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Evaluation of Adenosine Deaminase (ADA) Level in Serum of Patients with Prostate Cancer

Reza Saghiri*

Department of Biochemistry, Pasteur Institute of Iran, Tehran, Iran

ABSTRACT

Aim: Prostate cancer is a developing cancer in prostate gland. It is one of the common cancers among men. This cancer usually develops slowly but sometimes it is metastatic form. Screening of prostate cancer is done by measuring the PSA level, but it sometimes leads to over diagnosis in some cases. Therefore, finding another factor except PSA, for screening the cancer seems necessary. Elevation in the level of ADA is observed in some diseases like cancers. It is considered that measuring ADA level beside PSA level could be a helpful factor for screening prostate cancer.

Methods: In this study, blood sample were collected from 40 patients and 40 control participants matched for age. PSA, free PSA and ADA levels were compared in the serum of both groups. PSA assessment was based on sandwich ELISA although ADA level was measured by colorimetric methods. SPSS software was used for analyzing data.

Results: According to obtained data from patient and control groups the mean of PSA level was 23.9 ± 11.96 ng/ml and 1.33 ± 0.61 ng/ml, respectively which showed a significant increase in patients ($P<0.05$). ADA level was 30.99 ± 0.99 U/L and 9.8 ± 0.8 U/L in patient and control groups. It is significantly higher in patients than controls ($P<0.05$).

Conclusion: The study results showed a significant elevation in PSA and ADA levels in prostate cancer patients compared with control group. Therefore, serum ADA and PSA levels might be useful indexes in screening and monitoring of prostate cancer.

Keywords: Prostate cancer; Prostate specific antigen; Adenosine deaminase; Screening

INTRODUCTION

Prostate Cancer (PC) is a very common cancer among men [1,2]. It is located in the fifth place in cancers leading death in most countries and its prevalence is increasing annually [3-5]. Prostate cancer is usually diagnosed in 55 to 74 years old men and its incidence is higher in African American than other races [6,7]. It is not clear why this cancer arises, but there are some risk factors including age which is the most important one, race, genetics, diet and etc. that are related to this cancer [8,9]. The mortality rates of prostate cancer is low and most of men diagnosed with prostate cancer die of other reasons except this cancer. Prostate cancer is asymptomatic in many cases because its progression is very slowly [10]. Measuring Prostate-Specific Antigen (PSA) level is a screening method for identifying different kinds of prostate cancer [11]. PSA screening is a helpful way to diagnose prostate cancer at early stages and employ useful treatments to cure the disease but PSA level increases not only in prostate cancer but also in some other conditions like prostate inflammation and benign prostate enlargement [12-15]. Therefore, it cannot be a good marker for screening prostate cancer on its own and other tools should be used to aid in diagnosing the cancer more efficiently. Biopsy is one of the methods which is used for ensuring of exact diagnosis of prostate cancer but because of invasiveness and some possible side effects, it is preferred to make sure completely before using it for the final detection [16,17].

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Corresponding author: Reza Saghiri, Department of Biochemistry, Pasteur Institute of Iran, Tehran, Iran; E-mail: reza_saghiri@yahoo.com

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MRI is another way that is applied in some centers for evaluating patients.

Biological molecules like some enzymes, surface antigens and etc., may change in some pathological conditions and measuring them can be useful in screening and diagnosing of some diseases.

Adenosine Deaminase (ADA) is an enzyme which contributes in purine metabolism and catalyzes adenosine and deoxyadenosine and delaminates them to inosine and deoxyinosine [18,19]. These produced molecules have effects on different cells [20]. Adenosine which modulates cell function by adenosine receptor is regulated by ADA. The roles of adenosine in tumor progression have been described in some studies. Different blood cells like lymphocytes, mononuclear cells, neutrophils and red blood cells secret this enzyme, so it can be found in human serum. It is also expressed on various cells and tissues. ADA has an important role in differentiating and proliferating of T cells which are responsible for cellular immunity. The cellular immune response can be stimulated in different immune conditions like infectious diseases and cancers. Therefore, the activity of this enzyme in different body fluids can be associated with various diseases. Increased level of serum ADA activity is observed in diverse diseases like liver diseases, tuberculosis and some kinds of cancer such as breast cancer. So ADA can be considered as an auxiliary diagnostic marker in some diseases.

In this study we have measured the level of ADA in serum of patients with prostate cancer to show the relationship between this marker and the cancer. We are trying to find some markers for better screening of prostate cancer to help the patients to be safe from unnecessary treatment and also late diagnosis.

