Özgün araştırma / Original research

The value of procalcitonin in the diagnosis of acute scrotum

Akut skrotum tanısında prokalsitonin değeri

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Özet

Amaç: Bu prospektif çalışmanın amacı akut skrotumun ayrıcı tanısında akut faz proteinleri, prokalsitonin ve antioksidan enzimlerin önemini belirlemektir.

Yöntem ve Gereçler: Çalışmaya akut skrotumu olan 23 hasta (Grup 1) (epididimit n=17, testis torsiyonu n=6) ve aynı yaş grubundan 23 sağlıklı erkek (Grup 2) dâhil edildi. Tüm hastaların ve kontrol grubunun kan ve serumları beyaz küre (WBC), albumin, nötrofil oranı, C-reaktif protein (CRP), eritrosit sedimentasyon hızı (ESR), süperoksit dismutaz (SOD), katalaz (CAT), glutatyon peroksidaz (GPX) ve prokalsitonin açısından değerlendirildi. Sonuçlar klinik bulgular, rutin kan ve idrar tetkikleri ve doppler ultrasonografi ile kontrol edildi.

Bulgular: Tüm hastaların ortalama yaşı 30.17±12.46 yıl iken grup 1 de 29,96±15,85 ve grup 2 de 30,40±7,21 yıl idi. Bütün hastalarda şikayetin başlamasından hastaneye müracaat ettikleri zamana kadar geçen süre ortalama 89,6 saat (10-240) iken, epididimoorşit olan hastalarda bu süre 100 saat ve testis torsiyonu olanlarda ise 42 saat olarak tespit edildi. Ek olarak testis torsiyonu tanısı konulan hastalardan sadece 1 tanesi 18 yaşından büyük iken (42 yaş) epididimo-orşit tanısı alan hastaların 8 tanesi 18 yaşından küçüktü. Grup 1 ve grup 2 sonuçları karşılaştırıldığında WBC, nötrofil oranı, albumin, ESR, CRP, SOD, CAT ve GPX değerleri grup1'de istatiksel olarak anlamlı derecede yüksek idi. Ancak testis torsiyonu olan hastalarda, sadece prokalsitonin hem epididimoorşit olan hastalardan hem de kontrol grubundan istatiksel olarak anlamlı derecede

Abstract

Objectives: In a prospective study, we investigated the value of acute-phase proteins, procalcitonin and anti-oxidant enzymes in differential diagnosis of acute scrotum.

Material and Methods: A total of 23 patients (epididymitis n=17, testicular torsion n=6) with acute scrotum (Group 1) and 23 healthy men as a control group (Group 2) were included in the study. All patients were assessed by blood analysis for serum levels of white blood cells (WBC), albumin, neutrophil rate, C-reactive protein (CRP), eritrosit sediment rate (ESR), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), and procalcitonin. The results were confirmed by the clinical findings, routine blood and urine tests and Doppler ultrasound.

Results: The mean age of all patients was 30.17±12.46; while the mean ages of each group were 29,96±15,85 and 30,40±7,21 respectively. Mean time from the beginning of patient complaint to admission to hospital was 89.6 hours (range: 10-240 hours) in the patient group whereas the time was 100 hours in epididymo-orchitis patients and 42 hours in spermatic cord torsion. In addition, 1 patient (4.3%) with torsion was over 18 years old (42 years old), while 8 with acute epididymitis were younger than 18 years old. When group 1 was compared with group 2, WBC, neutrophil albumin, sedimentation, CRP, SOD, CAT and GPX were statistically higher in group 1. However, only procalcitonin was higher when compared with torsion and epididymo-orchitis patients and also higher than group 2 ($p<0.05$).

Conclusions: Acute-phase proteins (especi-

yüksek bulundu (p0.05).

Sonuç: Akut faz proteinleri özellikle prokalsitonin akut skrotumun ayırıcı tanısında testis torsiyonunu epididimin diğer enflamatuar hastalıklarından ayırt etmede kullanılabilir.

