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BANDS NEUTROPHILS LEVELS CHARACTERIZATION AND THEIR DYNAMICS AT TREATMENT OF ACUTE ALIMENTARY PANCREATITIS PATIENTS

Характеристика рівнів паличкоядерних нейтрофілів та їх динаміка при лікуванні хворих на гострий аліментарний панкреатит

Abstract

Purpose of the study. To evaluate changes of bands nuclear neutrophils level and their dynamics parameters during treatment in patients with acute alimentary pancreatitis based on repeated measurements and taking into account the severity of the course.

Materials and methods. Seventy patients with acute alimentary pancreatitis were examined, who treated in Surgical Department of Vinnitsa Regional M. I. Pirogov Clinical Hospital. Average age was $45,4 \pm 13,87$ years. Severe pancreatitis was found in 34 (48,57%) people, in 25 (35,72%) – moderate, 11 (15,71%) persons had mild forms. The severity of the disease was assessed using the Atlanta classification (2012). To achieve aim of study the repeated measurements of the stabs neutrophils levels were performed for all patients. Statistical analysis was performed using STATISTICA 13.

Results. The significant difference between the stabs neutrophils values identified in patients with acute alimentary pancreatitis was proved, taking into account the severity of the course, both during the primary measured ($p = 0,04$), during treatment ($p = 0,004$), and after its completion ($p < 0,00001$). The significant increase of stabs neutrophils level associated with increasing severity of acute pancreatitis, as in the primary treatment of patients ($\tau = 0,23, p = 0,005$), with determination during treatment ($\tau = 0,31, p = 0,0001$) and after its termination ($\tau = 0,49, p \leq 0,00001$) was determined. When comparing the indexes of stabs neutrophils

Резюме

Мета дослідження. Оцінити зміни рівня паличкоядерних нейтрофілів та їх динамічні параметри під час лікування у пацієнтів з гострим аліментарним панкреатитом на основі повторних вимірювань та з урахуванням тяжкості перебігу.

Матеріали та методи. Обстежено сімдесят хворих на гострий аліментарний панкреатит, які проходили лікування в хірургічному відділенні Вінницької обласної клінічної лікарні імені М. І. Пирогова. Середній вік становив $45,4 \pm 13,87$ років. Важкий панкреатит був виявлений у 34 (48,57%), у 25 (35,72%) – середній, 11 (15,71%) осіб мали легкі форми. Тяжкість захворювання оцінювали, використовуючи класифікацію Атланти (2012). Для досягнення мети дослідження було проведено багаторазові вимірювання рівня нейтрофілів кожного ряду для всіх пацієнтів.

Результати. Доведено значну різницю значень нейтрофілів, що виявилися у пацієнтів з гострим аліментарним панкреатитом, з урахуванням тяжкості перебігу, як під час первинного вимірювання ($p = 0,04$), під час лікування ($p = 0,004$), так і після його закінчення ($p < 0,00001$). Значне підвищення рівня паличкоядерних нейтрофілів, пов'язане з збільшенням вираженості гострого панкреатиту, як при первинному лікуванні хворих ($\tau = 0,23, p = 0,005$), з визначенням під час лікування ($\tau = 0,31, p = 0,0001$) та після

determined by repeated measurements, a rapid and continuous decrease of their values was found, as a whole in the group – by 3,76 times, and in the groups with a mild course of the inflammatory process – 6,75 times, the average degree of severity – in 5,11 times and severe forms – 3,05 times.

Conclusions. High informativeness of evaluation stabs neutrophils level and their dynamic during repeated measurements in patients with acute alimentary pancreatitis taking into account the severity of the course has been proved.

Keywords: acute alimentary pancreatitis, stabs neutrophils level, inflammatory process, damage to the pancreas, acute pancreatitis of alimentary genesis.

його було визначено припинення ($\tau = 0,49$, $p \leq 0,00001$). При порівнянні індексів паличкоядерних нейтрофілів, визначених повторними вимірюваннями, виявлено швидке і безперервне зниження їх значень у цілому в групі – в 3,76 рази, а в групах із легким перебігом запального процесу – 6,75 разів, середній ступінь тяжкості – у 5,11 рази, а важкі форми – в 3,05 рази.

