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# Meropenem Monotherapy versus Cefotaxime plus Metronidazole Combination Treatment for Serious Intra-Abdominal Infections

**Summary: In an open, randomised, multicentre trial, the efficacy and tolerability of empirical meropenem monotherapy (1 g intravenously every 8 hours) and cefotaxime (2 g every 8 hours) plus metronidazole (0.5 g intravenously every 8 hours) for 5 to 10 days was compared in 94 patients with serious intra-abdominal infection who required surgery. Eighty-three patients had an evaluable clinical response. Significantly more patients in the meropenem group had a satisfactory clinical response at the end of treatment (41/43 [95.3%] vs 30/40 [75.0%]; p = 0.008). The bacteriological response was also higher in the meropenem group (31/33 vs 26/32). In the bacteriologically evaluable population, a satisfactory clinical response was observed in 31/33 of those who received meropenem compared to 24/32 of the cefotaxime/metronidazole recipients (p = 0.03). Empirical meropenem monotherapy should prove a useful alternative to the currently standard combination treatment for serious intraabdominal infections.**

## Introduction

The management of serious intra-abdominal infections, diffuse peritonitis in particular, involves surgical intervention and supportive therapy, which may include artificial ventilation, in addition to appropriate antibiotic treatment. Since peritonitis is still associated with a mortality ranging from 3.5 to 60% depending on the site and duration of peritoneal contamination, the age of the patient and the pathogens involved [1], attempts to improve the clinical outcome with new antibiotic regimens are warranted.

Intra-abdominal infections are usually polymicrobial and antibiotic treatment must be effective against the most common causative pathogens, which include primarily gram-negative organisms and anaerobes [1]. Combination therapy has therefore been the standard form of treatment and cefotaxime plus metronidazole is an established combination regimen [2]. The broad spectrum of activity of the carbapenem, which includes gram-negative and gram-positive aerobic and anaerobic organisms, suggests that these agents should be suitable as monotherapy for intra-abdominal infections [3]. Indeed, imipenem/cilastatin has been shown to be effective in this context [4] and the results obtained from empirical monotherapy using the new carbapenem meropenem have been equally promising [5]. For these reasons, an open, randomised multicentre trial was conducted to compare empirical meropenem monotherapy with a combination of cefotaxime and metronidazole from the point of view of clinical and bacteriological efficacy and tolerance by the patient in the treatment of serious intra-abdominal infections.

## Patients and Methods

*Patients:* Hospitalised patients aged ≥ 18 years were eligible for the study if they were diagnosed as having an intra-abdominal infection requiring surgical treatment. Diagnosis of intra-abdominal infection was based on clinical signs and symptoms which included abdominal tenderness, guarding, rigidity and demonstration of infection when the operation took place (peritonitis). Patients in whom pathogens were identified prior to participation in the study were included if the pathogens were sensitive to both meropenem (MEM) and cefotaxime (CTX) or metronidazole (MTR). Patients with intra-abdominal infection as well as other sites of infection were included. All patients who participated gave written or witnessed verbal informed consent following a full explanation of the protocol. Pregnant or breast-feeding women were excluded from the study as were patients who had received other investigational agents within the previous 30 days, had participated in this study previously or had received antibiotics in the 3 days prior to the randomised treatment unless the organism had been shown to be either resistant or still present. Other exclusion criteria were as follows: hypersensitivity to any ß-lactam antibiotic, severe hepatic failure or neutropenia (neutrophil count $< 1{,}000 \times 10^6$/l), cystic fibrosis, a history of seizures and severe underlying disease such that completion of at least 48 hours of study drug therapy was unlikely.

