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Original Research

Microbial findings, sensitivity and outcome in patients with postoperative peritonitis a retrospective cohort study

Rainer Grotelueschen[a], Marc Luetgehetmann[b], Johannes Erbes[a], Lena M. Heidelmann[a], Katharina Grupp[a], Karl Karstens[a], Tarik Ghadban[a], Matthias Reeh[a], Jakob R. Izbicki[a], Kai Bachmann[a,*]

[a] Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, 20246, Hamburg, Germany
[b] Institute for Medical Microbiology, Virology and Hygiene, Medical Center Hamburg-Eppendorf, 20246, Hamburg, Germany

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ABSTRACT

Background: Acute postoperative peritonitis resulting from previous abdominal surgery is still a severe and potentially fatal disease, which is associated with high morbidity and mortality. The aim of the present study was to evaluate patients' outcome after postoperative peritonitis and identify the most effective empiric antibiotic regimes.

Methods: 422 patients with acute postoperative peritonitis as a result to earlier abdominal operation (e.g. anastomotic leakage) were analyzed retrospectively focusing on the origin of the peritonitis, microbial flora and resistance patterns. Furthermore, mortality was estimated according to sensitivity results of the tested antibiotics.

Results: In 50% of the patients, anastomotic leakage was located in the colon. The predominantly cultured microorganisms were *Escherichia coli* and Enterobacteriaceae. The combination of meropenem and vancomycin was effective in 96% of these microbes. The frequently used combinations of piperacillin/sulbactam and cefotaxime/metronidazole were effective in only 67% and 43%, respectively.

Conclusions: We were able to show that the currently used antibiotic regimes with piperacillin/sulbactam and cefotaxime/metronidazole are ineffective in a relevant number of patients with anastomotic leakage. Only meropenem or meropenem/vancomycin cover most of the microbes predominant in postoperative peritonitis.

1. Introduction

Peritonitis is a severe and potentially fatal disease associated with high morbidity and mortality. Abdominal infections following hollow organ perforation or anastomotic leakage play the most important role in the development of secondary peritonitis. Second to infections of the respiratory tract, they are one of the most frequent causes of septic episodes [1]. Despite advances in diagnosis and improvements in intensive care treatment, secondary peritonitis is still associated with a high mortality rate of 15–25% [2–7]. The severity can vary from mild peritonitis without sepsis or organ failure to severe peritonitis with sepsis and multi organ failure despite appropriate therapeutic interventions. A multidisciplinary team consisting of surgeons, intensive care specialists, microbiologists and radiologists is a precondition for optimal therapy. Outcome depends significantly on rapidly initiated source control and appropriate antimicrobial therapy [8,9]. Furthermore, initiating empiric antimicrobial therapy immediately after diagnosis can markedly reduce mortality in these patients [3,10–13].

In the surgical department and intensive care unit at the University Medical Center ***, an antibiotic regime consisting of piperacillin/tazobactam is frequently used in patients with secondary peritonitis. Selected patients with limited peritonitis sometimes receive a second or third generation cephalosporin (cefuroxime, ceftriaxone) in combination with metronidazole. In patients with severe peritonitis or even sepsis, the therapy is escalated to meropenem or meropenem in combination with vancomycin.

Several studies focus on appropriate antibiotic regimens in sepsis or peritonitis [14,15]. On the contrary, there is a lack of studies dealing with empirical antimicrobial therapy in patients with anastomotic leakage and postoperative peritonitis. This group of patients frequently undergoes previous antibiotic treatment, resulting in a different spectrum of bacteria and biological resistance.

Therefore, the aim of the present study was to analyze the occurring bacteria and biological resistances in relation to the location of the

* Corresponding author.
E-mail address: k.bachmann@uke.de (K. Bachmann).

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peritonitis so as to detect the most effective antibiotic therapy in patients with postoperative peritonitis. Furthermore, the commonly used antibiotic regimes were evaluated for their efficacy.

Additionally, the impact of the grade of antimicrobial resistance on mortality was evaluated.

2. Materials and methods

2.1. Patients

This is a retrospective, single center, cohort study including patients that underwent emergency laparotomy with intraoperatively verified postoperative peritonitis following earlier abdominal surgery. If patients required more than one re-laparotomy only the first of these was evaluated. In total, 422 patients with postoperative peritonitis qualified for this study. Patients were divided into five different groups according to the location of the leakage (colon, stomach, duodenum, small intestine and pancreas/biliary tract). All patients underwent adequate source control by experienced surgeons. The study was approved by the institutional review board of the University Medical Center meeting legal requirements (retrospective cohort study). Additionally the study was registered in the Research Registry (UIN 5001). The findings are reported according to the STROCSS criteria [16].