Висновки. Доведено високу інформативність оцінки рівня паличкоядерних нейтрофілів та їх динаміки під час повторних вимірювань у пацієнтів з гострим аліментарним панкреатитом з урахуванням тяжкості перебігу.

Ключові слова: гострий аліментарний панкреатит, паличкоядерні нейтрофіли, запальний процес, ураження підшлункової залози, гострий панкреатит аліментарного генезу.

INTRODUCTION

Acute pancreatitis is an acute inflammatory process located in the pancreas, which is accompanied by evident systemic body responses, rapid progression from local lesions to the development of multisystemic dysfunction involving all organs and systems. Acute pancreatitis is one of the most complex diseases in modern urgent abdominal surgery. The problem of its study is conditioned by high disease incidence and steady increase in the frequency of destructive forms [1]. The difficulties of early disease detection are related to the lack of proven clinical and laboratory criteria [2, 3]. Clinical manifestations of the disease, anamnesis data and findings of physical examination remain the priority in making the diagnosis [2, 4]. However, in view of considerable variability of clinical symptoms, even with the application of modern laboratory and instrumental methods, diagnostic errors, especially at early stages, are not uncommon [5].

Indicator values of laboratory findings are not considered to be perfect markers for the diagnosis of acute pancreatitis in view of high probability of false positives and their low peculiarity. The most common study in acute pancreatitis is to determine serum amylase level [6, 7]. In most cases, an increase in the level of amylase is observed in the first 24 h from the disease onset with a gradual decrease to normal values over the next 7–10 days.

It has been proven that hyperamylasemia preserving for several weeks from the disease onset signifies the development of complications such as pseudocyst, phlegmon or abscess [8]. In recent years, increasing attention has been paid to the analysis of band neutrophils role in the pathophysiology of acute pancreatitis development, especially its severe forms. There is a growing number of proofs that confirm the crucial role of leukocyte activation in the formation of a

complicated inflammatory process, regardless of trypsin activity [8, 9]. A number of research works have proved the relationship between the presence of increased values of band neutrophils and the development of systemic complications such as acute cardiovascular failure, acute respiratory distress syndrome, acute renal failure, and gastrointestinal bleeding [2, 10].

Taking into account that neutrophils play a central role in the formation and progression of the inflammatory process, their role in the diagnosis of disease and determination of the degree of inflammatory process, is significantly limited under modern conditions. Despite the low specificity of band neutrophils for inflammatory affect of the pancreas, a thorough analysis of indicator values determined by repeated measurements and evaluation of their dynamics in the process of treatment, taking into account disease severity requires further study.

PURPOSE OF THE STUDY

Research objective: to characterize the indices of band neutrophils in patients with acute alimentary pancreatitis and to evaluate the dynamics of their change when taking repeated measurements, taking into account disease severity.

MATERIALS AND METHODS

We have evaluated specific aspects of clinical course and treatment outcome of 70 patients with acute pancreatitis of alimentary genesis who underwent inpatient treatment at the department of surgery of Pirogov Memorial Regional Clinical Hospital, Vinnytsia for the period from 2014 to 2017. We have examined 48 (68,57%) men and 22 (31,43%) women. Patients were thoroughly examined and the tactics of their treatment met the requirements of the clinical protocol for providing

medical care to patients with acute pancreatitis, in accordance with the order № 297 of the Ministry of Health of Ukraine (02.04.2010).

Taking into account the severity of acute pancreatitis, we have created 3 groups among the examined patients. Most people had heavy severity level of acute pancreatitis – 34 (48,57%), 25 of them had moderate (35,72%), and 11 persons had mild cases (15,71%). The severity of acute pancreatitis was interpreted using the Atlanta Classification (2012) [3]. In order to achieve this goal, the level of band neutrophils was repeatedly measured in all patients from the study group at primary visit to a doctor, in the course of treatment and at the final stage.

According to the Kolmogorov-Smirnov test, the distribution of the study group differed from normal ($p < 0,05$). Non-parametric Kraskell-Wallis criteria and the τ -Kendall correlation coefficient were used to evaluate the probability of error-free prediction. The dynamics of band neutrophil indices during the study was evaluated by constructing and analyzing interval time series. The probability of an error-free prediction was determined at $p < 0,05$. Statistical processing of the obtained data was performed using computer

programs of the STATISTICA package (StatSoft Statistica v.13.0.).