*Study design and procedures:* Between December 1992 and December 1993, a total of 94 patients with intra-abdominal infections were recruited by five clinical centres into this open, parallel-group study. Patients were randomised separately at each centre to receive either Meronem® MEM (1 g infused intravenously over 20 to 30 min every 8 h) or Claforan® (CTX) (2 g) plus Clont® (MTR) (0.5 infused intravenously every 8 h) for 5 to 10

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Table 1: Demographic data and clinical status on joining the study of patients who were clinically evaluable.

| | Meropenem (n = 43) | Cefotaxime plus metronidazole (n = 40) |
|---|---|---|
| Gender | | |
| male | 22 | 24 |
| female | 21 | 16 |
| Mean age (years) (range) | 61.5 (23–89) | 56.6 20–87) |
| APACHE II scores | | |
| 0–10 | 26 (60%) | 28 (70%) |
| 11–20 | 14 (33%) | 11 (28%) |
| >20 | 1 ( 2%) | 1 ( 2%) |
| None recorded or taken after day 2 | 2 ( 5%) | |
| Site of infection: peritonitis | | |
| of the epigastric region | 14 (32%) | 11 (28%) |
| affecting the colon | 12 (28%) | 15 (37%) |
| due to perforated appendix | 17 (40%) | 14 (35%) |
| Extent of infection | | |
| local peritonitis | 31 | 22 |
| diffuse peritonitis | 12 | 18 |

days. A complete medical history was taken from each patient and a physical examination was performed prior to his or her participation in the study.

*Assessment:* Patients were considered evaluable if they had received at least 48 hours of study drug treatment, had no major protocol violations, and if the causative pathogens were susceptible to the study treatment regimen.

*Clinical response:* During the study, the patients were monitored daily with a clinical assessment of their general condition and measurement of body temperature. Definitive evaluations of the clinical efficacy were made on the last day of the study's drug administration (primary endpoint) and at a follow-up visit 2 to 4 weeks after treatment. Clinical response was considered satisfactory if the patient

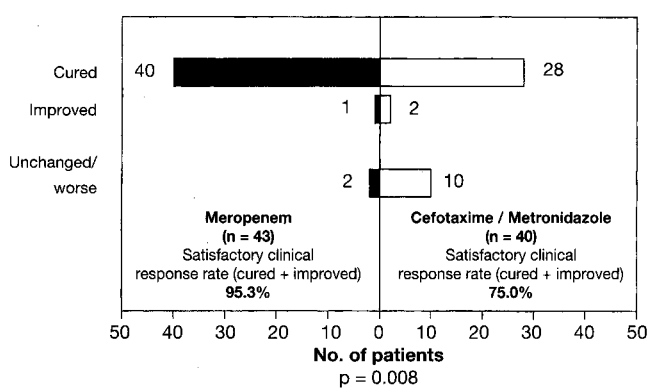


Figure 1: Clinical response at the end of treatment in clinically evaluable patients (n = 83) who received either meropenem 1 g intravenously every 8 hours or cefotaxime 2 g plus metronidazole 0.5 g intravenously every 8 hours.

was judged to be either cured or improved. Cure was defined as complete remission of local and systemic signs and symptoms of infection without the addition of other antibiotics and without subjective or objective evidence of recurrence. Improvement was defined as the attenuation of local and systemic signs of infection without complete remission. Patients with no improvement or with a deterioration of signs and symptoms were considered treatment failures. The same definitions were used to determine clinical efficacy at follow-up, with the addition of relapse. Clinical efficacy was determined both for the clinically evaluable population and for the bacteriologically evaluable population.

*Bacteriological response:* Prior to the trial therapy blood and other samples, e.g. peritoneal fluid, drainage fluid, pus or abscess, were collected for bacteriological assessment, including antibiotic sensitivity testing. Susceptibility to MEM was defined as zone diameter > 11 mm (using 10 µg discs) or minimum inhibitory concentration (MIC) ≤ 8 mg/l using the Kirby-Bauer method. Susceptibility to CTX was defined as zone diameter > 15 mm and susceptibility to MTR was defined as MIC < 4 mg/l. If necessary, cultures were repeated during treatment, immediately after treatment, and at a follow-up visit two to four weeks post-treatment. Bacteriological response was considered satisfactory if the original primary pathogen(s) was eradicated or presumed to be eradicated because no further culture was available due to clinical cure or improvement. Unsatisfactory response included persistence of the original pathogen(s) or an unchanged or worsened clinical status in cases where no culture samples were available.

