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■ Original Article

The evaluation of oxidative stress parameters in the benign prostatic hyperplasia, prostatitis and prostate cancer

Benign prostat hiperplazisi, prostatit ve prostat kanserinde oksidatif stres parametrelerinin değerlendirilmesi

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ABSTRACT

Aim: Recently, oxidative stress has been well known that it has especially important a role in benign prostatic hyperplasia, prostatitis, and prostate cancer. The present study has planned to estimate parameters of the oxidative stress and the antioxidant status in patients with benign prostatic hyperplasia, prostatitis and prostate cancer.

Material and Method: For this aim totally forty men with benign prostatic hyperplasia (n=14), prostatitis (n=15) and prostate cancer (n=11) without any other chronic disease, and who not use cigarettes and alcohol were subjected. Venous blood samples were taken. Thiobarbituric acid reaction (TBARS), total oxidant status (TOS), total antioxidant capacity (TAC), glutathione (GSH) levels, and catalase (CAT) activity in serum were assessed in patient with prostatitis, and prostate cancer compared to benign prostatic hyperplasia.

Results: It was viewed that GSH levels were significantly lower, TBARS and TOS levels were significantly higher in patients with of prostate cancer compared to benign prostatic hyperplasia. Also, GSH and CAT significant different was determined in prostatitis compared to BPH. Oxidative stress may be concluded in prostate cancer and prostatitis, proved via the higher TBARS levels and lower GSH levels.

Conclusion: The increased activity of antioxidant enzyme may be a compensatory regulation in response to oxidative stress.

Keywords: benign prostatic hyperplasia, prostatitis, prostate cancer, oxidative stress

ÖZ

Amaç: Son zamanlarda, oksidatif stresin iyi huylu prostat hiperplazisi, prostatit ve prostat kanserinde özellikle önemli bir rolü olduğu iyi bilinmektedir. Bu çalışma benign prostat hiperplazisi, prostatit ve prostat kanseri olan hastalarda oksidatif stres ve antioksidan parametreleri değerlendirmeyi planlamaktadır.

Gereç ve Yöntem: Bu amaçla benign prostat hiperplazisi (n = 14), prostatit (n = 15) ve prostat kanseri (n=11) diğer kronik hastalığı olmayan, sigara ve alkol kullanmayan toplamda kırk erkek hasta değerlendirmeye alındı. Venöz kan örnekleri alındı. Prostatit ve prostat kanserli hastalarda tirobarbitürik asit reaksiyonu (TBARS), total oksidan durum (TOS), total antioksidan kapasite (TAC), glutatyon (GSH) düzeyleri ve katalaz (CAT) aktivitesi iyi huylu prostat hiperplazisine göre değerlendirildi.

Bulgular: GSH düzeylerinin anlamlı derecede düşük olduğu, TBARS ve TOS düzeylerinin benign prostat hiperplazisine göre prostat kanserli hastalarda anlamlı olarak daha yüksek olduğu görülmüştür. Ayrıca, GSH ve CAT, BPH ile karşılaştırıldığında prostatitde önemli ölçüde farklı bulunmuştur. Oksidatif stres, daha yüksek TBARS seviyeleri ve daha düşük GSH seviyeleri ile prostat kanseri ve prostatit de görülebilir.

Sonuç: Antioksidan enzimin artan aktivitesi, oksidatif strese yanıt olarak telafi edici bir düzenleme olabilir.

Anahtar kelimeler: benign prostat hiperplazisi, prostatit, prostat kanseri, oksidatif stres

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most known urological diseases in aging men. It often progresses after the 40 age and ranges in prevalence from too 50% at 60 age to as high as 90% after 85 age [1]. BPH is defined as has high morbidity and low mortality rate, and is acceptable as a public health problem [2]. Prostate cancer (PCa) is one of the most frequently diagnosed malignancies in men [3]. The mechanism of prostate carcinogenesis is not entirely understood, but proof suggests that oxidative stress plays a role [4]. The correlation between risk of prostate cancer and oxidative stress has been well-known. There is remarkable proof defining oxidative stress conduces to pathogenesis and etiology of the prostate cancer [5,6]. Epidemiological research at the last years shows "prostatitis" to be one of the major medical healthcare problems in urology [7]. Recently, oxidative stress has been defined in patients with prostatitis and it is well adopted that areas of prostatic inflammation can produce free radicals, such as nitric oxide and many derived-oxygen radicals [8,9]. Chronic inflammation can initiate proliferative events and on the DNA modifications in prostate tissue by the oxidative stress. The reality in fact, recurred tissue damage and oxidative stress connected with this event may incite a compensative cellular proliferation with the risk of hyperplasia growth or neoplasm [8]. It is adopted that areas of prostate inflammation compose free radicals and many radicals derived oxygen. In particular, macrophages and infiltration of neutrophil supply an important origin of free radicals that can induce hyperplasia or precancerous transformations through the oxidative