Anahtar Kelimeler: Akut skrotum, testis torsiyonu, prokalsitonin

ally procalcitonin) are helpful in differentiating epididymitis from noninflammatory conditions like testicular torsion or tumor.

Key Words: Acute scrotum; testes torsion; procalcitonin

Introduction

Acute scrotum is a clinical syndrome which appears with intractable pain and scrotal swelling and/or pain and swelling of contents. Sometimes this clinical situation accompanies general symptoms and signs. Epididymitis, testicular torsion, testicular tumor or torsion of the testicular appendix are differential diagnoses for acute scrotum. The most important aim in the treatment of acute scrotum is to preserve torsioned testes. However, in most acute scrotum cases, while the main cause is inflammatory disease, testicular torsion must be excluded properly because the delay in diagnosis can result in ischemic injury and necrosis of affected testes.(1) Evaluation of acute scrotal pathology should include detailed history taking and a physical examination of the abdomen, testes, epididymis, cord, scrotal skin, and inguinal region. However, history-taking and physical examination are sometimes not enough for accurate diagnosis.(2-5) In suspicious cases, a urinalysis and color Doppler imaging of the scrotum are useful diagnostic modalities for differential diagnoses of testes torsion. In addition, testicular scintigraphy is also used for diagnosing testicular torsion accurately.(6)

Furthermore, blood samples are studied in terms of diagnosing acute scrotum or differential diagnoses such as either testes torsion or an inflammatory process. Erythrocyte sedimentation rate, white blood count, acute phase proteins, trace elements, mediators like cytokines and oxygen radicals are studied for differential diagnosis of acute scrotum. However, the literature is somewhat lacking and does not provide ample information for the accurate diagnosis of acute scrotum.

We designed a prospective study to enable rapid differential diagnosis of acute scrotum because the current diagnostic tools are time consuming and not always available. In this study we aimed to find the efficacy of serum levels of white blood cells (WBC), albumin, neutrophil rate, C-reactive protein (CRP), eritrosit sediment rate (ESR), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) and procalcitonin.

Material and Methods

In this prospective cohort study, we enrolled 23 consecutive patients with acute scrotum who were admitted to our emergency clinic between March 2010 and March 2012. Informed consent forms were obtained from all patients after approval from the local institutional review board was obtained. The exclusion criteria were the existence of one of the following conditions: immunocompromised diseases, administration of immunosuppressive or nonsteroidal anti-inflammatory drugs, rheumatoid arthritis, inflammatory bowel diseases, recent surgical operation, acute myocardial infarction, allograft rejection, malignancy, burns, infectious diseases with origins other than the scrotum, anemia, congestive heart failure, multiple myeloma, renal insufficiency, hypercholesterolemia, hyperfibrinogenemia, tuberculosis, and endocarditis. The patients were evaluated according to history, physical examination, laboratory tests, scrotal ultrasonography, and surgical exploration (when required). The final diagnoses were made after appropriate follow-up to evaluate outcomes. In patients with spermatic cord torsion –preceded by the taking of serum samples– manual detorsion was attempted and if successful, bilateral orchidopexy was performed immediately. If manual detorsion was not possible, or in cases of suspicion resting between epididymitis and spermatic cord torsion, surgical exploration would be carried out. Patients with acute epididymitis were recommended to rest, decrease scrotal temperature, and to elevate the testes. In addition, appropriate antibiotics and sedatives were commenced.

Patients were divided into two groups: 23 with acute scrotum (group 1) and 23 with any scrotal abnormality (group 2). Furthermore, the patients in group 1 were assessed as Testes torsion (TT) and epididymo-orchitis (EO) groups separately. Serum levels of WBC, albumin, neutrophil rate, CRP, ESR, SOD, CAT, GPX and procalci-

Table 1. The comparison of Group 1, EO,TT with Group 2.

