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Research Article

The Comparative Study of Prostate Specific Antigen Levels and Acid Phosphatase Activity in Patients with Prostate Hypertrophy

Manafa P.O, Chukwuma G.O*, Eze V.O, Onyenekwe C.C, Chukwuanukwu R.C, Ogenyi S.I, Oluboyo A.O, Ochiabuto O.M.T.B, Akulue J.C, Odiegwu .C.N.C

Department of Medical Laboratory Sciences, Faculty of Health Sciences and Technology, College of Health Sciences, Nnamdi Azikiwe University Nnewi Campus.

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Abstract
Prostate hypertrophy is common in men over 50 years. In the present work, a comparative study of prostate specific antigen (PSA) levels and acid phosphatase activity (ACP) in subjects with prostate hypertrophy was determined. One hundred and thirty male subjects aged 40 to 90 years were randomly recruited for the study. Of these, one hundred of the subjects with signs of prostate hypertrophy served as test subjects while thirty apparently healthy subjects were used as control. About 5mls of blood were collected from the subjects. Prostate Specific Antigen Levels were determined by the Enzyme-linked Immunosorbent Assay (ELISA). Results were analysed statistically, using the SPSS statistical system. There was positive correlation in total PSA with total ACP, % Free PSA with total ACP, total PSA with prostatic ACP but negative correlation in total PSA with non prostatic ACP and % Free PSA with non prostatic ACP. There was no significant difference between total PSA and total ACP ($P>0.05$). This same pattern was also observed between % Free PSA and total ACP, total PSA and prostatic ACP, and % Free PSA and prostatic ACP. In the age groups, there was no significant difference between the age groups in total PSA, prostatic ACP and % Free PSA ($P>0.05$). A slight decrease in the mean values was observed in the prostatic ACP with age groups of 71-80 and 81-90. Our findings from this study suggest that ACP determination may serve as a viable alternative to PSA especially in resource limited areas.

Key word: *Prostate Specific Antigen, Acid Phosphatase, Prostate Hypertrophy, Comparative*

INTRODUCTION

Serum activities of Acid Phosphatase (ACP) are still employed in most hospitals in Nigeria for the diagnosis of prostate cancer, because of lack of resources for prostate specific antigen (PSA) assay. Prostate cancer is a form of cancer that develops in the male reproductive system. It is a slow growing cancer and the most commonly diagnosed malignancy in males in the developing world (Pienta, 2008;Brawley, 2007). Acid phosphatase was first used as a tumor marker by Gutman and colleagues (2008), but clinical use of PAP (Prostatic acid phosphatase) has been replaced by PSA (Prostate specific antigen) assay (Andriole and Catalona, 1991 ; Bunting,1999) . PAP was measured first by its enzymatic activity, then using counter-immunoelectrophoresis, and subsequently, in the late 1970's by Radioimmunoassay (RIA). Its use was proposed as screening tool for prostate cancer (Gutman and Sproul, 2008). It has been used to detect the stage of prostate cancer, to correlate with the prognosis of the disease and to monitor therapy. PAP is not as sensitive as PSA for screening or for detection of early cancer (Andriole and Catalona, 1991; Bunting, 1999). It is less likely to be elevated in Benign Prostatic hyperplasia (BPH) than is PSA (Bunting, 1999). The measurement of acid phosphatase(ACP) isoenzymes is recommended as a routine screening test for patients whose serum ACP is abnormally high. This is because the isoenzyme study not only indicates the presence or absence of prostate cancer but also whether or not there is bony metastasis (Sun et al, 1981). However, with the advent of prostate specific antigen (PSA) measurement, assay of ACP and prostatic acid phosphatase (PAP) in the diagnosis, staging and monitoring of prostate cancer has taken a back-stage (Morote and de Torres, 1989). ACP and PAP estimations are still employed in most hospitals in Nigeria because of lack of resources for PSA (Eke and Sapira, 2002). On the other hand, heat stable alkaline phosphatase (HSAP), a placenta – type ALP that is expressed in gonadal and urologic cancers (Slack et al, 1981), including prostate carcinoma and metastatic diseases with bony lesions, (Schmidt et al, 1982), may play a role in the diagnosis of prostate cancer in the absence of facilities for PSA. Thus, the need for the evaluation and reappraisal of the serum activities of ACP in the presence or absence of PSA assay in the diagnosis and monitoring of prostate cancer in Nigeria. This may provide a simpler, more common and affordable method for the diagnosis of this disease and encourage hospital management to improve on the resources necessary for this diagnosis. PSA is one of the few organ- specific tumor markers. Prostate cancer is the leading cancer in older men. When detected early, it is potentially curable by