2.2. Clinicopathological data

The retrospectively analyzed data included patient's sex, age, date of operation, medical history, medication, co-morbidities, microbial findings and sensitivity, location of perforation or leakage and mortality. All items were acquired from the clinical records and from our prospective database.

2.3. Results of microbial findings and sensitivity

All microbial test were performed at the Department of Medical Microbiology, Virology and Hygiene at the University Medical Center ***. The sensitivity was analyzed for the relevant antibiotics. The microbes found in the samples were summarized in main groups. *Escherichia coli* were not counted to the Enterobacteriaceae group and were listed separately. Enterococcus faecium, *Enterococcus faecalis* and "Not otherwise specified Enterococcus species" were also analyzed separately due to frequent incidence and their differing resistance patterns.

We examined efficiency of and resistance to the following relevant antibiotics: ampicillin/sulbactam, piperacillin/sulbactam, meropenem, cefuroxime, cefotaxime, ceftazidime, tigecycline, ciprofloxacin, moxifloxacin, vancomycin and metronidazole.

In microbes with known natural resistance to an antibiotic, the resistance was determined correspondingly. If not tested separately, in case of distinct knowledge of sensitivity based on other tested antibiotics of the microorganism, the result was determined according to the "44th edition of The Sanford Guide To Antimicrobial Therapy" [17]. Furthermore, common antibiotic combinations such as cefuroxime and metronidazole, cefotaxime and metronidazole and meropenem and vancomycin, were evaluated. A microbe qualified as sensitive to a combination of two antibiotics if one of the antibiotics was determined as sensitive. Sensitivity results were analyzed for each microbial species and in correspondence to the location of the perforation/leakage.

2.4. Mortality

Mortality was evaluated in relation to the location of leakage. Additionally, the mortality was correlated to sensitivity results of our tested antibiotics. The combination of two different antibiotics was sensitive, if one of the antibiotics was determined as sensitive as aforementioned. Resistance against a combination of two different antibiotics was defined as resistance against both of the substances.

2.5. Statistics

Data were analyzed using SPSS® for Windows® (22.0; SPSS Inc., Chicago, IL). Data are reported in descriptive charts. Cross-tables were generated, followed by calculation of the P value by using the chi-squared test/Fisher's exact test. Statements of significance refer to P values for two-tailed tests of less than 0.05.

3. Results

Overall, 422 patients that underwent emergency laparotomy due to postoperative peritonitis caused by anastomotic leakage or abscess were included in this study.

234 males (55%) and 188 females (45%) were included; the mean age was 60.3 ± 17.4 years. In 214 (51%) patients, source of postoperative was located in the colon. The second most frequent localization was the pancreatobiliary tract with 86 (20%) patients followed by the small intestine with 80 (19%) patients. In 32 (8%) patients, localization of leakage was determined in the stomach and in 10 (2%) patients in the duodenum (Table 1). The patients were enrolled in our surgical department including a specialized HPB unit that performed more than 1700 HPB resections within the inclusion period. Therefore, the high number of patients with pancreatic fistula is explained percentage??. Up to four microbes were cultured per patient. The mean hospital stay was 22.6 ± 26.4 days.

Overall, the most common findings were *Escherichia coli* and Enterobacteriaceae, followed by yeasts. Only 16 probes revealed no microbes. Analyzing the distribution of the microbes, relevant differences were found in regards to the origin of the peritonitis. In patients with colon leakage, the predominant microorganism was *Escherichia coli* with 98 positive cultures (54%), followed by Enterobacteriaceae with 53%. Enterococcus species, Enterococcus faecium and *Enterococcus faecalis* were present in 12%, 14% and 17% respectively. Other gram-negative bacilli were found in 15%. In patients with pancreatic or biliary leakage Enterobacteriaceae were most frequently detected (46%) followed by yeasts (34%) and *Escherichia coli* (27%). In the small intestine group Enterobacteriaceae were the most frequently cultured microbes with 34 positive culture results (57%). In patients with leakage in the stomach or duodenum, staphylococcus was a common finding with a detection rate of 42% and 50% respectively. Yeasts were frequently found in all locations. They were detected in 34% of the patients with colon leakage; in patients with small intestine and pancreatobiliary leakage the rates were 47% and 34%, respectively. Overall, only 5% of the culture results showed no growth. The details of cultured microbes and the distribution in respect to the location are presented in Table 2.