	Hemogram		Acute phase reactants			Antioxidant Enzymes			Biomarker
	WBC (K/mL)	**NEUTROPHIL** (K/mL)	**ALBUMIN** (mg/dL)	**ESR** (mm/h)	**CRP** (mg/L)	**SOD** (U/mL)	**CAT** (U/mL)	**GPX** (nmol/min/L)	**Procalcitonin** (µg/L)
Group1 (EO+TT)	14.5±4.7	11.6±4.6	3.8±0.4	35±20.5	8.3±4.9	7.3±0.5	2.8±0.1	135.3±3.7	131.5±225.3
Group2 (control)	8.0±1.9	5.5±1.2	4.2±0.4	3.5	0.3±0.1	8.3±0.8	3.0±0.1	141.0±5.3	33.3±38.1
EO	15.2±4.9	12.1±4.8	3.7±0.4	38.5±19	9.5±4.3	7.3±0.4	2.8±0.1	135.3±4	66.4±119.4
TT	11.5±1.7	8.9±2.0	4.0±0.3	18.0±20	2.7±3.4	8.3±0.8	3.0±0.1	141.0±5.3	424.8±366.6
P^1	0.000	0.000	0.002	0.000	0.000	0.002	0.000	0.003	0.669
P^2	0.000	0.000	0.001	0.000	0.000	0.003	0.000	0.006	0.613
P^3	0.111	0.122	0.284	0.062	0.009	0.766	0.369	0.609	0.010
P^4	0.111	0.122	0.284	0.062	0.009	0.766	0.369	0.609	0.010

P^1: The comparison of Group 1 with Group 2
P^2: The comparison of EO with Group 2
P^3: The comparison of TT with Group 2
P^4: The comparison of EO with TT
EO: Epididymo orchitis
TT: Testes torsion
WBC: White blood cells
ESR: Eritrosit sediment rate
CRP: C-reactive protein
SOD: Superoxide dismutase
CAT: Catalase
GPX: Glutathione peroxidase

tonin were measured.

Each collected blood sample was immediately centrifuged at 5,000 rpm +4°C for 5 min and then sera of the samples were transferred into an Eppendorf tube. Samples were transferred on ice and kept in a -70°C deepfreeze until the end of the study. For hemocounting, blood samples were collected with Ethylenediaminetetraacetic acid (EDTA) and performed within 2 hours. WBC and neutrophil rates were measured with a CellDyne3700 automatic hemo-counter (Abbott Park, IL, USA). Albumin levels were measured in serum using an Architect c16000 auto analyzer (Abbott Park, IL, USA). Serum levels of C-reactive protein (CRP) were determined with the Rate Near Infrared Particle Immunoassay method (Immage high sensitive CRP, Beckman Coulter, USA) ESR was evaluated according to the Westergren method (cut-off 20mm/h).

Procalcitonin level was evaluated through the automated VIDAS BRAHMS PCT assay (bioMérieux, Marcy L'Etoile, France) and SOD activity was measured according to the method described by Fridovich.(7) Catalase activities were determined by measuring the decrease in hydrogen peroxide concentration at 230 nm using Beutler's method.(8) The GPx activity assay was based on Paglia's method.(9)

Statistical Analysis

All data were expressed as mean and standard deviation (SD). A one-sample Kolmogorov-Smirnov test was performed in order to determine whether the data assumed a normal distribution. Intergroup comparisons were performed using the Mann-Whitney U-test. Relationships between variables were analyzed by either the Pearson or Spearman correlation analyses, depending on how the variables were distributed. A p-value of 0.05 was considered to be significant. All data were processed using the Statistical Package For the Social Sciences (SPSS) 15.0 for Windows (SPSS INC., Chicago, IL, USA) statistical package.

