Bioequivalence, Antibacterial Activity and Therapeutic Outcome of A Generic Meropenem (Mapenem®)

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Background: *The authors aimed to compare the bioequivalence and antibacterial activity of a generic meropenem with the original meropenem and studied its preliminary therapeutic outcome.*
Material and Method: *A randomized, open-label, crossover study was employed to assess the bioequivalence and antibacterial activity. Twenty-six healthy males were recruited at Siriraj Hospital, Thailand and randomized to firstly receive either a single intravenous 30-minute infusion of a generic (Mapenem®) or original meropenem (Meronem®) and vice versa for the second period. The washout period was one week. Ten milliliters of blood samples were collected before meropenem infusion and at 0, 10, 15, 30, 45, 60, 90, 120, 150, 180, 240, 360, 470 and 480 minutes after the beginning of the drug infusion. Blood samples were coded and separated into plasma and serum samples. Plasma samples were used to determine drug concentrations by HPLC-UV detector and the data were analyzed for Cmax, AUC_{0-t} and AUC_{0-inf}. Serum samples were assayed in triplicate for measuring generic and original meropenems'inhibitory activities of a meropenem-susceptible E. coli ATCC 25922 in the same agar plate. An open-label design was used to preliminarily study of the therapeutic outcome and adverse effects of the generic meropenem in 30 patients.*
Results: *All enrolled twenty-six volunteers completed the whole study. The statistical analysis of 90% confidence interval of Cmax, AUC_{0-t} and AUC_{0-inf} of the generic and original meropenems were 87.7 to 101.7%, 96.3 to 102.4% and 96.3 to 102.3%, respectively. The results were within the standard range of bioequivalence acceptance criteria (80-125%) and the powers of the test were greater than 80%. Using E. coli ATCC 25922 in the blind assay of serum inhibition activity, the inhibitory zone sizes (mm) of the generic compared to original meropenems were not statistically different with respect to every time points of blood collections ($p < 0.05$). Correlation of mean values of serum meropenem levels and the widths of inhibitory zone sizes of the same samples collected at the same intervals showed good linear relationship with $r = 0.891$; $R^2 = 0.794$ ($p < 0.01$) for the generic meropenem and $r = 0.885$; $R^2 = 0.784$ ($p < 0.01$) for the original meropenem. The therapeutic result with the generic meropenem for various indications was successful or improved in 24 cases from 30 cases (80%) and the bacterial cure rate was 23 in 30 clinical isolates (76.7%). Adverse reactions probably related to the study medication were rash and elevated liver enzymes in 1 and 3 patients, respectively, and all resolved spontaneously.*
Conclusion: *In the present study, the generic meropenem exhibited indifferent bioequivalence and antibacterial activity compared to the original meropenem. There was also a good correlation between serum levels and inhibitory zone sizes produced by the same serum samples in every periods of blood collection. Clinical efficacy of the generic meropenem was shown to be satisfactory without notable severe adverse reaction.*

Keywords: *Generic meropenem, Serum inhibition assay, Bioequivalence study*

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Meropenem is a broad-spectrum antibiotic that has aroused considerable interest because of its exceptional potency against various gram-negative bacteria including ESBL-producing or AmpC-mediated beta-lactamase producing enterobacteriaceae[1-3]. It is often used empirically to treat serious infections until the pathogens are proven susceptible to narrow-spectrum antibiotics. When a generic meropenem becomes available, some physicians feel reluctant to use generic meropenem because there is no solid evidence to prove its quality comparable to the original Meronem®.

