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## THE USE OF PROCALCITONIN IN PATIENTS WITH SURGICAL FORMS OF ERYSIPELAS

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**Abstract.** **The use of procalcitonin in patients with surgical forms of erysipelas.** Shapoval S.D., Vasylevska L.A. *The ideal marker of bacterial infection should not only allow for early diagnosis, but also provide information about the course and prognosis of the disease. Nowadays the most well-studied and widely used in clinical practice is procalcitonin (PCT), but its value in surgical forms of erysipelas is insufficiently defined. The aim of the article is to determine the diagnostic and prognostic significance of procalcitonin in patients with surgical forms of erysipelas. 114 case histories of patients who were hospitalized in the center of purulent-septic surgery of the Non-profit municipal enterprise "City Hospital N 3" in Zaporozhye for 2019-2020 period were analyzed retrospectively and prospectively. It was found that most often the focus was localized on the lower extremities. In the complex treatment of patients with erysipelas, the main place belongs to antibiotic therapy (ABT) and early surgical treatment of the area of the pathological process. Determination of the level of procalcitonin in the serum makes it possible to assess the progression and generalization of the process and is a sensitive test for the effectiveness of treatment. Radical surgery and timely targeted ABT are key elements of success in the treatment of surgical forms of erysipelas and are not subject to revision. Procalcitonin is a diagnostic marker that can predict the development of sepsis.*

**Реферат.** *Использование прокальцитонина у больных с хирургическими формами рожи. Шаповал С.Д., Василевская Л.А. Идеальный маркер бактериальной инфекции должен не только давать возможность проводить раннюю диагностику, но и предоставлять информацию о ходе и прогнозе заболевания. На сегодняшний день наиболее хорошо изученным и достаточно широко применяемым в клинической практике является прокальцитонин (PCT), но его значение при хирургических формах рожи недостаточно определено. Цель исследования: выяснить диагностическую и прогностическую значимость прокальцитонина у больных хирургических форм. Ретроспективно и проспективно проанализированы 114 историй болезней пациентов, которые находились на стационарном лечении в центре гнойно-септической хирургии КНП «Городская больница № 3» г. Запорожье за период 2019-2020 гг. Установлено, что наиболее часто очаг локализовался на нижних конечностях. В комплексном лечении больных рожей главное место принадлежит антибиотикотерапии (АБТ) и ранней хирургической обработке зоны патологического процесса. Определение уровня прокальцитонина в сыворотке крови дает возможность оценить прогресс и генерализацию процесса и является чувствительным тестом на эффективность проводимого лечения. Радикальное хирургическое вмешательство и своевременная направленная АБТ являются основными элементами успеха в лечении хирургических форм рожи и не подлежат пересмотру. В качестве диагностического маркера, который позволяет своевременно предусмотреть развитие сепсиса, является прокальцитонин.*

In recent years, there has been a significant increase in infections caused by B-hemolytic streptococcus of group A. According to sample data, the average incidence of erysipelas in European countries is 4.3 per 10,000 adults. In the structure of the morbidity there is a tendency to increase the number of young and middle-aged patients, as well as an increase in complicated forms of erysipelas and its recurrence [2, 5].

Changes in clinical symptoms and course of the disease with the development of severe complications and sepsis are observed more and more often. Mortality among the necrotic form of the disease ranges from 5.8 to 81% and, as a rule, is due to the development of sepsis [1, 10]. In this context, it is important to timely recognize the development of sepsis, assess the general condition of the patient and determine further treatment strategy.

It is known that the ideal marker of bacterial infection should not only allow for early diagnosis, but also provide information about the course and prognosis of the disease [6].

Biomarkers are understood as molecular substances or physiological parameters, the change of the level of which indicates the development of a certain pathological process and/or its severity.

From the standpoint of maximum clinical benefit, the following requirements for the "ideal" biomarker of sepsis were formulated: high sensitivity and specificity. Concentration in biological media should be different from inflammation of non-infectious origin; accessibility; quick result; correlation with the severity of the condition and the result; coincidence of the dynamics of the content with the clinical response to the therapy [12].

To date, the most well-studied and widely used in clinical practice is procalcitonin (PCT). The concentration of PCT in the serum is normally insignificant – less than 0.1 ng/ml. However, with

inflammation induced by bacteria, there is an increase in its content in the blood in the range from 1 ng/ml to 1000 ng/ml and above [3].

In addition to prognostic significance, among other advantages of PCT, attention should be paid to the possibility of a significant reduction in the duration of antibacterial therapy (ABT) in assessing its dynamics, in contrast to traditional clinical and laboratory parameters.