*Tolerability:* Adverse events were classified according to their intensity and relationship to the study drug and the outcome was recorded. Samples were collected for clinical chemistry and haematological testing before treatment was initiated, once weekly during treatment and within 24 hours of discontinuing treatment.

*Statistical analysis:* The analysis was carried out on the per protocol population excluding all protocol violators. An intention to treat analysis was also performed and the results were similar. The power calculations were based on the clinical response at the end of treatment. Assuming a clinical evaluability rate of 95% and a satisfactory response rate of 90% with CTX plus MTR, then 40 patients per treatment group would be sufficient to detect a 25% lower response rate with MEM (power = 65%; significance = 5%). Assuming these response rates, 40 patients per group would give an approximate 95% confidence interval for the difference between the treatments to be 25% ± 18%. The numbers of patients with a satisfactory response (cured or improved with respect to clinical response, eradication or presumed eradication of the causative agent(s)) in each treatment group were compared using Pearson's chi-squared test (not continuity corrected). The 95% confidence limits for the difference in proportions were calculated using the normal approximation to the binomial distribution (not continuity corrected).

Table 2: Patients classified as clinical failures (clinical signs and symptoms unchanged/worse).

| Centre/No. Pat./No. | Drug | No. of treatment days | Indication (APACHE II SCORE) | Pathogen | Sensitivity: s = sensitive r = resistant MEM | CTX | MTR | Elimination | Comment |
|---|---|---|---|---|---|---|---|---|---|
| 001/006 | MEM | 6 | Perforated sigmoid | *Escherichia coli* | – | – | – | Presumed persistence | Persistent fever |
| | | | Perforated rectum | *Prevotella prevotii* | s | s | s | Presumed persistence | |
| | | | Fecal peritonitis (APACHE II SCORE: 28) | | | | | | |
| 007/006 | MEM | 6 | Perforated appendix | *Stenotrophomonas maltophilia* | r | r | r | Resistant | Defervescence since day 5 of trial therapy |
| | | | Peritonitis (APACHE II SCORE: 11) | *Pseudomonas aeruginosa* | s | r | r | Persistence | |
| 001/004 | CTX/MTR | 4 | Colorectal anastomosis | *Escherichia coli* | s | s | r | Presumed persistence | Patient died due to septic shock due to progression of peritonitis |
| | | | Dehiscence | *Pseudomonas aeruginosa* | – | – | – | Presumed persistence | |
| | | | Peritonitis (APACHE II SCORE: 25) | *Enterococcus faecium* | r | r | r | Resistant | |
| 001/005 | CTX/MTR | 6 | Colorectal anastomosis Dehiscence Peritonitis (APACHE II SCORE: 17) | *Peptostreptococcus magnus* | s | r | s | Presumed persistence | Persistent fever |
| 001/009 | CTX/MTR | 4 | Perforated sigmoid Diverticulitis Peritonitis (APACHE II SCORE: 5) | *Escherichia coli* | s | s | r | Eradication | Recurrent fever |
| 001/017 | CTX/MTR | 5 | Perforated gallbladder Peritonitis (APACHE II SCORE: 6) | *Escherichia coli* | s | s | r | Eradication | Persistent fever |
| 0001/026 | CTX/MTR | 6 | Perforated colon | *Klebsiella pneumoniae* | s | s | r | Presumed persistence | Persistent fever |
| | | | Peritonitis | *Escherichia coli* | s | – | – | Presumed persistence | |
| | | | (APACHE II SCORE: 10) | *Enterococcus faecium* | r | r | r | Resistant | |
| 001/028 | CTX/MTR | 7 | Perforated cholecystitis | *Escherichia coli* | s | s | r | Presumed persistence | Persistent fever |
| | | | Peritonitis (APACHE II SCORE: 16) | | | | | | |
| 001/030 | CTX/MTR | 4 | Colorectal anastomosis Dehiscence | *Escherichia coli* | s | s | r | Presumed eradication | Persistent fever |
| | | | | *Bacteroides fragilis* | s | s | s | Presumed eradication | |
| | | | Peritonitis (APACHE II SCORE: 14) | | | | | Superinfection with *Enterococcus* spp. + *Pseudomonas* spp. | |
| 001/035 | CTX/MTR | 3 | Perforated sigmoid Fecal peritonitis (APACHE II SCORE: 5) | No pre-therapy pathogen isolated | – | – | – | Unevaluable | Persistent fever |
| 001/038 | CTX/MTR | 10 | Small bowel necrosis | *Pseudomonas* | s | r | r | Resistant | Recurrent fever |
| | | | Peritonitis | *aeruginosa* | s | s | r | Presumed persistence | |
| | | | | *Escherichia coli* | | | | | |
| | | | (APACHE II SCORE: 18) | *Proteus mirabilis* | s | s | r | Presumed persistence | |
| | | | | *Proteus vulgaris* | – | s | – | | |
| | | | | *Enterococcus faecalis* | r | r | r | Resistant | |
| 001/041 | CTX/MTR | 7 | Perforated sigmoid Diverticulitis | No pre-therapy pathogen isolated | – | – | – | Unevaluable *Enterococcus* isolated later on as new pathogen | Persistent fever |
| | | | Peritonitis (APACHE II SCORE: 4) | | | | | | |

