

Comparative Analysis of Immunobiochemical Indicators in Biological Fluids in Patients with Acute Purulent-Destructive Orchioepididymitis

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Abstract Acute purulent-destructive orchioepididymitis (APDOE) is a severe inflammatory disease of the male reproductive system with complex immune pathogenesis. Objective: to study the role of immunobiochemical and antioxidant markers in the development of acute purulent orchioepididymitis. Methods: 110 patients were examined. Concentrations of immunological markers were measured (IL-6, IL-18, TNF- α , CRP, SOD) by ELISA (Verctor Best). Results: In patients with acute purulent-destructive orchioepididymitis, the levels of IL-6, IL-18, TNF- α and C-reactive protein in the blood serum were significantly higher than the control values (2.5–4.2 times; $p < 0.05$), while the activity of superoxide dismutase decreased by 1.6 times ($p < 0.05$). In urine, IL-6 and IL-18 significantly increased (by 1.3–1.9 times; $p < 0.05$), while TNF- α increased insignificantly. Conclusion: Acute purulent-destructive orchioepididymitis is characterized by pronounced activation of proinflammatory cytokines and systemic imbalance of antioxidant defense, which confirms their diagnostic and prognostic significance.

Keywords Orchioepididymitis, Cytokines, IL-6, IL-18, TNF- α , Ejaculate, Urine, Systemic inflammation, Local immunity, Immune markers

1. Introduction

Acute purulent-destructive orchioepididymitis (APDOE) is a severe inflammatory lesion of the male reproductive system, characterized by severe tissue damage, intense pain syndrome, fever, and a high risk of reproductive dysfunction. The pathology often develops against the background of ascending urogenital infections and is a complex interaction between microbial factors and the host's immune response. Despite surgical interventions and antibacterial therapy, some patients continue to have inflammation and develop complications, including testicular atrophy and infertility [2,5,8,10].

In recent years, interest in the role of proinflammatory cytokines in the pathogenesis and progression of APDOE has increased significantly. Mediators such as interleukin-6 (IL-6), interleukin-18 (IL-18), and tumor necrosis factor- α (TNF- α) are involved in leukocyte recruitment, increased vascular permeability, and tissue destruction. However, their diagnostic and prognostic value is largely determined by the biological environment in which they are

measured. While serum analysis reflects systemic inflammation, local biofluids, such as urine, more accurately indicate the intensity and localization of the immune response in the reproductive tract. This emphasizes the need for comparative analysis of the cytokine profile in various biological fluids for a comprehensive understanding of inflammatory processes in APDOE [1,4,7,13].

Another important aspect of APDOE is oxidative stress. Excessive production of reactive oxygen species (ROS) at the site of inflammation leads to lipid peroxidation, DNA damage, and additional cellular damage. The body's antioxidant defense system, in particular the enzyme superoxide dismutase (SOD), plays a key role in counteracting these processes. A decrease in SOD activity reflects a systemic imbalance in oxidative processes and can serve as an indicator of the severity of inflammation and the body's ability to recover. Evaluation of SOD levels in combination with cytokines provides a more complete picture of the immune-oxidative status of patients and can be used to justify therapeutic approaches [3,6,9,12].

2. Purpose of the Research

Purpose of the study is to study the role of immunobiochemical and antioxidant markers in the development of acute purulent orchitis epididymitis.

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3. Materials and Methods

The study included 110 men aged 18 to 85 years with a confirmed diagnosis of APDOE, who were treated in the surgical department of the Bukhara branch of emergency medical care, which was the base of the Department of Urology of the Bukhara State Medical Institute. Inclusion criteria: confirmed diagnosis of APDOE, no previous immunosuppressive therapy, consent to participate. Exclusion criteria: chronic renal or hepatic failure, systemic autoimmune pathologies, oncological processes, decompensated metabolic disorders. The control group for immunological studies consisted of 20 healthy men of the same age.

Concentrations of IL-6, IL-18, TNF- α and CRP in blood serum and urine were determined by ELISA (Vector Best, Russian Federation). Determination of the level of superoxide dismutase (SOD) in blood serum was carried out by ELISA using ELISA-SOD test systems (OOO Cytokine, St. Petersburg, Russia).