Measurement of the plasma levels of the active ingredient after using an intravenous form of generic meropenems by HPLC method is generally accepted as a standard mean to ensure its bioequivalence. However, the bioequivalence is definitely not identical to "antibacterial equivalence" though discordance of the two equivalences may seldom exist with intravenous antimicrobials. The authors have witnessed difference of antibacterial potency between ofloxacin and levofloxacin due to difference in isomer structure that has influence on the MIC values[4]. The stability of generic drug in the human body is another problem that can affect drug potency as recently reported with a generic cefuroxime[5]. Once meropenem is mixed with normal saline, its concentration was reported to decrease 11.85% after 8 hours storage at 32-37°C.[6] Hence, in addition to bioequivalence study of a generic meropenem, the authors performed serum inhibition test to compare their antibacterial activities after infusion into human volunteers and aimed to correlate their inhibitory zone sizes with corresponding plasma concentrations. A preliminary study of the clinical efficacy and adverse effects of a generic meropenem was also investigated separately.

Material and Method

A generic meropenem (Mapenem®) produced by Siam Pharmaceutical Co. Ltd. lot A7ME00201/3 was used as the generic or test product and compared with Meronem® of AstraZeneca Ltd. lot DV826 as the original or reference product. The present study protocol was approved by the Ethics Committee (SiEC protocol no. 404/2549) and the written informed consent was obtained from each volunteer prior to the participation in the present study.

Study design

An open-label, randomized, crossover single-dose study, using two period, two sequences, with a washout period of 7 days, was used. Twenty-six healthy Thai male volunteers, aged 20 to 40 years were recruited at Siriraj Hospital. Their health conditions were assessed by the medical history, clinical examination and blood chemistry analysis. Subjects were randomly divided to receive either one gram of generic or original drug as a single-dose of meropenem by intravenous infusion for 30 minutes by an infusion pump. After the 7-day washout period, the subjects were crossed over to receive the other preparation by the same protocol. Serial 10 milliliters of blood samples were collected by venous catheterization at hand or forearm of each volunteer before and 10, 15, 30, 45, 60, 90, 120, 150, 180, 240, 360, 470 and 480 minutes after the beginning of the infusion. Each 5 ml of blood samples were kept in heparinized and ordinary tubes and coded. Plasma and serum specimens were separated and stored at -80°C until analysis. Plasma concentrations of meropenem at each interval were blindly determined using high-performance liquid chromatographic method with ultraviolet light detection (HPLC-UV detector). The plasma area under concentration-time curve (AUC) and maximum plasma concentration (C_{max}) were calculated and used for bioequivalence study of generic meropenem. C_{max} and AUC were determined by the statistical analysis. The 90% confidence interval of the means and log transformed data must reside within the 0.80 to 1.25 in order to meet the accepted criteria of bioequivalence.

HPLC analytical method

Determination of meropenem concentrations in plasma was performed using validated high performance liquid chromatography (HPLC) method, modified from Allergranzi B et al[7]. Meropenem and internal standard theophylline were extracted from sample by solid phase extraction on Oasis cartridges. Fifty-microliter samples were injected into C18 reverse phase column at the temperature of 30°C with a mobile phase of ammonium acetate 50 mM, pH 5: acetonitrile (9:1) at a flow rate of one milliliter per minute and with ultraviolet (UV) light detection at 296 nm. Quantitation of meropenem was determined by linear regression analysis of the peak area ratios of the internal standard. The detention limit was 0.1 to 50 microgram per milliliter. The inter-day and intra-day relative standard deviation were lower than 10.67 per cent and per cent recovery of meropenem was between 97.66 and 106.55. The mean extraction recoveries of meropenem and internal standard were 81.36 to 97.77 per cent, respectively.

