V.V. Grebenyuk, K.A. Kovtunov, A.A. Nazarov, I.V. Chumachenko Microflora Features in Patients with Surgical Sepsis

ABSTRACT

The authors present a retrospective analysis of archival materials of bacteriological laboratories and case histories of patients with surgical infections, hospitalized in the "Municipal Clinical Hospital", Blagoveshchensk and Amur Regional Clinical Hospital from 1985 to 2014.

Microbiological investigation of the material from the surgical and urological patients identified etiologic role mainly of Gram-negative bacteria in patients with surgical sepsis. The role of microbial associations (E. coli with Staphylococcus aureus, Staphylococcus epidermidis and with bacteria of the genus Proteus) went up and the share of Pseudomonas aeruginosa and Candida fungi increased.

The authors concluded a preferred application for empirical antimicrobial therapy of surgical sepsis with cephalosporin group III - IV generation drugs (ceftazidime, cefepime, cefpirome) and carbapenems (meropenem, imipenem, doripenem) after analysis of antibioticogramms.

Keywords: microbial landscape, antibiotic sensitivity, empirical antibiotic therapy, surgical sepsis.

INTRODUCTION

According to the literature currently sepsis in developed countries is 200 - 275 per 100,000 population per year. In the United States recorded 500,000 cases of sepsis to a mortality of 20 - 50%. There are official Russian data on the proportion of sepsis in the structure of hospital-acquired infections, as in 2007, Russia recorded 7738 cases of nosocomial infections in health - care facilities surgical profile, the main share of which are the purulent-septic infections 95.0% [4]. Timely and effective empirical antimicrobial therapy allows 1.5 - 2 times to reduce mortality and prevent the development of septic shock patients [3]. In this regard, the study of the structure and dynamics of antibiotic resistance and sensitivity of micro-organisms allocated in microbiological research submissions from septic patients, in our opinion important. The aim of our study was to investigate the dynamics of the bacterial landscape in the etiology of surgical sepsis and sensitivity of microbes to antimicrobial therapy.

MATERIALS AND METHODS

A retrospective analysis of archival materials bacteriological laboratories and 369 case histories of patients with surgical infections treated in the surgical intensive care unit and in the

"Municipal Clinical Hospital" (building 1 and 3) of Blagoveshchensk and Gause JSC "Amur Regional Clinical Hospital" since 1985 to 2014. The analysis included verified during surgery and confirmed by microbiological methods of surgical infections, appropriate diagnostic criteria for sepsis [1,2]. We have highlighted a group of patients with surgical sepsis, in which studied the causes and place of occurrence, taking into account the severity of the septic process, especially bacterial landscape and its sensitivity to antibiotics, as well as the start of antibiotic therapy, schemes of its implementation, the total duration. In the study of medical records of patients recorded the following complications: suppuration of postoperative wounds, intra-abdominal abscesses and inflammatory infiltrates after surgery, bile leakage of drainage and into the free abdominal cavity, insolvency holedohoduodenalnogo anastomosis, cholangitis, eventration, intestinal fistulas, nosocomial pneumonia, infection of the urinary tract, thrombophlebitis. The analysis of microbiological studies was subjected to: peritoneal fluid, bile (cystic and ductal), discharge of drainage, blood, wound secretions, urine, tissue, and others. Planting material was produced on plates with 5% blood agar, VSA, Endo agar and Saburo. To separate blood culture using a double impact. Identify obligate anaerobes was conducted on Wednesday, Blair Wilson and agar Tseyslera. Bile duct was seeded at a dilution of 1:10, 1: 100, 1: 1000 in a dose of 0.1 ml of inoculum. Incubation was carried out at 37 ° C for 24-48 hours followed by counting the number of colonies and determining the titer of microorganisms isolated in CFU / g (ml). Identification of microorganisms was carried out based on the data microscopy, culture properties, oxidase and catalase activity, and conventional biochemical tests. The sensitivity of the studied strains of microflora with the preparation of the inoculum to individual antimicrobial drugs used in the department for the treatment of septic infections. Statistical analysis of the results of research carried out using the program «Statistica 6.0 for Windows».