3.1. Analysis of biological resistance and microbial flora

Considering the obtained culture results in all the patients, piperacillin/sulbactam reached an overall sensitivity rate of 67%. In detail,

Table 1
Location of peritonitis and mortality.

Location	Patients	Mortality
	n = 422	
Colon	214 (50.7%)	19.6%
Stomach	32 (7.6%)	37.5%
Duodenum	10 (2.4%)	40%
Small intestine	80 (19.0%)	35%
Pancreas/biliary tract	86 (20.4%)	25.6%

Table 2
Microbial flora related to location.

	Colon	Stomach	Duodenum	Small intestine	Pancreas/ biliary tract
Enterococcus, not specified	12.1%	0%	0%	20.0%	22.0%
Enterococcus faecium	14.3%	33.3%	25.0%	16.7%	14.6%
Enterococcus faecalis	16.5%	0%	0%	6.7%	17.1%
Escherichia coli	53.8%	25%	50.0%	23.3%	26.8%
Enterobactericae	52.7%	33.3%	50.0%	56.7%	46.3%
Staphylococcus	8.8%	41.7%	50.0%	13.3%	17.1%
Streptococcus	5.5%	25.0%	0%	0%	2.4%
Bacteroidaceae	11.0%	16.7%	0%	6.7%	0%
Other gram positive	3.3%	0%	25.0%	3.3%	2.4%
Other gram negative	15.4%	0%	0%	16.7%	7.3%
Yeast	34.1%	58.3%	50.0%	46.7%	34.1%
Sterile	3.3%	0%	0%	3.3%	9.8%

the sensitivity was 100% for *Enterococcus faecalis*, 93% for Bacteroidaceae and 92% for Staphylococcus species.

Sensitivity rates of meropenem for *E. coli*, Streptococcus and Bacteroidaceae were found to be 100%, for Enterobacteriaceae 99% and 92% for Staphylococcus species, the sensitivity rate over all microbes was 73%.

The combination of cefuroxime or cefotaxime plus metronidazole showed an overall sensitivity rate of 43% and 53%, respectively. The sensitivity rate for Streptococcus and Bacteroidaceae was 100% for both combinations, while it reached 86 and 89%, respectively for *E. coli*.

The combination of meropenem and vancomycin achieved a sensitivity of ≥99% in almost all microbes with the exception of the group of other gram-negative microbes in which the rate was 77%. Furthermore, tigecycline achieved a high sensitivity in the groups of not further specified Enterococcus, Enterococcus faecium, *Enterococcus faecalis*, Staphylococcus, Streptococcus and other gram-positive microbes. The sensitivity rate for *E. coli* was found to be 99%, while the rate for Enterobacteriaceae was only 71%. Overall, tigecycline offers the best overall sensitivity rate (84%) of all single antibiotics, only the combination of meropenem and vancomycin achieved better results with a response rate of 97%. The details of cultured microbes with their biological sensitivity are presented in Table 3.

3.2. Analysis of biological resistance and location

Overall, 646 microbes were detected in the abdominal fluids from the included patients. 352 microbes were cultured in patients with colon perforation or leakage, 128 from pancreatobiliary tract leakages and 98 in leakages of the small intestine. Additionally, 42 microbes were isolated in the gastric group and 26 in the duodenal group.

Piperacillin/sulbactam was found to be sensitive in 80% in the pancreatobiliary tract group, while the sensitivity rate of the therapy was just 61–67% in patients with peritonitis originating from stomach, small intestine or colon.

The range to the sensitivity of meropenem was found to be between 64% in the pancreatobiliary tract group and 81% in the gastric group. In microbes isolated in patients with secondary peritonitis after colon perforation or leakage, sensitivity of meropenem was 74%.

Furthermore, the combination of cefuroxime or cefotaxime plus metronidazole achieved a sensitivity rate of only 33–57% in the different locations. The therapy with moxifloxacin showed response rates of 53–67%.

When analyzing the response rates of single antibiotics, only tigecycline showed good sensitivity rates (78–91%) over all the different locations.

