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IMIPENEM IN SURGICAL INFECTIONS

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Cerrahi infeksiyonlarda imipenem.

Infectious complications, including septicemia, remain a major problem in surgery. This is especially true for patients with intra-abdominal infections. As hospital infections, they are often caused by multiply resistant bacterial strains and choice of the appropriate antibacterial drug is difficult. For empiric treatment of intraabdominal infections, a broad spectrum antimicrobial or a combination of antimicrobials is thought to be essential. Life-threatening infections are often used to be treated with a combination of three antimicrobials.

Imipenem, as the first drug in a new class of β-lactams, the carbapenems, has a broad antibacterial spectrum, including most Gram positive and Gram negative aerobic, microaerophilic and anaerobic pathogens. Imipenem penetrates well to peripheral compartments and has a high degree of β-lactamase stability. Cilastatin is an inhibitor of the renal metabolism of imipenem and is used as an 1:1 combination.

EXPERIENCE WITH IMIPENEM/CILASTATIN IN THE TREATMENT OF SERIOUS POSTOPERATIVE INFECTIONS

At the Department of Surgery, Clinic of Visceral Surgery, University Hospital of Zurich we compared the effectiveness of Imipenem/Cilastatin versus our standard combination, consisting of tobramycin (in the first 4 patients) or netilmycin + amoxicillin + clindamycin in patients with severe postoperative infections.

84 adult patients, all of whom underwent abdominal surgery and had life-threatening or potentially life-threatening acute infections were entered into the study. Patients with uncomplicated urinary tract infections or wound infections, and patients who had received antimicrobials during the preceding three days were excluded. The patients were randomized into two groups: I/C (Imipenem/Cilastatin) and COMB (aminoglycoside+amoxicillin+clindamycin). In the I/C group all patients received 1g q 8 h (as g Imipenem). Patients in the combination group received routine doses as depicted in table 1. All antimicrobials were administered as intravenous infusions using saline as a diluent and an infusion time of 30 min or 60 min (for aminoglycosides). When necessary, doses were adjusted for reduced renal function. Before therapy was started, aerobic and anaerobic cultures were taken from accessible sites (drainages, bronchial secretion in ventilated patients, operative sites, etc.) Blood cultures were taken routinely before, and also during therapy if the patient had fever >38.5°C. During therapy, all obtainable materials from sources other than the primary infection area were cultured regularly.

Table 1. Antimicrobial agents and doses.

I/C	Imipenem/Cilastatin	1g q 8h	42 patients
COMB	Amoxicillin	2g q 8h	42 patients
	Clindamycin	0.6 g q 6h	
	Aminoglycoside	Acc. serum level	

Outcome of treatment was assessed as,

cured: No need for further antimicrobial treatment within 10 days after end of therapy and no reappearance of the causative pathogen.

improved: Marked clinical effect but persistence of the causative pathogen or reappea-

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rance within 10 days after end of therapy, and

failure: Death due to infection, poor response to therapy or need for change of therapy.

RESULTS: There were no differences between the two groups with respect to mean age, sex distribution, infectious diagnoses (Table 2), underlying diseases and risk factors.

Tablo 2. Infectious diagnoses.

	I/C	COMB
Lower resp.tract	14	7
Peritonitis	8	13
A.cholecystitis	–	6
Perf. appendicitis	4	6
Bowel perf. (sm+1)	4	4
Septicemia	9	3
Other infections	3	3

Mean duration of treatment with Imipenem/Cilastatin was 8.0±3.0 days, with the combination 8.5±2.8 days. Patients in the I/C group were hospitalized for a period of 30.8 days (6-118), in the combination group 24.9 days (6-107). Pathogens isolated are shown in table 3. 25 patients had polymicrobial aerobic/microaerophilic, and 16 had mixed anaerobic/aerobic infections. 18 patients had infections caused by a single aerobic or microaerophilic species, 2 had polymicrobial anaerobic infection.

Tablo 3. Pathogens isolated before treatment.

	I/C	COMB
Coag. neg. Staphylococci	33	28
Enterococci	14	13
Staph. aureus	4	6
Other Gram-positives	5	1
E. coli	19	25
Pseudomonas spp.	19	13
Klebsiella spp.	8	7
Enterobacter spp.	9	4
Haemophilus spp.	8	10
Other Gram-negatives	12	4

There was no statistically important difference in the outcome of patients between the two treatment groups. The overall frequency of cured and improved patients was 84.2 % in the Imipenem/Cilastatin and 83.3 % in the combination group (Tablo 4) ($p>0.05$).

Tablo 4. Clinical results (%).

	I/C	COMB
Cured	34 (81.8)	30 (71.4)
Improved	1 (2.4)	5 (11.9)
Failed	6 (14.3)	7 (16.7)
Not assesable	1 (2.4)	

OTHER EXPERIENCE WITH IMIPENEM/CILASTATIN IN SURGICAL INFECTIONS

JS. Solomkin et al. (Ann. Surg. 1990; 212: 581) compared in a multicenter study with 162 patients Imipenem/Cilastatin against the combination of tobramycin+clindamycin for intraabdominal infections. There was a significant improvement in outcome for I/C-treated patients ($p=0.043$).

D.Poenaru et al. (Can. J. Surg. 1990; 33:415) concluded in a study comparing I/C to an aminoglycoside-based antibiotic regimen for the management of intra-abdominal infections that "patients treated with I/C had fewer febrile episodes and occurrences of breakthrough bacteremia, less antibiotic resistance and need for drug change; ... their hospital stay was shorter and that the death rate from sepsis was less."

In contrast to these favourable results with Imipenem/Cilastatin, it is documented in different studies (U.Hartenauer et al.: J.Hosp.Infec. 1990;15A:61), that *Pseudomonas spp.* could not be eradicated with I/C, or resistance to *Pseudomonas spp.* emerged during therapy with I/C (T.Krech et al.: Immun.Infekt. 1986; 14:224). Because of these observations and our empirical experience, our policy in treating *Pseudomonas* infections since 1981 is to use two drugs against *Pseudomonas* and to change the combination every 7-10 days.

CONCLUSIONS

Despite meticulous surgical technique, infectious complications remain a major problem, even in elective clean abdominal surgery. Although surgery is the most important clinical procedure in the treatment of intra-abdominal infection, antimicrobial therapy - with a broad spectrum regimen - is an essential part of the therapeutic concept. With the above mentioned results we feel that Imipenem/Cilastatin monotherapy is as effective as more conventional and "routine" antimicrobial combinations in treating severe intra-abdominal infections. In our patients, treatment times of seven to eight days seemed sufficient; longer times were not correlated to improved therapeutic outcome. Therefore, if clinical or laboratory signs of infection persist, reoperation and/or change of antimicrobial therapy should be considered. It should be stressed again that antimicrobial drugs cannot substitute for surgical revision and drainage of infectious foci.

In conclusion, Imipenem/Cilastatin is an effective and well tolerated alternative to combination antimicrobial therapy in serious postoperative infections. Obvious advantages of Imipenem/Cilastatin are that the number of drug doses per day can be reduced and that there is no need for serum level monitorisation.