ARTICLE ORIGINAL

Microbiological profile of postoperative peritonitis in intensive care units

Profil microbiologique des péritonites postopératoires dans les unités de soins intensifs

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Abstract

Introduction

Postoperative peronitis (POP) is a serious complication, difficult to control especially with the emergence of multidrug resistant bacteria. The aim of this work was to study the epidemiological characteristics and the bacteriological profile of POP.

Material and methods

This is a retrospective study over a period of 6 years, from 01/01/2014 to 31/12/2019.

Results

Thirty-nine cases were collected, 31 of which have a positive culture of peritoneal swab. POP were characterized by a male predominance (*sex-ratio*: 1.61). Patients over 60 years old were mainly affected (64.7%). The main antecedents observed were abdominal surgery (89.7%) and neoplastic disease (77%). The most frequent etiology of postoperative peritonitis was anastomotic leakage (38.5%). The culture was multi-microbial in 48.4% of cases. Sixty-nine strains have been isolated. Seventy one per cent were aerobic bacteria, 21.7% were anaerobic and 7.3% were yeasts. The distribution of germs varied according to the stage of the initial intervention. Enterobacteriaceae were more prevalent in the supramesocolic stage (62.5%). In the sub-mesocolic stage, anaerobes and enterobacteriaceae accounted respectively for 28.9% and 31.1% of isolated microorganism. Multidrug resistant bacteria (n=19) were isolated in 61.3% of cases.

Conclusion

Considering the high rate of multi-resistant bacteria, the prevention and management of POP is a major challenge. Constant analysis of microbiological data remains essential.

Key word *: Postoperative peritonitis, epidemiology, bacteriology*

Résumé

Introduction

Les péritonites postopératoires (PPO) sont des complications graves, difficile à contrôler surtout avec l'émergence de bactéries multi-résistantes. L'objectif de ce travail est d'étudier les caractéristiques épidémiologiques et le profil bactériologique des péritonites postopératoires.

Matériel et méthodes

Il s'agit d'une étude rétrospective sur une période de 6 ans, allant du 01/01/2014 au 31/12/2019.

Résultats

Trente-neuf cas ont été colligés dont 31 à culture bactériologique positive. Les PPO sont à prédominance masculine (*sex-ratio* : 1.61) et touchent essentiellement les sujets de plus de 60 ans (64.7%). Les principaux antécédents observés sont la chirurgie abdominale (89.7%) et les néoplasies (77%). L'étiologie la plus fréquente est le lâchage des anastomoses (38.5%). La culture était plurimicrobienne dans 48.4% des cas. Soixante-neuf souches ont été isolées dont 71% sont des bactéries aérobies, 21.7% des anaérobies et 7.3 % des levures. La répartition des germes était variable selon l'étage de l'intervention initiale. Les entérobactéries primaient dans l'étage sus-mesocolique (62.5%). Quant à l'étage sous-mesocolique les anaérobies et les entérobactéries représentaient respectivement 28.9% et 31.1% des germes isolés.Les bactéries multi-résistantes (n=19) ont été isolées dans 61.3% des cas.

Conclusion

Devant un taux élevé de bactéries multi-résistantes, la prévention et la prise en charge des péritonites postopératoires posent un défi important et l'analyse régulière des données microbiologiques reste indispensable.

Mots clés : *Péritonite postopératoire, épidémiologie, bactériologie*

INTRODUCTION

Postoperative peritonitis (POP) corresponds to secondary and tertiary health care associated infection, occurring in the aftermath of abdominal surgery. The usual criteria for diagnosing peritonitis are less reliable because of the postoperative context. Untreated POP are rapidly associated with organ failure and a severe prognosis (1). In the same way, both late treatment and antibiotic therapy not considering all isolated germs are factors of therapeutic failure, persistence of infection, and even death (2, 3). Careful multidisciplinary management, involving surgeons, radiologists, intensive care anesthetists, and microbiologists, is therefore essential.

Unlike community acquired peritonitis in which the microbial findings reflect the usual digestive flora, in POP the microbial ecology is modified both in terms of bacterial type and susceptibility profile (3). Although several studieshave been conducted on POP, few of them focused on microbiological data.

The aim of this work was to study epidemiological characteristics and microbial findings of POP diagnosed in the intensive care units as well as antibiotic susceptibility patterns of isolated bacteria for better therapeutic management.