The best response rates were found for the combination of meropenem plus vancomycin. This combination was associated with a sensitivity of 95% in the colon group, 98% for small intestine and pancreatobiliary origin and 100% in patients with leakage of the stomach or duodenum. The overall response rate of meropenem plus vancomycin was > 97%. Details of biological sensitivity related to origin of peritonitis are represented in Table 4.

3.3. Mortality

The overall in-hospital mortality of the included patients was 26%. Allocated to different origins of the peritonitis, the highest mortality rate was detected in patients with duodenal and gastric leakages (40% and 28% respectively). Perforations in the small intestine were associated with a mortality rate of 35%, while 26% of the patients in the pancreatobiliary group and 20% patients in the colon group died during the hospital stay (Table 1).

As shown in Table 5, sensitivity had no impact on mortality in the majority of the tested antibiotics. However, we were able to show that patients with proven resistance patterns to antibiotics frequently used

Table 3
Biological sensitivity related to microbial flora.

	Enterococcus, not specified (n = 52)	Enterococcus faecium (n = 58)	*Enterococcus faecalis* (n = 48)	*Escherichia coli* (n = 144)	Enterobactericae (n = 180)	Staphylococcus (n = 52)	Streptococcus (n = 18)	Bacteroidaceae (n = 28)	Other gram positive (n = 12)	Other gram negative (n = 44)
Ampicillin/ Sulbactam	53.8%	0%	91.7%	50%	32.2%	15.4%	100%	100%	66.7%	4.5%
Piperacillin/ Sulbactam	61.5%	0%	100%	61.1%	76.7%	92.3%	33.3%	92.9%	66.7%	72.7%
Meropenem	7.7%	0%	0%	100%	98.9%	92.3%	100%	100%	66.7%	77.3%
Cefuroxime	11.5%	0%	0%	86.1%	44.4%	15.4%	100%	35.7%	66.7%	4.5%
Cefotaxime	11.5%	0%	0%	88.9%	80%	7.7%	100%	35.7%	66.7%	4.5%
Ceftazidime	11.5%	0%	0%	87.5%	80%	0%	33.3%	35.7%	66.7%	90.9%
Tigecycline	100%	100%	100%	98.6%	71.1%	100%	100%	87.5%	100%	0%
Ciprofloxacin	7.7%	0%	0%	83.3%	96.7%	38.5%	0%	0%	16.7%	81.8%
Moxifloxacin	19.2%	0%	20.8%	83.3%	96.7%	38.5%	100%	42.9%	16.7%	0%
Vancomycin	100%	96.6%	100%	4.2%	1.1%	100%	100%	0%	100%	0%
Metronidazole	0%	0%	0%	0%	1.1%	0%	0%	100%	66.7%	0%
Cefuroxime/ Metronidazole	11.5%	0%	0%	86.1%	45.6%	15.4%	100%	100%	66.7%	4.5%
Cefotaxime/ Metronidazole	11.5%	0%	0%	88.9%	81.1%	7.7%	100%	100%	66.7%	4.5%
Meropenem/ Vancomycin	100%	96.6%	100%	100%	98.9%	100%	100%	100%	100%	77.3%

Table 4
Biological sensitivity related to location.

	Colon	Stomach	Duodenum	Small intestine	Pancreas/ biliary tract
Ampicillin/ Sulbactam	44.3%	47.6%	12.5%	34.7%	42.2%
Piperacillin/ Sulbactam	64.2%	61.9%	37.5%	67.3%	79.7%
Meropenem	74.4%	81.0%	75.0%	73.5%	64.1%
Cefuroxime	43.2%	52.4%	37.5%	34.7%	32.8%
Cefotaxime	51.7%	57.1%	50.0%	44.9%	48.4%
Ceftazidime	57.4%	42.9%	50.0%	53.1%	46.9%
Tigecycline	83.5%	90.5%	87.5%	77.6%	87.5%
Ciprofloxacin	55.7%	42.9%	62.5%	61.2%	56.3%
Moxifloxacin	57.4%	66.7%	62.5%	53.1%	57.8%
Vancomycin	31.8%	57.1%	50%	38.8%	50.0%
Metronidazole	7.4%	9.5%	0.0%	8.2%	0.0%
Cefuroxime/ Metronidazole	45.5%	52.4%	37.5%	40.8%	32.8%
Cefotaxime/ Metronidazole	54.0%	57.1%	50.0%	51.0%	48.4%
Meropenem/ Vancomycin	94.9%	100%	100%	98.0%	98.4%

Table 5
Mortality related to biological sensitivity.