One of the main advantages of PCT over other markers is its early and highly specific increase in response to severe systemic bacterial infections and sepsis. Therefore, with the development of sepsis, an increase in PCT levels can be observed 3-6 hours after the development of infection [7].

Preliminary analysis of the cost-effectiveness of PCT in diagnosis has shown that the systematic use of PCT for the diagnosis and control of sepsis can reduce the use of antibiotics, thus reducing the length of stay in the intensive care unit and reducing its cost per patient [8]. It is recommended to discontinue antibacterial therapy when PCT is reduced to levels from 0.1 to 0.25 ng/ml.

The decision to prescribe or forego ABT should be reviewed within the next 6-24 hours based on the patient's clinical condition and PCT level. These values should also be taken into account in the decision-making process regarding the duration of ABT, as well as the clinical course of the disease.

The aim is to determine the diagnostic and prognostic significance of procalcitonin in patients with surgical erythema.

#### MATERIALS AND METHODS OF RESEARCH

114 case histories of patients who were hospitalized in the center of purulent-septic surgery of the City Hospital "City Hospital No. 3" in Zaporizhzhia for the period 2019-2020 were retrospectively and prospectively analyzed. All patients were diagnosed with erysipelas during

hospitalization by forms: erythematous – 24 (21.0%), bullous – 28 (24.6%), phlegmonous form – 48 (42.1%), necrotic – 14 (12.3%). Recurrent cases of the disease were noted in 21 patients. Of these: in erythematous form – 4 (16.7%), in bullous – 5 (17.9%), phlegmonous – 9 (18.7%), necrotic – 3 (21.4%).

In terms of gender: men – 47 (41.2%), women – 67 (58.8%). The age of patients was  $62.1 \pm 2.6$  years. Verification of the diagnosis was performed on the basis of clinical and anamnestic data according to the classification of V.L. Cherkasov (1986) [4].

Among hospitalized patients, middle-aged patients accounted for 38.2%, elderly – 32.7%. If among men this disease was observed mainly in young and middle age – 49.2%, in women – in middle (74%) and elderly age – 26%.

It should be noted that the microflora of primary foci in destructive forms of erysipelas has changed both quantitatively and qualitatively. Increasingly, streptococcus is inoculated in content of microbial associations.

The qualitative composition of the microflora and the sensitivity of the isolated cultures to antibiotics were determined on automatic microbiological analyzers "Vitek-2" and "BaCT/ALERT" (France). Modern automatic methods of studying inoculation of wounds of the wound environment allow to record the growth of microorganisms within 6-8 hours, which allows to obtain an accurate identification of the pathogen in 24-48 hours.

At this time, procalcitonin is considered as a highly sensitive and specific marker of inflammation, with which it is possible to assess the severity of the patient's condition. As the infection and multiorgan failure progress, the concentration of procalcitonin increases, which is confirmed by the correlation between the assessment of the severity of the condition and the vulnerability of multiorgan dysfunction, which is characterized by APACHE II and SOFA scale systems [11].

Determination of serum procalcitonin allows to assess the progression and generalization of the process, being a sensitive test for the effectiveness of treatment. This is important in the choice of treatment methods, duration and scope of surgery.

Upon admission to MNPE "City Hospital No. 3" ZRC in all patients with destructive forms of erysipelas on day 1-2 procalcitonin level was determined. It should be noted that in patients with erythematous erythema, both at the time of hospitalization and thereafter, there was no increase in PCT. In patients with bullous erysipelas, only 1 patient had a slight increase in serum PCT levels of 1-1.5 ng/ml, but on day 3 the PCT level returned to normal.

With the development of destructive forms of the disease, the pain syndrome decreases somewhat, but the general condition worsens. Some patients hope that everything will pass, and do not hurry to visit the doctor, and only the phenomena of general intoxication force them to seek help.

In patients with phlegmonous form of erysipelas with primary form, the PCT level exceeded 0.25 ng/ml (14 (35.9) patients, but on day 2-3 of treatment its normalization was observed. In patients with recurrent disease, PCT levels greater than 0.25 ng/ml were observed in 5 patients (55.6%). Its normalization occurred on day 4-5. It should be noted that we did not observe a significant increase in PCT in patients with primary and recurrent forms of the disease ( $p > 0.05$ ).

The most severe complication of streptococcal infection is a necrotic form of erysipelas, which is characterized by severe disease, development of infectious-toxic shock, respiratory distress syndrome, multiple organ failure and is accompanied by 80% of mortality [13]. In the treatment of this pathology it is necessary to recognize the onset of sepsis as early as possible and to timely prescribe the necessary treatment.