Bioassay of the antibacterial activity

Serum inhibition bioassay was blindly performed using coded samples and measured in the term of inhibitory zone sizes[8]. Three milliliters of Muller Hinton broth (Difco) containing meropenem-susceptible *Escherichia coli* ATCC 25922 at the concentration of 1 x 10^8 CFU per milliliter was mixed thoroughly with 300 milliliters of Muller Hinton agar at 50°C. Then 15 milliliters of the mixture were poured over a sterile petri dish with a diameter of 90 millimeters. The dish was left to cool down and form agar at room temperature for 30 minutes. A cox borer with 7 millimeters in internal diameter was used to punch holes to make agar wells in each plate. The agar plugs were removed gently to avoid disturbing or tearing of the adjacent agar. Then 50 microliters of serum samples collected at the same time point from the same volunteer after receiving generic or original meropenem were added in triplicate into the alternative wells on the same dish (Fig. 2). The dishes were incubated for 18 hours at 37°C. Then they were inverted, and the diameters of inhibitory zones were read with a vernier caliper through the back of the dish to the nearest 0.1 millimeter. Serum inhibitory zone sizes exhibited by generic and original meropenems at the same period of collections were averaged and compared to show the level of similarity of potency. The correlation between serum meropenem levels and inhibitory zone sizes of the same generic or original samples collected at each interval was determined to indicate the level of causal strength and pattern of a relationship between the two variables.

The preliminary efficacy and safety test

The efficacy and safety of the generic meropenem for the treatment of severe or antimicrobial-resistant infections were assessed in 30 patients at Siriraj Hospital according to the indication under supervision of the attending physicians. Treatment outcome was evaluated by clinical and microbiological responses. Adverse reaction was also noted if there was any. The present study protocol was approved by the Ethics Committee (COA no. Si 252/2007) and informed consent was obtained before starting the study drug.

Results

All twenty-six Thai healthy male volunteers, aged 20 to 40 years completed the open-label, randomized, crossover single-dose study without any notable adverse reaction. Results of pharmacokinetics study and drug levels at each interval in the volunteers receiving generic and original meropenems are shown in Table 1 and Fig. 1. The peak concentrations or C_{max} (mean ± SD) were found to be 50.31 ± 11.35 and 53.26 + 11.12 μg/ml; AUC_{0-t} (mean ± SD) 3751 ± 501.03 and 3798 ± 654.25 μg.min/ml and $AUC_{0-\infty}$ (mean ± SD) 3769 ± 503.29 and 3818 ± 658.37 μg.min/ml respectively. The 90% CI of the relative means and log transformed data of C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ of the generic to original

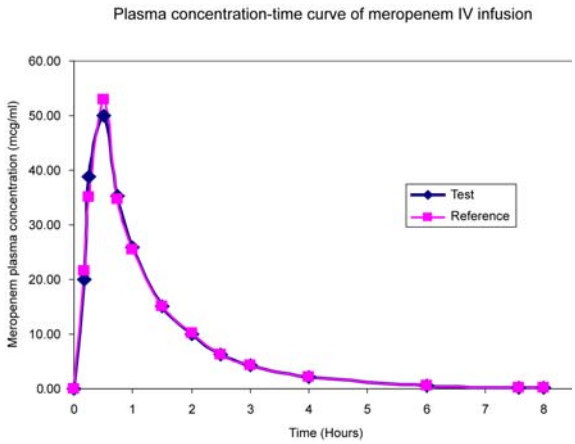


Fig. 1 Mean plasma concentration-time curves of intravenous (IV) generic and original meropenem infusions (n = 26)

Table 1. Comparison of pharmacokinetic parameters after one gram, 30-minute intravenous infusion in 26 volunteers between the generic and original meropenems

Parameter	Generic meropenem	Original meropenem	90% confidence interval
C_{max} (μg/ml) (mean ± SD)	50.31 ± 11.35	53.26 ± 11.12	87.8-101.7
AUC_{0-t} (μg.min/ml) (mean ± SD)	3751.00 ± 501.03	3798.00 ± 654.25	96.3-102.4
$AUC_{0-\infty}$ (μg.min/ml) (mean ± SD)	3769.00 ± 503.29	3818.00 ± 658.37	96.3-102.3
$T_{1/2}$ (hr) (mean ± SD)	1.02 ± 0.11	1.01 ± 0.12	-
T_{max} (hr) (mean ± SD)	0.52 ± 0.07	0.49 ± 0.09	-
Kel (hr^{-1}) (mean ± SD)	0.69 ± 0.07	0.69 ± 0.08	-

Table 2. Serum concentrations and inhibitory zone sizes exhibited by serum samples from generic and original meropenem volunteer groups at each period of sample collections

