

**SERUM ZINC AND COPPER LEVELS IN BENIGN AND MALIGNANT LESIONS OF PROSTATE****C. REKHA* AND V. PRAVEENA**

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ABSTRACT

To estimate the levels of serum zinc, copper and prostate specific antigen in patients with benign prostatic hyperplasia (BPH) and prostate carcinoma (PCa) and to correlate their levels as screening test in the diagnosis of prostate neoplasms. Serum zinc and copper were estimated in 25 patients of BPH and 18 patients with PCa over a period of one year. All patients were males and aged between 55 and 75 years. Age matched 25 male patients without BPH or PCa were taken as controls and serum zinc and copper were estimated in them also. An attempt was made to correlate the zinc/copper levels ratio in both diseases. The mean levels of serum zinc were raised significantly in BPH ($152 \pm 25.94 \mu\text{g/dl}$) and lowered significantly in PCa ($84.8 \pm 33.11 \mu\text{g/dl}$) than in controls ($110.0 \pm 20.20 \mu\text{g/dl}$), $p < 0.001$. The mean levels of serum copper were raised significantly in both BPH ($179.10 \pm 55.19 \mu\text{g/dl}$) and in PCa ($154.10 \pm 45.45 \mu\text{g/dl}$) than in controls ($112.00 \pm 17.95 \mu\text{g/dl}$), $p < 0.05$. Prostate specific antigen was increased significantly in PCa ($47.18 \pm 8.53 \text{ ng/ml}$) than in BPH ($6.50 \pm 2.25 \text{ ng/ml}$) and controls ($2.78 \pm 0.73 \text{ ng/ml}$), $p < 0.05$. The mean value of copper/zinc ratio was significantly more in PCa (2.08 ± 0.81) than in BPH (1.23 ± 0.55) and controls (1.04 ± 0.19), $p < 0.05$. The significantly high level of serum zinc in BPH and low level in PCa, along with high copper/zinc ratio and markedly increased levels of prostate specific antigen in PCa helps to differentiate BPH from PCa.

KEY WORDS: Serum zinc, serum copper, prostate specific antigen, benign prostatic hyperplasia, prostatic cancer.

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INTRODUCTION

Among the diseases of the prostate, benign prostatic enlargement (BPH) and prostate cancer (PCa) are of great clinical importance. It is well known that normal human prostate accumulates higher zinc than any other soft tissue in the body¹. Globally, many studies have shown that serum zinc levels are raised in BPH and lowered in PCa¹⁻⁵. Zinc and copper are homeostatically regulated minerals which are components of metalloenzymes and are important for cell growth, replication, osteogenesis and immunity³. The pub med search revealed few studies only from north India on serum zinc and copper levels in prostate neoplasms^{1,2,4} and none from south India. Therefore, we undertook this study to estimate the levels of serum zinc and copper in patients with benign prostatic hyperplasia(BPH) and prostate carcinoma (PCa) and to correlate their levels as screening test in the diagnosis of prostate neoplasms.

MATERIALS AND METHODS

The estimation of serum zinc, copper and prostate specific antigen was done in 25 patients with BPH and 18 patients with prostate cancer, admitted in the urology ward of Gandhi hospital over a period of one year. All the patients were males and aged between 55 and 75 years. Age matched 25 subjects without urinary symptoms and clinical findings of BPH or PCa were taken as controls (normal) for this study.

Inclusion criteria

BPH and PCa patients were included. Patients with grade III and IV hyperplasia of prostate were included in this study. The symptoms of urgency and difficulty in passing urine, findings of per rectal examination and findings of ultrasound examination of lower abdomen were used for grading of prostate hyperplasia. Fine needle aspiration cytology was performed to rule out the malignancy. The diagnosis of prostate cancer was based on the symptoms of haematuria, raised serum prostate specific antigen levels and biopsy confirmed histopathological features of

malignancy. Some patients had symptoms of spread of malignancy in the bladder and urethra.

Exclusion criteria

All the patients were subjected to routine blood investigations like full blood count, blood sugar, serum proteins, blood urea, serum creatinine, and lipid profile; and patients with anaemia and hypoproteinemia were excluded from the study since these two conditions are associated with low serum zinc level and high serum copper level⁴. All the patients and control subjects were informed about the purpose of taking blood samples and a consent was taken. This study was approved by the Ethics committee of Gandhi Hospital. Collection and processing of samples: 5 ml of blood was collected by the vein puncture in specific bottles (zinc and copper free containers issued by the laboratory of the National Institute of Nutrition (NIN), Tarnaka, Hyderabad. In all cases, care was taken to prevent haemolysis of red blood cells as they contain high zinc element. The collected blood samples were centrifuged within one hour and the serum was refrigerated in polypropylene screw capped test tubes, and stored at - 20^o C and transported to NIN. Two (2) ml of serum was diluted with deionised water and then 5 ml of analar concentrated nitric acid was added. After mixing the samples well, they were allowed to stay at room temperature for three hours. Then, they were centrifuged for 10 minutes at 2500 rpm. The supernatant obtained was transferred to plastic bottles using chemically cleaned pipette; after adding double distilled water was preserved at room temperature. The sample thus obtained was subjected to atomic absorption spectrophotometer (AAS) analysis technique for serum zinc and copper levels using GBC Aventa 2.01 equipment. Prostate specific antigen was estimated by solid phase enzyme linked immunosorbent assay (ELISA) technique. The data was expressed as mean \pm standard deviation and analysed statistically using Man-Whitney test as the data of zinc, copper, prostate specific antigen, copper/zinc ratio were non-Gaussian in nature. P value of < 0.05 was considered as significant.

