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MICROBIOLOGICAL CHARACTERISTICS OF CAUSES OF HOSPITAL-HOSPITAL INFECTIONS AND DEVELOPMENT OF A METHOD FOR DIAGNOSIS OF HOSPITALIZED STRAINS

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ABSTRACT

Hospital-acquired infections (HAIs) are a major health problem for the entire global community. In the world, they develop annually in 2-2.2 million people, and the length of hospital stay as a result of their development increases by an average of 5-9 days. Layering on top of the underlying disease and increasing its duration, nosocomial infections give rise to new problems - postoperative mortality. They are a common cause of neonatal mortality, affecting child mortality in general. The number of nosocomial infections according to various studies amounted to 10-70% of the number of hospitalized people and in 2% of cases the disease ended in death. The epidemic spread of nosocomial infections is facilitated by the formation and widespread distribution of strains multiresistant to modern antimicrobial drugs, characterized by high virulence and increased resistance to environmental factors, including disinfectants. As a result of the occurrence of nosocomial infections, the cost of antibacterial drugs accounts for a third of all drugs sold.

Key words: Nosocomial infections (HAIs), hospital infection, microbiological characteristics, indication method, Enterobacteriaceae, Staphylococcus spp.

INTRODUCTION

Based on long-term observations, the leading pathogens in the etiological structure of nosocomial infections in different clinics and hospitals were identified

- S.aureus, S.epidermidis, E.coli. Differences in the spectrum of microflora from individual biotopes of the human body were revealed: *P.aeruginosa, Enterobacter* spp., S.aureus dominated in postoperative wounds; for conjunctivitis - S. epidermidis, Hafnia spp.; for urinary tract infections - P.aeruginosa, Citrobacter spp. and Proteus spp. A direct correlation was established between the frequency of isolation of nosocomial pathogens in patients and microorganisms isolated from 4 swabs of objects in the hospital environment. Isolation of a certain type of pathogen from individual biotopes and types of studied material makes it possible to predict the formation of hospital strains and conduct microbiological diagnostics of nosocomial infections [2, 4]. The frequency (7 - 20%) of the spread of antibioticresistant strains in a multidisciplinary clinic among pathogens of nosocomial infections has been established. Oxycillin-resistant strains of S.aureus, E.faecalis, E.faecium, K.pneumoniae, P.aerugmosa were classified as multiresistant. Antibiotic-resistant strains were isolated from throat and wound discharge (S. aureus) and external ear discharge (P. aeruginosa) [7, 9]. Purpose of the study. To establish the etiological structure of microorganisms isolated from nosocomial infections in the region, to present the microbiological characteristics of pathogens of nosocomial infections and to develop a method for indicating hospital strains [1, 5, 8].

MATERIAL AND METHODS OF RESEARCH

To assess the dynamics and trends of long-term morbidity, a retrospective analysis of data from the last 5 years was carried out. The etiological structure of nosocomial infections was studied based on the results of microbiological studies of clinical material obtained from parents, newborns, postoperative patients, and studies of swabs from objects in the external environment of healthcare facilities. In addition to the generally accepted microbiological studies of various secretions from patients with health care facilities, the work used the original "Method for determining the plasma-coagulating activity of pathogenic staphylococci", including determining the plasma-coagulating activity of pathogenic staphylococci based on recording resistance indicators of a liquid nutrient medium containing plasma during the cultivation of these microorganisms. Determination of the electrical resistance of a suspension of bacteria in a nutrient medium is carried out within 2000 kohm for a period of 3-5 hours of bacterial cultivation at a temperature of 37°C. When the electrical resistance of the solution is 64 - 84 kohm, the isolated bacterial culture is classified as plasma-coagulating [3, 6, 10]. Species identification of bacteria of the family Enterobacteriaceae was carried out using test systems on ethonium cultures. In bacteria Staphylococcus spp. lecithinase activity and pigment formation were determined on JSA media, the

fermentation of sugars and monohydric alcohols was assessed under aerobic and anaerobic conditions on Hiss media with mannitol and glucose; Catalase production was studied in a test with a 1% hydrogen peroxide solution. Cytochrome oxidase was recorded using the standard method in the Oxy test. Bacteria Pseudomonas spp. identified using the OF test, determination of catalase, cytochrome oxidase, gelatin hydrolysis and growth at 43°C. Identification of hospital strains was carried out by determining the sensitivity of strains to antibiotics, compiling and comparing antibiograms of bacterial cultures isolated from patients and from environmental objects. Hospital strains included bacteria with multiple antibiotic resistance (3 or more antibiotics).