RESULTS AND DISCUSSION

Major disease causes abdominal surgical infections were: positive forms of destructive pancreatitis (48 cases), perforated gastric ulcer and duodenal ulcer (30 cases), acute appendicitis (20 cases), bowel ischemia due to intestinal obstruction (24 cases), a destructive cholecystitis (22 cases), insolvency HDA (8 cases), bile leakage into the free abdominal cavity (32 cases), acute obstructive suppurative cholangitis (119 cases); causes of urinary infection - acute pyelonephritis, chronic pyelonephritis, urolithiasis (IBC), benign prostatic hyperplasia (BPH) 2-3 stage, patients with nephrostomy and (or) epitsistostomoy (67). Since 1985, much has changed, and the ratio of gram negative microorganisms. According to the results of microbiological studies of wound material from 1985 to 1996 as a causative factor of negative microorganisms was dominated only when the intestinal form of abdominal sepsis and complicated urinary tract infection (E. coli -



62.5%, P. aeruginosa - 24.8%). By 1997, the etiological structure of surgical sepsis incidence of gram-negative organisms has increased. In 2008 indicated an almost equal ratio of the detection rate of gram-positive and gram-negative flora. Since 2009, we registered an increase of etiological significance gram-negative microorganisms. The proportion of Gram-negative organisms has increased due to increase in frequency allocation from the wound contents and other biological fluids of Pseudomonas aeruginosa, Proteus spp bacteria and Klebsiella from 5.5% in the period up to 2004, to 67.8% in 2014, as well as frequency of detection of fungi Candida to 6% (Figure 1). An increasing number of mixed - infection: in the period from 1985 to 2000, the frequency of their isolation varied from 1.7 to 2.5% by 2007, increased to 4.6% of cases in 2014 was 16.1%. Most associations were found with E. coli Staphylococcus aureus - 7.7%. The urine when reseeding intestinal shelves with Pseudomonas shelf - 10%, from fungi of the genus Candida - 6.8%, Klebsiella - 7%. In crops separated from the abdominal cavity, resulting in the first operation, also dominated by Gram-negative flora (E.soli - 34,5%, Proteus spp. -16,5%). Repeating in crops of abdominal registered preferential growth of Pseudomonas aeruginosa (37,2%), Klebsiella pneumoniae (26,3%), Staphylococcus aureus (26,5%). During the period 1997 - 2009 years. Bile studied in 160 patients who underwent surgical treatment of choledocholithiasis (including 60 patients with obstructive suppurative cholangitis severe disease complicated by biliary sepsis). In 70 patients with bile for bacteriological examination obtained intraoperatively (during choledochotomy before operative cholangiography through drainage Halstead - Pikovsky), others 80 - endoscopically. Bacteriological examination of the bile duct, and received intraoperative endoscopy revealed the presence of bakterioholii at 92.7% of the patients. The most frequently detected E. coli, Pseudomonas aeruginosa, Klebsiella pneumoniae as a monoculture (20.2%) or in the form of mixed - infection (73.8%), often in combination with Staphylococcus aureus. The bacterial content ranged from 1,8h103 to 1,27h108 CFU / g. Most seeded bacterial and microbial diversity of landscape found in patients with cholelithiasis complicated with choledocholithiasis, acute suppurative obstructive cholangitis, obstructive jaundice and severe biliary sepsis (60 cases). At the same time, we noted no correlation between the level of bacterial contamination of bile and morphological changes of the gallbladder wall. The microflora of the bile duct is almost always corresponded to the gallbladder bile, monoculture were allocated only 18.0% of cases. Anaerobic flora was found in 1 case (Clostridium perfringens) patient phlegmonous calculous cholecystitis complicated by choledocholithiasis with cicatricial papillostenozom and suppurative obstructive cholangitis. The most common representatives of the bacterial microflora of bile in patients with severe sepsis were biliary (as well as other patients with abdominal sepsis) Gram-negative bacteria: Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae. Similar results were

