ORIGINAL ARTICLE

Trait Marker IGF1 is More Diagnostic than PSA in Ca Prostate, Study at Local Population of Karachi

MUHAMMED ILTAF[1], JAGDESH[2], JAI PARKASH PANJWANI[3], *MUKESH KUMAR ADVAI[4], MUHAMMED YOUSIF MEMON[5], KHALILULLAH[6]*

ABSTRACT

Objective: To evaluate the serum level of insulin like growth factor-1 (IGF-1) and prostate specific antigen in diagnosed prostate cancer patients and age matched normal healthy subjects in local population of Karachi and to compare the mean values of these parameters in CA prostate patients with normal control subjects and also to observe the sensitivity of these parameters.

Material and methods: This study was carried out in the Department of Biochemistry, BMSI, JPMC, Karachi a total of 70 subjects were included with their consent in this study. 35 subjects were of prostate cancer and 35 normal age matched healthy control subjects for comparison. The diagnosed cases of prostate cancer were taken from Department of urology and Radiotherapy, JPMC, Karachi and control subjects were taken from general population.

Results: The result showed that mean value of IGF-I in the control group was 190.60±5.59 and that of patient group was 230.68±4.25; showing statically significant difference ($p < 0.005$). Whereas the PSA value in control and patient group were 0.83±0.10 and 63.35±9.78 with a highly significant difference $p < 0.005$. The PSA value was found significantly high in patient group but when we sub-grouped these patients on the basis of PSA value (0-4ng/ml) we found that the majority of the cancer patients had raised PSA value, 30 out of 35(85.52%) had PSA value more than 4ng/ml, whereas 5 out of 35 (14.28%) although suffering from prostate cancer had PSA value within normal limit of less than 4ng/ml. The IGF-I value was found significantly high in patient group but when we sub-grouped these patients on the basis of IGF-I value we found that the majority of the cancer patients had raised IGF-I value, 33 out of 35(94.28%) had IGF-I value more than 200ng/ml, whereas only 2 out of 35 (5.72%) although suffering from prostate cancer had IGF-I value within normal limit of <200ng/ml.

Conclusion: We strongly recommend serum IGF-1 level should be routinely done as a diagnostic biochemical tool along with PSA in carcinoma of prostate.

Keywords: IGF-1, prostate cancer, PSA.

INTRODUCTION

Prostate cancer is one of the most common male cancers in developed countries. Meanwhile, in Asia where the risk of prostate cancer has previously been known to be much lower, prostate cancer incidence is currently rising rapidly[1]. The increase in survival may be attributed to increasing awareness of prostate cancer among practicing physicians, general public and increasing interest in cancer detection as a result of serum prostate specific antigen (PSA) testing, with subsequent earlier diagnosis.

[1]Medical Technologist, Biochemistry, Basic Medical Sciences Institute/JPMC, Karachi. [2]Associate Prof, Biochemistry, Bhitai Dental & Medical College, Mirpurkhas
[3]Assistant Professor Biochemistry, Baqai Medical University, Karachi
[4]Assistant Professor Pathology, Shaheed Mohtrama Benzir Bhutto Medical College, Karachi
[5]Associate Professor Biochemistry, LUMHS, Jamshoro
[6]M.Phil student Biochmistry, BMSI/JPMC, Karachi
Correspondence to Mr. Muhammed Iltaf, Email: drmukeshadvani@yahoo.com

Though PSA has established itself as a valuable tool for cancer detection using a cutoff value of 4.0ng/ml, but the specificity of PSA is problematic[2]. Our understanding is that most cancers detected among men with PSA levels less than 4.0ng/ml can be considered clinically significant. Thus, it is evident that there is need for new tools to improve the specificity of PSA levels in the “diagnostic gray zone” and the cancer detection in men with low PSA levels.

Prostate-specific antigen (PSA) is a protein produced by normal prostate cells. This enzyme participates in the dissolution of the seminal fluid coagulum and plays an important role in fertility. The highest concentration of PSA is found in the seminal fluid; some PSA escapes the prostate and can be found in the serum. This serum component has been used to track the response to therapy in men with prostate cancer.

After observations that certain hormones, such as testosterone and insulin-like growth factor-1 (IGF-1), can affect prostate cancer cell growth, several

researchers have investigated the significances of these hormones regarding risk and/or prognosis of prostate cancer in Europeans and Americans. Certainly, the responsiveness of prostate cancer to hormonal therapy supports the view that testosterone might indeed play an important role in the pathogenesis of prostate cancer.