Minutes after infusion	Concentration of generic meropenem (μg/ml)	Inhibitory zone size of generic meropenem (mm) (mean ± SD)	Concentration of original meropenem (μg/ml)	Inhibitory zone size of original meropenem (mm) (mean ± SD)
-0*	0	0	0	0
10	20.09	26.95 ± 3.81	21.49	26.42 ± 4.46
15	33.81	28.78 ± 4.17	35.05	28.10 ± 4.53
30	50.00	30.64 ± 4.87	52.94	29.58 ± 4.64
45	35.25	27.18 ± 2.66	34.61	27.09 ± 2.52
60	25.92	25.82 ± 2.06	25.42	26.01 ± 2.15
90	15.08	23.47 ± 2.03	15.13	23.44 ± 1.99
120	10.01	23.72 ± 2.59	10.14	23.72 ± 2.65
150	6.28	21.33 ± 2.40	6.26	21.36 ± 2.36
180	4.24	21.20 ± 1.47	4.25	21.20 ± 1.77
240	2.16	19.89 ± 1.63	2.12	19.86 ± 1.74
360	0.60	16.70 ± 1.59	0.59	16.72 ± 2.00
470	0.24	13.58 ± 2.44	0.24	14.26 ± 1.92
480	0.20	13.44 ± 2.48	0.22	13.62 ± 2.14

-0* = immediately before starting antibiotic infusion

meropenems were 87.8 and 101.7, 96.3 and 102.4, 96.3 and 102.3 respectively, which resided within 80 to 125 percent. Hence the two products were considered bioequivalent according to standard criteria.

The diameters (milliliter) of inhibitory zone sizes produced by meropenem in both groups are shown in Table 2 and Fig. 2 and 3. Comparison of the diameters between both groups at the same time point revealed almost identical mean values and the minute differences were not statistically significant by the paired t-test. Homogeneity of variance for each pair of serum samples was demonstrated using Levene's test for equality of variances. Hence, antimicrobial potency of the generic and original meropenems was comparable at least up to eight hours after intravenous infusion into the volunteers.

The correlation between mean plasma concentrations of meropenem and diameters of inhibition zones at the same time points in both groups were analyzed and both lines had a curvilinear relationship and almost coincided as shown in Fig. 4. Statistical values for the correlation analysis were $r = 0.891$; $R^2 = 0.794$ ($p < 0.01$) for generic meropenem group and $r = 0.885$; $R^2 = 0.784$ ($p < 0.01$) for the original meropenem group.

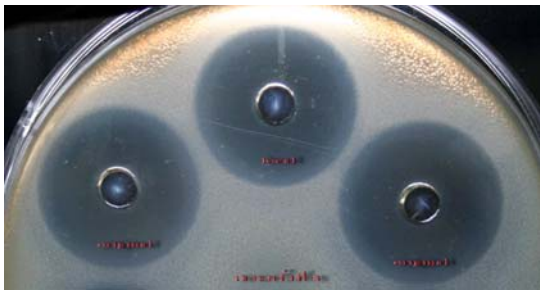
Baseline clinical characteristics, comorbid illness and demographic data of the 30 patients including adverse reactions are shown in Table 3. A preliminary study of clinical efficacy and microbiological eradication rate are shown in Table 4. Treatment with generic meropenem in 30 patients showed that clinical and microbiological responses were found in 24 cases (80%) and 23 (76.7%) patients respectively which were within the expected range. The incidence of adverse

Table 3. Baseline clinical characteristics, demographic data of 30 patients and adverse reactions