RESULTS

The mean values of serum zinc, copper, prostate specific antigen and copper/zinc ratio estimated in BPH, PCa patients and control subjects are shown in Table 1. The serum zinc was raised significantly in BPH and lowered significantly in PCa than in controls ($p <$

0.001). On the other hand, serum copper was raised significantly in both BPH and in PCa than in controls ($p < 0.05$). The prostate specific antigen was increased significantly in PCa than in BPH and controls ($p < 0.05$). The copper/zinc ratio was significantly more in PCa than in BPH and controls ($p < 0.05$).

Table 1
Mean serum values of zinc, copper, prostate specific antigen and copper/zinc ratio

Parameter	Control subjects (n=25) mean \pm $\mu\text{g/dl}$	Benign prostatic hyperplasia(n=25) mean \pm $\mu\text{g/dl}$	Prostate cancer (n=18) mean \pm $\mu\text{g/dl}$	P value
Zinc	110.0 \pm 20.2	152.1 \pm 25.94	84.8 \pm 33.11	< 0.001
Copper	112.0 \pm 17.95	179.1 \pm 55.19	154.1 \pm 45.45	< 0.05
Prostate specific antigen	2.78 \pm 0.73	6.5 \pm 2.25	47.17 \pm 8.53	< 0.05
Copper/zinc ratio	1.04 \pm 0.19	1.23 \pm 0.55	2.08 \pm 0.81	< 0/05

DISCUSSION

Human prostate gland epithelial cells have the unique capability of accumulating high levels of zinc. The cellular accumulation of zinc inhibits mitochondrial terminal oxidation and respiration. Zinc accumulates exhibit anti-proliferative effects via its induction of mitochondrial apoptosis. Zinc accumulation also inhibits the invasive/ migration activities in malignant prostate cells, and this process

occurs through zinc activation of specific intracellular signalling pathways. Consequently, these effects impose anti-tumour actions by zinc trace element. In our study serum zinc levels were increased in BPH and decreased in PCa. Similar studies were reported by Jain et al⁴, Tiwari et al¹, Goel and Shankwar², Lekili et al⁵.

Table 2
Comparison of serum zinc levels in benign prostatic hyperplasia (BPH) and prostate carcinoma (PCa)

Author	Controls $\mu\text{g/dl}$	BPH $\mu\text{g/dl}$	P Ca $\mu\text{g/dl}$
Jain et al ⁴	105.0 \pm 8.5	114.5 \pm 10.5	91.9 \pm 13.4
Tiwari et al ¹	94.5 \pm 10.38	172.7 \pm 5.27	59.6 \pm 3.08
Goel and Shankwar ²	94.5 \pm 10.38	172.7 \pm 5.27	59.6 \pm 3.08
Lekili et al ⁵	---	93.1 \pm 15.19	62.8 \pm 12.71
Present study	110.0 \pm 20.2	152.1 \pm 25.94	84.8 \pm 33.11

Lowered serum zinc levels in PCa patients was reported by Adaramoye⁶, Whelan et al⁷, Brys et al⁸, Li et al⁹, Costello et al^{10,11}, Chirulescu et al¹², Ozomen et al¹³. Christudoss et al¹⁴ reported a reduction in the levels of tissue zinc, plasma zinc and an

increase in urine zinc/creatinine ratio in BPH and PCa patients. However, Habib et al³ reported that plasma zinc levels were not affected by disease, whereas the plasma copper levels were significantly higher in the benign and malignant lesions of prostate.

Table 3
Comparison of serum copper levels in benign prostatic hyperplasia (BPH) and prostate carcinoma (PCa).

Author	Controls µg/dl	BPH µg/dl	P Ca µg/dl
Habib ³	84.0	124	
Jain et al ⁴	93.3 ± 9.31	113.2 ± 10.5	105.5 ± 8.2
Present study	112.0 ± 17.95	179.1 ± 55.19	154.1 ± 45.45

In our study, copper/zinc ratio was significantly raised in PCa patients when compared to BPH patients and control subjects. This is supportive of the diagnosis of prostate cancer. Zinc is known to be physiological antagonist of copper and this may be responsible for hypozincemia and hypercupremia observed in malignant lesion of the prostate. Raised PSA levels in BPH and highly raised levels in PCa patients observed in our study proves to be an important

biological tumour marker for prostate neoplasms as reported by Sardana et al¹⁵.

CONCLUSION

From the results of our study, it is concluded that the significantly higher level of serum zinc in BPH and low level in PCa, along with high copper/zinc ratio and markedly increased levels of prostate specific antigen in PCa helps to differentiate BPH from PCa.

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