MATERIALS AND METHODS

This is a retrospective study carried out in the microbiology laboratory over a period of 6 years, from 01/01/2014 to 31/12/2019. The inclusion criteria was intensive care units patients diagnosed with POP and having a peritoneal sample sent to laboratory.

Clinical and epidemiological data were collected from the patients'medical records. Data were analyzed using Excel software. Samples were processed according to the laboratory's standard methods. Identification of isolates was performed using the API identification galleries or VITEK 2 system cards (Biomérieux Inc). Antibiotic susceptibility was performed and interpreted according to Eucast/CASFM Guidelines using the agar diffusion method and Vitek 2 system (Biomerieux Inc).

RESULTS

During the study period, 39 cases of POP were managed at the intensive care units.

1. Epidemiological characteristics

Patients were predominantly male (61.8%) and over 60 years old in 64.7% of cases. The mean age was 63 years. Most cases (n=31) had two or three underlying diseases. Abdominal surgery (89.7%) was the most common past medical history followed by neoplastic disease (77%). Nearly 30% of patients had diabetes and around 70% had at least one chronic disease (Table I). Initial surgery characteristics are summarized in Table II. The most common etiology of POP was anastomotic leakage (38.5%) followed by intestinal perforation (17.9%).

Bacteriological and mycological characteristics Peritoneal fluid culture was positive in 31 cases. Negative cultures were observed following triple therapy with carbapenems, aminoglycosides and glycopeptides.

Table I : Underlying pathologies

Pathology	n	%
Abdominal surgery	35	89.7
Neoplasia	30	77
Chronic pathologies (renal, cardiovascular, pulmonary)	16	41
Diabetes	11	28.2
Radio-chemotherapy	3	7.7
Immunosuppressants	2	5.1
Chronic Inflammatory Bowel Disease (IBD)	1	2.6
Pulmonary tuberculosis	1	2.6
Adenomatous polyposis	1	2.6

n: Number of patients, % : Pathology frequency

Table II : Type and site of initial pathology

Site	Type of pathology	n	%
supramesocolic		**12**	**30.8**
Stomach	-Gastrictumor	3	7.7
	-Gastrectomy sleeve	2	5.1
Duodenum	-Duodenal adenocarcinoma	2	5.1
	-Duodenalulcer	1	2.6
Pancreas	-Pancreatic head tumor	2	5.1
Liver	-Hepatocellular carcinoma	1	2.6
Gallbladder	-Bladder tumor	1	2.6
Sub-mesocolic		**25**	**64**
Colon	-Hemorrhagic rectocolitis	1	2.6
	-Colon tumor	10	25.5
Rectum	-Tumor of the upper rectum	1	2.6
	-Tumor of the middle rectum	5	12.8
	-Tumor of the lower rectum	3	7.7
Small intestine	Occlusion	4	10.2
Appendix	Appendicitis	1	2.6
Others		**2**	**5.2**
	Urothelial carcinoma	1	2.6
	Details of the initial surgery not specified	1	2.6
Total		39	100

2. Distribution of isolated germs

Sixty-nine strains have been isolated. Seventy one per cent were aerobic bacteria, 21.7% were anaerobic and 7.3% were yeasts (Table III). Enterococci were isolated from 25.8% of POP positive culture.The culture was multi-microbial in 48.4% of cases (n=15). The distribution of germs was variable according to the stage of surgery (Table IV). Enterobacteriaceae were more prevalent in the supramesocolic stage (62.5%). In the sub-mesocolic stage, anaerobes and enterobacteriaceae accounted respectively for 28.9% and 31.1% of isolated microorganism.

2.2 Resistance profiles

Antimicrobial resistance profiles of Gram-negative bacilli (GNB) are described in Table V. The two isolated strains of *Staphylococcus aureus* were resistant to methicillin without cross-resistance to aminoglycosides and fluoroquinolones. All strains of the genus *Streptococcus* were sensitive to the tested antibiotics. For enterococci, all strains of *Enterococcus faecalis* were sensitive to ampicillin and showed low level of resistance to aminoglycosides. All strains of *Enterococcus faecium* were resistant to beta-lactam antibiotics and showed a high level of resistance to aminoglycosides.