## Results

*Patients Enrolled*

Forty-eight patients received MEM and 46 received CTX/MTR. The mean duration of treatment was 7.3 (-range 2–11) days in the MEM group and 6.9 (1–14) days in the CTX/MTR group. The mean daily dose was 2.5 g (-range 1.25 – 3.6 g) and 6.6 g (range 2.5 – 8.0 g) for the MEM and CTX/MTR groups respectively. 83 patients in all were clinically evaluable and 65 were bacteriologically evaluable.

*Demographic Data*

The characteristics of the patients with respect to demographic data (Table 1), concurrent diseases, APACHE II score and site and spread of infection were broadly similar in both treatment groups. Six of the clinically evaluable patients in the MEM group had received antibiotics up to 3 days before the start of the study treatment compared to eight in the CTX/MTR group.

*Clinical Efficacy*

Among the clinically evaluable patients, 41/43 (95.3%) of the MEM group had satisfactory clinical responses at the end of treatment compared to 30/40 (75%) of those who received CTX/MTR. This difference between the two treatments (20.4%) was statistically significant (p = 0.008, 95% CI [5,5%, 35.2%]) (Figure 1). There were two clinical failures in the MEM group and ten in the CTX/MTR group (Table 2). No relapses were detected in either treatment group at follow-up. Seven patients at centre six inadvertently received MEM 0.5 g intravenously three times daily. All had a satisfactory clinical response at the end of treatment and at follow-up. Clinical response rates at the end of treatment according to the site of infection were 11/12 (colon), 14/14 (epigastric region) in the MEM group and 8/15 (colon) and 14/14 (complicated appendicitis) in the CTX/MTR group (Table 3).

Clinical response rates according to the spread of infection at the end of therapy were 31/31 for local peritonitis in the MEM group and 22/22 in the comparator group. As regards diffuse peritonitis, however, a satisfactory response was achieved in 10/12 in the MEM group compared to only 8/18 in the CTX/MTR group (Table 4).

According to the APACHE II score in the MEM group all patients (26/26) with a score of ≤ 10 had a satisfactory clinical response, whereas in the CTX/MTR group this applied to 23/28. According to the APACHE II score of > 10, 13/15 of patients in the MEM group and 7/12 in the CTX/MTR group were cured or improved (Table 5).