Statistical data processing was performed using the standard Microsoft Excel 2016 package (Microsoft Corp, USA). During the analysis, the arithmetic mean (M), standard deviation (m), standard error of the mean (m) and Student's criterion (t) with calculation of the significance level (p) were calculated. Differences were considered statistically significant at $p < 0.05$.

4. Results and Discussion

Studying serum cytokine concentrations in patients with AGDOE allows assessing the nature of the systemic immune response and identifying immunological markers associated with the severity of the disease, the degree of tissue destruction, and the prognosis of the course. However, it should be taken into account that serum indices do not always fully reflect the local destructive process, since blood cytokine levels may depend on many factors: concomitant diseases, endocrine status, age and sex differences, and the general reactivity of the body. Nevertheless, in combination with local inflammation markers determined in urine, serum analysis provides a comprehensive picture of the development and activity of the inflammatory process, complementing the clinical and diagnostic assessment with the systemic immune background. Studying the IL-6 level in acute purulent-destructive orchiepididymitis (APDOE) is important, since this marker reflects the intensity of the inflammatory response, the degree of destructive changes, and the potential risk of systemic complications. The study found that in patients with OGDOE, the concentration of IL-6 in the blood serum was

20.2 ± 0.21 pg/ml, which is statistically significant ($p < 0.05$) and 3.77 times higher than the same indicator in the control group, where the level of IL-6 was 5.36 ± 0.05 pg/ml.

IL-18 in acute purulent-destructive orchiepididymitis (APDOE) is involved in the initiation of purulent inflammation, tissue destruction and the development of a systemic inflammatory response, and can also serve as a marker of the severity of immune activation. The results of this study showed that the level of IL-18 in the blood serum of patients with APDOE was 482.5 ± 1.14 pg/ml, which was significantly ($p < 0.05$) higher than the control group indicator by 2.55 times (188.8 ± 1.33 pg/ml).

TNF- α is involved in the formation of purulent inflammation and tissue destruction, and can also serve as a biomarker of the severity of the immune response and the severity of the condition. The study revealed that in patients with OGDOE, the level of TNF- α in the blood serum was 43.3 ± 0.51 pg/ml, which is significantly higher by 3.30 times ($p < 0.05$) than in the control group, where this indicator was 13.1 ± 0.19 pg/ml.

In acute purulent-destructive orchiepididymitis, determination of the CRP level in the blood serum has diagnostic and prognostic value, since its increase reflects the intensity of inflammation, the degree of tissue destruction and the risk of systemic complications. According to the data obtained, in patients with APDOE, the CRP level in the blood serum was 16.0 ± 0.28 mg/l, which is statistically significant ($p < 0.05$) 4.21 times higher than the values of the control group - 3.80 ± 0.13 mg/l.

Superoxide dismutase (SOD) is a key antioxidant enzyme that protects cells from the toxic effects of superoxide anion, one of the main active forms of oxygen [11]. The concentration of superoxide dismutase (SOD) in patients with pathology was 949.0 ± 1.66 pg/ml, which is significantly lower compared to the control group, in which this indicator reached 1504.8 ± 6.85 pg/ml (Table 1). A 1.59-fold decrease in the SOD level ($p < 0.05$) reflects a pronounced inhibition of the activity of the enzymatic link of the antioxidant system, which is probably associated with increased production of active forms of oxygen against the background of inflammation and tissue destruction.

In addition to blood serum, determination of proinflammatory cytokine levels in urine has significant diagnostic value, reflecting local immune-inflammatory processes in the lower urinary tract and scrotal organs [5]. In acute purulent-destructive orchiepididymitis (APDOE), inflammation affects not only the tissues of the testicle and its appendage, but can also affect the urinary tract, in particular through the spread of urogenital infection. Based on this, we further studied the concentration of cytokines in urine.

Table 1. Serum cytokine levels in surveyed groups (M \pm m), pg/ml

Serum	IL-6	IL-18	TNF α	SRB	SOD
Control (n=20)	5.36 ± 0.05	188.8 ± 1.33	13.1 ± 0.19	3.80 ± 0.13	1504.8 ± 6.85
Patients (n=110)	$20.2 \pm 0.21^*$	$482.5 \pm 1.14^*$	$43.3 \pm 0.51^*$	$16.0 \pm 0.28^*$	$949.0 \pm 1.66^*$

* $P \leq 0.05$ significantly increased compared to the control group

Table 2. The level of cytokines in urine in the examined groups (M±m)