stress to the tissue and DNA [10]. Reactive oxygen species (ROS) increase the risk for DNA damage and inhibition of DNA repair in tumor cells [11]. Increased ROS production has conventionally been associated with tissue or DNA damage. But new and thrilling knowledge points to a main role for its increased production in different cellular processes connected with neoplastic transformation and abnormal growth and proliferation [12]. Moreover, ROS is the basis of many disease such as inflammatory diseases, neurodegenerative diseases, atherosclerosis, cancer and so on [13]. The human body is constantly exposed to the attack of free radicals. In the origin of the numerous diseases, inclusive tumors, known as increased in production of ROS resulting with oxidative stress. Level of prostatic hyperplasia and growth are frequently accompanied with inflammation initiated by improved production of ROS, oxidizing halogen derivatives, and reactive nitrogen species [14]. Increased amount of the ROS cause to damage of the biological structures [15]. DNA damage may seriatim reason to modifications in transcription and replication, initiation of signal transmission pathways, and genomic instability, which forms the basis for carcinogenesis [16]. Alive organism is protected against the detrimental ROS activity through a quite complex antioxidant system. Enzymatic antioxidants turbot contains, within other component, superoxide dismutase (SOD), which catalyses superoxide anion dismutation, as well as catalase (CAT) and glutathione peroxidase, as dissociate hydrogen peroxide [17,18].

In the previous studies have defined the changed oxidant-antioxidant status in semen, serum, plasma, and the

prostatic tissue of human and rats, or in persistent cell lines [19-22]. In this way, massive generation of ROS and/or deficiency in antioxidant defense system of the healthy cells can result with oxidative stress and the increased of ROS may play an important role in cellular processes associated with induction and improving of prostate inflammation, BPH, and numerous cancer species involving PCa. The present study was conceived to detect the oxidative stress markers and antioxidant status such as TBARS, TAC, TOS, GSH levels, CAT activity in patients with BPH, prostatitis, and PCa.

MATERIAL AND METHOD

Patients and Blood Samples

This study was included between 55–70 aged patients with BPH, prostatitis, and PCa without any other chronic disease and who not use cigarettes and alcohol, diagnosed at the Clinic of Urology, Faculty of Medicine, Erzincan University, Erzincan, Turkey. Also, Patients with medical conditions that alter oxidative status, such as another malignant disease, active inflammatory disease, thyroid disease, ischemic disease, diabetes mellitus, vascular disease, and severe dysfunction of the kidney, liver or heart were excluded from study. A complete medical history and physical examination were provided by all study participants. The study was authorized by Health Science Human Researches Ethical Committee of Erzincan University (No. 5/1-29.11.2013). Benign prostatic hyperplasia, prostatitis, and prostate cancer were divided into 3 groups. Group 1(BPH): this group was created patients diagnosed with BPH. Group 2 (prostatitis): this group was conducted patients diagnosed with prostatitis. Group 3 (PCa): this group was composed patients diagnosed with PCa. Blood samples were obtained after fasting 12 hour period. Samples were withdrawn from an antecubital vein into blood tubes and immediately stored in ice at 4 °C. Serum was separated from the blood after allowing it to stay in a test tube for about 30 minutes, followed by centrifugation at 3000 rpm for 10 minutes and stored at -20 °C until used for the ELISA assays.

Biochemical Analysis

ELISA assays

Serum CAT activity, GSH and TBARS levels were quantified by using an ELISA kit (Cayman Chemical Company, Michigan, USA). TOS and TAC levels were quantified by using an ELISA kit (Real Assay Diagnostics, Gaziantep, Turkey). All assay procedures were carried out according to the manufacturer's instructions. The absorbance of standards and samples were obtained at 450 nm wavelength using an

Table 1. The mean \pm SD values of Total antioxidant capacity (TAC), Total oxidant status (TOS), Glutathione (GSH), Thiobarbituric acid reaction (TBARS), and Catalase (CAT) in patients with BPH, Prostatitis, and PCa

	TAC (mmol/l)	TOS (μ mol/l)	CAT (nmol/ min/ml)	GSH (nmol/ml)	TBARS (nmol/ml)
BPH (n=14)	1.62 \pm 0.25	8.78 \pm 3.73	51.41 \pm 22.44	5.29 \pm 1.36	2.10 \pm 0.68
Prostatitis (n=15)	1.49 \pm 0.32	9.79 \pm 3.23	45.26 \pm 20.95	5.24 \pm 1.54	2.66 \pm 0.84
PCa (n=11)	1.32 \pm 0.34	11.73 \pm 2.76	39.14 \pm 23.96	3.96 \pm 1.22	2.93 \pm 1.1

Epoch spectrophotometer (Biotech Instruments, Inc., Winooski, VT, USA). A standard curve was plotted with standard concentration on the x-axis and absorbance on the y-axis to determine levels of CAT (nmol/min/ml), GSH (nmol/ml), TBARS (nmol/ml), TOS (μ mol/l) and TAC (mmol/l).

