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Features of Antibiotic Therapy of Patient with Complicated Diabetic Foot Syndrome and Sepsis

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Summary

Examined and treated 1246 patients with complicated diabetic foot syndrome (DFS) for the period from 2010 to 2015 (326 patients - a comparison group, 888- main groups - representative) and of 32 patients in the Development of Sepsis. Found that in patients with pyonecrotic processes of DFS in which surgery is performed in an ambulatory, ABT can be administered in the tablet forms. Patients of groups II-III the one should remember that in the presence of sensitivity to multiple antimicrobials, use sequence - from the weaker to the stronger, and at the risk of MRSA – linezolid, daptomycin. With the development of sepsis - drugs of choice are fluoroquinolones of III - IV generation, carbapenems, and the presence of MRSA – linezolid, daptomycin or vancomycin. Suggested tactics of ABT contributed to the reduction of length of hospitalization, with an average of (31,4±1,8) to (19,4±2,3) patient days (t=3,32; P<0,05), and the reduction of postoperative mortality from 7,5 to 3,8% (x2=6,74; P<0,05).

Keywords: diabetic foot syndrome; sepsis; antibiotic therapy

Introduction

More than 1.8 million diabetes patients are officially registered in Ukraine. According to world statistics, the number of patients doubles every 13-15 years [1, 6].

Every year, 18-20 million cases of sepsis with mortality are registered in the world: 10% - from systemic inflammatory response syndrome (SIR), 20% - from sepsis, 32 - 40% - from severe sepsis and more than 70% from septic shock (SSH). That is, 4.5-6 million patients die from sepsis every year, which is twice as many as from tuberculosis and HIV infections combined [9].

Diabetic foot syndrome (DFS) develops in 20–80% of patients with DM and is the cause of high amputations with a postoperative mortality of 5–42%, and mortality within 5 years after amputation varies from 30 to 68% [3, 5].

One of the significant complications of SDS is purulent-necrotic lesions of the foot of a diabetic and sepsis, which require hospitalization of patients in a hospital and complex therapy, the main component of which is antibacterial therapy (ABT) [7, 8].

Unfortunately, today there are no standards for conducting ABT in various clinical forms of complicated SDS, the circumstance of taking chemotherapeutic agents at the pre-hospital stage is not taken into account, the severity of the patient's condition, as well as complications in the form of sepsis, are not emphasized.

At the 22nd congress of surgeons of Ukraine (Vinnytsia, 2010), we proposed a classification of complicated SDS, and at the 4th congress of vascular surgeons and angiologists of Ukraine (Uzhhorod, 2012), this classification was approved and recommended for wide implementation [2, 4].

The classification of complicated SDS (CZE system) takes into account: clinical form - Clinical form (C); anatomical zone - Anatomy zona (Z); etiological factor - Etiological factor (E). The clinical form involves the identification of a specific complication of SDS and is denoted by symbols from C1 to C18. The prevalence of the local pathological process is assessed according to anatomical criteria, which are denoted by symbols from Z1 to Z4 and reflect the increasing severity of foot tissue damage. The etiological factor is taken into account as the presence of infection - E1, ischemia - E2, or infection and ischemia - E3. The symbolic designation of the clinical diagnosis of complicated SDS according to the CZE system can have four main groups of options: C1-5Z1E1-3, C6-12Z2E1-3, C13-16Z3E1-3, C17-18Z4E1-3.

The purpose of the work is to optimize the regimens of antibacterial therapy in patients with complicated diabetic foot syndrome and with the development of sepsis.

Materials and Methods

During the period from 2010 to 2015, 1,246 patients with complicated SDS were examined and treated on the basis of the department of ambulatory, purulent-septic surgery and ultrasound of the ZMAPO Ministry of Health of Ukraine in the purulent-septic center with beds for the diabetic foot of the City Clinical Hospital No. 3".

