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Analiza wyników badań mikrobiologicznych i zastosowanej antybiotykoterapii u pacjentów z ranami przewlekłymi

SUMMARY

Background: Chronic wounds, including diabetic foot syndrome (DFS) and venous leg ulcers (VLU) are a global health problem, the treatment of which consumes huge financial resources, in particular the treatment of complications.

Globally, over 422 million people and over 3 million people in Poland are living with diabetes mellitus (DM) and this number will be increasing due to obesity, which is more and more frequently observed among the population. DFS is the most serious complication of diabetes that affects 15-25% of diabetics. The occurrence of obesity and diabetes is associated with a change in lifestyle and nutrition. Consumption of high-calorie, irregular meals, lack of physical activity, sedentary or standing work also contributes to the development of venous insufficiency, which in turn leads to the creation of VLU. In the USA this problem affects nearly 7 million people, and in Poland occurs in 1% of the population in the group between 60 and 80 years old and mainly concerns women. The most serious complication in the treatment of chronic wounds are infections that in the case of DFS, they can lead to amputation of the lower limb and disability.

The analysis of individual elements of therapy used in the treatment of DFS and VLU and its effectiveness may prove helpful in unification the treatment process, especially in the field of antibiotic therapy, the use of which is currently being discussed in the light of the increasingly common bacterial resistance. Treatment of wounds in the course of DFS and VLU should be conducted comprehensively by an interdisciplinary team, and should also include the treatment of comorbidities that may interfere with the wound healing process.

Objective: The aim of the study was to analyze of bacterial flora in infected wounds of DFS and VLU, the analysis of empirical and targeted antibiotic therapy in the treatment of DFS and VLU and the analysis of factors influencing the time of antibiotic therapy and healing time of DFS and VLU.

Materials and methods: The study used retrospective analysis of data in 118 cases of DFS in 98 patients and 30 patients with VLU who reported at the Wound Clinic in Warsaw in 2014-2018. The selection of the group was random, based on the accepted criteria for inclusion in the study.

In order to obtain data for analysis, an analysis of the patient's medical records was performed. Collected data included: sociodemographic data, information on wounds, used treatment, results of microbiological tests that were collected on the day of admission, and data on the empirical and targeted antibiotic therapy used in the treatment of DFS and VLU infections.

For purposes of identifying the empirical and targeted antibiotic compatibility, patients with DFS and VLU were divided into the following subgroups: NEA (no empiric antibiotic), NTA (no targeted antibiotic), ETA (empiric, targeted antibiotic), ETA + (compatibility of empiric-targeted antibiotic), ETA- (non-compatibility of empiric-targeted antibiotic).

Data was collected in Excel 2016 and subjected to statistical analysis using the statistical program R (ver. 3.5.3) using the tidyverse and ggplot2 packages. The basic descriptive statistics, Pearson correlation coefficient, Mann-Whitney U test, Kruskal-Wallis test with Dunn post-hoc test with Holm correction for multiple testing were used for the analysis and the bootstrap method power analysis was also performed. The significance level was set to $p < 0.05$.

Significant results are also presented in point or bar charts showing the mean with standard deviation (box plot).

Results: The study group of DFS consisted of 71 men ($N = 71$; 72.4%) and 27 women ($N = 27$; 27.6%), and an average age of group was 65.1 ± 13.6 years. Obese according to the Body Mass Index classification occurred in 20 patients with DFS (20.4%). The most common bacterial strain in DFS wounds was *Staphylococcus aureus* ($N = 53$; 24.4%) and *Enterococcus faecalis* ($N = 41$; 18.9%). Sixteen patients (13.6%) in the study group with DFS received topical treatment with gentamicin. The most commonly used antibiotics as empirical therapy were: amoxicillin with clavulanic acid, clindamycin and levofloxacin, while targeted therapy most often used amoxicillin with clavulanic acid and levofloxacin. The empirical and targeted antibiotic therapy were compatible in 65 cases (55.1%). The average wound healing time was 173.0 ± 116.6 days. It did not differ between selected subgroups, but was longer in group with obese ($p = 0.001$, Mann-Whitney U test), by an average of 100 days. Other variables did not influence on the healing time of DFS. The average duration of antibiotic therapy in the treatment of DFS wounds was 41.7 ± 34.1 days and was longer in the ETA + group (compatibility of empirical and targeted antibiotic therapy) compared to the NEA group (without empirical antibiotic) and in the group of patients receiving topical treatment with gentamicin ($p = 0.031$, Mann-Whitney U test). There were no significant correlations between the time of antibiotic therapy and other variables.

However, in the case of the study group with VLU, the majority were women (N = 23; 76.7%) and 7 were men (N = 7; 23.3%). The average age of participants with VLU was 74.7 ± 9.8 years. In this group obese occurred in 5 patients (16.7%). The most common bacterial strain were *Staphylococcus aureus* (29.0%) and *Pseudomonas aeruginosa* (17.7%). In half of the study group with VLU (50.0%), no empirical antibiotic was used, while in the remaining group, as the empirical antibiotic, the most commonly used was amoxicillin with clavulanic acid, which together with levofloxacin was the most commonly used targeted antibiotic. The compliance of empirical and targeted antibiotic therapy was only 13.3%. The average healing time of VLU was 163.4 ± 97.1 days and did not differ between subgroups. Of the all analyzed factors that could affect healing time, only the number of bacterial strains in the wound affected the healing time of VLU - with each subsequent bacterial strain, healing time increased by 28.4 days ($p=0.041$). The average time of antibiotic therapy in the treatment of VLU was 20.4 ± 18.7 days and did not differ in individual subgroups. The occurrence of obese ($p = 0.047$, Mann-Whitney U test) did a statistically significant effect on the duration of antibiotic therapy, which was significantly longer in this group than in the group of patients without obese.

Conclusions: The study showed that the most common bacterial strains in DFS wounds is *Staphylococcus aureus* and *Enterococcus faecalis*, and in the case of VLU *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The most commonly empirical used antibiotics in the treatment of DFS infections and VLU were: amoxicillin / clavulanic acid, clindamycin and levofloxacin. The study showed the low range of compliance of empirical and targeted antibiotic therapy for both DFS and VLU treatment, which indicates that empirical antibiotic therapy should be given with caution and if the patient's clinical condition allows it. The decision on the antibiotic should be withheld until the result of the microbiological test with the antibiogram. Especially that in both the group with DFS and VLU the healing time it was independent of the antibiotic therapy used. In the addition, in the group with DFS the topical treatment with gentamicin application also did not shorten the wound healing time.

The basic diagnostic element in the treatment of wound infections is proper collection of material from the wound bed for microbiological tests.

Patients with chronic wounds should be treated for obese, which has a negative effect on wound healing. Obese should also be considered when prescribing the appropriate dose of antibiotic.

Key words: antibiotic therapy, chronic wounds, diabetic foot syndrome, wound infection, venous leg ulcers.