In patients with necrotic erythema, the PCT level in 10 patients was more than 2 ng/ml. This afforded us ground to consider them as patients with sepsis. In the dynamics of the study, the level of PCT in them remained high for 2 weeks and only with the stabilization of the general condition and clinical recovery it returned to normal. It should be noted that in these patients the blood test for blood culture was negative. 6 patients died, mortality was 60.0%.

Statistical processing of the obtained research results was performed using biometric analysis methods implemented in the EXCEL-2007<sup>®</sup> software packages and the STATISTICA 6.1 non-parametric statistics module (StatSoft Inc., serial No. AJAR909E415822FA) [4].

## RESULTS AND DISCUSSION

It was found that the most often a local focus was on the lower extremities.

The most common clinical manifestations of intoxication in bullous and phlegmonous forms of erysipelas were: general weakness, hyperthermia, muscle pain. In the necrotic form of erysipelas, patients showed signs of severe intoxication with nausea, vomiting and confusion.

A significant proportion of patients (52%) with erysipelas were admitted to the hospital in the long terms from the onset of the disease. This was due to self-medication, long-term outpatient examination and treatment. It should be noted that the longer the

pre-hospital period, the more pronounced the symptoms of intoxication.

In the complex treatment of patients with erysipelas the main place belongs to antibiotic therapy (ABT) and early surgical treatment of the pathological process. This statement does not apply only to the erythematous form of erysipelas, when with the help of local and non-surgical treatment it is possible to eliminate the pathological process.

In patients with bullous form of erysipelas, surgery consists of opening the bulla with the evacuation of pathological fluid and drainage. In phlegmonous and necrotic forms of erysipelas, it is a decompression contour dermatomy.

In complicated forms of erysipelas, surgery should be both earlier and as radical as possible, and include extensive opening of the local infection focus, removal of devitalized tissues, complete drainage.

The most complete surgical intervention is required for patients with circular erythema lesions, when the incision is performed within the area of inflammation with longitudinal and transverse wave-like incisions throughout the pathological focus. This method provides complete drainage, outflow of infected lymph and reduction of pressure deep into the underlying tissues.

The nature of the clinical course of the disease, including the nature of the local inflammatory focus, depends on the set of pathogenetic features of the microbes that form the microbial landscape.

The trigger for the development of any form of erysipelas is group A streptococcus (*S. pyogenes*) in 58-68% of cases, group C (*S. equisimilis*) – 14-25%, group B (*S. agalactiae*) – in 3-9%. It should be noted that the microflora of primary foci in destructive forms of erysipelas has changed both quantitatively and qualitatively. Increasingly, streptococcus is sown in microbial associations.

In our clinic we adhere to restrained surgical tactics in the treatment of patients of this profile. The general condition of the patient comes to the fore. In case of septic shock and unstable hemodynamics, surgery is postponed until the condition

stabilizes or there is a positive response to infusion therapy; we use the same principles when indicating repeated sanitation of purulent foci, without defining a strict time frame. In addition, during necrectomy, only non-viable tissues are removed, widely opening leakages. Active local treatment allows to control the wound process, to timely indicate repeated necrectomy. Tactics of maximum possible preservation of viable tissues during surgery, the use of longitudinal rather than circular and wave-like incisions, ultimately reduce the area of wounds and prevent the further formation of transverse scars, which contribute to the progression of lymphostasis.

The clinical effectiveness of treatment in patients with surgical forms of erysipelas was evaluated on the basis of local manifestations of the disease and PCT data (in the necrotic form). Thus, in patients with necrotic form of erysipelas after a single surgery there was a slight increase in PCT more than 2 ng/ml, with repeated necrectomies and sanitation of purulent foci it decreased on day 7-8, PCT levels usually returned to normal on day 14-16 of treatment. It should be noted that there was a significant positive local dynamics.

The term of inpatient treatment of bullous form was  $10.2 \pm 1.7$  days, phlegmonous form –  $24.4 \pm 2.3$  days, necrotic form – more than 1 month (depending on the dermatoplastics). Thus, the more severe the form of erysipelas, the longer the duration of inpatient treatment and the greater the material costs of this category of patients.

## CONCLUSIONS

1. More than 60% of patients with erysipelas are at the age of 40 and older, mostly women.
2. The frequency of recurrent erysipelas among the studied patients was 18.4%.
3. Determination of serum procalcitonin allows to assess the progression of the generalization of the process, being a sensitive test for the effectiveness of treatment.

Conflict of interest. The authors declare no conflict of interest.

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