**Author for correspondence* -
E-mail: georgechuma@yahoo.com
Tel: +234-8034101608

prostatectomy. This study is aimed at finding an alternative diagnostic tool for prostate cancer diagnosis in resource limited settings..

MATERIALS AND METHODS

The study was carried out at the Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi Anambra State, Nigeria. The age groups were made up of men above 40 years. One hundred and thirty subjects were recruited. The first group consist of one hundred subjects who have prostate hypertrophy. These are the test group while the next group consist of thirty subjects who had no prostate enlargement. They served as the control group. Blood was collected from the subjects using plain sample bottles. The subjects PSA using Enzyme linked immunosorbent assay method (ELISA) and ACP using the tartrate resistant method were determined. Finally, the results obtained were analysed statistically using SPSS system.

Ethical approval: This was obtained from the Ethical committee of the Nnamdi Azikiwe University Teaching Hospital Nnewi and informed consent of the participants was sought and obtained.

Acid phosphatase (ACP) determination: This was done according to the method of tartrate resistant (Bais and Edward, 1976). Three 19mm clean tubes were set up in tube rack for each known serum and labeled total, non prostatic and blank. One milliliter of buffer and substrate were pipette into each tube. One tube for the standard was set up and 1ml of substrate and buffer was transferred to this tube. Then 50ul of tartrate buffer was added to all tubes labeled non prostatic. Also 100ul of sample was added to all tubes labeled total test and non prostatic test. Blanks and standard were incubated at 37oc for 1hour. At the end of 1 hour, all the tubes were removed from the incubator. Then 1ml of 0.5N NaOH, 0.5NSodium bicarbonate, 4-aminophenazone, potassium ferricyanide was added and mixed after 1hour. Absorbance was then read at 520nm.

Prostate specific antigen (PSA) assay: This was carried out using a solid phase enzyme linked immunosorbent assay system. Here, 25ul each of the serum reference and control was pipette into appropriate well. Then 100ul of the PSA enzyme reagent was added to each well. The microplate was gently swirled for 20-30 seconds to mix, and then was covered and incubated for 30minutes at room temperature. The contents of the microplate were decanted. Then 300ul of wash buffer was added, this was followed by decantation. This process was repeated two times. After, 100ul of working substrate solution was added to all well. It was incubated at room temperature for 15 minutes. Also 50ul of stop solution was added to each well, it was mixed gently for 15-20 seconds. The absorbance was read at 450nm in a microplate reader within 30 minutes of adding the stop solution.

RESULTS

Serum mean Total PSA, Total ACP and Prostatic ACP were significantly higher in the test group compared with the controls but %Free PSA was higher in the control group (P<0.05).

Table 1:
T- Test table comparing the means of total PSA, total ACP, % free PSA and prostatic ACP of the test and control subjects respectively.

Parameters	Control (n =30) Mean ± SD	Test (n=100) Mean ± SD	F Value	P Value
Total PSA	2.85 ± 0.85	53.81 ± 40.0	48.50	P<0.05
Total ACP	7.29 ± 1.73	25.60 ± 10.57	88.76	P<0.05
% free PSA	43.16 ± 20.77	13.42 ± 3.94	186.01	P<0.05
Prostatic ACP	2.43 ± 0.94	7.80 ± 4.71	38.30	P<0.05

Table 2:
Correlation table comparing the relationship between total PSA and total ACP , total PSA and non prostatic ACP, total PSA and prostatic ACP , % free PSA and prostatic ACP.