The definition of "complicated SDS" combined purulent-necrotic lesions of the foot: ulcer, abscess, phlegmon, purulent tendovaginitis, osteomyelitis, gangrene, as well as diabetic osteoarthropathy. Criteria for inclusion in the study: type II diabetes, the presence of SDS with purulent-necrotic lesions of the tissues of the foot or aseptic lesions of the bones of the foot on the background of diabetic osteoarthropathy. Exclusion criteria: type I diabetes; SDS with intact skin (stage 0 according to the Wagner classification); isolated diabetic neuropathy; patients on hemodialysis.

The distribution was carried out as follows: the comparison group - 326 patients who were examined and treated in the period 2008 - 2009, the main group - 888 patients (including 32 patients with sepsis), the period 2010 - 2015. The age of the patients varied. from 38 to 86 years, the average was (61.7 ± 2.3) years. The largest share of patients fell on patients of the mature and elderly age category, and the groups were representative in terms of sex and age, concomitant pathology.

The complex of microbiological studies consisted of determining the sensitivity of microorganisms to antibiotics, the qualitative composition of microbial pathogens (microbial landscape), quantitative microbial insemination of the wound using the Veitek-2 analyzer.

Statistical data processing was carried out taking into account the principles of evidence-based medicine, calculations were performed using the software package for statistical data analysis "STATISTICA 6.1".

Results and Discussion

The results of our research show that the wound microflora of primary purulent foci in patients with complicated SDS changed both quantitatively and qualitatively during the period 2008-2015.

Thus, the dominant role of gram (-) pathogens at the end of the last century - (53.6 %) changed to the present in favor of gram (+) - (54.3 %). In addition, the seeding capacity of microbial associations increased from 22.6 to 29.4%, i.e. 1.3 times.

Of particular concern is the phenomenon of growth among gram (+) flora of methicillin (oxacillin) resistant strains of staphylococci (MRSA). According to our data, an increase in MRSA staphylococcal strains from 16.9 to 36.9% was registered in our center between 1995 and 2015. The latter are insensitive to conventional antibiotics and require the appointment of special chemotherapeutic agents.

ABT in patients with a mixed form of complicated SDS should provide the maximum therapeutic effect with minimal impact on the patient's body, who suffers from severe concomitant diseases.

The technological features of antibacterial therapy were:

- ABT in these patients was built according to the type of step therapy;
- The state of tissue concentration of antibiotics was taken into account: the highest concentrations in tissues (exceeding the content in serum) are achieved when prescribing fluoroquinolones of the III-IV generation, protected penicillins, linezolid, daptomycin, while the tissue concentration of beta-lactams, aminoglycosides, vancomycin, usually, 1.5 – 3 times lower than serum;
- Empirical ABT was carried out before receiving the result of a microbiological study, its effectiveness depends on the correct choice of the drug and its effect on all potentially possible pathogens;
- Directed ABT was prescribed only after receiving the results of seeding. In cases of necessity, repeat ABT correction taking into account the isolated microflora and its sensitivity to antibacterial drugs;
- Directed ABT was carried out in a short course (10-14 days) until a clear clinical result was obtained;
- When conducting ABT no later than 10 days after its start, prescribe a prophylactic dose (150 mg once a week) of antifungal drugs - fluconazole (diflucan, fucis, etc.).

It should be noted that our center has been monitoring microbiological flora in patients with purulent pathology for many years. Thanks to such a "passport" in most cases empirical therapy was directed and there was no need for its correction.

ABT for patients of group I – C1-5 Z1 E3 was prescribed taking into account the previous ABT at the outpatient stage of treatment. If it was not effective and the patient was sent to the hospital, then taking into account the previous intake of antibiotics, the hospital prescribed parenteral drugs: cefazolin - intravenously, 2.0 g three times a day; cefuroxime - intravenously, 1.5 g three times a day; amoxicillin / clavunate - IV, 1.2 g 3-4 times a day; ampicillin / sulbactam - IV, 3.0 g 4 times a day; clindamycin - IV, 0.3 - 0.6 g 3 - 4 times a day.

For patients of the II group - C6-12 Z2 E3, they were guided by the fact that in the presence of sensitivity to several antibacterial drugs, the sequence should be used - from weaker to stronger.

