Original Article

Association of Plasma Zinc and Prostate-Specific Antigen in Patients with Prostatic Cancer in Khartoum

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Abstract

Background: Prostate cancer is the most common visceral cancer in males, ranking as the second most common cause of cancer-related deaths in men older than 50 years of age, after carcinoma of the lung. It is predominantly a disease of older males, with a peak incidence between the ages of 65 and 75 years. This study aimed to estimate the plasma zinc level and plasma prostate-specific antigen (PSA) level in patients suffer from prostate cancer. **Materials and Methods:** A case–control study was conducted in Khartoum on 100 males aged more than 50 years old which were divided into 50 apparently healthy as control and 50 with prostate cancer as case. A 5 ml of blood specimens was collected in lithium heparin anticoagulants for the estimation of plasma zinc level using Buck model 210 VGP Atomic Absorption Spectrophotometer (East Norwalk, CT 06855) made in the USA and the plasma total PSA that was measured by immunoassay Sandwich principle HITACHI ROCHE COBAS E 411 (serial number 04641655190 V 13.0). **Results:** The mean level of plasma zinc was 0.35 mg/L ± standard deviation [SD] 0.14 in case and in control was 0.68mg/L ± SD 0.13, so the *P* value was 0.002 and PSA was 43.08 ng/ml ± SD 20.08 in case and 3.53 ng/ml ± SD 3.90 in control, so the *P* value was 0.000, the correlation between the level of plasma PSA with plasma zinc in patients with prostate cancer give *R* was 0.01 and R^2 was 0.001. **Conclusion:** This study concluded that PSA is significantly increased in patients with prostate cancer and plasma zinc level is significantly decreased in patients with prostate cancer. However, it is statistically significant.

Keywords: Cancer, prostate, zinc

Introduction

The prostate gland is often described as walnut-shaped organ that surrounds the beginning of the urethra in the male.[1]

The most commonly occurring disorders of prostate include prostatitis, benign prostatic hyperplasia (BPH), and prostatic carcinoma.[2]

Prostate cancer is the most common visceral cancer in males, ranking as the second most common cause of cancer-related deaths in men older than 50 years of age, after carcinoma of the lung.[3]

Genetic factors have also been implicated, based on the increased risk of the disease among first-degree relatives of prostate cancer.[4]

It is well-known that normal human prostate glands accumulate almost 10-fold higher zinc as compared to other soft tissues, such as liver and kidney.[5,6] Accumulation of cellular zinc and secretion of zinc into the prostatic fluid in prostate glands are essential functions of the prostate secretory epithelial cell. [7] In addition low zinc concentration in seminal plasma may affect the mobility of sperm which can result in infertility in men.[8,9]

The cancer detection rate using measurement of prostate-specific antigen (PSA) is between 2% and 4%, and approximately 30% of men with an elevated PSA will have prostate cancer confirmed by biopsy. Unfortunately, 20% of men with clinically significant prostate cancer will have PSA values within the normal range. There is therefore controversy over the usefulness of PSA alone as a screening procedure.[10]

Access this article online

Quick Response Code:

Website: www.matrixscimed.org

DOI: 10.4103/mtsm.mtsm_8_21

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How to cite this article: Mohammed N, Saeed AA, Mahdi MA. Association of plasma zinc and prostate-specific antigen in patients with prostatic cancer in Khartoum. Matrix Sci Med 2022;6:23-6.

Received: 16-04-2021, **Revised:** 05-10-2021, **Accepted:** 07-10-2021, **Published:** 25-01-2022