Statistical Analysis

The results are presented as the mean \pm S.D. Normality test (Shapiro Wilk and Levene test) to assay the homogeneity of variance for variables were evaluated. While data were analysed, previously the one-way analysis test was made for comparison of three more group and later Bonferroni-Dunn's test of Kruskal-Wallis from multiple comparison test was used in the situation that Tukey HSD test from the multiple comparison tests were not provided. The significance level was shown as $p < 0.05$. SPSS 20 for data analysis (Released 2011. IBM Corp. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) Statistical package program was used.

RESULTS

It has been focused on the importance of free radical damage in the determined of BPH, prostatitis, and PCa. Besides, it has been intensely worked to prevent its initiation or progression. Also, recently in several preclinic and clinic studies have been demonstrated that therapies supporting antioxidant system have been made to decrease and minimize development of the BPH, prostatitis, and PCa. The mean \pm SD of serum TAC, TOS, TBARS, CAT, and GSH are indicated in **Table 1**. There was a statistically significant for the GSH levels between PCa with BPH and Prostatitis with BPH. The TAC levels were significantly higher in Prostatitis and PCa group compared to group BPH ($P < 0.05$; **Figure 1**). The levels of plasma CAT showed significant different between BPH and Prostatitis ($P < 0.05$; **Figure 1**). In the present study GSH an antioxidant was significantly lower in patients with PCa compared to Prostatitis and BPH ($P < 0.05$;

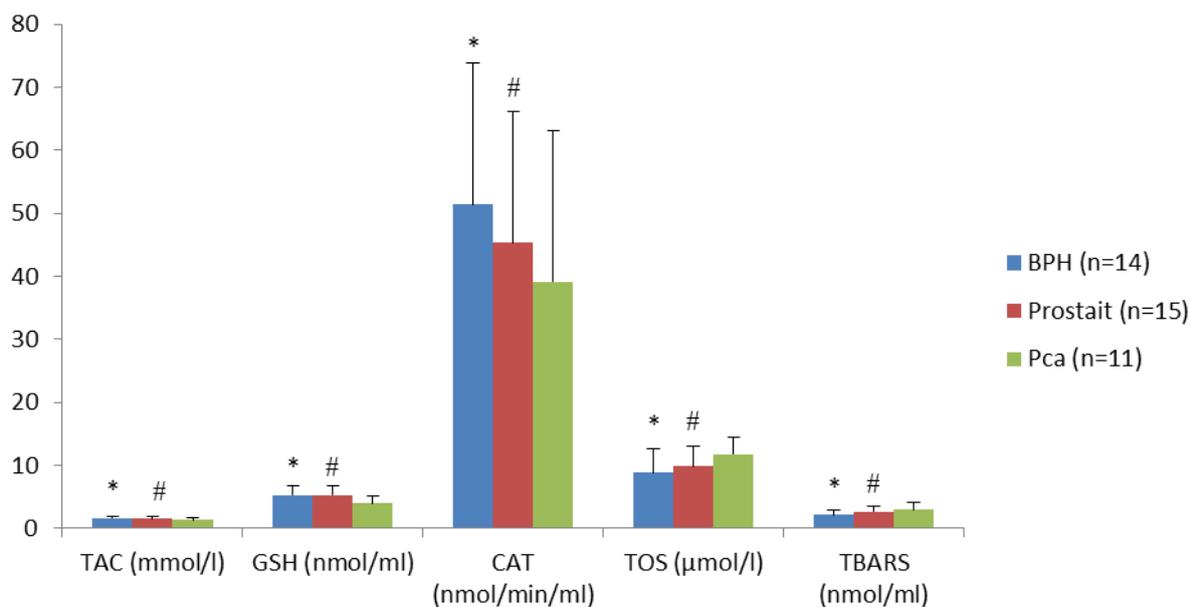


Figure 1. Statistically significant values of Total antioxidant capacity (TAC), Total oxidant status (TOS), Glutathione (GSH), Thiobarbituric acid reaction (TBARS), and Catalase (CAT) in patients with BPH, Prostatitis, and PCa

*: Compared to between the prostatitis and BPH ($p < 0.05$)

#: Compared to between the BPH and PCa ($p < 0.05$)

Figure 1). TBARS levels more increased in PCa group compared to BPH and in Prostatitis compared to BPH ($P < 0.05$; **Figure 1**). TOS level was improved, as a biomarker of the oxidative stress, in PCa and Prostatitis. This situation was lower in group of patients with BPH as seen in the **Table 1** and **Figure 1**.

