุประสงค์*: โรงพยาบาลศิริราชได้มีการนำยาสามัญ meropenem (Penem®) มาใช้ทดแทนยาต้นแบบในการรักษาโรคติดเชื้อ อย่างไรก็ตามยังมีความไม่มั่นใจด้านประสิทธิผลและความปลอดภัยของยา*

วัสดุและวิธีการ*: ศึกษาข้อมูลแบบย้อนหลังจากฐานข้อมูลยาระหว่างเดือน กรกฎาคม พ.ศ. 2550 ถึง เดือน กรกฎาคม พ.ศ. 2553 โดยวิเคราะห์ข้อมูลผู้ป่วยที่มีอายุตั้งแต่ 18 ปีขึ้นไป ซึ่งถูกรับไว้รักษาในโรงพยาบาลและได้รับยา meropenem นานอย่างน้อย 48 ชั่วโมง โดยต้องมีผู้ป่วยอย่างน้อย 260 รายต่อกลุ่ม เพื่อศึกษาความไม่ด้อยกว่าของยาสามัญ meropenem (Penem®) เปรียบเทียบกับยาต้นแบบในด้านการหายหรือดีขึ้นจากการติดเชื้อ*

ผลการศึกษา*: จากผู้ป่วยที่ได้รับยาต้นแบบ meropenem 275 ราย และได้รับยาสามัญ meropenem (Penem®) 273 ราย พบว่าผู้ป่วยหายหรือดีขึ้นจากการติดเชื้อไม่แตกต่างจากกลุ่มที่ได้รับยาต้นแบบ (ร้อยละ 72.5 เทียบกับ ร้อยละ 65.8, p = 0.108) และมีอัตราการเสียชีวิตไม่แตกต่างกัน (ร้อยละ 38.6 เทียบกับ ร้อยละ 39.3, p = 0.918) รวมถึงไม่พบความแตกต่างในด้านผลข้างเคียงของยา เมื่อทดสอบความไม่ด้อยกว่ากันของผลการรักษาหลัก พบว่ายาสามัญมีผลการรักษาทางคลินิกและอัตราการตายรวมไม่ด้อยกว่ายาต้นแบบ (p < 0.001, p = 0.005, ตามลำดับ) สำหรับปัจจัยอิสระที่มีผลต่อการรักษาทางคลินิก ได้แก่ การได้รับยาต้านจุลชีพอื่นนำมาก่อนการติดเชื้อในระบบทางเดินหายใจ การได้รับยา meropenem ในขนาดต่ำหรือระยะเวลาสั้น สำหรับปัจจัยอิสระที่มีผลต่ออัตราการตายรวม ได้แก่ การมีโรคประจำตัวเดิมเป็นโรคปอด การได้รับยาต้านจุลชีพอื่นนำมาก่อน การติดเชื้อในระบบทางเดินหายใจ หรือสายสวนหลอดเลือดโดยพบว่าชนิดของยา meropenem ที่ใช้ไม่มีความสัมพันธ์กับการหายหรือดีขึ้นจากการติดเชื้อ (p = 0.320) หรืออัตราการตายรวม (p = 0.640)*

สรุป*: ยาสามัญ meropenem (Penem®) ไม่ด้อยกว่ายาต้นแบบ meropenem ในการรักษาโรคติดเชื้อในผู้ป่วยที่รับไว้ในโรงพยาบาลศิริราช*