	Mortality rate		p value
	Cultured bacterias: sensitive	Cultured bacterias: resistant	
Ampicillin/Sulbactam	24%	27%	0.500
Piperacillin/Sulbactam	22%	32%	**0.018**
Meropenem	23%	33%	**0.024**
Cefuroxime	23%	27%	0.363
Cefotaxime	22%	29%	0.096
Ceftazidime	23%	28%	0.124
Tigecycline	20%	53%	**0.001**
Ciprofloxacin	22%	30%	0.059
Moxifloxacin	24%	27%	0.344
Vancomycin	23%	27%	0.423
Metronidazole	25%	26%	0.851
Cefuroxime/ Metronidazole	22%	28%	0.176
Cefotaxime/ Metronidazole	21%	30%	**0.03**
Meropenem/Vancomycin	23%	88%	< **0.001**

in peritonitis had a significantly increased mortality rate. The presence of bacteria resistant to frequently used antibiotics was associated with higher mortality. Piperacillin/Sulbactam (32% vs. 22%; $p = 0.018$) Meropenem (33% vs. 23%; $p = 0.024$) and Tigecycline (53% vs. 20%; $p = 0.001$).

These findings are also true for the combination of Cefotaxime/ Metronidazole (30% vs. 21%; $p = 0.03$) and Meropenem/Vancomycin (88% vs. 23%; $p < 0.001$).

4. Discussion

In this study, we were able to demonstrate that the detected bacteria and the biological resistance patterns in postoperative peritonitis markedly differ from those in secondary peritonitis. The mortality of postoperative peritonitis is still very high. Patients with bacteria resistant to commonly used antibiotics for peritonitis have a significantly increased mortality rate.

Postoperative peritonitis is a common and severe complication after major abdominal surgery. After colorectal resections the rate of anastomotic leakage is 2–25%, resulting in peritonitis [18]. The mortality of severe intraabdominal infections with peritonitis has decreased form 90% in 1900 to 23% in 2002 due to improved surgical, antibiotic and intensive care treatment [19]. Source control remains the most crucial aspect of successful treatment of intraabdominal infections. The role of surgical treatment of peritonitis is uncontroversial and independent of the origin or cause (primary hollow organ perforation or anastomotic leakage) [20]. The kind of surgical management depends on location, severity of the peritonitis and the patient's general condition [20].

In the most recent guideline for diagnosis and management of intraabdominal infections, recommendations are given for health care associated intraabdominal infections on the one hand and community acquired infections in regards to the above mentioned facts on the other. In health care associated infections, the empiric coverage should include agents active against gram-negative aerobe and facultative bacilli. The antibiotics recommended are meropenem, imipenem, piperacillin/tazobactam, ceftazidime/cefepime plus metronidazole, aminoglycosides or colistin [21].

Acute postoperative peritonitis following previous abdominal surgery is still a severe and potentially fatal disease associated with high morbidity and mortality. The clinical presentation and natural course differs markedly from peritonitis resulting from hollow organ perforation.

Because patients are hospitalized, clinical deterioration may well be detected early. Additionally, abdominal drainages can allow for early detection of anastomotic leakage by alteration in the quality of the fluids. In contrast to this, pain is attenuated by the regular use of analgesic medication and reduced general condition is frequently found after major abdominal surgery. Furthermore, elevated infection parameters may also be explained by operative trauma, or other foci such as urinary tract infection or pneumonia and clear fluids in drainages may prolong the time to diagnostic procedures and re-laparotomy.

The mean duration from operation until diagnosis of anastomotic leakage is 8.6 days. The mean duration from onset of symptoms or first signs until diagnosis of the leakage is 3.5 days. Early symptoms such as fever, abdominal tenderness, reduced bowel movements, leukocytosis and elevated CRP are unspecific and may also be explained by the operative trauma [18].

Considering these facts, the operative treatment of peritonitis due to postoperative complications, such as anastomotic leakage, might be delayed compared to secondary peritonitis. Additionally, clinical experience shows that these patients commonly underwent antibiotic pretreatment. Therefore, the expected rate of resistances is higher.