RESULTS AND DISCUSSION

The long-term dynamics of the incidence of nosocomial infections over a 5year period, was characterized by a pronounced downward trend (T sn = 6.09). In general, there has been a decrease in the incidence of nosocomial infections in Uzbekistan. However, according to a number of experts, the annual decrease in the incidence of these infections occurs mainly due to the lack of registration or underregistration of some nosological forms. The average incidence rate of nosocomial infections among the population of the region was 0.81±0.09%, and among the urban population it was 1.4 times higher (1.12±0.1%) compared to the rural population. Apparently, in rural areas, due to defects in their registration, there was an undercount of nosocomial infections. In the structure of the incidence of nosocomial infections, obstetric institutions accounted for an average of 63.4% of the total number of diseases, while in Uzbekistan the same figure was observed over 5 years. Amounted to 20.3% the share of surgical hospitals accounted for 19.9% of cases of nosocomial infections (for hospitals - 28.5%), for children's hospitals - 1.06% (for hospitals - 11.2), for others - 3.6%. In outpatient clinics, this figure was 12.0%, while in the Republic it did not exceed 8.1%. In maternity institutions, the incidence rate of newborn nosocomial infections was 27.4±1.54 per 1000 live births, with a pronounced tendency towards a decrease in incidence by the end of the observation period (Tsn=9.35%). Among the clinical forms of purulent-septic infections in newborns, the leading ones were conjunctivitis $(33.2\pm1.0\%)$, diseases of the skin and subcutaneous tissue $(10.5\pm0.6\%)$, and omphalitis (6.8±0.5%). According to the research results, a variety of species with a predominance of S.aureus (23.35±0.4%) was noted in the structure of pathogens of nosocomial infections; S.epidermidis (16.6±0.4%); E. coii (14.0+0.4%); the role of fungi of the genus Candida is noticeable (3.7±0.2%).

The following changes have been noted in the microlandscape under certain pathological conditions. S.aureus bacteria were isolated more often during

infections $(17.1\pm0.3\%)$ and conjunctivitis (16.4±0.3%). postoperative S.epidermidis was most often isolated from conjunctivitis (55.8+0.5%), urological $(16.9\pm0.4\%)$ and gynecological diseases $(14.9\pm0.4\%)$. On the contrary, S. saprophytics was found in 58.0±4.8% and 36.0±4.8% of cases of urological and gynecological diseases, respectively. In diseases of streptococcal etiology, S. pyogenes was isolated from conjunctivitis (14.6 \pm 0.4%), while S. haemoliticus was more typical for urinary tract infections (52.0 \pm 5.0%). In isolates from postoperative purulent infections, *P.aeruginosa* was recorded in 38.6+1.6%, and in urinary tract infections in 20.2±1.3% of cases. In urological diseases, Acinetobacter spp. accounted for 16.2±1.5%, E. coii - 71.6+0.5%, Klebsiella spp. -27.9+1.0%, a Proteus spp. (38.2±1.5%). In case of gynecological diseases, bacteria related to Moraxella spp were inoculated in 99.4±0.2% of cases. Moraxella catarrhalis is a Gram-negative diplococcus that causes infections of the ear, upper and lower respiratory tract.

Although bacteremia is rare, half of patients die within 3 months due to intercurrent illnesses. Patterns of M. catarrhalis colonization depend on age. Approximately 1–5% of healthy adults have an upper respiratory tract infection. Nasopharyngeal colonization with M. catarrhalis is common in early childhood and may increase during the winter months, and is also a risk factor for the development of acute otitis media; early formation of colonization is a risk factor for the development of recurrent otitis media. There are significant regional differences in carriage rates. Living conditions, hygiene, environmental factors (e.g, smoking at home), genetic characteristics of the population, home environmental factors, and other factors influence carriage rates. The microorganism spreads from sites of colonization in the respiratory tract to lesions. A strong direct relationship was found between the frequency of pathogen isolation during purulent-septic infections circulating in different types of health care facilities (in obstetric institutions and in surgical hospitals) ($r = 0.76 \pm 0.1$).

Almost equally occurred both independently - in $51.8\pm6.6\%$ of cases, and in associations - in $48.3\pm6.6\%$ of cases. As part of microbial associations, grampositive bacteria were more often found in combination with gram-negative (60.3 \pm 12.4%) than gram-positive bacteria of other species (33.3 \pm 12.0%).Grampositive bacteria were detected in $51.3\pm4.6\%$ of patients, and in two thirds of them the pathogen was isolated in monoculture, and only in a third - in microbial associations. Gram-negative bacteria, identified in $48.1\pm4.6\%$ of patients, Gramnegative bacteria were more often associated with gram (-) bacteria of other species (in $46.4\pm9.6\%$ of cases), and in $26.4\pm8.4\%$ of cases - with mixed microflora. Among the causative agents of nosocomial infections, *S. aureus*