RESULTS AND DISCUSSION

In the study group of patients, the average value of band neutrophils was $12,13 \pm 9,63\%$ when taking primary measurements. The vast majority of patients in the group – 58 (82,86%) showed an increase in the level of band neutrophils, while for the remaining 12 (17,14%) persons, the values corresponded to the limits of the reference normal range (table 1). When comparing the studied indicators, established at a primary visit to a doctor, we have established a statistically significant difference in the groups of patients, taking into account the degree of severity between the indicators, ($p = 0,01$).

A statistically higher frequency of increased indices of band neutrophils was recorded for the patients with severe acute pancreatitis at admission ($p = 0,01$). There was a direct correlation of low force ($\tau = 0,23$, $p = 0,005$) between the severity of acute pancreatitis and the values of band neutrophils, certifying an accurate increase in the level of band neutrophils with increasing severity of acute pancreatitis.

Table 1

Evaluation of band neutrophils level in patients with acute alimentary pancreatitis, taking into account the severity of the latter

Values	Severity level			p-level
	Mild	Moderate	Heavy	
1 measurement				
M \pm SD	7,36 \pm 3,50	11,44 \pm 8,47	14,18 \pm 11,20	0,04
1–6%	5 (45,45%)	5 (20,0%)	2 (5,88%)	0,01
$\geq 7\%$	6 (54,55%)	20 (80,0%)	32 (94,12%)	0,01
2 measurement				
M \pm SD	6,73 \pm 3,72	9,96 \pm 8,39	12,94 \pm 7,49	0,004
1–6%	7 (63,64%)	10 (40,0%)	5 (14,71%)	0,006
$\geq 7\%$	4 (36,36%)	15 (60,0%)	29 (85,29%)	0,006
3 measurement				
M \pm SD	1,09 \pm 0,94	2,24 \pm 1,64	4,65 \pm 3,37	0,00001
1–6 %	11 (100%)	24 (96%)	27 (79,41%)	0,06
$\geq 7\%$	0	1 (4,0%)	7 (20,59%)	0,06

In the process of measurement during medical treatment, band neutrophils indices remained increased in all groups, but their gradual decrease was observed compared to the previous data. The average level in the group was $10,90 \pm 7,65\%$ and signified the preservation of active inflammatory process in the patients of the study group. The increase of the studied parameters was recorded in the vast majority of patients with severe course – 29 (85,29%) and 15 (60,0%) patients with

moderate severity of acute alimentary pancreatitis, while we have established the preservation of the values within normal limits – 5 (14,71%) and 10 (40,0%) of respective groups under study. In the group of patients with mild disease, active inflammation was observed in 4 (36,36%) patients on the group, in most – 7 (63,64%) indices met the reference normal range. When comparing the prevalence of high indices and the frequency of values corresponding to the reference normal

range, we have established a significant difference of outcomes ($p = 0,006$). When comparing the average levels of band neutrophils, the highest indices were observed in patients with severe course – $12,94 \pm 7,49\%$, in patients with moderate and mild course the indices remained increased as well – $9,96 \pm 8,39\%$ and $6,73 \pm 3,72\%$ respectively. When comparing the studied indices the established difference is statistically significant ($p = 0,004$). Direct correlation relationship of average force ($\tau = 0,31$, $p = 0,0001$) between the severity of acute pancreatitis and the level of band neutrophils, indicates a significant increase in the level of band neutrophils in patients with elevated disease severity in the course of treatment.

Analyzing the indices of band neutrophils upon completion of medical treatment, it was found that their average level was $3,23 \pm 2,93\%$. In the majority of the patients under study – 62 (88,57%) the level of band neutrophils met the reference normal

range, while in 8 patients (11,43%) there was an increase in the studied parameters. The difference between the indices of band neutrophils determined in patients after the performed treatment taking into account disease severity is statistically significant ($p < 0,00001$).

We have established a direct correlation connection of average force ($\tau = 0,49$, $p \leq 0,00001$) between the severity of acute pancreatitis and the level of band neutrophils, indicating a significant increase in the level of band neutrophils in patients with increased disease severity. In the group of patients with severe course of acute pancreatitis, a significantly higher incidence of high level of stab neutrophils was recorded, even upon completion of treatment ($p = 0,06$).