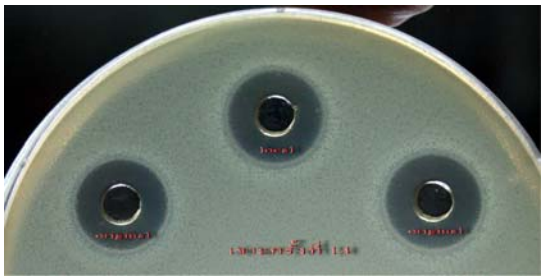
Male : female	1:2
Mean age; year (range)	67.8 (34-92)
Comorbid illness [n, (%)]	28 (93.3)
Diabetes mellitus	15 (50.0)
Hypertension	11 (36.7)
Chronic kidney disease	7 (23.3)
Malignancy	6 (20.0)
Coronary artery disease	5 (16.7)
Cerebrovascular disease	4 (13.3)
Chronic liver disease	3 (10.0)
Chronic lung disease	1 (3.3)
Others (dementia, COPD, SLE etc.)	10 (33.3)
Antimicrobial administration prior to enrollment [n, (%)]	29 (96.7)
Mean APACHE II score (range)	15.6 (5-26)
Mean duration of meropenem administration (range)	8.2 (1-14)
Adverse reactions [n, (%)]	4* (13.3)

* Adverse reactions probably related to study medication were rash and elevated liver enzymes in 1 and 3 patients, respectively, and all resolved spontaneously

Before the infusion



Two hours after the infusion



Eight hours after the infusion

Fig. 2 Inhibitory zone sizes exhibited by serum samples from generic and original mereopenem before the infusion and at two and eight hours after the infusion

reaction was not significantly different from what has been observed in the treatment with original meropenem. Adverse reactions probably related to generic meropenem were rash and elevated liver enzymes in 1 and 3 patients, respectively. All reactions resolved spontaneously.

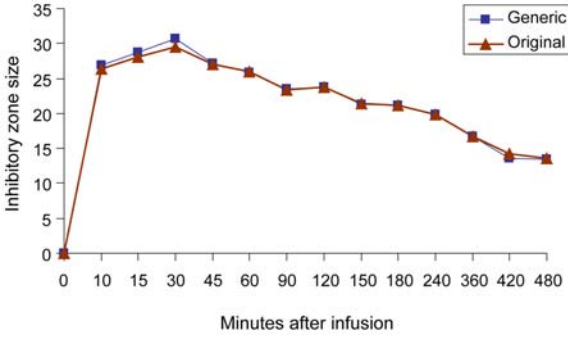


Fig. 3 Inhibitory zone sizes produced by serum samples at each interval from generic and original meropenems before and up to 8 hours after initiation of the infusion (n = 26)

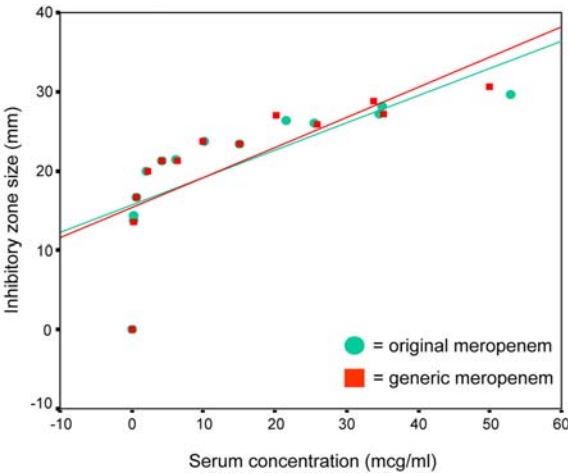


Fig. 4 Correlation between mean plasma concentrations of meropenem and diameters of inhibition zones at the same time points in the generic and original meropenem groups (n = 26)

Discussion

This present study was conducted to compare bioequivalence and antibacterial activity of a generic to the original meropenems in order that the generic meropenem could be widely accepted as a reasonable alternative to the original meropenem. In the context of bioavailability study, the "power of study" was adequate to detect a significance of 20 per cent difference between mean of C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ of the generic to original meropenems if the differences actually existed between the two products in the study of 26 volunteers. The 90% confidence interval of the ratio of $AUC_{0\ to\ 8}$, $AUC_{0-\infty}$ and C_{max} between generic and

Table 4. Response rate by site of infection and type of causative bacteria in 30 cases