Two vancomycin-resistant *Enterococcus faecium* (VREF) were found and were only sensitive to linezolid.

Table III : Isolated germs from peritoneal samples

Germs	**n**	**%**
Aerobicgerms	**49**	**71**
Gram-negativebacilli	**34**	**49.3**
Enterobacteriaceae	**27**	**39.1**
Escherichia coli	12	17.4
Klebsiella pneumoniae	9	13
Other Enterobacteriaceae	6	8.7
Non-fermenting Gram-negative bacilli	**7**	**10.1**
Acinetobacter baumannii	3	4.3
Pseudomonas aeruginosa	4	5.8
Gram-positive Cocci	**15**	**21.7**
Staphylococcus aureus	2	2.9
Streptococcus	5	7.2
Enterococcus	8	11.6
Anaerobicgerms	**15**	**21.7**
Prevotella	7	10.1
Bacteroides	5	7.2
Others	3	4.3
Yeast	**5**	**7.2**
Candida albicans	4	5.8
Candida glabrata	1	1.4
Total	**69**	**100**

n= number of strains, % frequency

Table IV : Distribution of microorganisms according to the stage of the initial surgery

Germs (n=69)	Space		
	Supramesocolic n (%)	Sub-mesocolic n (%)	Supramesocolic and Sub-mesocolic n (%)
Enterobacteriaceae	10 (62.5)	14 (31.1)	3
Non fermenting Gram-negative bacilli	1 (6.2)	6 (13.3)	0
Gram-positive Cocci	2 (12.5)	11 (24.5)	2
Anaerobes	0	13 (28.9)	2
yeast	3 (18.8)	1 (2.2)	1
Total	16 (100)	45 (100)	8

n : number of strains, % : frequency in each space

Table V : Antibiotic Susceptibility profile of *aerobic Gram-negative bacilli*

	Aerobic Gram-negative bacilli		
	Enterobacteriaceae (n=27)	Non fermenting (n=7)	Total (n=34)
Antibiotic	**R (n)**	**R (n)**	**R (n) (%)**
Amoxicillin	27	NT	- -
Amoxicillin + clavulanicacid	19	NT	- -
Ticarcillin	23	4	27 (79.4)
Ticarcillin + clavulanicacid	NT	4	- -
Piperacillin	23	4	27 (79.4)
Piperacillin + Tazobactam	11	4	15 (44.1)
Cefuroxime	11	NT	- -
Cefotaxime	11	NT	- -
Ceftazidime	11	4	15 (44.1)
Ertapenem	3	NT	- -
Imipenem	3	4	7 (20.5)
Gentamicin	10	4	14 (41.1)
Amikacin	0	3	3 (8.8)
Ofloxacin	10	NT	-
Ciprofloxacin	9	4	13 (38.2)
Trimethoprim+			
Sulfamethoxazole	12	5	17 (50)
Fosfomycin	3	NT	- -

R : Resistant/ intermediate , n : number of strains, NT : Not tested

Concerning anaerobic bacteria, they were sensitive to imipenem, metronidazole as well as amoxicillin-clavulanic acid and piperacillin-tazobactam combinations. Resistance rates of these isolates were 33.3% to clindamycin and 86.6% to amoxicillin.
All strains of *Candida albicans* were susceptible to fluconazole and amphotericin B. The only strain of *Candida glabrata* was resistant to fluconazole but sensitive to echinocandins.

2.3 Multi-resistant bacteria

Multidrug-resistant (MDR) bacteria were isolated from 61.3% of POP positive culture and represent 38.8% of the aerobic germs isolated in our series. Among the 19 MDR strains, five were emerging extensively drug-resistant bacteria (eXDR): three strains of carbapenemase-producing enterobacteriaceae and two strains of VREF. The other MDR bacteria were third generation cephalosporin-resistant enterobacteriaceae (n=8), imipenem-resistant non fermenting GNB (n=4) and methicillin-resistant *Staphylococcus aureus* (n=2).

DISCUSSION

POP is a serious complication that raises two main issues for medical practitioners: difficult diagnosis and challenging treatment (3). As national studies on POP are extremely rare, it is crucial to identify POP specificities in order to get a better management.