Insulin like growth factors (IGFs) are polypeptide hormones, have structures resembled to that of pro-insulin and they generally mediate anabolic cellular effect via endocrine, paracrine and autocrine mechanisms. In normal and transformed prostate epithelial cells, Insulin like growth factors (IGFs) are reported to have mitogenic and anti-apoptotic effects & are thought to be implicated in the development & progression of prostate cancer[3]. Circulating IGF-I & IGFBP-3 levels may be altered in prostate cancer patients. In these patients the circulating IGF-I level was shown to be often increased, whereas the circulating or the prostatic tissue levels of IGFBP-3 were often decreased[4,5]. Where as Harman et al (2000) stated that the association between circulating IGF-I & risk of prostate cancer was stronger than that of any previously reported risk factors. Male mice with deletion of the IGF-I gene are infertile and have a significant reduction in the mass of the prostate gland. IGF-I has mitogenic and anti-apoptotic influences on human prostate epithelial cells[7].

The most widely studied effect of IGFs in vitro is the stimulation of DNA synthesis and cell replication, by causing cells to traverse the successive phases of the cell cycle. IGF-I has been shown to function as a progression factor in the cell cycle[8].

SUBJECTS AND METHODS

This case control study was carried out in the department of Biochemistry. Basic Medical Sciences institute, Jinnah Postgraduate Medical Centre, Karachi in collaboration with urology and Radiotherapy Department, JPMC, Karachi. A total of 70 subjects were included in this study. The subject were classified into two groups as follows.

Group I (control): Comprised of 35 subjects with no urinary tract symptoms. The age was 50 years and above. The control subjects were taken from general population.

Group II (CA Prostate): Comprised of 35 diagnosed cases of prostate cancer which were mostly taken from urology and radiotherapy dept of JPMC Karachi.

Collection of serum specimens: Fasting blood samples were collected from all study subject including 35 diagnosed cases of prostate cancer and 35 control subjects under all aseptic measures. Blood samples were allowed to stand at room temperature (25°C) and then centrifuged for 5-10 minutes to obtain serums which were stored in small serum cups and kept in deep freezer(-50°C) till analyze.

Laboratory assays: The serum IGF-I was determined by IGF-I ELISA- using Kit Cat No. EIA - 2947, manufactured by DRG diagnostics GmbH, Germany. The estimation of PSA was done by AxSYM Total PAS assay, list number 3C19; 69-2399/R4, manufactured by Abbott Laboratories USA, on AxSYM system. The basic principle of this system is Enzyme Linked Immuno Sorbent Assay (ELISA).

RESULTS

Table 1 shows the comparison of Biochemical parameters between control and patients group. The mean value of IGF-I in the control group was 190.60±5.59 and that of patient group was 230.68±4.25; showing statically significant difference ($p<0.005$). Whereas the PSA value in control and patient group were 0.83±0.10 and 63.35±9.78 with a highly significant difference $p<0.005$.

Table 1: Comparison of mean values of biochemical parameters in both groups

Parameter	Control Group (n = 35)	Patient Group (n = 35)
IGF-1(ng/ml)	190.60 ± 5.59	230.68 ± 4.25*
PSA (ng/ml)	0.83 ± 0.10	63.35 ± 9.78

Table 2 shows the distribution of Prostate Specific Antigen (PSA) concentrations in carcinoma of prostate patients. Although the PSA value was found significantly high in patient group but when we sub-grouped these patients on the basis of PSA value (0-4ng/ml) we found that the majority of the cancer patients had raised PSA value, 30 out of 35 (85.52%) had PSA value more than 4ng/ml, whereas 5 out of 35(14.28%) although suffering from prostate cancer had PSA value within normal limit of less than 4ng/ml. This table explains that PSA alone should not be taken as confirmative diagnostic tumor marker for prostate cancer.

Table 3 shows the distribution of IGF-I concentration in patients with carcinoma of prostate. Although the IGF-I value was found significantly high in patient group but when we sub-grouped these patients on the basis of IGF-I value we found that the majority of the cancer patients had raised IGF-I value, 33 out of 35 (94.28%) had IGF-I value more than 200ng/ml, whereas only 2 out of 35 (5.72%) although suffering from prostate cancer had IGF-I value within normal limit of less than 200ng/ml. The table shows the superiority of IGF-I over PSA in the diagnosis of prostate cancer. This clearly indicates that IGF-I can be used as a strong diagnostic marker along with PSA for the prostate cancer.