The prostate examination

Prostate-specific antigen

PSA is a glycoprotein that is a serine protease. Its function may be to facilitate liquefaction of semen, but it is a marker for prostatic disease. It is measured by an immunoassay, and the normal range can differ a little from laboratory to laboratory. The levels increase with age, with prostate cancer, and with BPH. There are age-related values, but, in general, in men aged 50–69 years, a level of about 3–4 ng ml^{-1} would prompt a discussion about the need for prostate biopsy. Cancer usually has serum PSA levels <10–15 ng ml^{-1}. Although PSA is a reliable marker for the progression of advanced disease, it is neither specific nor sensitive in the differential diagnosis of early prostate cancer and BPH, as both diseases are compatible with PSA in the range of 3–15 ng ml^{-1}. PSA measurement has superseded measurement of serum acid phosphatase. In summary, about 25% of men with a PSA of 4–10 ng ml^{-1} have prostate cancer (i.e., it is not very specific), and about 15%–20% of men with a PSA of 1–4 ng ml^{-1} have prostate cancer. The majority of PSA circulates in serum while bound to protease inhibitors, such as a1-antichymotrypsin and a2-macroglobulin, while the remaining PSA exists unbound or free. Processes, such as inflammation, hyperplasia, and neoplasia, within the prostate, lead to disruption of physiological barriers and increased basement membrane permeability and thus increased release of PSA into the circulation.[11]

Zinc

Zinc is an essential trace element and deficiency is common throughout life, especially in individuals that do not ingest meat. The usual methods for zinc determination in serum plasma[12] have been flame atomic absorption spectrometry or instrumental neutron activation analysis.[13]

Zinc as an antitumor agent in prostate cancer

The normal human prostate gland epithelium has the function of accumulating high levels of zinc. In prostate cancer, this capability is lost as an early event in the development of the malignant cells. The mechanism and factors responsible for the ability of the normal epithelial cells to accumulate and loss of this capability in the malignant cells need to be identified.[14-17] Although zinc is an essential mineral in human nutrition, many people have insufficient zinc status due to low dietary intake, the recommended daily intake of zinc is 12 mg for women and 15 mg for men.[18]

Objectives

General objective

- To associate between the levels of plasma zinc and PSA among Sudanese patients with prostate cancer.

Specific objectives

- To estimate the level of plasma zinc and PSA in control and in case
- To compare between the levels of plasma zinc and PSA in control and in case
- To correlate between the levels of plasma zinc with plasma PSA in patients with prostate cancer.

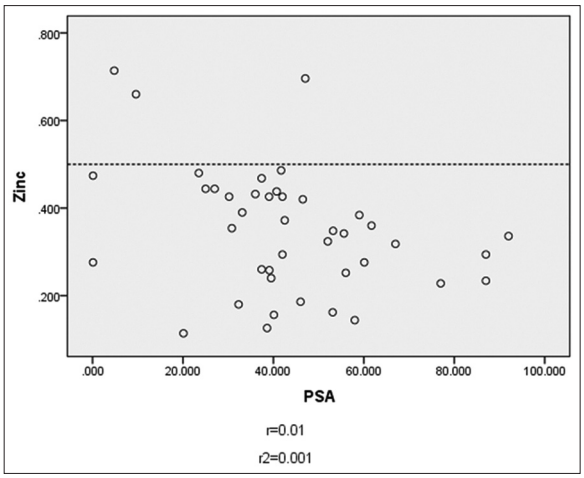

Figure 1: Correlation between the levels of plasma prostate-specific antigen with plasma zinc in patients with prostate cancer

Table 1: Comparison between the means of plasma zinc in healthy individuals as control and in patients with prostatic cancer as case group

Case/control	*n*	Mean±SD	*P*
Zinc (mg/l)			
C: Means control	49	0.68±0.13	0.002
P: Means patient	48	0.35±0.14	

P<0.5 significant. SD: Standard deviation

Table 2: Comparison between the mean of plasma prostate-specific antigen in healthy individuals as control and in patients with prostatic cancer as case group

Case/control	*n*	Mean±SD	*P*
PSA (ng/ml)			
C: Means control	48	3.53±3.90	0.000
P: Means patient	44	43.08±20.80	

P<0.5 significant. SD: Standard deviation, PSA: Prostate-specific antigen

Materials and Methods

Materials

A case–control study was conducted in Khartoum hospital and International hospital during the period between September and October 2019 on 100 males aged more than 50 years old which were divided into 50 apparently healthy as control and 50 with prostate cancer as case.