Site of infection	Clinical cure rate Number of case/total (%)	Microbiological cure rate Number of case/total (%)
Lower respiratory tract	6/12 (50)	5/12 (41.7)
Blood stream	8/8 (100)	8/8 (100)
Urinary tract	8/8 (100)	8/8 (100)
Abdomen	2/2 (100)	2/2 (100)
Total	24/30 (80)	23/30 (76.7)
Causative bacteria		Microbiological eradication rate Number of isolate/total (%)
ESBL-producing *Escherichia coli*		10/10 (100)
Non-ESBL-producing *E. coli*		2/2 (100)
ESBL-producing *Klebsiella pneumoniae*		6/9 (67)
Non-ESBL-producing *K. pneumoniae*		1/1 (100)
Pseudomonas aeruginosa		3/6 (50)
Acinetobacter baumannii		0/2 (0)
Salmonella sp.		1/1 (100)
Providentia sp.		1/1 (100)
Total		24/32* (75)

* Two cases were each infected with two micro-organisms

original meropenems were indeed in the range of 0.80-1.25 as recommended by the USP24-NF 19 guidelines for bioequivalence study. Therefore, bioequivalence can be indicated between this generic and original meropenems[9].

Although the establishment of bioequivalence is usually unnecessary for intravenous formulation of antibiotics, once it has gained regulatory approval by Thai FDA, the prices of generic intravenous antibiotics are sometimes very seductive compared to the originals that physicians are greatly concerned about their qualities especially if they are classified as life-saving antibiotics. Meropenem is among one of the most useful weapons against resistant pathogenic bacteria causing serious infections. Bioequivalence study is a universal method to assure quality but the cost of the study is relatively expensive for Thailand and the method needs sophisticated equipment. The alternative of less expensive and feasible test to directly measure antimicrobial activity after it has been administered to human would be preferred. The present study proved that serum inhibition assay can be used to serve this purpose. The inhibitory zone sizes of the generic and original meropenems were comparable and correlated well with levels of serum concentrations. This method can assure the equivalence of antibacterial activity in comparison with the bioequivalence study of the generic meropenem and reflects level of antibacterial activity and stability of generic meropenem within the human body to eight hours after administration. The technique is simple, reproducible though laborious but gives precise and accurate comparison of antibacterial activity and degree of stability of the infused meropenems. Kongthaisong et al[10] used a similar concept to assay the anti-malarial activities of three oral formulations of dihydroartemisinin manufactured in the People's Republic of China, Belgium and Thailand. They found that the ex vivo blood schizontocidal activity profiles generally coincided with plasma concentration-time profiles and the ex vivo model may be a useful tool for evaluating and comparing the schizontocidal activities in addition to bioequivalence study of the interesting drugs. Though the Thai FDA continuously checks and regulates pharmaceutical manufacturing and product quality with current good manufacturing practice program to obviate the necessity of conducting clinical trials, the present study's result will augment Thai FDA's pharmaceutical product of the quality assurance program. The authors believe that the addition of serum inhibition assay to bioequivalence study of a generic meropenem is a significant initiative to enhance the regulation of pharmaceutical manufacturing and product quality of life-saving antibiotics. Since the generic manufacturers

do not incur the cost of drug discovery and do not bear the burden of proving the safety and efficacy of the drugs through clinical trials, the authors encourage generic manufacturers to ensure comparable product activity of their preparations with serum inhibition assay in order to gain confidence for physicians and the cost is cheaper compared with the bioequivalence study. In addition, serum samples could be reduced to four samples per one drug for the assay of antibacterial activity. After generic meropenem has been used in the hospitals, a periodic serum inhibition assay or bioequivalence study is required to prove that the local firms can consistently manufacture meropenem with the comparable activity in large quantity. In the United States, the law even allows generic-drug manufacturers to apply for FDA approval and conduct tests of bioequivalence before the relevant patents expire without being subject to patent-infringement claims[11]. In Thailand, the availability of a generic good-quality antibiotic is needed to help control medical costs and insurance premiums. Therefore, bioequivalence study of a generic drug before marketing is becoming an acceptable method for generic manufacturers to assure physicians for the drug quality[12]. Alternatively, serum inhibition assay is a reasonable option if bioequivalence study is too costly or not feasible due to limited availability of the sophisticated equipment.