Urine	IL-6	IL-18	TNF α
Control (n=20)	2.50±0.09	55.2±1.43	17.7±0.42
Patients (n=110)	4.71±0.05*	71.9±0.59	24.3±0.11

* $P \leq 0.05$ significantly increased compared to the control group

According to the study results, the IL-6 level in urine of patients with APDOE was 4.71 ± 0.05 pg/ml, which is 1.88 times significantly higher than in the control group (2.50 ± 0.09 pg/ml), ($p < 0.05$). Damage to the urothelium activates the expression of IL-6 in its cells, and the cytokine is released into the urine. As studies have shown, an increase in IL-6 in urine is observed in pyelonephritis, cystitis, urethritis, and bacterial prostatitis [7]. A similar mechanism can be realized in OGDOE, where the ascending route of infection and the local inflammatory response induce the production of IL-6, which is recorded in the urine. The level of IL-18 in urine was 71.9 ± 0.59 pg/ml, which is 1.30 times higher than in the control group (55.2 ± 1.43 pg/ml). These data may be due to the activation of the signaling complex of the innate immune response NLRP3 (nucleotide-binding domain, leucine-rich repeat-containing family, pyrin domain-containing-3), which is responsible for the production of active IL-18 during microbial inflammation [13]. In patients with APDOE, the concentration of TNF- α in urine was 24.3 ± 0.11 pg/ml, which is only slightly higher than the value of the control group (17.7 ± 1.28 pg/ml), an increase of 1.37 times (Table 2). The absence of a significant increase in the level of TNF- α in urine may be due to the fact that active production of this cytokine occurs predominantly in the inflammatory focus, i.e. in the tissues of the scrotum, and not in the epithelium of the urogenital tract. This may indicate a limited release of TNF- α through the urinary tract in isolated orchepididymitis without clinically significant involvement of the bladder or urethra.

In the process of determining the microbiological status in the intraoperative fluid in 30 patients with acute purulent-destructive orchepididymitis, the studied proinflammatory

cytokines were also determined. Active production of proinflammatory cytokines was revealed. It was established that the local concentration of IL-6, IL-18 and TNF- α exceeded similar indicators in both blood serum and urine, which reflects the intensity of the local immune response.

Table 3. Cytokine levels in intraoperative fluid, pg/ml

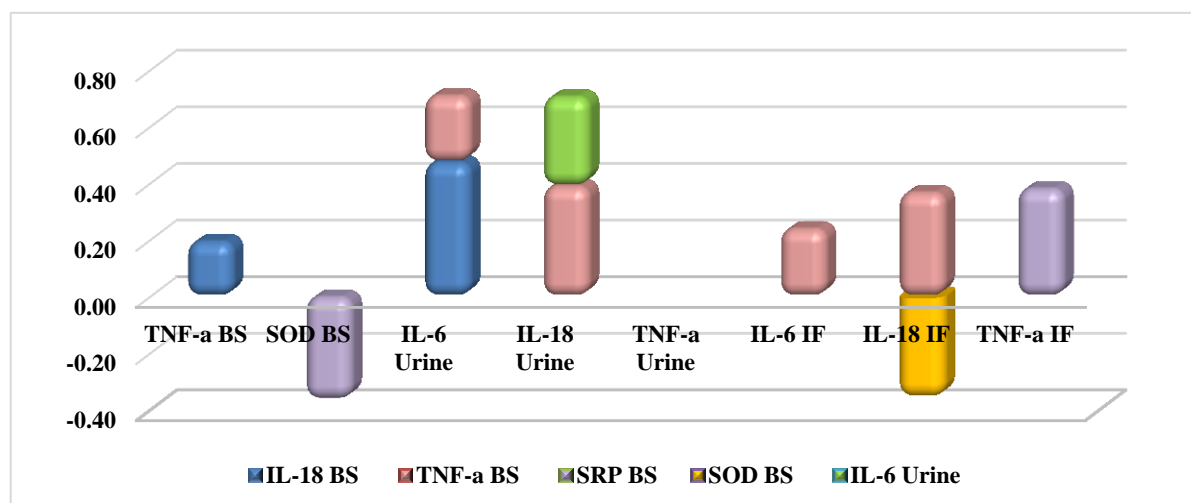
Cytokines	Patients (n=30)
IL-6	43.9±3.24
IL-18	502.4±16.6
TNF-a	46.1±2.19

The increase in the level of these mediators is closely related to the severity of destructive tissue changes and the degree of bacterial contamination.

