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Lipoprotein lipase - the important genetic factor of 2 type diabetes development in the native population of Yakutia

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High association of gene LPL, Int8 SNP (rs320) with 2 type diabetes let us possible to make out proposition about mechanism and role of LPL in 2 type diabetes developing.

Keywords: lipoprotein lipase LPL, Int8 SNP (rs320), hypertension, macrophage.

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ANALYSIS OF AEROBIC CAUSATIVE AGENTS OF GENERAL PERITONITIS

IN PATIENTS OF MULTITYPE HOSPITAL

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SUMMARY: Objective: The study of the structure and antibiotics resistance of aerobic causative agents of general peritonitis (GP) for the optimization of empirical antibacterial therapy.

Materials and Methods: The results of the microbiological study of peritoneal exudates of 147 patients with GP are presented. Results: All in all 160 (51,4%) strains of the family *Enterobacteriaceae*, 86 (27,7%) strains of non-enzyming gram-negative bacteria and 65 (20,9%) gram-positive causative agents were obtained. During staged debridement extra-hospital strains are replaced by nosocomial ones.

Conclusion: Initial antibacterial treatment of GP should be based on the local data on the range and

antibiotics resistance of intra-abdominal infection causative agents. Besides it is necessary to take into consideration the origin of peritonitis and the future technique of the abdominal cavity management.

Key words: general peritonitis, aerobic microflora, antibiotics resistance.

Introduction

Despite the sufficient arsenal of antimicrobial preparations the choice of adequate antibacterial therapy of general peritonitis (GP) remains a problem of urgent surgery and intensive care [3, 4, 6, 9, 10]. Early and adequate empirical antibacterial treatment influences the incidence of complications in patients and their mortality [5]. As a rule, deferred adequate therapy already does not affect the clinical outcome. It is of special actuality in the intensive care of post-operative peritonitis and in staged abdominal cavity management [1]. Inadequate initial antibacterial therapy in this contingent of patients is mainly conditioned by insufficient information on the range of causative agents of GP in a given hospital and their antibiotics resistance [1, 2].

Objective: The study of the structure and antibiotics resistance of aerobic causative agents of GP for the optimization of empirical antibacterial therapy.

Materials and Methods

147 patients with GP who were being treated in the department of purulent surgery and the intensive care department of MI of HS “City Clinical Hospital N6 named after N.S.Karpovich” in Krasnoyarsk were examined. Peritoneal exudates for microbiological study were obtained from all the patients with GP during the primary laparotomy and subsequent planned debridements.

Identification of the strains was carried out with the help of traditional methods. Determination of antibiotic susceptibility was done by the technique of dilution in Muller-Hinton’s broth in accordance with the recommendations and criteria of the National Committee on clinical laboratory standards (CLSI/NCCLS) [8].

For the interpretation of susceptibility to cefoperazon/sulbactam the criteria of cefoperazon were used. The results of determination of susceptibility of *P. aeruginosa* to polymixin B were interpreted according to the criteria SFM of 2003 [7].

For characterizing the microorganisms’ susceptibility to antibiotics the universally accepted categories - susceptible, moderately resistant and resistant – were used. For integral characteristics of drug resistance the term ‘non-susceptible strains’ combining moderately resistant and resistant microorganisms was applied.

Statistical processing of the data obtained was carried out with the methods of variation statistics on the PC using the applied programs «Statistics for Windows’ 6.1» (StatSoft, USA). The descriptive statistics is represented as percentage fractions and standard fraction error. For

comparison of rates of binary sign in the two unrelated groups the criterion χ^2 was used. On verification of the statistical hypotheses the differences at $p < 0.05$ were considered significant.

Results and Discussion

In 78.9% (116/147) patients GP developed as a complication of acute inflammatory diseases and traumas of the abdominal organs (extra-hospital peritonitis). In 21.1% (31/147) of cases GP was of nosocomial origin and complicated the course of the postoperative period after planned and urgent operations on the organs of the abdominal cavity (postoperative peritonitis). In 37.1% (43/116) of patients with extra-hospital GP and 77.4% (24/31) of patients with nosocomial GP staged debridements of the abdominal cavity were performed because of the intensity of the inflammatory process.

In patients with extra-hospital peritonitis etiologically important aerobic microorganisms were obtained in 145 cases (positive inoculations), from which 182 strains of aerobic causative agents were obtained. In 77.9% (113/145) of positive inoculations monocultures of microorganisms were found and in 22.1% (32/145) of cases – microbial associations. At the same time during the first operation and the first planned relaparotomy (PR) associations of microorganisms were seen in 7.1% and 13.8% of cases, respectively, on the third PR – in 88.9%, and on the fourth planned debridement – in all the patients.

In postoperative peritonitis 129 strains of aerobic microorganisms were obtained in 74 positive inoculations, out of which monocultures 35.1%, microbial associations – 64.9%. If the inflammatory process in the abdominal cavity was not stopped during 1-2 debridements, on the 3-4th debridements the infection was caused only by associations of microorganisms.