A preliminary study of efficacy and adverse effect of the generic meropenem for various indications in 30 patients with mild to moderate severity of infections revealed that the generic meropenem exhibited therapeutic outcome and the adverse effects do not differ from what the authors have observed with the original meropenem. Clinical and microbiological responses were found in 24 cases (80%) and 23 cases (76.7%) respectively. Adverse reactions possibly related to generic meropenem were rash and elevated liver enzymes in one and three patients, respectively and all reactions resolved spontaneously. Since the study is not a comparative trial, the authors can only conclude that the therapeutic outcome and adverse effect do not differ from what the authors had experienced with the original meropenem.

Conclusion

The present study revealed that the generic and original meropenems exhibited pharmacokinetic and antibacterial equivalence. Pharmacodynamic study using serum inhibition assay is not too sophisticated to perform and its result was comparable with that of the pharmacokinetic study. Both or either test should be repeated periodically to ensure antibacterial equivalence of the generic meropenem in the postmarketing phase. Preliminary study of therapeutic outcome and adverse reaction of the generic meropenem showed the good therapeutic outcome without serious adverse events. Accordingly, patients should have the option whether to choose the generic or original meropenems according to their preferences.

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การศึกษาชีวสมมูล ฤทธิ์ทำลายแบคทีเรีย และผลการรักษาของยาสามัญเมโรพีเนม (Mapenem®)

อมร ลีลารัศมี, ยงค์ รงค์รุ่งเรือง, สุวรรณา ตระกูลสมบูรณ์, พิณทิพย์ พงษ์เพ็ชร, พีรชา ธนวัฒนาวนิช, พรสิรี จิตรถเวช

ภูมิหลัง: *เพื่อเปรียบเทียบค่าชีวสมมูล ฤทธิ์ทำลายแบคทีเรีย และศึกษาผลการรักษาเบื้องต้นของยาสามัญเมโรพีเนมหนึ่งขนาน*

วัสดุและวิธีการ: *รูปแบบงานวิจัยที่ใช้ศึกษาชีวสมมูลและฤทธิ์ทำลายแบคทีเรีย คือ แบบเปิดฉลาก สุ่มแบ่ง และข้ามกลุ่ม ในอาสาสมัครชาย 26 รายในโรงพยาบาลศิริราชและให้ยาเมโรพีเนมสามัญ (Mapenem®) หรือ ยาต้นแบบ (Meronem®) ในช่วงแรกแล้วสลับกับยาต้นแบบหรือยาสามัญในช่วงที่สอง โดยมีเวลาพักระหว่างช่วงนาน 1 สัปดาห์ ได้เจาะเลือด 10 มิลลิลิตร ก่อนให้ยา และหลังเริ่มให้ยา 10, 15, 30, 45, 60, 90, 120, 150,180, 240, 360, 470 และ 480 นาที ตัวอย่างเลือดแยกเป็นซีรัมและพลาสมาโดยให้รหัสแก่ตัวอย่างเพื่อปกปิดผู้วิเคราะห์ ระยะเวลาที่ให้ยาหยดเข้าหลอดเลือดดำนาน 30 นาที การวัดระดับยาในพลาสมาใช้เครื่อง HPLC-UV detector และวิเคราะห์ข้อมูลเปรียบเทียบกับยาต้นแบบ โดยคำนวณหาช่วงความเชื่อมั่นร้อยละ 90 ของค่า C_{max}, AUC_{0-t} และ AUC_{0-inf} การศึกษาฤทธิ์ทำลายแบคทีเรียของยาสามัญและยาต้นแบบในซีรัมใช้การยับยั้งการเจริญเติบโตของแบคทีเรีย E. coli ATCC 25922 ในอาหารเลี้ยงเชื้อจานเดียวกันและเปรียบเทียบค่าเส้นผ่าศูนย์กลางของวง (มิลลิเมตร) ที่ยายับยั้งการเจริญเติบโตของเชื้อ ส่วนการศึกษาผลการรักษาเบื้องต้นและฤทธิ์ไม่พึงประสงค์ ใช้รูปแบบเปิดฉลากในการใช้ยาสามัญเมโรพีเนม รักษาผู้ป่วยโรคติดเชื้อ 30 รายตามข้อบ่งชี้ทั่วไปของการใช้ยาขนานนี้*