1. Epidemiological characteristics

The mean age in our data was 63 years. This result was consistent with other published studies, where the mean age reported was around 60 years (4-7). This finding can be explained by the increased susceptibility of elderly subjects to infections due to immunosenescence, malnutrition, and a large number of age-related physiological and anatomical alterations (8).
The male predominance noticed in our data is in accordance with other studies conducted in Africa and Europe (4-7, 9, 10) and is probably related to etiological factors. In fact, digestive system neoplasms, a common reason for initial surgery in POP, is more prevalent in men than in women (11).
In our data, 77% of patients had a malignant pathology and 28.2% were diabetic. In two studies conducted in France, neoplastic disease was found to be around 40%, while diabetes was found in 10% to 19% of cases depending on the POP subgroup, but neither of these two parameters was considered a risk factor for persistent POP nor POP due to MDR bacteria (12, 13).
In our study, the initial surgery was digestive for almost all patients. Only one case of urological surgery was found. The colonic region was the most concerned site (28.1%) as in previous published data (40 % to 51%) (4, 5, 14, 15). In 38.5% of cases, POP occurred as a result of anastomosis release causing a rupture of the gastrointestinal tract seal. Anastomosis release is a major complication in gastrointestinal surgery and the most common etiology of POP in several studies (32% to 66%) (4, 7, 10, 14, 15) despite all the advances in surgery.

2. Bacteriological and mycological characteristics

The nature of germs isolated in the POP varied according to the stage of the initial intervention. This finding is explained by the distribution of germs in the digestive system. Indeed, a large majority of aerobic germs is found in the stomach as well as in the jejunum. At the level of the ileum, there is an aero-anaerobic balance. However, in the colon, we find the most important bacterial load with a large majority of anaerobes (16).
In previous published studies *Escherichia coli* was the most commonly found enterobacterium (18 to 50%) followed either by the genus *klebsiella* or by the genus *Enterobacter* (13, 15, 17, 19). This is in accordance with our data showing a predominance of *Escherichia coli* (17.4%) and *Klebsiella pneumoniae* (13) Enterococci were isolated from 25.8% of the positive culture. In previous studies enterococci were found in 19 to 44% of cases (13-15). According to certain authors, isolation of enterococci from peritoneal fluid is associated with a high mortality rate, particularly when virulence factors are expressed (20-22). However in the study conducted by Seguin *et al.*(14), the presence of enterococci was associated with a higher rate of intraperitoneal abscess and did not affect the mortality rate.
In addition, some risk factors for intra-abdominal enterococcal infection have been identified: immunocompromised patient, prior antibiotic therapy with cephalosporin or broad-spectrum beta-lactam (23).
As for anaerobic germs, the *Bacteroides* genus was the most frequently found (7% to 17%) while the *Prevotella* genus was not particularly reported (13,15,17,18). However, in our study, the genus *Prevotella* was the most commonly found anerobe (10.1%) followed by the genus *Bacteroides* (7.2%).
As for MDR bacteria, they were isolated from 61.3% of positive culture in our data study. MDR bacteria were found in 41% of POP cases in the study presented by Augustin *et al.* (13) and in 17% of POP cases by Seguin *et al.* (18). These authors showed that hospitalization longer than 5 days and prior antibiotic therapy were two independent risk factors for MDR bacteria (18). Indeed, these two factors seem to have consequences on the patient's digestive flora. Moreover, the frequency of MDR bacteria can be particularly high in multiple surgical revisions and tertiary peritonitis. In fact it seems to be progressively increasing with the number of re-interventions (3,12). Seguin *et al*. reported that MDR bacteria were found in 75% of POP cases at the third reoperation (18), while Montravers *et al.* reported a 15% increase in MDR bacteria frequency at each reoperation (12).
Our study has its limitations, namely the small sample size and the absence of a control group for statistical validation of POP characteristics. Nevertheless, it highlights a fearsome infectious complication for which national publications focusing on microbiological data are lacking.

CONCLUSION

POP are frequently multi-microbial. Nature of isolated

germs varies according to the stage of the initial intervention. The antibiotic resistance rates are alarming in our institution. Therefore, the main challenges consist of preventing the spread of eXDR and rationalizing broad-spectrum antibiotics prescription. Furthermore, local and national antibiotic treatment protocols must be established and regularly revaluated on the basis of local microbiological data.

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