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PRIMARY PERITONITIS IN IMMUNOCOMPROMISED PATIENTS

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Abstract:
This study is basically conducted to recognize the primary peritonitis in immunocompromised patients, for the purpose all patients admitted to the (ICU) intensive care unit of the Hospital from 1 January 2016 to 31 July 2017 with a diagnosis of primary peritonitis were retrospectively included. The medical record of the patients was gathered from the data recordings of the Department of Critical Care and Emergency and the Departments of Surgery. APACHE II (Acute Physiology and Chronic Health Evaluation II) was the main source in the calculation for every patient at the time of admission. Antimicrobial treatment management before and after the diagnosis of peritonitis was studied. According to the above-mentioned details of methods, 120 were included and the results concerning mortality, etiology of peritonitis and microbiological data were in accordance with previous studies. According to the APACHE II score (P = 0.005), age (P = 0.002), the existence of enterococcus in the peri-operative samples (which is defined P = 0.02) and the period between diagnosis and surgery (P = 0.04) were prognostic about the death within thirty days after peritonitis diagnosis. There was no prominent difference was shown in the mortality rate in patients whose post-operative antibiotic treatment was changed following results of intra-operative peritoneal cultures versus patients having inappropriate treatment (P = 0.96). The same observations were noted for anti-enterococcal treatment. This study concentrates on the importance of significant treatment of surgery and represents modern antibiotic treatment impact. The mortality and morbidity linked with the existence of enterococcus which basically not inspired by the treatment with an antibiotic would represent to advised the pro-inflammatory role of Enterococcus. Therefore, the studies of potential randomize are required to analyze the actual contribution ofthe contribution of enterococcal antibiotic coverage in this background.

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INTRODUCTION:

The basic bacterial peritonitis refers to the spontaneous bacterial invasion of the peritoneal cavity. This mainly occurs in infancy and early childhood, in cirrhotic patients and immunocompromised hosts.Primary peritonitis remains a major cause of morbidity, with a mortality of ∼30%.The Acute Physiology and Chronic Health Evaluation II (APACHE II) is the most studied severity index in peritonitis and has been shown to be equal or superior to specific peritonitis scores such as the Mannheim Peritonitis Index (MPI) and the Peritonitis Index of Altona II (PIA II). The APACHE II score does not include microbiological data and according to some authors, the results of microbiological cultures do not seem to influence peritonitis prognosis (Ohno, 2017).

However, Enterococcus was shown to increase postoperative morbidity both in animal models and in humans. In the same way, when the surgical procedure is effective, the role of suitable empirical antimicrobial therapy remains controversial, particularly the necessity to systematically treat Enterococcus at an early stage. The impact of potential post-operative antimicrobial alteration inaccordance with microbiological samples is still poorly documented (JIANG, YEN and WANG, 2017).

2.0 METHODS AND MATERIALS:

All patients admitted to the intensive care unit (ICU) of a tertiary care hospital from 1 January 2016 to 31 July 2017 with a diagnosis of primary peritonitis were retrospectively included. Patients' medical records were collected from the data recordings of the Department of Critical Care and Emergency and the Departments of Surgery. Primary peritonitis was defined as the result of the loss of integrity of the gastrointestinal or genito-urinary tract leading to contamination of the peritoneal space. A distinction was made between community-acquired peritonitis and post-operative or nosocomial peritonitis (JIANG, YEN and WANG, 2017).

Data Gathering

Data has been gathered through pre-existing comorbid disorders as per the give below criteria: current smoking was defined as a cigarette consumption >10 per day; alcoholism was defined as a current consumption exceeding 20 g per day for women and 60 g per day for men; the body mass index; and allergy was defined as a clinical history of anaphylactic reaction. Comorbid conditions were collected with the following criteria: dyslipidaemia, patient receiving a specific treatment (e.g. statin, fibrates); diabetes mellitus, the patient was on insulin or oral anti-diabetic therapy; cardiovascular disease, the patient was having treatment for congestive heart failure and/or coronary artery disease; chronic pulmonary disease, a clinical history of chronic obstructive, restrictive or vascular pulmonary disease giving rise to moderate to severe reduction of exercise tolerance, or the patient was on bronchodilator treatment or long-term oxygen; immunodeficiency conditions (chemotherapy, radiotherapy, high doses of corticosteroids); or malignant progressive diseases. Previous abdominal surgery was also recorded (Baothman, Md and Reddy, 2016). The patient's history was recorded: the date of the onset of symptoms, the date and reason for the patient's admission, date of peritonitis diagnosis and etiology of peritonitis. APACHE II scores were calculated for each patient upon admission. The date and the type of surgical treatment of peritonitis were recorded (JIANG, YEN and WANG, 2017).