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Results

A total of 23 patients with acute scrotum (Group 1) and 23 control subjects (Group 2) were included in the study. Of 23 men with acute scrotum, 17 (73.9%) had epididymo-orchitis (EO) and 6 (26.1%) of those had spermatic cord torsion (TT). The mean age of all patients was 30.17±12.46 years; while the mean ages of each group were 29.96±15.85 years and 30.40±7.21 years respectively. The mean time from the beginning of the complaint to admission to hospital was 89.6 hours (range: 10-240 hours) in the patient group whereas the time was 100 hours in epididymo-orchitis patients and 42 hours in those with spermatic cord torsion. In addition, 1 patient (4.3%) with torsion was over 18 years old (42 years old), while 8 (17.4%) patients with acute epididymitis were younger than 18 years old.

All patients were assessed by blood analysis of serum levels for WBC, albumin, neutrophil rate, CRP, ESR, SOD, CAT, GPX, and procalcitonin. The mean value of samples for group 1 and group 2 are described in Table .

White Blood Count

The mean value of WBC in group 1 and group 2 was 14.5 K/mL and 8.0 K/mL respectively. When we measured the patients separately in group 1, the mean value of WBC in the EO group was 15.2 K/mL while it was 11.5 K/mL in the TT group. The difference was statistically significant when comparing group 1 with group 2 (Table). Although there was a statistically significant difference between the EO group and group 2 (Table), there was no statistically significant difference between the TT group and group 2 (Table) nor was there any statistically significant difference between the TT and EO groups (Table). Additionally, there was only a statistically significant difference between group 1 and group 2 in terms of neutrophil counts.

Acute Phase Reactants

Albumin, erythrocyte sedimentation rate and CRP were studied as acute phase reactants. The mean value of albumin, ESR and CRP in group 1 were 3.8 mg/dL, 35 mm/h, 8.3 mg/L and then 4 mg/dL, 3.5 mm/h, and 0.3 mg/L in group 2, respectively. All parameters were statistically different between group 1 and group 2 (Table). But when the EO and TT, and TT and Group 2 (Table) were compared with each other, there was no statistically significant difference for any of the parameters.

Antioxidant Enzymes

Superoxide dismutase, CAT, and GPX were studied from antioxidant enzymes. The mean values of SOD, CAT, and GPX in group 1 were 7.3 U/mL, 2.8 U/mL, 135.3 nmol/min/L respectively, while these were 8.3 U/mL, 3.0 U/mL, 141 nmol/min/L respectively in group 2. All the parameters for each antioxidant enzyme were lower in group 1 compared with group 2 (Table). There was no statistically significant difference between EO and TT groups and TT and group 2 (Table).

Procalcitonin

The procalcitonin parameter was 131.5 μg/L in group 1 and 33.3 μg/L in group 2. The level of procalcitonin was extremely high only in the TT group. There was no statistically significant difference between group 1 and group 2, EO and group 2 (Table). But the level of procalcitonin was statistically higher in the TT group when compared with group 2 and the EO group (Table).

Discussion

The accurate diagnosis of acute scrotum is still difficult in emergency departments. However in many cases, the time from the beginning of the patient's complaint until accurate diagnosis is so important in preserving the testes in patients who have acute scrotum due to testes torsion. Differential diagnosis of acute scrotum may be difficult, even for experienced staff such as pediatric surgeons and urologists. Surgical exploration should be the unique choice when the etiology is uncertain. In recent developments in health instruments, scrotal color Doppler ultrasonography (CDUS) is widely used all over the world for evaluating acute scrotum. However, it is reported that CDUS is a very valuable diagnostic tool but it is highly dependent on the expertise and technique of the investigator.(10) In this study we aimed to evaluate different laboratory tests for differential diagnosis of acute scrotum in order to help clinicians to manage acute scrotum when diagnoses are inaccurate.