ผลการศึกษา: *อาสาสมัครชายทั้ง 26 รายเข้าร่วม การศึกษาโดยตลอด การศึกษาชีวสมมูล โดยวัดช่วงความเชื่อมั่นร้อยละ 90 ของ C_{max}, AUC_{0-t} และ AUC_{0-inf} ของอัตรา ส่วนของยา mapenem® และ meronem® ได้ค่าร้อยละ 87.7-101.7, 96.3-102.4 และ 96.3-102.3 ตามลำดับ ผลการศึกษาแสดงว่า ค่าชีวสมมูลของยาสามัญเมโรพีเนมอยู่ในเกณฑ์มาตรฐานคือระหว่างร้อยละ 80-125 โดยมีกำลังของการทดสอบมากกว่าร้อยละ 80 ค่าความเข้มข้นของยาสามัญและต้นแบบใกล้เคียงกันในทุกตัวอย่างที่เก็บ ในเวลาเดียวกัน การศึกษาฤทธิ์ทำลายเชื้อแบบปกปิดโดยเปรียบเทียบค่าเส้นผ่าศูนย์กลาง (มิลลิเมตร) ของวง ที่ยับยั้งการเจริญเติบโตของเชื้อ E. coli ATCC 25922 ในจานอาหารเลี้ยงเชื้อ พบว่า ให้ค่าไม่ต่างกันอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) ทั้งยาสามัญและยาต้นแบบจากตัวอย่างซีรัมทุกตัวอย่างที่เก็บทุกระยะ การหาความสัมพันธ์ระหว่างระดับยา และค่าเส้นผ่าศูนย์กลางของวงที่ยับยั้งแบคทีเรียทั้งของยาสามัญและยาต้นแบบพบว่ามีความสัมพันธ์ในเชิงเส้นตรงที่ดี โดยได้ค่า $r = 0.891$; $R^2 = 0.794$ ($p < 0.01$) สำหรับยาสามัญ และ $r = 0.885$; $R^2 = 0.784$ ($p < 0.01$) สำหรับยาต้นแบบ ผลการรักษาของยาสามัญพบว่า ผู้ป่วย 24 รายหายจากโรค (ร้อยละ 80) และกำจัดเชื้อได้ 23 ราย (ร้อยละ 76.7) ฤทธิ์ไม่พึงประสงค์ที่อาจจะเกิดจากยาพบว่า มีผื่น 1 ราย และระดับ เอนไซม์ของตับเพิ่มขึ้น 3 ราย แต่หายได้เองทั้งหมด*

สรุป: *การศึกษาครั้งนี้ไม่พบความแตกต่างในด้านชีวสมมูลและฤทธิ์ทำลายแบคทีเรียระหว่างยาเมโรพีเนมสามัญและต้นแบบ ความสัมพันธ์ระหว่างระดับยาในพลาสมาและค่าเส้นผ่าศูนย์กลางของวงที่ยับยั้งเชื้อของตัวอย่างเดียวกันที่เก็บในเวลาต่าง ๆ อยู่ในเกณฑ์ที่ดี ผลการรักษาเบื้องต้นของยาสามัญเมโรพีเนมอยู่ในเกณฑ์ที่พอใจและไม่พบฤทธิ์ไม่พึงประสงค์ที่ผิดปกติ*