Statistical analysis

For the statistical analysis, the expression was used through quantitative parameters as mean ± S.D. or as median (5th and 95th percentiles) according to their distribution. The $\chi 2$ test or Fisher's exact test was used for comparing distributions of the qualitative parameters. Prognostic factors at the day of peritonitis diagnosis were determined considering demographic data, patient's history, the severity of the illness, surgical management, microbiological data and patient's outcome (death at 30 days after diagnosis of peritonitis) (Ohno, 2017).

RESULTS:

Generally, 120 patients (48 females, 40%) were included. Peritonitis was post-operative in 38 cases. Median age was 61 years (5% to 95% percentiles, 25–87). Underlying diseases are reported in Table 1.

Table 1. Pre-existing comorbid disorders at the time of admission for 120 peritonitis patients

Comorbid conditions	Patients *n*	Patients %
Current smoking	30	25
Alcoholism	9	7.5
Obesity	11	9.2
Allergy	9	7.5
Metabolic diseases		
dyslipidaemia	12	10
diabetes mellitus	10	8.3
Cardiovascular diseases		
congestive heart failure	11	9.2
coronary artery disease	5	4.2
Chronic pulmonary disease	12	10
Immunocompromised patients		
corticotherapy	3	2.5
HIV infection	1	0.8
Malignant disease		
solid tumour	22	18.3
haemopathy	2	2.5
Previous abdominal surgery	40	33

Source: (JIANG, YEN and WANG, 2017)

The basic reason of the patients' admission was an abdominal pain in 64 patients (54%), mechanical ileus in 17 (14%), deterioration of health in 11 (9.3%) and miscellaneous in 28 (22.7%). Upon admission to the ICU, the median APACHE II score was 10 (range 2–26). The median period between the onset of symptoms and diagnosis was 3 days (range 0–70 days). The median period between diagnosis and surgery was 0 days (range 0–5 days). Aetiologies of peritonitis were: perforation of the large bowel (n = 48), perforation of the stomach (n = 23), appendicitis (n = 14), pancreatitis (n = 13), cholecystitis (n = 10), perforation of the small bowel (n = 9) and miscellaneous (n = 3). In all patients, surgical treatment was completed by evacuation of pus and peritoneal lavage (Cuff, 2017).

According to the plan the type of surgery carried out was as follows: appendicectomy (n = 14), gastric or duodenal suture (n = 18), gastric resection (n = 5), cholecystectomy (n = 14), pancreatic necrosectomy (n = 13), small bowel suture (n = 4), small bowel resection with anastomosis (n = 5), small bowel anastomosis resection without anastomosis (n = 5), Hartman's operation (n = 23), colonic resection (n = 25) and miscellaneous (n = 3). Mortality was not significantly different in patients needing re-operation (23.5% versus 25.2%, P = 0.87). Patients were mechanically ventilated post-operatively for 1 day (range 0–32 days). The median lengths of stay at the ICU and in the hospital were 4 (range 0–36) and 18 (range 4–70) days, respectively. Post-operative extra-abdominal nosocomial infection occurred in 22 patients (18.3%); it was most frequent in patients with peri-operative peritoneal sample isolates [10 (34.5%) versus 12 (13.2%), P = 0.01]. Thirty patients died within 30 days of admission (25%). Peri-operative intra-abdominal samples were taken in 90 patients and were positive in 68 patients. The median number of bacterial species per patient was 1 (range 0–4). The microorganisms isolated are shown in Table 2.

Table 2. Microorganisms isolated from peri-operative intraperitoneal samples

Organisms	Patients with samples available from cultures		
	community acquired (*n* = 59)	post-operative or nosocomial (*n* = 31)	total (*n* = 90)
Aerobic			
Gram-negative aerobic and facultative			
E. coli	26	13	39
Klebsiella spp.	6	3	9
Pseudomonas aeruginosa	4	3	7
others	11	8	19
Gram-positive aerobic and facultative			
Enterococcus spp.	18	11	29
Streptococcus spp.	13	4	17
S. aureus	7	5	12
Anaerobic	12	6	18
Fungi			
Candida albicans	5	3	8
Candida tropicalis	2	–	2
Candida parapsilosis	–	1	1
Total no. of microorganisms			161

Source: (JIANG, YEN and WANG, 2017)

Escherichia coli, Enterococcus, Staphylococcus aureus,and fungi wereisolated in 39, 29, 12 and nine patients, respectively. Among the cases of E. coli, 43.6% were resistant to amoxicillin, 25.6% to a combination of amoxicillin and clavulanic acid and 5.1% to fluoroquinolones. Among the isolates of Enterococcus (n = 29), none was resistant to glycopeptides. Among Enterococcus faecalis (n = 26), none was resistant to gentamicin and one (3.8%) was resistant to amoxicillin. Among Enterococcus faecium (n = 3), one (33.3%) was resistant to gentamicin and two (66.6%) were resistant to amoxicillin. Among S. aureus, 25% were resistant to oxacillin(Cuff, 2017).