Parameters	Pearson correlation coefficient (r)	P- value
Total PSA and total ACP	0.039	(P>0.05)
Total PSA and non prostatic ACP	-0.013	(P>0.05)
% free PSA and total ACP	0.055	(P>0.05)
Total PSA and prostatic ACP	0.070	(p>0.05)
% free PSA and non prostatic ACP	-0.026	(P>0.05)

This table shows that there was a positive correlation between Total PSA and Total ACP, and between Total PSA and Prostatic ACP though the values were not significantly different (P>0.05). Also there was a negative correlation between Total PSA, and non Prostatic ACP and between %Free PSA and non Prostatic ACP and the values are equally not significant (P>0.05).

Table 3:
Comparison of Age, Total PSA, % Free PSA and Prostatic ACP

Age	Total PSA	% Free PSA	Prostatic Acp
51-60 N=17	37.0±40.7	12.83±4.4	6.20±4.1
61-70 N=36	48.73±38.7	13.46±4.0	8.27±4.4
71-80 N=33	64.73±38.8	13.74±3.5	8.02±5.1
81-90 N=17	65.28±39.7	14.02±5.1	8.00±5.0
P Value	0.079	0.898	0.493

This tables shows the relationship between Age, Total PSA , % Free PSA and Prostatic ACP . There was no significant difference between the age groups in Total PSA, % Free PSA and Prostatic ACP (P>0.05)

DISCUSSION

This study shows that there is significant difference in PSA and ACP levels in the test subjects when compared with the control subjects (P>0.05). The relationship of total PSA with

prostatic ACP had weak positive correlation. However, the values obtained were not of significant difference (P>0.05). These results agree with the work of (Taira et al, 2007). They reported an increase in both total PSA and total ACP in prostate hypertrophy. These were as a result of concomitant increase in the tumours and the rise in the secreation of PSA and the production of ACP. There had been an earlier report on elevated PAP in malignant conditions and bone metastasis of other cancers by (Gutman and Sproul, 2008). Similarly, prostatitis and acute urinary retention can also raise PSA concentration. This pattern was also observed by Stamey et al, (1991), who found out that the pathological stages of tumor extension and metastases are associated with increase in both PSA and ACP, since tumors secreate PSA and produce ACP.

On the other hand, there was a negative correlation between total PSA with non prostatic ACP, and %free PSA with non prostatic ACP but again, the values obtained were not significantly different (P>0.05). This collaborates with the work of Taira et al, (2007), which reported an increase in Total PSA and Total ACP in prostate hypertrophy. The non Prostatic ACP is a fraction of Total ACP which comes from other tissues like erythrocytes, and platelets. Also the relationship between Age, Total PSA, % Free PSA and Prostatic ACP is shown in this study. There was no significant difference between the age groups in Total PSA, % Free PSA and Prostatic ACP (P>0.05). There was a difference in the PSA mean values in the different age classifications (37.07±40.7, 48.43± 38.7, 64.73±38.8 and 65.28±39.7), respectively. A similar scenario was noticed in % Free PSA (12.83±4.4, 13.46±4.0, 13.74±3.5 and 14.02±5.1), respectively. A slight decrease in the mean values was observed in the Prostatic ACP within age groups of 71-80 and 81-90. This may be explained by the fact that most of the patients under these age groups may have been on therapy.

In conclusion, Prostatic ACP may be useful as an alternative tool for prostate cancer diagnosis. Its usefulness is invaluable in rural settings where resources are mostly limited and skilled personnel difficult to find. However, PSA assay still remain the gold standard procedure for early detection and subsequent management of prostate cancer.

Competing Interests: The authors wish to state that there is no competing interest whatsoever.

Author's Contributions

MPO, EVO & CGO conceived the study, collected samples and drafted the manuscript. OCC, CRC & OCNC were involved with sample analyses, data collection, literature search and statistical analysis while OSI, OAO, OOMTB & AJC were involved with sample collection, analyses and review of the manuscript.

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