The enrolled patients who presented with leakages from the stomach mainly underwent distal gastrectomy. The anastomotic leaks were managed either by a total redo of the anastomosis or by suturing when appropriate in patients with minor leakage. Biliary or pancreatic fistulas were found after major hepatic resections, bilioenteric anastomoses, Whipple's procedures or distal pancreatectomies. In most patients, these fistulas could be managed conservatively or interventionally (e.g. CT guided drainage). Indications for surgical management were early onset (< 48–72 h postOP) of major leakage or rapid deterioration with no option for interventional treatment. The management options range from simple drainage of fluid collections and the leakage itself, over suturing or redo of the anastomosis to total pancreatectomy in rare cases. Leakages from colonic anastomoses were found in all locations of the colon anastomosis. The management depended on the severity of the peritonitis and the patient's general condition and involved suturing, redo of the anastomosis, additional loop ileostomy or Hartman procedure in critically ill patients.

This trial was designed to analyze the bacteria present in peritonitis in correlation to the underlying location and biological resistance so as to reason the best possible antibiotic therapy in patients with postoperative complications. The term postoperative peritonitis was established to describe this specific form of secondary peritonitis. Postoperative peritonitis is an independent risk factor for mortality in patients with secondary peritonitis (18 fold increased risk) [18]. In patients with secondary peritonitis the mortality was found to be 36% [22].

The antimicrobial treatment is a major challenge due to the diverse spectrum of bacteria. Prospective trials provide relatively little data regarding high-risk patients or postoperative peritonitis. The mortality rates in these trials are often < 5% and do not represent severe peritonitis. In the special condition of health care acquired peritonitis, the empiric treatment should consider previous antibiotic treatments [19].

Postoperative peritonitis is different to tertiary peritonitis. Tertiary peritonitis is characterized as recurrent or persistent (> 48 or 72 h) peritonitis developing form secondary peritonitis, especially when surgical source control is unsuccessful. It is often associated with the presence of fungi or low-grade pathogenic bacteria [23].

The mortality of intraabdominal infections varies in regard to their origin. For intraabdominal infections originating from the stomach and duodenum, the mortality rate was found to be 21%, while perforations of small bowel and colon are associated with a mortality of 38% and 45%, respectively. These findings are in accordance to the findings of this trial [19]. The most commonly found microbes were Enterococci (21%), E coli (19%) and Enterobacter species (12%) [24]. This in addition, is consistent with our trial, where *E. coli* and other Enterobacteriaceae were the most frequently found microbes. In addition, the frequent appearance of Enterococcus species and Yeast is often described [15,25–34].

The most common aerobe bacteria in intraabdominal infections are E coli; in unaerobe cultures Bacteriodes (fragilis) are most common as in our data. The presence of enterococci should be taken into account when selecting the empiric antibiosis in high risk patients.

The distribution of postoperative peritonitis in our results is comparable to previously published data with the following origins: colon in 40%, stomach in 20%, small intestine in 13% and pancreas in 15% of patients. The most frequent cause was anastomotic leakage in 66% [24]. The sensitivity results are in accordance to other published studies, too. However, sensitivity rates in correlation to the location of leakage have not been studied extensively so far.

In the past, double or triple antimicrobial therapy was considered standard of care. In recent years, monotherapies with piperacillin/tazobactam, imipenem/meropenem or tigecylin have been established as the gold standard. Other authors have suggested piperacillin/tazobactam, imipenem or meropenem, ciprofloaxaxin plus metronidazole and 3rd or 4th generation cephalosporine plus metronidazole for severe abdominal infections. The initial empiric treatment should be deescalated, when definitive culture results are available [35].

Piperacillin/sulbactam achieved a sensitivity of over 60% with the exception of duodenal leakage where sensitivity was relatively low at 38%. The response rate of empiric antibiotic treatment with cefoxitin in secondary peritonitis was reported to be 72% compared to imipenem with 98%; surprisingly no impact on the mortality rate was detected [24]. An empiric antibiotic therapy with cephalosporines in combination with metronidazole cannot be recommended due to the sensitivity resulting between 33 and 57% in our data.

Meropenem reached sensitivities of over 73% and almost 100% when combined with vancomycin independent of the location. This supports our current antibiotic regime with piperacillin/sulbactam and with meropenem with or without vancomycin in severe peritonitis. The value of combining broad spectrum beta lactamase and aminoglycosides for intraabdominal infections is discussed controversially. A RCT was not able to detect any advantage of this treatment and is therefore not recommended [29]. Moxifloxacin is also approved for treatment of intraabdominal infections. In trials, the response rate was found to be 80% in secondary peritonitis. In comparison to this finding, the response rate in the present study was far lower with 58% [36] and can therefore not be recommended for the treatment of postoperative peritonitis.