Of the 65 bacteriologically evaluable patients, a satisfactory clinical response was observed in 31/33 MEM recipients at the end of treatment compared to 24/32 patients in the CTX/MTR group. The difference between the two treatments was statistically significant (p = 0.03, 95% CI [1.9%; 36.0%]). A satisfactory response was maintained in all successfully treated patients who attended the follow-up visit.

*Bacteriological Efficacy*

The original pathogen(s) was eradicated or presumed to be eradicated in 31/33 of MEM recipients and 26/32 of those who received CTX/MTR (Figure 2) (p = 0.12, 95% CI [−3.1%, 28.5%]). The two cases of bacteriological failure in the MEM group were also clinical failures (Table 2). There were five cases of bacteriological failure in the CTX/MTR group and one case of superinfection, all of which were associated with clinical failure (Table 2). Although bacteriological response was higher in the MEM group, the difference (12.7%) did not achieve statistical significance. At follow-up, bacteriological efficacy was maintained in 25/26 and 18/19 of the MEM and CTX/MTR groups, respectively. Pathogens were eradicated or presumed to be eradicated at the end of treatment and at follow-up in all seven patients who received MEM 0.5 g intravenously three times daily.

The pathogens isolated in bacteriologically evaluable patients and the response to treatment are shown in Figure 3. A majority of patients had polymicrobial infections (19/33 in the MEM group vs 16/32 in the CTX/MTR group). The maximum number of organisms isolated from one patient was four. Enterobacteriaceae, primarily *Escherichia coli*, accounted for the largest proportion of single-organism infections (9/14 in the MEM group vs 11/16 in the CTX/MTR group). As expected, anaerobes were generally co-infecting organisms, although anaerobes alone were isolated in one patient in the MEM group (*Bacteroides fragilis*) and in three patients in the CTX/MTR group (*Prevotella bivia*, *Bacteroides fragilis* and *Peptostreptococcus magnus*). Gram-positive organisms only were identified in four patients in the MEM group (*Enterococcus durans*, Group F streptococci, viridans streptococci, and Group G streptococci) and in two patients in the CTX/MTR group (*E. durans* in both cases). MEM-resistant organisms were isolated from three patients: *Enterococcus faecium* (MIC 32 mg/l), *Staphylococcus saprophyticus* (MIC 64 mg/l) and *Stenotrophomonas maltophilia* (> 64 mg/l). However, other organisms were also isolated from all three patients. The two patients from whom *E. faecium* and *S. saprophyticus* were isolated had satisfactory clinical responses and these organisms were thus not considered causative pathogens. All enterococci and anaerobes were resistant to CTX, as expected, and all gram-negative rods and gram-positive cocci (aerobic and anaerobic) were resistant to MTR. In addition, CTX-resistant *E. coli* (32 mg/l) was isolated from one patient and CTX-resistant *Pseudomonas aeruginosa* (MIC 16, 16 and > 64 mg/l) was isolated from three patients. The nature of the CTX- and/or MTR-resistant organisms and the fact that some were isolated from patients who were classified as having a satisfactory clinical response suggested that these organisms were unlikely to be the causative pathogen in these cases.

## Tolerability

All 94 patients who participated in the study were evaluated for adverse events. A total of 12/48 patients who received MEM experienced adverse events as compared

with 13/46 (28.3%) CTX/MTR recipients Adverse events were considered drug-related in six (12.5%) patients in the MEM group (headache, diarrhoea, mild changes shown by liver function tests and moderately increased creatinine) and in one (2%) patient in the CTX/MTR group (mildly increased alanine amino transferase).
Three deaths occurred during the study treatment (one MEM patient, two CTX/MTR patients) and five occurred during the follow-up period (two MEM patients, three CTX/MTR patients). The reasons in the MEM-patients were cardiogenic shock, cardiac failure, myocardial infarction and in the CTX/MTR patients pulmonary embolism, adult respiratory distress syndrome, the progression of peritonitis, septic shock and circulatory collapse. None of these deaths was considered drug-related.