Prognostic factors

Using univariate and multivariate analyses, the APACHE II score (P = 0.005), age (P = 0.002), the presence of Enterococcus in the peri-operative samples (P = 0.02) and the period between diagnosis and surgery (P = 0.04) were predictive of death within 30 days after diagnosis of peritonitis. There was a trend to significance for post-operative or nosocomial peritonitis as predictors of death (P = 0.06) (Tables 3 and 4)

Table 3. Univariate analysis of demography, history, clinical and paraclinical factors present at the time of admission that were associated with death within 30 days

Risk factors	Univariate analysis				
	deaths ($n=30$)		survivors ($n=90$)		
	n	%	*n*	%	*P*
Male sex	16	53	56	62	0.4
Alcoholism	3	10	6	7	0.69
Current smoking	7	23	23	26	1
Diabetes mellitus	6	20	4	4	0.02
Dyslipidaemia	2	7	10	11	0.73
Allergy	3	10	6	7	0.69
Prior abdominal surgery	9	30	31	34	0.82
Corticotherapy	0	0	3	3	0.57
Congestive heart failure	7	23	4	4.5	0.002
Coronary artery disease	3	10	2	2	0.1
Respiratory insufficiency	5	17	7	8	0.17
Haemopathy	1	3	2	2	1
Solid tumour	11	37	11	12	0.003
HIV infection	0	0	1	1	1
Post-operative or nosocomial peritonitis	14	47	24	27	0.05
Enterococcus	13	43	16	18	0.005
Fungus	5	17	4	4	0.005
Post-operative extra-abdominal nosocomial infection	11	37	11	12	0.003
	median (5% to 95% pc)		median (5% to 95% pc)		
Age (years)	78 (40–92)		53 (19–82)		0.001
Body mass index	23 (16–30)		24 (17–32)		0.13
Maximal temperature (°C)	39 (38–40.6)		38.5 (37.2–39.5)		0.002
APACHE II	18 (10–36)		9 (2–22)		0.0001
Period between onset of symptoms and diagnosis (days)	6 (0–95)		2 (0–47)		0.03
Period between diagnosis and surgery (days)	0 (0–15)		0 (0–3)		0.07
Maximal leucocytosis (cells/mm^3)	20 500 (3700–53 100)		14 550 (7800–28 700)		0.02
Number of sites infected	1 (0–3)		1 (0–2)		0.05
Number of microorganisms isolated per patient	2 (0–6)		1 (0–3)		0.02

pc, percentiles.

Table 4. Multivariate analysis of factors present at the time of admission associated with death within 30 days

Risk factors	Coefficients	Odds ratio (95% CI)	*P*
Post-operative or nosocomial peritonitis	1.44	4.2 (1.0–18.2)	0.06
Enterococcus[a]	1.99	7.2 (1.4–36.5)[b]	0.02
		1.0 (0.2–5)[c]	0.96
Age (years)	0.09	–	0.002
Maximal temperature (°C)	0.69	–	0.11
APACHE II	0.22	–	0.005
Period between diagnosis and surgery (days)	0.35	–	0.04

[a]The reference level is considered as 'absence of *Enterococcus*'.
[b]Presence of *Enterococcus*.
[c]Missing data.

Source: (JIANG, YEN and WANG, 2017)

DISCUSSION:

The treatment of primary peritonitis is subject to debate, and several fundamental questions remain unanswered. Should the antibiotics are chosen to be effective against all the intra-peritoneal microorganisms? Should a single broad-spectrum β-lactam or combination with an aminoglycoside be used? What is the optimal duration of this treatment? What abdominal lavage should be performed? This study showed results that were comparable to previous studies, confirming that our population of patients was representative(Cuff, 2017).

The mortality rate was 25% compared with other studies that report it to be ∼30%, with a wide range (0–70%). The predictive factors that we found were reported in other studies. APACHE II appears to be the most reliable prognosis index for peritonitis. Sites of perforation causing peritonitis were comparable with those described in the literature. The need for further surgical intervention did not have any influence on prognosis. The types of microorganisms identified were those commonly observed(Cuff, 2017).