DISCUSSION

BPH is the most often benign neoplasm for men as an endocrine disorder. Significant majority men will be treated in their lifetimes related to the symptoms of BPH [23]. PCa is disease of the male above the age of 50 years worldwide [24]. The numerous people endure with prostatitis which is one of the most prevalent problems in urinary and andriatry surgery/therapy [25]. In fact we can say that in these three diseases importantly is associated with oxidative stress. Oxidative stress is one of the results unavoidable in the aerobic life. Gradually increasing evidences show that the accumulation and generation of the ROS and reactive nitrogen species play a main role in the aging process and age-related various diseases such as prostate cancer [26,27]. These extremely reactive oxidant molecules have connected and oxidation of lipid, DNA, and proteins, also they reacts with neighborhood structures. When the oxidative damage is not repaired that can cause mutations, increasing the risk of carcinogenesis [28]. ROS are related to dissimilar grades of carcinogenesis, through either immunological mechanisms or DNA damage, as interact coaction with tumor suppressor genes, oncogenes [29]. Furthermore, ROS

may also lead to the generation of DNA adducts indirectly by starting autocatalytic lipid peroxidation, which creates a great range of potentially genotoxic breakdown products, containing aldehyde and lipid proxyl radicals (ROO), such as malondialdehyde [30,31]. Consequently, the DNA is intensely oxidatively modified and damaged [32,33]. The oxidative hydroxylation causes a lack of base with quite mutagenic lesion of nuclear DNA, that it is resulted with faulty reading of the modified base and adjacent residues. When any oxidative lesion is not repaired can results mutations, increasing the risk of carcinogenesis [28,34-37]. Moreover, oxidative damage are tightly associated with chronic prostatitis [38]. Also, the grade of oxidative damage induced by ROS can be intensified due to derogation in the performance of antioxidant defense system. This defense systems against the ROS involve antioxidant enzymes such as: glutathione peroxidase, catalase, and superoxide dismutase [39]. In previous various human and animal studies have been evaluated some parameters of oxidative stress in patients with benign prostatic hyperplasia, prostatitis, and prostate cancer. For example Sarafinovska et al., reported that antioxidant enzyme activities decreased and oxidative stress parameters increased in prostate cancer [4].

When balance of ROS-antioxidant in prostatic tissue is destroyed, the activities of prostatic antioxidant enzymes (such as SOD, CAT and GPx) are obviously decreased while the level of TBARS is significantly improved [40]. It has been

reported that the activities of SOD, CAT and GPx are increased by the treatment of antioxidant for 4 weeks obviously, and decreased the level of TBARS in prostate tissue compared to carrageenan-induced bacterial prostatitis group [41]. It has been well known lead to DNA damage of the ROS but also, these products are extremely make prone to the malignant transformation from the prostate hyperplasia [42,43]. In previous a study, it has been determined that levels of antioxidants in blood of patients with PCa was reduced [44] and increased of markers lipid peroxidation [44,45]. Adedapo et al.'s in study, TAC level higher in patients with PCa compare to the BPH [46]. In a study that comparison of semen characteristics and measures of oxidative stress between healthy men (control) and patients with chronic prostatitis, TAC was higher in patients with chronic prostatitis according to the control group [21]. In the other study, in patients with chronic bacterial prostatitis compared to healthy men volunteers erythrocyte malondialdehyde levels increased and erythrocyte SOD, CAT and GPx activities significantly decreased [40]. Our study has been demonstrated that TBARS, as an indicator of lipid peroxidation level, increased. TAC and CAT decreased, as specifier of antioxidant enzymes in the blood of patients with BPH is a disease nearly related to oxidative stress. But severity of oxidative tissue damage more increased in group of the patients with Prostatitis and PCa due to TBARS levels much more improved. Fundamentally increased lipid peroxidation can be devastating to different tissues if not scavenged by antioxidant defense system as a consequence of overwhelming free radicals. Consequently, the serum antioxidant enzymes might be used to set against the rised lipid peroxidation in the tumor or inflammation-affected tissue. Another speculation is that the increased lipid peroxidation consists as conclusion of the inadequate force of consumed antioxidant defense system for a prolonged time. Additionally, in group of the patients with Prostatitis and PCa dropped significantly CAT activity, TAC, and GSH levels. In the light of literature and our own findings we can say that the CAT activity, TAC, and GSH levels may possibly decreased to detoxify substantially of the hydrogen peroxide. Because these antioxidant enzymes may be used in the start and continue of defense against the raised lipid peroxidation in the touched tissue [47].

The results in this study suggest that there exist increased oxidative stress as more severe and damage in patients with chronic bacterial prostatitis and prostate cancer according to patients with BPH.

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DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest associated with this manuscript.

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