obtained in patients with urinary infection [7]. This microbial landscape was detected in the urine of patients primarily with urolithiasis, urodynamics disorders of the upper and lower urinary tract after instrumental and surgical procedures on the urinary system, especially after prolonged drainage of the urinary system. When blood cultures for sterility results were positive in 28% of patients, most often identified by Gram flora: Escherichia coli (28,6%), Pseudominas aeruginosa (25%), Klebsiella pneumoniae (14.0%). Regardless of the blood culture (positive or negative) with the overt clinical manifestations of severe surgical sepsis and septic shock (multiple organ failure, the primary suppurative focus, hypotension, pronounced intoxication syndrome) were treated according to the rules of purulent surgery. We have analyzed antibiotikogrammy pathogens isolated in 1997, 2009. and 2014. A significant part of the strains was resistant to most antibiotics used that reflects the general trend in the department of purulent surgery [5]. The analysis revealed that the most polyresistance showed gram-negative microorganisms: Escherichia coli, Pseudomonas aeruginosa and Klebsiella pneumoniae. Multidrug-resistant E. coli increased from 73.0% in 1997 to 89.6% in 2014, and Ps. aeruginosa from 80.4% to 87.0% respectively. Resistant strains studied spread to previously used antibiotics: ampicillin, oxacillin, gentamicin, cefazolin. In this connection, since 2009 these drugs were excluded from use in septic patients. In the last decade marked a significant change in antibiotic resistance and gram-positive microorganisms. In 2004, staphylococci and enterococci are highly sensitive to vancomycin, carbapenems and amikacin. Beginning in 2009 was an increase in the stability of staphylococci to cephalosporins, fluoroquinolones (especially ciprofloxacin), amikacin, erythromycin. Maximum sensitivity is saved only to the drugs group of carbapenems. Cephalosporin III-IV generation of 70.3% were sensitive isolates of staphylococci. Regarding streptococci (Streptococcus haemolyticus) were also most effective cephalosporins generation III-IV, whereas ampicillin, ciprofloxacin, erythromycin, they exhibited a high resistance. The drugs of choice for this group began to carbapenems and fluoroguinolones (except ciprofloxacin), they found sensitivity of 86.0% of the isolated strains. The most effective currently against pseudomonads were III-IV cephalosporins and carbapenems generation. Enterobacteriaceae susceptible to cephalosporins III-IV generation, carbapenems and amikacin, high resistance enterobacteria registered to cephalosporins I-II generation and gentamicin (Table. 1).

CONCLUSIONS

Thus, in the bacterial landscape of biological fluids of patients with surgical sepsis Gramnegative bacteria (Escherichia coli, Klebsiella and Pseudomonas aeruginosa) dominated. There was noted increased incidence of microbial associations and fungi genus Candida. Susceptibility

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was noted mainly to drugs of carbapenems (meropenem, imipenem, doripenem) and cephalosporins III - IV generation (ceftazidime, cefepime, cefpirome, cefotaxime).