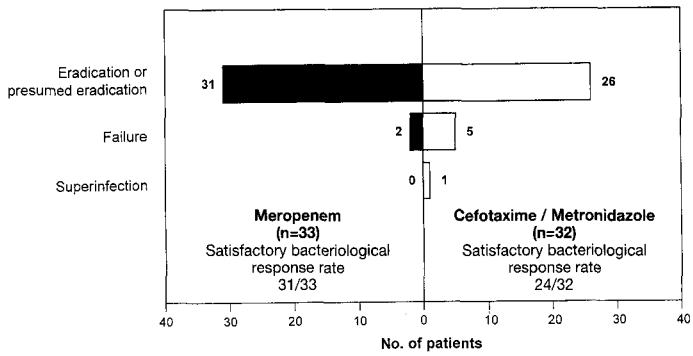


Figure 2: Bacteriological response at the end of treatment in bacteriologically evaluable patients (n = 65) who received either meropenem 1g intravenously every 8 hours or cefotaxime 2 g plus metronidazole 0.5 g intravenously every 8 hours.

## Discussion

The CTX/MTR antibiotic combination is an effective treatment for diffuse peritonitis and has been found to be equivalent to the standard combination of CTX plus clindamycin [2]. However, in the treatment of intra-abdominal infections, the advantage of monotherapy is that it is a simplified treatment regimen by comparison with standard combination therapy. The benefits of monotherapy include a reduction in the number of times the drug is administered and exposure to fewer drugs, potentially reducing the risk of adverse events and interactions between drugs as well as the cost of treatment.
An increasing body of experience with carbapenem monotherapy, specifically MEM or imipenem/cilastatin, is being accumulated. MEM monotherapy has previously been compared with CTX/MTR, at the same dosages used in this study, in 160 patients with peritonitis, and was shown to be as effective as the combination regimen [6]. These earlier results are confirmed by the findings of the present study: the overall clinical response rate for MEM was indeed significantly better than that for CTX/MTR (41/43 vs 30/40; p = 0.008). With respect to bacteriological efficacy, MEM monotherapy had a higher satisfactory response rate than CTX/MTR, but the difference did not achieve statistical significance (31/33 vs 24/32). Although compared with the CTX/MTR group a lower percentage of patients in the MEM group had the more serious diagnosis of lower gastrointestinal tract infection (37% vs 28%, respectively), this was probably offset by the higher percentage of patients in the MEM group who had APACHE II scores > 10. Moreover, the clinical response rate at the end of treatment in those patients with infection of the lower gastrointestinal tract was markedly higher in the MEM group than in the CTX/MTR group (11/12 vs 8/15). With respect to the APACHE II score of > 10 a similar higher response rate was found (13/15 vs 7/12). Both treatment regimens were well tolerated with a low incidence of adverse effects.
It was interesting that in the present study all seven patients with severe intra-abdominal infection who inadvertently re-

Table 3: Satisfactory clinical response (cured plus improved) in clinically evaluable patients at the end of treatment according to the site of infection.

| Site of infection: peritonitis | Meropenem (n = 43) | Cefotaxime/ Metronidazole (n = 40) |
|---|---|---|
| Epigastric region | 14/14 | 8/11 |
| Affecting the colon | 11/12 | 8/15 |
| Perforated appendicitis | 6/17 | 14/14 |
| Total | 41/43 (95%) | 30/40 (75%) |

Table 4: Satisfactory clinical response (cured plus improved) in clinically evaluable patients at the end of therapy according to extent of the infection.

| | Meropenem (n = 43) | Cefotaxime/ Metronidazole (n = 40) |
|---|---|---|
| Local peritonitis | 31/31 | 22/22 |
| Diffuse peritonitis | 10/12 | 8/18 |

Table 5: Satisfactory clinical response (cured and improved) in clinically evaluable patients at the end of treatment according to the Apache II score.