Five milliliter of venous blood specimen was collected in heparinized containers, plasma was separated by centrifugation at 3000 rpm for 5 min.

Ethical consideration

The study was approved by the Ethical Committee of National University, Sudan.

Verbal consent

Participants were provided a written informed consent.

Methods

Instruments

Plasma PSA was measured using HITACHI ROCHE E COBAS 411 (serial number 04641655190 V 13.0), the reagent that was used in this method to estimate total PSA was M. Streptavidin coated micro particles (transport cap), R1 anti–PSA-AB-biotin (gray cap), R2 Anti-PSA-Ab labeled with ruthenium complex.

Plasma zinc was measured using Buck model 210 VGP Flame Atomic Absorption Spectrophotometer (East Norwalk, CT 06855). Zinc standards are prepared by diluting the stock standard solution, described in the "Standard Conditions" for zinc, with 5% (v/v) glycerol.

Principles

- Sandwich principle for PSA: Total duration of the assay was 18 min.
- First incubation: 20 µL of sample, a biotinylated monoclonal PSA-specific antibody, and a monoclonal PSA-specific antibody labeled with a ruthenium complex were react to form a sandwich complex.
- Second incubation: After addition of streptavidin-coated microparticles, the complex was bound to the solid phase via interaction of biotin and streptavidin
- The reaction mixture was aspirated into the measuring cell where the microparticles were magnetically captured onto the surface of the electrode. Unbound substances were then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which was measured by a photomultiplier
- Results were determined via a calibration curve which is an instrument specifically generated by 2-point calibration and a master curve provided via the reagent barcode or barcode.

For zinc, the buck 210 VGP atomic absorption spectrophotometer was designed to measure the concentration of elemental metal in solution, it provides integrated measurements in absorbance or emission intensity, as well as sample concentration in comparison to standard solutions.

Results

The mean level of plasma zinc was 0.35 mg/L ± standard deviation [SD] 0.14 in case and in control was 0.68mg/L ± SD 0.13, so the P value was 0.002 and PSA was 43.08 ng/ml ± SD 20.08 in case and 3.53 ng/ml ± SD 3.90 in control, so the P value was 0.000, the correlation between the level of plasma PSA with plasma zinc in patients with prostate cancer give R was 0.01 and R2 was 0.001 [Figure 1, Table 1 and Table 2].

Discussion

There is a statistically significant difference between the level of plasma zinc in patients with prostate cancer and healthy individuals, the plasma zinc level in prostate cancer patients is lower than healthy and also there is a statistically significant difference between the level of plasma PSA in patients with prostate cancer and healthy individuals, the plasma PSA level in prostate cancer patients is higher than healthy, this study agree with that prostate cancer is the second leading cause of cancer death among men after lung cancer, and it has been shown that plasma zinc level in blood was decreased in many kinds of malignancies including prostate cancer,[3] and a study by Tiwari *et al*. in September 2004 in India stated that plasma zinc level (compared to normal individuals) decreased in patients with carcinoma prostate and level of plasma PSA high when compared to normal individuals.[19]

Pamela *et al*. stated that BPH or prostate carcinoma may be associated with a reduction in the levels of tissue zinc, plasma zinc, and an increase in urine zinc/creatinine.[20]

Another study by Pamela Christudoss *et al*. stated that prostatic carcinoma associated with a reduction in the level of plasma zinc.[20]

Another study by Rahman *et al*. found that zinc level has got statistically significant difference between control and prostatic cancer patients ($P < 0.000$) and total PSA was also significantly different between case and control ($P < 0.006$).[21]

Conclusion

PSA is significantly increased in patients with prostate cancer. Plasma zinc level is insignificantly decreased in patients with prostate cancer.

Recommendation

More studies must be done in this area, the results suggested that screening for prostate cancer using PSA in men at ages 50–60 years should focus on those with PSA levels in the top quartile, zinc level for patients with prostate cancer must be estimated, and men aged over 40 should consider zinc supplementation for a variety of reasons including maintaining healthy prostate tissue zinc levels.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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