(31.7±4.3%) and E. coii (22.6±3.8%) predominated. S. aureus was found in associations in 10.7±5.0% of cases, and E. coii - in 46.7±9.7% of cases, respectively. When studying the microbial landscape of isolated pathogens, a direct strong correlation was established between the location of microorganisms and the studied material from which they were isolated ($r = 0.8 \pm 0.2$). Thus, *S. aureus* was isolated from any tissue (usually from sputum, throat discharge, and urine - in 37.7-57.8%). S. epidennidis (heme+), which has dermatotropic properties, was more often detected in the discharge of the genitals, wounds, and ears (55.6-68.9%). E. coli was isolated from urine in 45.3% of cases. Fungi of the genus Candida were isolated from sputum, throat discharge and outer ear in 12.7-15.5%. It was noted that E. coli was more often the cause of endogenous infection, and S. aureus - exogenous. The formation of hospital strains is more often noted among opportunistic microflora. Under the influence of the use of broad-spectrum antimicrobial drugs, which have a bactericidal and bacteriostatic effect not only on pathogenic, but also on conditionally pathogenic and saprophytic flora, Changes in the intestinal microbiocenosis of patients were identified, consisting in the selection of more resistant types of microorganisms that led to the development of intestinal dysbiosis. The diagnosis of dysbacteriosis was confirmed in children under 1 year of age in 98.6±0.46%, and in older patients - in 90.78±0.75%. With dysbacteriosis in the microlandscape of the intestinal flora of children under 1 year of age, the deficiency of bifidobacteria was more pronounced, while in children of older age groups - lactobacilli, E. coli and enterococci. This contributed to the creation of an ecological niche favorable for the development of opportunistic and pathogenic bacteria. Among the causative agents of nosocomial infections S.aureus, E.coli, P. aeruginosa, K.pneumoniae, isolated from patients of a clinical hospital, a high frequency of multidrug-resistant strains of microorganisms that remain sensitive only to drugs of the fluoroquinolone group was noted. Among opportunistic microorganisms, oxacillin-resistant strains of Staphylococcus spp were often found and multidrug-resistant strains of E. faecalis, E. faecium, K. pneumoniae and P. aeruginosa. A large proportion of mixed infections involving E.coli and other opportunistic microorganisms, predominantly highly resistant to antibiotics used in medical institutions, has been noted E.faecalis, E.faecium, E.coli and other enterobacteria isolated from patients were highly resistant to a number of semisynthetic penicillins, cephalosporins and aminoglycosides. Strains environmental objects of surgical isolated from hospitals (S.aureus, K.pneumoniae) were resistant to most antibiotics used to treat patients, with the exception of streptomycin and gentamicin. Of the isolated strains, oxacillinresistant S.aureus accounted for 9.7±4.9%, S.epidermidis - 28.6+10.8%. It seems

that in surgical and therapeutic departments, among patients and in environmental objects, strains with the same spectrum of antibiotic resistance circulated. Peculiarities in the spectrum of antibiotic resistance among gram-positive and gram-negative microflora were identified (Table 2). Table 2 Proportion of strains of microorganisms resistant to average therapeutic doses of antimicrobial drugs isolated from patients.

From the data presented in Table 2 it follows that, in comparison with gramnegative flora, almost all isolated strains of *E.faecium* and the majority of E.faecalis turned out to be resistant to oxacillin (100.0+2.5% and 84.6±1.6%, respectively). These same microorganisms were highly resistant to a number of semisynthetic penicillins, cephalosporins and aminoglycosides. On the contrary, gram-positive flora showed sensitivity to furagin, while some gram-negative microorganisms showed slight resistance to this drug in 33.0-95.7% of cases. In some cases, among S. aureus strains, maximum sensitivity to ampicillin in combination with subactam (87.5%) was observed, while the majority of P. aeruginosa strains (90.5%) were resistant to this combination of antibacterial drugs. The largest number of P.aeruginosa strains were sensitive to amikacin (94.0±16.7%), as well as the combination of amoxicillin and clavulanic acid (87.5%). The proportion of strains of Staphylococcus spp., E.coli, K.pneumoniae, *P.aeruginosa* that are resistant to amikacin is quite small. Dioxidin showed some activity against gram-negative bacteria, with the exception of *P.aeruginosa*, among which 67.3+13.4% of strains were resistant. That is, among the most common isolates are S. aureus, E. coii, and P. aeruginosa. Of K.pneumoniae, a high frequency of isolation of strains multiresistant to AMPs was observed, which retained sensitivity only to drugs of the fluoroquinolone group. Antibiotic-resistant strains of nosocomial pathogens, in contrast to antibiotic-sensitive ones, had some differences in cultural and biochemical properties. When analyzing the data presented in Figure 3, it was revealed that antibiotic-resistant strains of S.aureus, in contrast to antibiotic-sensitive ones, showed lower fermentation of mannitol under anaerobic conditions on the 1st day compared to antibiotic-sensitive strains (74±8.9 and 98±2.7, respectively,