| Apache II score | Meropenem (n = 41) | Cefotaxime/ Metronidazole (n = 40) |
|---|---|---|
| ≤ 10 | 26/26 | 23/28 |
| > 10 | 13/15 | 7/12 |
| Total | 39/41 (95%) | 30/40 (75%) |

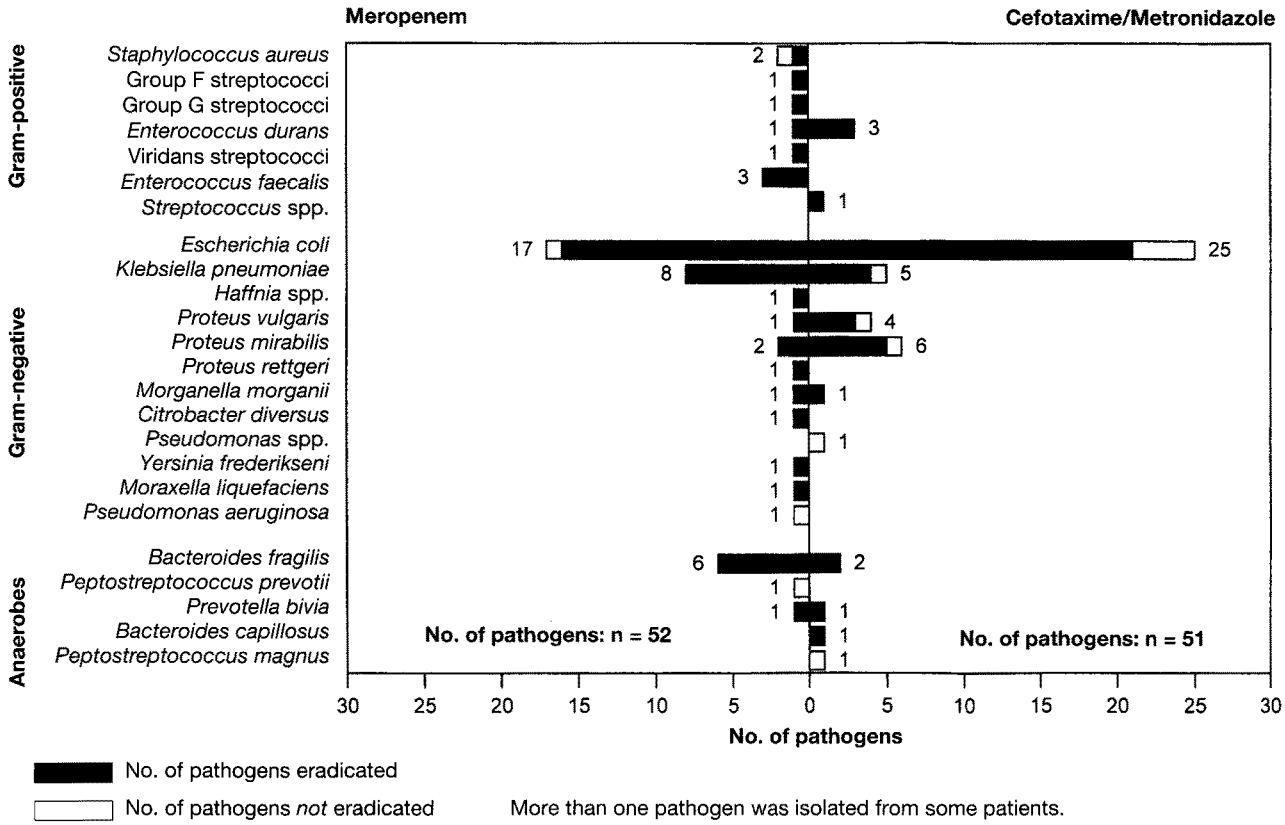


Figure 3: Response by organism in patients with intra-abdominal infection treated with either meropenem 1 g intravenously every 8 hours or cefotaxime 1 g plus metronidazole 0.5 g intravenously every 8 hours.