Next, we conducted a correlation analysis of immunological parameters in various biological fluids in order to identify possible mechanisms of their interaction and pathogenetic significance.

The conducted correlation analysis showed multidirectional relationships between immunological indices in various biological fluids. The obtained data reflect the complex nature of the interaction of the systemic and local inflammatory response in acute purulent-destructive orchepididymitis. The presence of both positive and negative relationships indicates the existence of several pathogenetic mechanisms, including both activation and regulation of inflammation. The most pronounced associations were noted between systemic cytokines and local markers.

A moderate positive correlation was found between the level of IL-6 in urine and IL-18 in serum ($r = 0.47$). This indicates a close interaction between the systemic inflammatory response and the local reaction of the urogenital tract. IL-18, as a key inducer of the production of proinflammatory mediators, enhances the activity of IL-6, which reflects the severity of the inflammatory cascade. Thus, their synchronous increase demonstrates the consistency of systemic and local inflammation.

**Figure 1.** Correlation analysis of markers of general blood analysis and immunological parameters in patients with APDOE

A moderate positive correlation was found between IL-18 in urine and TNF- α in serum ($r = 0.39$). This correlation confirms that local inflammation in the urogenital structures is accompanied by activation of the systemic cytokine response. TNF- α is a key mediator of tissue damage and the initiation of a cascade of inflammatory reactions. Accordingly, the obtained results demonstrate its participation in the pathogenesis of both systemic and local levels.

A similar positive correlation was found between TNF- α in the intraoperative fluid and C-reactive protein (CRP) in the serum ($r = 0.38$). This reflects the synchronous activation of the humoral component of the inflammatory response involving both local mediators and acute phase proteins. CRP is traditionally used as an indicator of the severity of systemic inflammation. Its relationship with TNF- α confirms that local cytokine activity directly affects systemic markers of inflammation.

A positive association was also found between IL-18 in the intraoperative fluid and TNF- α in the serum ($r = 0.37$). These data indicate a close relationship between the local cytokine cascade and the body's systemic response. An increase in IL-18 at the site of inflammation is accompanied by activation of TNF- α in the serum, which intensifies the inflammatory process. As a result, a self-sustaining inflammatory cycle is formed, including both local and systemic mechanisms.

A negative correlation was found between the level of C-reactive protein and superoxide dismutase (SOD) in serum ($r = -0.36$). This result confirms that the increase in systemic inflammation is accompanied by a decrease in antioxidant activity. SOD is a key enzyme that neutralizes superoxide radicals and prevents oxidative damage to tissues. Accordingly, inhibition of its activity reflects an imbalance between inflammation and antioxidant protection.

A similar inverse relationship was recorded between IL-18 in the intraoperative fluid and the SOD level ($r = -0.35$). An increase in IL-18 in the inflammation focus is accompanied by a decrease in the antioxidant potential of the body. This indicates that local activation of proinflammatory cytokines directly affects systemic defense mechanisms. Thus, IL-18 can be considered as one of the markers of oxidative stress progression.

Thus, in general, the obtained data indicate that in acute purulent-destructive orchiepididymitis, a complex network of relationships between systemic and local immunological indices is formed. Strong positive relationships confirm the participation of cytokines in coordinating the inflammatory response at different levels. At the same time, negative correlations emphasize the role of oxidative stress and decreased antioxidant protection in the progression of the pathological process. All this allows us to consider correlation analysis as a tool for an in-depth understanding of the pathogenesis and clarification of prognostic criteria for the disease.

5. Conclusions

Based on the obtained data, it was established that patients

with acute purulent-destructive orchiepididymitis have a reliable increase in the levels of the studied systemic activation of innate immunity and intensity of the inflammatory response, possibly associated with concomitant pathology, age factors underlying destructive processes in the tissues of the testicle and epididymis. The analysis of the cytokine profile in the urine of patients with acute purulent-destructive orchiepididymitis showed the presence of local immunoinflammatory activity reflected by a reliable increase in the levels of IL-6 and IL-18 compared to the control group. At the same time, the level of TNF- α in the urine did not demonstrate significant differences, which may be due to its predominantly systemic production and limited excretion through the urinary tract.

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