In patients with peritonitis, a response rate of 80–86% for tigecyline and imipenem was found [19,36]. In our trial, tigecycline had an overall sensitivity rate of 84%. Therefore, this antibiotic can be used as an alternative empiric antibiotic in patients without adequate response to the initially conducted empiric therapy. The initial treatment of peritonitis is empiric as culture and sensitivity results take 48 h till available. The aim of empiric treatment is to begin antibiotic treatment as soon as possible, since any delay increases mortality and morbidity [36].

Our data shows with just a few exceptions that mortality increases in patients infected with microbes resistant to commonly used antibiotics as compared to infections with sensitive microbes. This supports the notion that an empiric antimicrobial therapy initiated immediately after diagnosis can reduce mortality, if the microbes are sensitive to it. Delayed antibiotic therapy will have a similar effect on outcome as an ineffective antibiotic regime against resistant microorganisms. Previously, some trials were able to show the impact of empiric antibiotic therapy on mortality, while other trials revealed contradictory results. The main differences concerning survival were found between patients with adequate empiric treatment and those without effective therapy for the detected microbes [24].

In previous multivariate analyses, the presence of Enterococcus was associated with a 7.2 fold increase in mortality [24,37]. This is in accordance to our data showing a mortality rate of 32.1% in patients with Enterococcus cultures.

Most guidelines do not include antifungal therapy for patients with secondary or postoperative peritonitis. Therefore, this trial does not focus on the sensitivity results of yeasts. This is reasonable since antifungal prophylaxis is only recommended in selected patients at risk of candidiasis. Furthermore, some authors do not recommend antifungal agents even if yeasts are discovered. However, antifungal therapy is indicated in patients with immunosuppression or on-going abdominal infection [34,38,39]. In the majority of cases, yeasts are sensitive to Amphotericin or Fluconazole. Therefore, empiric treatment for fungal infections is simpler compared to empiric treatment for bacteria.

5. Limitations

This is a retrospective analysis of data from our prospectively collected database. Some patients had to be excluded due to lack of intraoperative microbiological testing. This might cause a certain selection bias. Postoperative complications including abscess or anastomotic leakage are rare, therefore, the case load is limited, especially when analyzing subgroups with different locations.

Nevertheless, to our knowledge this is the first such evaluation of microbes and their biological resistance in this special group of patients correlated with a detailed analysis according to the origin of the peritonitis. Therefore, this trial may well help in improving the clinical outcome of postoperative peritonitis, one of the most important complications after major abdominal surgery, by optimizing individually calculated antibiotic treatment.

6. Conclusions

This trial shows that the currently applied antibiotic regimes with piperacillin/sulbactam and cefotaxime/metronidazole are only effective in 67% and 53% of patients with anastomotic leakage. Therefore, their administration cannot be recommended as initial empiric antimicrobial therapy before sensitivity results are available. Only meropenem or meropenem/vancomycin cover most of the microbes over all origins of secondary peritonitis (besides second line antibiotics such as tigecycline) and is recommended as empiric antimicrobial therapy till sensitivity results become available. The presence of resistant microbes is associated with increased mortality. To improve the evidence, multicenter trials with higher numbers of included patients are required.

Ethical approval

The study was approved by the institutional review board of the hospital.

(No approval number exist).

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Author contribution

Rainer Grotelueschen.
Drafting of the manuscript, Interpretation of results Design of Tables.
Marc Luetgehetmann.
Evaluation of data, drafting of the manuscript.
Johannes Erbes.
Data collection, statistical analysis, assistance in drafting the manuscript.
Lena M. Heidelmann.
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Katharina Grupp.
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Interpretation of results revision of manuscript.
Matthias Reeh.
Interpretation of results revision of manuscript.
Jakob R. Izbicki.
Study design. supervised the work.
Kai Bachmann:
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All authors discussed the results and commented on the manuscript.

Conflicts of interest

No conflicts of interest exists.

Research Registration Unique Identifying Number (UIN)

The study was registered in the Research Registry.
(UIN researchregistry: 5001).
Link: https://www.researchregistry.com/browse-the-registry#home/registrationdetails/5d22f97f076ccc0010fc2cfd/

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Kai Bachmann & Rainer Groteluschen

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.08.020.

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