The next step was to evaluate the dynamics of changes in the values of band neutrophils during treatment in the groups of patients, taking into account the severity of acute alimentary pancreatitis (table 2).

Table 2

Comparative analysis of band neutrophils level in patients with acute pancreatitis in the process of treatment

Severity level	1 measurement	2 measurement	3 measurement	p-level
Mild	$7,36 \pm 3,50$	$6,73 \pm 3,72$	$1,09 \pm 0,94$	0,00001
Moderate	$11,44 \pm 8,47$	$9,96 \pm 8,39$	$2,24 \pm 1,64$	0,00001
Heavy	$14,18 \pm 11,20$	$12,94 \pm 7,49$	$4,65 \pm 3,37$	0,00001
Overall	$12,13 \pm 9,63\%$	$10,9 \pm 7,65\%$	$3,23 \pm 2,93\%$	0,00001

When comparing the indices of band neutrophils determined by repeated measurements, a statistically significant difference was established as a whole in the group ($p < 0,00001$) and when comparing the outcomes of obtained results in patients with mild ($p < 0,00001$), moderate severity ($p < 0,00001$) and severe course ($p < 0,00001$). There was a rapid and continuous decrease in the indices of

band neutrophils during the study, as a whole in the group – by 3,76 times, and separately in the groups of patients with acute pancreatitis – by 6,75 times, the average severity – by 5,11 times and heavy severity – by 3,05 times. The dynamics of change in the indices of band neutrophils in the group of patients with acute alimentary pancreatitis in the course of treatment is presented in Figure 1.

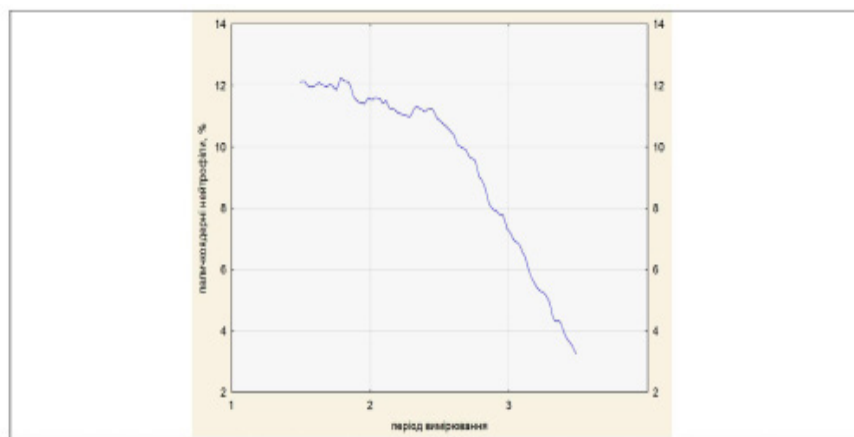


Figure 1. Bands neutrophils indices dynamics in the group of patients with acute alimentary pancreatitis in the course of treatment

CONCLUSION

Thus, we have determined a significant difference between the values of band neutrophils determined in patients with acute pancreatitis of alimentary genesis, taking into account disease severity, both during a primary visit to a doctor ($p = 0,04$), in the course of treatment ($p = 0,004$), and upon its completion ($p < 0,00001$).

Besides, we have established a significant increase in the level of band neutrophils with increasing severity of acute pancreatitis, as during a primary visit to a doctor ($\tau = 0,23$, $p = 0,005$), in the course of treatment ($\tau = 0,31$, $p = 0,0001$) and upon its completion ($\tau = 0,49$, $p \leq 0,00001$).

When comparing the indices of band neutrophils determined by repeated measurements, a rapid and

continuous decrease of their values was found, as a whole in the group – by 3,76 times, and in the groups with a mild course of the inflammatory process – by 6,75 times, average severity level – by 5,11 times and severe forms – by 3,05 times.

PROSPECTS FOR FUTURE RESEARCH

Necessary for further study and more specific indices of acute alimentary pancreatitis, with subsequent evaluation of their dynamics in the course of treatment, taking into account disease severity. The established outcomes will allow to determine the early criteria for predicting the severity of inflammatory pancreatic affection and to develop an algorithm for choosing a treatment regimen.

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