The total count of WBC and neutrophil are increased, especially in inflammatory processes in the body. Accordingly, these were used to follow up the treatment of inflammatory situations. Mestrovic J. et al. reported a series of patients who had acute scrotum for inflammatory or non-inflammatory reasons. In that study they found that the values for WBCs and neutrophil were increased in both groups.(11) Similarly, we demonstrated that the values were increased either in WBC or neutrophil in acute scrotum or TT or EO groups. Although the increase was statistically significant in the acute scrotum group (also in the EO and TT groups), compared with the control group it was not significant when the EO and TT groups were compared with each other.

Blood samples are routinely obtained from patients with acute scrotum. Likewise, blood samples are routinely studied for patients who have acute scrotum. The proteins which increase or decrease during an acute process by more than 25% are called acute phase proteins. (12) Although the levels of ESR and CRP increase during inflammatory processes of the body, albumin decreases because it is a negative acute phase reactant.(12) In a

study it is reported that CRP is increased four-fold in the inflammatory process where it is found that CRP had a sensitivity of 96,2% and a specificity of 94,2%. It is also reported that the increase is not as significant as in testes torsion and tumor.(1) In another study, Asgari et al. reported that CRP and ESR were significantly increased in acute scrotum due to epididymitis compared with non-inflammatory reasons.(13) Albumin is not studied for the purposes of evaluating acute scrotum in the English literature according to the best of our knowledge. CRP and ESR are widely used in all clinics and albumin should also be studied in all clinics. In the present study, we demonstrated that CRP and ESR were increased ten-fold in acute scrotum compared with the control group. Despite the findings of the other studies discussed above, we investigated that the increase for CRP and ESR is as high in TT as in epididymitis. This situation should be explained by the lower number of patients with TT in our study. As albumin levels also decreased in the acute scrotum group and the EO and TT groups, the difference was statistically significant when acute scrotum and control groups were compared – but the difference was not significant when we compared the EO group with the TT group.

It is reported that the main pathophysiology of the testes is a result of ischemia reperfusion injury.(14) When testicular ischemia and reperfusion occurs, ROS are overproduced and this results in testicular injury.(15) ROS (hydrogen peroxide, superoxide anions etc…) are eliminated with antioxidant enzymes such as SOD, GPX and catalase.(16, 17) Wei et al. reported an experimental study with rats with a model of testes torsion. In that study they found that superoxide dismutase and catalase levels are significantly lower in torsioned testes.(14) In the present study we found that the levels of antioxidant enzymes were higher in the acute scrotum group. This discrepancy may be due to the experimental structure of the study. Furthermore, the authors studied levels of antioxidant enzymes in the testes but in our study, the results were studied from the peripheral blood.

Procalcitonin was first studied in patients with sepsis and infection by Assicot et al.(18) And procalcitonin has since been popularized in studies of inflammatory processes such as sepsis, pneumonia, pyelonephritis etc. Kim et al. reported that the cut-off value of procalcitonin is 0.4 ng/ml for exclusion of bacteremia in patients with fever. (19) However, procalcitonin is not evaluated in patients with epididymo-orchitis or testes torsion. Only one paper focuses on testes torsion which was designed experimentally in rats.(20) In that study, the authors reported that the procalcitonin levels are statistically higher in rats with testes torsion. Although the procalcitonin level is higher in patients with inflammatory processes, in our study we demonstrated a significant increase in patients with testes torsion compared with epididymo-orchitis patients and healthy subjects. The limited number of patients with testes torsion in our study was a major limitation. Therefore, we could not give the cut-off value for procalcitonin in patients with testes torsion. Further studies with large samples are needed to determine the cut-off value for procalcitonin in patients with acute scrotum.

Conclusions

Differential diagnosis of acute scrotum is very important for preserving the testes in patients with testes torsion. Although it is well known that color Doppler ultrasonography and nuclear scintigraphy are highly appreciated techniques which are used for differential diagnosis of acute scrotum, procalcitonin should be used for differential diagnosis of acute scrotum for rapid and easy diagnosis. However, for determining the exact and cut-off value for procalcitonin, further studies with large samples are needed.

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