REFERENCES

- 1. Konferentsiya Standartyi diagnostiki i lecheniya v gnoynoy hirurgii [The Conference Standards in diagnosis and treatment of purulent surgery] Razdel 3 [Section 3]. Standartyi klassifikatsii, diagnostiki i lecheniya hirurgicheskogo sepsisa [Standards classification, diagnosis and treatment of surgical sepsis]. Hirurgiya, 2002, N 8, pp 67 – 68.
- 2. Molchanov I.V. Bolyakina T.K. Vlasenko A.V. Klinicheskaya anesteziologiya i reanimatologiya [clinical anesthesiology and critical care medicine], 2008, V 5, 2, pp 17 – 23.
- 3. Galkin D.V. Optimizatsiya antibakterialnoy terapii sepsisa v mnogoprofilnyih statsionarah [Optimization of antibiotic therapy for sepsis in general hospital] avtoref. dis. kand. med. Nauk. Smolensk, 2005, 26 p.
- 4. O sanitarno epidemiologicheskoy obstanovke v Rossiyskoy Federatsii v 2007 godu: Gosudarstvennyiy doklad [On the sanitary - epidemiological situation in the Russian Federation in 2007 State report]. Moskow: Federalnyiy tsentr gigienyi i epidemiologii Rospotrebnadzora [Federal Center of Hygiene and Epidemiology], 2008, 397 p.
- 5. Sazhin V.P. Rannyaya diagnostika vnutribolnichnoy infektsii na osnove monitoringa ranevoy mikrofloryi v otdelenii gnoynoy hirurgii [Early diagnosis of nosocomial infection based on the monitoring of wound microflora in the department of purulent surgery]. Moskow: Hirurgiya [Surgery], 2007, № 10, p. 32-35.
- 6. Gelfand B.R., Burnevich S.Z., Gelfand E.B. Antibakterialnaya terapiya abdominalnogo sepsisa [Antibiotic therapy of abdominal sepsis]. Moskow: Vestn. intens. ter.: Sb. Antibakterialnaya terapiya [Antibiotic therapy], 2008, 32-38 p.
- 7. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis / R.C. Bone, R.A.B. Balk, F.B. Cerra et al. // Crit. Care Med. -2009. - 20; 6. -864-874.
- 7. New criteria for selecting the proper antimicrobial chemotherapy for severe sepsis and septic shock / P. Periti, T. Mazzei // Int. J. Antimicrob. Agents. - 2010. - 12; 2. - 97-106.

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Fig. 1.

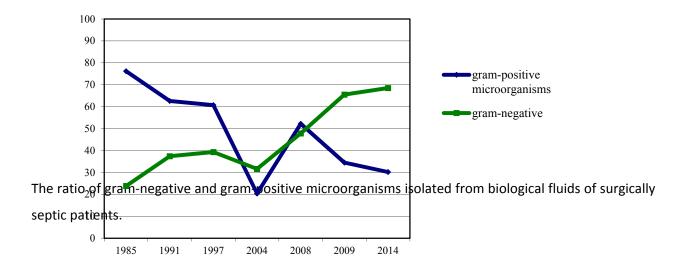


Table 1 Susceptibility of abdominal surgical infections to antibiotics,% (2014)

Microorganisms		Staphylococcus spp.			Streptococ- cus spp.			Pseudomonas spp.			Enterobac- teriaceae spp.		
		R	MR	S	R	М	S	R	MR	S	R	М	S
ampicillin		90,3	2,4	7,3	-	40	60	70	-	30	71	28,	-
Cephalosporins (CA I – II)		2	26	72	30	-	70	23	10	67	9	40	51
CA III - IV		-	33,3	66,7	5	-	95	3-55*	-	45-97**	23	15	62
carbapenem		6	-	94	11	-	89	7	3	90	-	18	82
fluoroquinolones	Tsiprofloxatsi	62,5	16,7	20,8	60	-	40	23,3	16,7	60	43	32	25
	pefloxatsina Norfloxacin Ofloxacin	35,3	-	64,7	4	7	89	6	2	92	35	20	45
aminoglycosides (amikacin)		18,7	75	6,3	-	-	-	20	13,3	66,7	9	12	79
macrolides mycin)		75	12,5	12,5	30	30	40	-	-	-	-	-	-
lincomycin		56,6	13,3	30,4	-	-	-	-	-	-	60	20	20
Tetracycline (doxycycline)		75	-	25	70	-	30	70	-	30	75	25	-

R - resistant

MR - moderately resistant

S - sensitive

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^{*} Resistance to cefotaxime and ceftazidime 55% to 3% of cefoperazone

^{**} Sensitivity cefotaxime and ceftazidime 45% to 97% of cefoperazone



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