ceived MEM in a dosage of 500 mg rather than 1 g intravenously every 8 h responded clinically and bacteriologically. *Geroulanos* et al. compared MEM with imipenem/cilastatin administered as 1 g of intravenous infusion (or bolus injection for MEM) every 8 h in 232 patients with intra-abdominal infections and found no difference in the clinical or bacteriological response rates [5]. *Wilson* reviewed three prospective trials of MEM in intra-abdominal sepsis: one versus CTX/MTR and two versus imipenem/cilastatin and found no significant difference in the cure rates (91–100%) between MEM and the other treatments [11]. In addition, MEM was tolerated as well as the other antibiotic regimens. There was no report of nausea, vomiting or seizures in the MEM group. Meropenem was judged to be highly effective as a monotherapy for local or diffuse peritonitis. Although MEM and imipenem/cilastatin have shown equivalent clinical and bacteriological efficacy in intra-abdominal infections, MEM appears to offer some advantage over imipenem/cilastatin. MEM can be administered either by a short intravenous infusion (20 to 30 min) or as an intravenous bolus over a period of approximately 5 minutes. By contrast, imipenem/cilastatin must be administered by intravenous infusion over a period of 30 to 60 minutes to minimise the incidence of nausea and vomiting. Moreover, imipenem/cilastatin has been associated with a high incidence of nausea and vomiting in seriously ill patients when administered in a dosage of 4 g daily [12, 17]. The spectrum of pathogens isolated in this study corresponds to the microbiological aetiology of intra-abdominal infections as reviewed by other authors, to be precise a predominance of *E. coli* and *Bacteroides* spp. [13–15]. In this study, the susceptibility of the pathogens to MEM is in agreement with *in vitro* results reported previously [16]. By contrast, the incidence of CTX-resistant organisms was higher than in reported *in vitro* results [16]. CTX is virtually inactive against anaerobic pathogens whereas the antibacterial activity of MTR is limited solely to anaerobic organisms. With these agents, therefore, combination treatment is always indicated. Overall, monotherapy with MEM was more active against a wider range of organisms causing peritonitis than the dual therapy of CTX/MTR. In this study, MEM was clinically and bacteriologically more effective than the standard CTX/MTR regimen. In view of these results and those of earlier studies, empirical monotherapy with MEM should prove to be a useful alternative to currently available combination treatments for serious intra-abdominal infections.

## Acknowledgements

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**Zusammenfassung: Meropenem Monotherapie im Vergleich zu Cefotaxim plus Metronidazol in der Therapie schwerer intraabdomineller Infektionen.** In einer offenen, randomisierten Multicenter-Studie wurden die Wirksamkeit und Verträglichkeit einer initialen Monotherapie mit Meropenem (MEM, 1 g 3 × tägl. i.v.) mit der etablierten Kombinationstherapie Cefotaxim (CTX) plus Metronidazol (MTR) (2 g CTX + 0.5 g MTR 3 × tägl. i.v.) verglichen. 94 Patienten mit operationspflichtigen schweren intraabdominellen Infektionen wurden einbezogen. Davon waren 83 Patienten bezüglich klinischem Ansprechen auswertbar. Die klinische Wirksamkeit war in der MEM-Gruppe signifikant höher (41/43 Pat. = 95.3% vs 30/40 Pat. = 75%; p = 0.008). Das bakteriologische Ansprechen war in der MEM-Gruppe ebenfalls höher im Vergleich zur Kombinationsgruppe (31/33 vs 26/32), der Unterschied war jedoch statistisch nicht signifikant. In der bakteriologisch auswertbaren Population war das klinische Ansprechen in der MEM-Gruppe signifikant höher als im Vergleichskollektiv (31/33 vs 24/32; p = 0.03). MEM erscheint somit für die initiale empirische Monotherapie bei schweren intraabdominellen Infektionen geeignet.

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