Patients who did not receive antibiotics on an outpatient basis: amoxicillin / clavunate - IV, 1.2 g 3-4 times a day; ampicillin / sulbactam - IV, 3.0 g 4 times a day; clindamycin - i.v., 0.3 - 0.6 g 3 - 4 times a day in combination with cefuroxime - i.v., 1.5 g 3 times a day or with ceftriaxan, i.v., 2.0 g 1 – 2 times a day or with cefotaxime, IV, 2.0 g 3-4 times a day.

For patients who received ABT at the pre-hospital stage: ofloxacin - IV, 0.4 g 2 times a day + clindamycin - IV 0.6 g three times a day; piperacillin / tazobactam - IV 4.5 g 4 times a day; levofloxacin, IV, 0.5 g once a day; moxifloxacin, IV, 0.4 g once a day; ceftaroline, IV, 0.6 g 2 times a day; ertapenem, IV, 1.0 g once a day. At risk of MRSA - linezolid, IV, 0.6 g 2 times a day.

For patients of III and IV groups: levofloxacin - IV, 0.5 g 2 times a day + metronidazole, IV, 0.5 g three times a day; piperacillin / tazobactam - IV, 4.5 g 3-4 times a day; cefaperazone / sulbactam - IV, 4.0 g 2-3 times a day; ceftaroline - IV, 0.6 g 2 times a day; ertapenem - IV, 1.0 g once a day; imipenem / cilastatin - IV, 0.5 - 1.0 g three times a day; meropenem - IV, 1 - 2.0 g three times a day. In the presence of MRSA strains - linezolid or vancomycin before any ABT regimen.

The introduction of an optimized scheme of antibacterial therapy in combination with active surgical tactics and radical local treatment of the primary purulent center led to a decrease in the impact of endogenous intoxication and antigenic load, which was expressed in a faster restoration of the body's regenerative properties and faster wound healing.

Prospects for further development are, first of all, the creation of an industry network of "diabetic foot" clinics and the search for antibacterial drugs not only with a spectrum of action against aerobic and anaerobic pathogens, but also against MRSA strains of staphylococci, which would be affordable to a wide range of patients for complicated SDS.

Analysis of the duration of treatment in patients with complicated SDS shows that the length of stay of patients in each clinical group, as well as the total length of their stay in the hospital in the main group, was significantly ($P<0.05$) shorter than that of patients in the comparison group.

That is, the average length of stay of patients with complicated SDS in the hospital decreased by 1.6 times ($t=3.32$; $P<0.05$).

The proposed optimized tactics of ABT contributed to the reduction of postoperative mortality from 7.8% in the comparison group to 4.3% in the main group ($x2=6.74$; $P<0.05$).

As a result of the analysis of this study, it was established that the use of optimized tactics of ABT, along with active surgical and local treatment of patients with complicated SDS, made it possible to reliably ($P<0.05$) reduce the frequency of postoperative complications, "high" amputations, and shorten the length of stay of patients in the hospital and reduce postoperative mortality.

Conclusions

1. Optimizing the regimen of antibacterial therapy for patients with complicated SDS and sepsis in the main group in combination with active surgical and local treatment made it possible to positively influence the phases of the wound process: the wound was cleaned at a faster ($P<0.05$) pace; the speed of wound healing was significantly ($P<0.05$) higher; the total number of postoperative complications decreased by 4.2% ($P<0.05$).
2. The proposed tactic of ABT contributed to reducing the length of stay of patients in inpatient treatment on average from (27.6+1.8) bed/day in the comparison group to (21.4+2.2) bed/day in the main group ($t=3.32$; $P<0.05$), as well as a decrease in postoperative mortality from 7.8 to 4.3% ($x2=6.74$; $P<0.05$).
3. Prospects for further development are, first of all, the creation of an industry network of "diabetic foot" offices and the search for antibacterial drugs not only with a spectrum of action against aerobic and anaerobic pathogens, but also against MRSA strains of staphylococci, which would be affordable to the general public circle of patients with complicated SDS.

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