Table 2: Distribution of prostate specific antigen (PSA) concentrations in carcinoma of prostate

S.No.	High PSA sub-group (>4ng/ml)	Normal PSA sub-group (≤4ng/ml)
1	36.00	-
2	36.80	-
3	65.00	-
4	-	2.10
5	100.70	-
6	105.70	-
7	146.00	-
8	-	3.60
9	36.60	-
10	8.05	-
11	18.50	-
12	60.00	-
13	150.00	-
14	11.40	-
15	18.50	-
16	-	2.50
17	189.00	-
18	41.72	-
19	250.00	-
20	-	2.90
21	104.00	-
22	52.30	-
23	15.20	-
24	-	2.40
25	98.50	-
26	58.50	-
27	76.30	-
28	34.40	-
29	30.60	-
30	18.30	-
31	48.00	-
32	89.20	-
33	90.60	-
34	110.10	-
35	104.00	-
n =	30	05
%	85.72	14.28

Table 3: The Distribution of IGF-I concentrations in patients with carcinoma of prostate

S.No.	High IGF-I sub-group (>200ng/ml)	Normal IGF-I sub-group(≤ 200ng/ml)
1	240.05	-
2	236.00	-
3	211.15	-
4	225.62	-
5	265.07	-
6	281.11	-
7	236.85	-
8	281.15	-
9	251.86	-
10	211.30	-
11	269.06	-
12	249.11	-
13	270.14	-
14	201.96	-
15	209.08	-
16	238.52	-
17	216.03	-
18	225.51	-
19	200.67	-
20	204.54	-
21	219.75	-
22	246.57	-
23	-	180.82
24	200.15	-
25	221.00	-
26	230.18	-
27	209.56	-
28	249.00	-
29	219.65	-
30	240.00	-
31	238.00	-
32	241.10	-
33	-	188.85
34	217.00	-
35	248.15	-
n	33	02
%	94.28	5.72

DISCUSSION

Though prostate specific antigen (PSA) is the first line test for prostate cancer screening, early detection, staging and monitoring, the inadequacies of this test have surfaced. It has poor specificity in the range of 4.0 to 10ng/ml (the so-called diagnostic gray zone) and may miss clinically significant prostate cancer using a cutoff of 4.0ng/ml. lowering the threshold will magnify the problem of poor specificity and low positive predictive value. New tumor markers are required urgently. In the connections of trial studies where researchers are keep busy to obtain new and more accurate biochemical parameters which help for early diagnosis and prompt treatment. Our data support the hypothesis that higher plasma IGF-I levels are associated with higher rates of malignancy in the prostate gland.

We found significantly higher Prostate Specific Antigen (PSA) value in prostate cancer subjects when compared to normal controls. PSA is used as a diagnostic tool in prostate cancer but when sub grouped these cancer patients on the basis of normal value of PSA (< 4.00ng/ml) we found that not all cancer patients had raised PSA level. In 5 out of 35 patients (14.8%) had normal PSA although were suffering from cancer. It showed that PSA alone can not be taken as diagnostic tool. Similarly when we sub grouped these cancer patients on the basis of normal level of IGF-I (≤ 200ng/ml) we found that most of the cancer patients had higher IGF-I levels. Only 2 out of 35 (5.71%) had normal IGF-I level although were suffering from prostate cancer; showing that IGF-I could be taken as a better diagnostic marker than PSA. These results are justified with study of Chan et al (1998) who stated that the association between circulating IGF-I level & risk of prostate cancer was stronger than that of any previously reported risk factor. IGF-I remained a significant predictor of prostate cancer in men with low (<4.00ng/ml) and high (>4.00ng/ml) PSA value. He also concluded that IGF-I concentration may be a better predictor of prostate cancer than PSA. Similarly Chan (1998) found that men at greater risk of advanced prostate cancer were those with high levels of IGF-I than those with normal IGF-I levels.

CONCLUSION

We strongly recommend serum IGF-1 as a diagnostic biochemical tool along with PSA in carcinoma of prostate and must be routinely available in the laboratories of Urology Department.

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