MATERIALS AND METHODS

Patients

This study was performed from April 2015 to March 2016. The specimens were obtained from men who were referred to Imam Hossein hospital and Pasteur institute. 40 men who were diagnosed with prostate cancer and 40 healthy men as control group were enrolled in the study and the same factors were assessed in both groups. The average age in test and control group was 77.1 ± 4.41 and 71.6 ± 6.4 respectively (**Figure 1**).

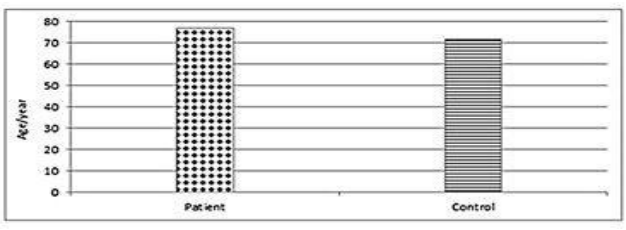

Figure 1: Mean age of participants in the control and patient groups.

According to the inclusion criteria, patients with PSA level equal or more than 10 ng/ml were participated in the study. We received consent from participants.

Assays

3 ml of blood was collected from each patients and healthy controls without any previous preparation. The serum was separated based on the following protocol:

The sample remained in room temperature for 30 minutes then it was centrifuged at 1200 g for 10 minutes. Finally, the serum was collected and stored at -70°C for future assays.

PSA was assayed by Pishtaz kit which was based on sandwich ELISA. The normal range of PSA is ≤ 4 ng/ml in men.

ADA was measured by ADA assay kit (Diazyme kit, USA) based on colorimetric method. The intensity of produced color has a direct relationship with the amount of ADA in the sample. If its level is less than 15 U/L, it is considered normal in serum.

Statistical Analyses

We showed the data as mean ± SD and determined the differences between control and patients group by t test. If the P value was less than 0.05 it would be considered significant.

RESULTS

Comparison of obtained data from test and control group showed that the average levels of PSA in patients and healthy control were 23.9 ± 11.96 ng/ml and 1.33 ± 0.61 ng/ml. The mean of free PSA level in prostate cancer patients was 2.69 ± 0.99 ng/ml and it was 0.33 ± 015 ng/ml in control group. Comparing data between test and reference group showed a significant increase in patients than control. (**Figure 2**) ADA level has a mean of 30.99 ± 0.99 U/L and 9.8 ± 0.8 U/L in patient and reference group, respectively which showed a statistically significant difference between two groups. (P< 0.05) (**Figure 3 and Table 1**).

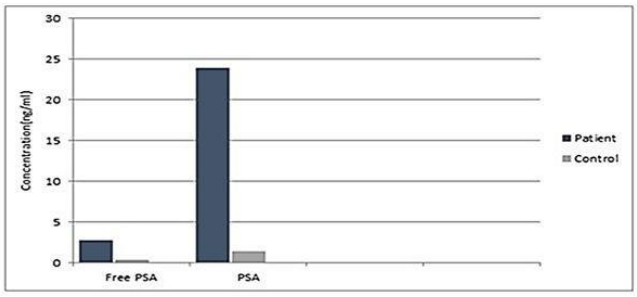

Figure 2: Mean serum level of PSA and free PSA in patients and control group.

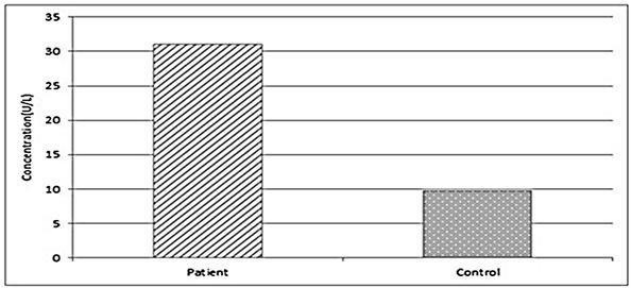

Figure 3: Mean serum level of ADA in patients and control group.

Table 1: The mean and standard error of mean of PSA, free PSA and ADA in controls and patients with prostate cancer.