A variety of antimicrobial regimens were initiated because the choice of antibiotic treatment was at the discretion of physicians. Numerous combinations of treatment are commonly used because a large number of antimicrobial agents are effective. It should be noted that in a study by Mosdell et al. there were over 24 different combinations of antibiotics, and in another study by Cuff (2017), there were 123. The difficulty of antimicrobial management lies in the diversity of the microbiological etiology and the variation of quantity and quality of bacteria according to the position of perforation in the gastrointestinal tract. Empirical broad-spectrum antimicrobial treatment appears to be effective. In the peri-operative period, most of the patients received a combination of a β-lactam with an aminoglycoside when the diagnosis of peritonitis was made. Antimicrobial treatment was changed in 49 patients. In the 36 patients with available cultures, the changes were in accordance with microbiological data. Among the 71 patients with no change in antimicrobial agents, 14 should have had changes according to the microbiological data and 13 others for the reduction of the antimicrobial spectrum (Cuff, 2017).

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Age (years)	0.09	–	0.002
Maximal temperature (°C)	0.69	–	0.11
APACHE II	0.22	–	0.005
Period between diagnosis and surgery (days)	0.35	–	0.04

[a]The reference level is considered as 'absence of *Enterococcus*'.
[b]Presence of *Enterococcus*.
[c]Missing data.

Table 5. Modification of the peri-operative antimicrobial treatment in the post-operative period for 120 patients with secondary peritonitis

Patient category	No. of patients ($n = 120$)	Death ($n = 30$)
Patients without modification of the peri-operative antimicrobial treatment in the post-operative period	$n = 71$	$n = 19$
No culture data (on the peri-operative samples) available or premature death	39	10
Cultures showed that a modification of the peri-operative antimicrobial treatment was indicated in the post-operative period[a]	14	4
Cultures showed that peri-operative antimicrobial treatment was appropriate and no reduction of spectrum was possible in the post-operative period[b]	5	2
Cultures showed that peri-operative antimicrobial treatment was appropriate but reduction of spectrum was possible in the post-operative period[b]	13	3
Patients with modification of the peri-operative antimicrobial treatment in the post-operative period	$n = 49$	$n = 11$
No culture data available[c]	11	0
Cultures showed that a modification of the peri-operative antimicrobial treatment was indicated in the post-operative period[b]	26	9
Cultures showed that peri-operative antimicrobial treatment was appropriate but modification was made in order to reduce the spectrum[b]	10	1
Modification was made due to adverse effects	2	1

[a]Inappropriate treatment strategy.
[b]Appropriate strategy.
[c]Change was motivated by clinical failure because microbiological samples were not contributive or available.

Source: (JIANG, YEN and WANG, 2017)

The absence of correlation between the expected outcome and susceptibility of the isolated microorganisms is frequently reported in the literature. For peri-operative samples may not be justified because the culture results were ignored by the physician in the post-operative period and an appropriate change did not seem to influence the outcome. There are several contributing factors.

(i) The period between the onset of symptoms and diagnosis. In this study, it was greater in patients who died, 6 versus 2 days (P = 0.03 by univariate analysis)(Ohno, 2017).

(ii) (ii) An early and efficient surgical treatment. In this study, the period between diagnosis and surgery was a predicting factor of mortality by multivariate analysis (P = 0.04).

(iii) The delay in finding suitable post-operative antimicrobial treatment according to the culture results. However, the time required to obtain culture results is at least 2 days (up to 4 days for anaerobic bacteria)(Ohno, 2017).

(iv) The virulence of the microorganisms and the large inoculum size,32 which may explain the failure of antimicrobial treatment even though the bacteria were susceptible. In our study, a number of infected sites and the number of microorganisms isolated per patient were associated with mortality by univariate analysis(Ohno, 2017).

(v) The host defense responses. Therefore, the outcome is probably determined in the first few hours of the history of peritonitis, and these factors must be taken into account in clinical trial procedures to investigate the efficiency of antimicrobial treatment(Ohno, 2017).

Although other studies do not suggest it, there are several bibliographic arguments for thinking that there could be a linear relationship between the time from diagnosis to surgical intervention and the increase in mortality.

CONCLUSION:

In conclusion, this study confirms the ability of the APACHE II score to predict the severity of peritonitis at the time of admission and emphasizes the importance of prompt surgical treatment, in contrast to the modest impact of adapted antibiotic treatment on prognosis. The latter seems to be decisive in the first hours of the evolution. The morbidity and mortality associated with the presence of Enterococcus in peritoneal fluid, not influenced by the treatment of this microorganism, would seem to suggest a pro-inflammatory role of Enterococcus, as shown in animal models and evoked in humans. Specific, prospective, randomized studies are needed to evaluate the real contribution of enterococcal antibiotic coverage in this context, where underlying diseases and surgical techniques are important

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