All in all 160 (51.4%) strains of the family *Enterobacteriaceae*, 86 (27.7%) strains of non-enzyming gram-negative bacteria (NGB) and 65 (20.9%) gram-positive causative agents were obtained.

Obtaining of *E. coli* was seen more often both in extra-hospital and nosocomial peritonitis – in 30.8% and 25.6% of cases, correspondingly. The results were similar for *Enterococcus* spp. – 15.4% и 14%, respectively. Statistically significant in nosocomial peritonitis were *P.aeruginosa* – in 17.8% of cases in comparison with extra-hospital peritonitis – 9.3% ($p = 0.0276$), and also *Acinetobacter* spp. – 20.9% and 10.4% ($p = 0.0102$), respectively. The rate of obtaining *S.aureus* in extra-hospital peritonitis was 7.1%, in comparison with 4.7% - in nosocomial peritonitis.

Both in extra-hospital and nosocomial peritonitis representatives of the family *Enterobacteriaceae* prevailed among the causative agents. But while in extra-hospital origin of peritonitis their share in the structure of causative agents was significantly higher than that of non-enzyming gram-negative microorganisms: 57.7% (105/182) and 19.8% (36/182), respectively ($p < 0,001$), in nosocomial

peritonitis the share of the problem causative agents (*Acinetobacter* spp. and *P.aeruginosa*) increased and did not differ from the family of *Enterobacteriaceae* – 38.8% and 42.6%, respectively ($p = 0.5263$).

It should be noted that in choosing the staged surgical treatment of extra-hospital general peritonitis the microbial landscape of peritoneal exudates changed with each subsequent planned debridement. If in bacteriological inoculations of peritoneal exudates on the first operation or the first planned debridement *E. coli* (39.6% and 30.3%, respectively), *Enterococcus* spp. (15.4% and 18.2%), *Proteus* spp. (8.8% and 6.1%) prevailed, then on the third-fourth debridements *Acinetobacter* spp. (20.7% and 33.3%, respectively), *P.aeruginosa* (20% and 22.2%), *K.pneumoniae* (15% and 11.1%) prevailed in the inoculations. On the primary operation the ratio of the family *Enterobacteriaceae* and NGB was 69.2% and 7.7%, accordingly, and on the second-fourth planned relaparotomy – 39.7% and 41.4%.

In nosocomial origin of general peritonitis in case of planned abdominal cavity management the similar dynamics of the microbial landscape of the peritoneal exudates was not noted.

All the obtained strains of the family *Enterobacteriaceae* preserved maximum susceptibility to carbapenems (imipenem, meropenem). Susceptibility of the strains obtained in nosocomial peritonitis was significantly lower than in extra-hospital peritonitis to the following antibacterial preparations: ampicillin – 50.9% and 86.7%, respectively ($p < 0.05$), amoxicillin/clavulanat – 20% and 44.8% ($p < 0.05$), cefepim – 67.3% and 87.6% ($p < 0.05$), cefoperazon – 29.1% and 56.2% ($p < 0.05$), cefotaxim – 27.3% and 71.4% ($p < 0.05$), ciprofloxacin – 47.3% and 89.5% ($p < 0.05$), gentamycin – 21.8% and 55.2% ($p < 0.05$), piperacillin – 17% and 41.9% ($p < 0.05$). Presence, in cases of extra-hospital peritonitis, of the strains *Enterobacteriaceae*, resistant to the majority of the used antibiotics is first and foremost explained by the fact that in performing staged debridements the extra-hospital strains are replaced by the nosocomial ones. Table 1 presents the dynamics of antibiotics susceptibility of the most frequently occurring in GP representative of the family *Enterobacteriaceae* – *E. coli*.

According to the data obtained, from the first operation up to the second-fourth debridements of the abdominal cavity susceptibility of *E. coli* had decreased to all groups of antibacterial preparations, except carbapenem. Thus, susceptibility decreased from 100% up to 80% to cefoperazon/sulbactam; up to 70% – to ampicillin, ceftazidim, cefepim and piperacillin/tazobactam; up to 50% – to ceftriaxon and ciprofloxacin; up to 40% – to cefotaxim and gentamycin. The number of insusceptible to amoxicillin/clavulanat and cefoperazon strains has significantly increased – from 13.9% and 11.1%, respectively, up to 70%.

NGB had maximum susceptibility only to polymyxin. Good susceptibility of the strains obtained in both extra-hospital and nosocomial peritonitis was to imipenem – 91.7% and 92%, meropenem – 86.1% and 88% and cefoperazon/sulbactam – 72.2 % and 74%, respectively. To all the rest antibiotics under investigation susceptibility was 50% and lower.

One should pay attention to low activity of NGB to the antibacterial preparations which are widely used for the treatment of severe infections, including intra-abdominal ones. Thus, susceptibility of the microorganisms obtained in extra-hospital and nosocomial peritonitis was 55.6% and 34% to ampicillin, 50% and 36% to cefepim, 44.4% and 34% to ceftazidim, 41.4% and 18% to ciprofloxacin, respectively.