Noteworthy is the uniformity of the resistance spectrum of the studied strains, reflected in the graphical plane. A similar pattern can be seen from the results of studies of pseudomonad isolates presented in Figures 4c and 4d. In comparative terms, the classical and developed methods were tested in the bacteriological laboratory of a multidisciplinary clinic. For the study, known strains of bacteria isolated from patients and from environmental objects were used, their seroidentification and phage typing were carried out, and their sensitivity to

antibiotics was determined. In a laboratory setting using conventional testing methods, the use of methods for indicating hospital strains typically varies depending on the type of microorganism. The hospital strain of *P.aeruginosa* is diagnosed based on determining its sensitivity to antibiotics, phagotype and serotype, resistance to disinfectants, plasmid profile, and adhesion coefficient on the surface of epithelial cells. The strain is classified as a hospital strain based on the same phagoserotype, similar plasmid profile, as well as the adhesion coefficient on the surface of epithelial cells. The strain is classified as a hospital strain based on the same phagoserotype, similar plasmid profile, adhesion coefficient > 15 \pm 0.2, as well as in the absence of sensitivity to nine or more antibiotics, resistance to five disinfectants. It is known that hospital strains maintain stability of genotypic and phenotypic properties over a certain period of time, which support the ability of microorganisms to secrete enzymes that destroy antimicrobial drugs. A strain isolated from surrounding objects is diagnosed as a hospital strain if it is resistant to 3 or more antibiotics and the type of antibiogram of microorganisms matches, isolated from patients and from surrounding objects.

The developed method allows saving the cost of material resources for carrying out 1 analysis by more than 6 times and reduces the working time of a bacteriologist by approximately 1.5 times. Identification of hospital strains is the basis for carrying out preventive measures aimed at preventing the circulation of hospital strains in hospital settings.

CONCLUSIONS

1. The long-term dynamics of the incidence of nosocomial infections during the studied period from the moment of its registration characterized by a downward trend (Tsn = 8.6), which coincides with the general trend in Uzbekistan as a whole. The average incidence rate of nosocomial infections among the population of the region was $0.81\pm0.09\%$, prevailing among the urban population compared to the rural population. The incidence of nosocomial infections during the analyzed period decreased among obstetric institutions (63.4%), surgical hospitals (19.9%), outpatient clinics (12%), and children's hospitals - 1.06%.

2. In the healthcare facilities of in the structure of pathogens of nosocomial infections, a diversity of species composition was noted with a predominance of *S.aureus* (23.35±0.4%), *S.epidennidis* (16.6±0.4%), *E.coli* (14.0±0.4%). In the etiology of postoperative purulent infections, the leading ones were *P.aeruginosa* (30.6±1.6%), *Enterobacter spp.* (29.2±1.6%), *S.aureus* (17.1±0.3%), for conjunctivitis - *S.epidermidis* (55.8±0.5%), Hafnia spp. (26.6±0.6%), for urinary tract infections - *P.aeruginosa* (20.2±1.3%), *Citrobacter* spp. (29.8+1.4%), *Proteus spp.* (38.2±1.5%). At hospital facilities, the microbial landscape of isolated

cultures included bacteria of the family Enterobacteriaceae (67.0±5.6%), S.aureus (22.0±1.8%), *P.aeruginosa* (9.0+0.6%), *Klebsiella spp.* (1.5+0.1%) and *Proteus spp.* $(1.0\pm0.06\%)$. Between the frequency of isolation of nosocomial pathogens from patients and from swabs from objects in the hospital environment, a direct correlation was established (r=0.76±0.1). A strong direct correlation was noted between the biotope of nosocomial pathogens and the studied material from which they were isolated (r=0.8±0.2). S.aureus was more often isolated from sputum, throat discharge, urine (37.7-57.8%), S.epidermidis (hem+) - from discharge from the genitals, mouth, ears (55.6-68.9%); E. coii - from urine (45.3%); fungi Candida spp. - from sputum, throat discharge, external ear in 12.7-15.5%. Among the causative agents of nosocomial infections, isolated from patients, S.aureus strains were 20.5±0.9% antibiotic-resistant and 10.3±0.7% moderately resistant to antibiotics; P.aeruginosa strains - in 17.7±1.9 and 7.4±1.1%, respectively. In isolates of S.aureus, E.coli, P.aeruginosa, K.pneumoniae, a high frequency of isolation of multidrug-resistant strains that retained sensitivity only to drugs of the fluoroquinolone group was noted.

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