Variable	Control group (n=40) Mean (SEM)	Patient group (n=40) Mean (SEM)	P Value
PSA (normal range= ≤ 4 ng/ml)	1.33 (0.66)	23.9 (0.18)	< 0.05
Free PSA	0.33	2.69	< 0.05
ADA (normal range= <15 U/L)	9.8 (0.39)	30.99 (0.46)	< 0.05
	(P<0.05)		

The correlation between data (PSA and age, ADA and age, PSA and ADA) in patient and control groups was evaluated by Pearson correlation test. The results are presented in **Tables 2-4.**

Table 2: The correlation coefficient between age and PSA in study groups.

Age and PSA	Correlation	P value
Control group	0.169	0.296
Patient group	0.32	0.544

Table 3: The correlation coefficient between age and ADA in study groups.

Age and ADA	Correlation	P value
Control group	-0.105	0.519
Patient group	0.244	0.129

As shown in Tables 2 and 3 no significant was observed between age and PSA or age and ADA in patient or control groups. Although, **Table 4** demonstrated a weak positive correlation between PSA and ADA among the study groups.

Table 4: The correlation coefficient between ADA and PSA in study groups.

PSA and ADA	Correlation	P value
Control group	0.377*	0.033
Patient group	0.610*	0
	*= Significant	

DISCUSSION

PSA level has been a major marker for screening prostate cancer for a long time. Although the screening of PSA causes reduction in risk of prostate cancer mortality, it may result false positive in some cases which would lead to some complicated diagnostic criteria. According to growing incidence of prostate cancer, it seems to be necessary to find some other markers for screening the disease to help for accurate diagnosis. ADA is an enzyme which changes its level has been reported in some diseases. In our study, we measured the ADA and PSA level in patients with prostate cancer which showed that in all cases with increased level of PSA, an elevated level of ADA can be seen which is statistically significant. This result might be due to leakage of ADA enzyme from prostatic tumors [19]. Also another explanation for the elevation in ADA level in cancers is due to increase in production of adenosine in cancerous tissues which is the substrate of ADA. Because of higher metabolism of nucleotide, the level of ADA will increase too. It is also suggested that ADA level increases to neutralize toxic effects of elevated adenosine level, Most of the studies on ADA have considered the importance of the level and role of ADA in tuberculosis. A lot of researches have evaluated ADA level in different cancers, but there are some controversial results in these studies. For example, Dasmahapatra, et al., believed

that ADA level in lymphocyte decreases in patients with head and neck cancer and in 1985 Kojima and colleagues also showed the same result in patients with gastric cancer. These results may be an indicator of the suppression of cell mediated immunity in cancers. Elevation in ADA level in patients with different kinds of cancer has also been reported in other studies. In 2010, Aghai and colleagues indicated the level of ADA increased in serum of breast cancer patients. A study by Pirincci group in 2012 on patients with bladder cancer showed higher level of ADA in patient's serum than in references. In the same year, Mahajan, et al., found that ADA level increased in breast cancer patients and it decreased after treatment. In 2016, Pirincci group also showed that the level of ADA was increased in patients with renal cell carcinoma and it might be an additional biomarker for RCC diagnosis. Another study in 2016 which was done by Ghaderi, et al. assessed the level of ADA activity in serum of CLL patients and showed its elevation in patients. Therefore, according to the results of these studies increase in ADA level can be seen in various cancers. These results are compatible with the result that we have obtained in our research. A few studies have assessed the serum level of ADA in prostate cancer patients in Iran and other countries. Our study is the first research in Iran for evaluating the ADA level in prostate cancer cases. In our research we found two other studies that had measured ADA level in prostate cancer patients and as a result decrease in the level of ADA was observed in patients compared to control in them which is against our result. Since our study is the first research in Iran for evaluating the ADA level in prostate cancer cases and according to the existing contradictions further research seems to be necessary. Based on the results of our study, ADA level in serum might be potentially a useful index in screening of prostate cancer. However, because its elevation is also observed in other cancers, it is better to use both PSA and ADA level for the screening. PSA and ADA also can be useful in follow up the patients after treatment. They can prevent patients from unnecessary diagnostic criteria like biopsy. Owing to the limited number of studies on ADA and prostate, It seems that conducting further research with larger number of participants could bring about more precise results. It is a good suggestion to try to find a relationship between PSA and ADA level that could be applied in accurate diagnosis or finding some other biological markers that their elevation is only specific for prostate cancer [21,22].

CONCLUSION

The study results showed a significant elevation in PSA and ADA levels in prostate cancer patients compared with control group. Therefore, serum ADA and PSA levels might be useful indexes in screening and monitoring of prostate cancer.

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