Also low activity to these causative agents was noted in inhibitor-protected penicillins: piperacillin/tazobactam and ticarcillin/clavunat: 44.4% and 52.9% in extra-hospital, 38% and 56.5% in nosocomial general peritonitis, respectively.

Out of all antibiotics used for the treatment of severe abdominal infection ertapenem, imipenem, meropenem and sulperazon/sulbactam have a clinically significant activity against the strains of *Acinetobacter* spp. Polimixin B has the highest activity against the investigated strains *P.aeruginosa* but, unfortunately, this antibiotic is not available for usage in Russian in-patient departments. The preparations of choice for the treatment of extra-hospital general peritonitis caused by blue pus bacillus are imipenem, meropenem, piperacillin/tazobactam, cefepim, ceftazidim and ampicillin. As for nosocomial strains *P.aeruginosa*, only imipenem and meropenem are clinically significantly active.

Gram-positive microorganisms make 20.9% in the general structure of causative agents of general peritonitis. We obtained 19 strains *Staphylococcus aureus* – 6.1% (19/311) of all causative agents of general peritonitis. The frequency of obtaining *S. aureus* in extra-hospital and nosocomial peritonitis was 7.1% (13/182) and 4.7% (6/129), respectively. *Enterococcus* spp. was obtained significantly more often – 14.8% (46/311) ($p < 0.001$). It was characteristic for both extra-hospital – 15.4% (28/182) and nosocomial general peritonitis – 14% (18/129).

All the obtained strains *Enterococcus* spp. preserved maximum susceptibility only to vancomycin. Out of 28 strains obtained in extra-hospital peritonitis 78.6% of strains preserved susceptibility to ampicillin, 67.9% - to ciprofloxacin and gentamycin, and 57.1% - to tetracyclin. The strains *Enterococcus* spp. obtained from peritoneal exudates in nosocomial peritonitis were susceptible to ampicillin in 66.7%, to ciprofloxacin in 22.2%, to gentamicin in 16.7%, to tetracycline in 27.8% (Fig. 4.8.).

Out of 13 identified in extra-hospital peritonitis strains *S.aureus*, 4 were MRSA. All strains MRSA in extra-hospital peritonitis were obtained from peritoneal exudates taken in planned debridements of the abdominal cavity. In nosocomial peritonitis the frequency of MRSA was 66.7% (4/6). All strains MRSA preserved susceptibility to vancomycin.

Conclusions

1. In staged treatment of extra-hospital GP with each subsequent operation there is a shift of microbe landscape to microbe associations and replacement of extra-hospital strains by antibiotics-resistant nosocomial ones. In nosocomial (postoperative) GP no similar dynamics was noted.

2. The data received in our investigation show that *in vitro* carbapenems are the most active preparations in general peritonitis caused by nosocomial aerobic microflora.

3. While administrating empirical antibacterial therapy of GP one should take into consideration not only its origin (extra-hospital or nosocomial) but also the planned technique of the abdominal cavity management.

4. Antibiotics resistance of extra-hospital and nosocomial strains NG(-)B is a serious medical problem nowadays. In relation to NG(-)B only imipenem and meropenem have a clinically significant activity.

5. Microbiological investigation of intra-operative material in patients with general peritonitis is the basis for both adequate and timely individual antibacterial therapy and prognosis and planning of antibacterial therapy in the future.

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Table 1

**Dynamics of antibiotics susceptibility of strains *E. coli*,
obtained in staged treatment of extra-hospital GP (%)**

Antibiotic	Primary operation (n=36)		1 PR (n=10)		2-4 PR (n=10)		All operations (n=56)	
	P	±m	P	±m	P	±m	P	±m
Amicacin	100,0	0	100,0	0	70,0	14,5	94,6	7,1
Amoxicillin/Clavulanat	86,1	5,8	50,0	15,8	30,0	14,5	69,6	14,5
Ampicillin	44,4	8,3	30,0	14,5	20,0	12,6	37,5	15,3
Gentamycin	100,0	0	70,0	14,5	40,0	15,5	83,9	11,6
Imipenem	100,0	0	100,0	0	100,0	0	100,0	0
Meropenem	100,0	0	100,0	0	100,0	0	100,0	0
Piperacillin	61,1	8,1	40,0	15,5	20,0	12,6	50,0	15,8
Piperacillin /Tazobactam	100,0	0	90,0	9,5	70,0	14,5	92,9	8,1
Cefepim	100,0	0	90,0	9,5	70,0	14,5	92,9	8,1
Cefoperazon	88,9	5,2	60,0	15,5	30,0	14,5	73,2	14,0
Cefoperazon /Sulbactam	100,0	0	80,0	12,6	80,0	12,6	92,9	8,1
Cefotaxim	100,0	0	80,0	12,6	40,0	15,5	85,7	11,1
Ceftazidim	100,0	0	90,0	9,5	70,0	14,5	92,9	8,1
Ceftriaxon	100,0	0	80,0	12,6	50,0	15,8	87,5	10,5
Ciprofloxacin	97,2	2,8	100,0	0	50,0	15,8	89,3	9,8

Note: n – number of strains *E. coli*.

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