Original Article

Comparative study of zinc levels in benign and malignant lesions of prostate

V. S. Tiwari, Asha Agrawal, Suhel Mohd., Vipul Agrawal
Department of Surgery and Pathology, G.S.V.M. Medical College, Kanpur - 208002, India.

ABSTRACT

Background: Normal human prostate accumulates higher level of zinc than any other soft tissue in the body. In contrast, the zinc levels in prostate cancer are markedly decreased from the levels detected in non-prostate tissues. Earlier techniques of estimation of Zinc ion (chemical estimation or polarography) did not help to arrive at a specific correlation of the metal ion with development of disease. Atomic absorption spectrophotometry (AAS) has been used in this study to find out if there is any change occurring in the serum zinc levels under diseased conditions.
Aims: This study aims to investigate the serum zinc levels in disorders of prostate, so as to find a correlation to either reinforce or refute any claims of a relationship between them as a diagnostic or screening tool.
Materials and Methods: This study was conducted on 80 patients with symptoms of prostatic diseaseof prostatic disease (normal baseline group comprised of 20 men, who had normal prostate on initial workup).Blood samples of all 80 cases and prostate tissue of 60 patients with enlarged prostate were taken for analysis. Serum sample was subjected to Atomic Absorption Spectrophotometry (AAS) for analysis of serum zinc levels. For statistical analysis student's 't' test (unpaired) was used.
Results: Serum zinc levels showed an approximate rise of 78% in cases of benign prostatic hypertrophy while a fall of approximately 37% in those with prostate cancers as compared to normal individuals.
Conclusion: The plasma zinc levels (as compared to normal individuals) were markedly raised in cases of benign prostatic disease and were dramatically lowered in patients with carcinoma prostate. This clearly indicates that both these diseases signify the opposite ends of the wide spectrum with regards to serum zinc levels; and that it can prove as an evaluation tool for the diagnosis / screening of prostate diseases.
Also, the mean plasma zinc level in cases of carcinoma prostate with dissemination was not very diverse from those without metastasis. This indicated that metastasis in cases of carcinoma prostate had practically no effect on plasma zinc levels.

KEY WORDS

Benign Prostatic Hypertrophy , prostate cancers, serum zinc levels.

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INTRODUCTION

The prostate gland is one of the most intriguing organs of the human body, a very valuable member of the male genital constellation. This disease finds mention in the Egyptian papyri as early as 1500 BC. Prostate has been found to undergo benign hypertrophy and neoplastic transformation in a considerable number of men during old age. It is well known that normal human prostate accumulates higher level of zinc than any other soft tissue in the body. In contrast, the zinc levels in prostate cancer are markedly decreased from the levels detected in non-prostate tissues. Despite these relationships, the possible role of zinc in the growth of normal and malignant prostate has not been determined as yet. Further study is needed to

Address for correspondence: Dr. V. S. Tiwari, Department of Surgery, G.S.V.M. Medical College, Kanpur - 208002, UP, India.
E-mail: vipags@yahoo.co.in, shreevant_t@rediffmail.com
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investigate the direct role as the anthropometric association with prostate disease is weak.

Zinc ion had earlier been determined with the help of chemical estimation or polarography. These techniques did not help to arrive at a specific correlation of the metal ion with development of disease. Atomic absorption spectrophotometry (AAS) has been used, which can precisely determine the most minute quantity of any metal in the tissue or plasma. Accordingly, this technology is used in this study to find out if there is any change occurring in the serum zinc levels under disease and normal conditions.

This study aims to investigate the serum zinc levels in disorders of prostate, so as to find a correlation to either reinforce or refute any claims of a relationship between them as a diagnostic or screening tool; to strengthen or disapprove the hypothesis that serum zinc levels are protective against the development of prostate cancers; and to utilize the results in formulating ways and methods in dealing with prostate pathology in question, either prognostically or therapeutically.

MATERIALS AND METHODS

This study was conducted on 80 patients of prostatic disease. The normal baseline group comprised of 20 men (age matched) who presented with some symptoms of prostatic disease, but upon investigating no disease of prostate gland could be elicited and the symptomatology was due to some other disorder like urethritis, urinary tract infection, neurogenic bladder, etc. A blood sample was obtained from these patients. The disease cases, were patients (60 in number) presenting with complaints of prostate disease and of age group 35 to 84 years. A sample of prostatic tissue along with a blood sample was taken from them. Then, depending upon the final histopathological diagnosis they were divided into two groups:

Control group: comprising of normal baseline group and patients with benign prostatic hypertrophy
Study group: comprising of patients with prostate cancers.

A sample of prostatic tissue was obtained from patients with benign prostatic hypertrophy (either by open or transurethral prostatectomy) and prostate cancers (age group 35 to 84 years) either via FNAC or by closed perineal biopsy with Vim Silvermann needle or specimen obtained during transrectal ultransongraphy using a biopsy forceps or tissue removed during an operative procedure like TURP or open prostatectomy.

From all these patients and those in the baseline normal group blood sample was collected. The blood was allowed to stand at room temperature (25 ± 2° C) for approximately 6 hours and then centrifuged to obtain a serum sample, which was stored in small aliquots and kept in deep freeze (-20° C) till analysis. The serum sample thus obtained was subjected to Atomic Absorption Spectrophotometric (AAS) analysis technique and the serum zinc levels were analysed. The AAS applied was Beckman System Model 495, which is based on atomic property unique to each element. For statistical analysis we have used the student's 't' test (unpaired) to calculate the pooled estimate or variance in the data obtained from our present study; leading to calculation of the significance or "*P*" value. '*P*' value thus obtained is considered significant if $P<0.05$ and highly significant if $P<0.01$.

RESULTS

Serum zinc levels showed an approximate rise of 78% in cases of benign prostatic hypertrophy while a fall of approximately 37% as compared to normal individuals in those with prostate cancers (Table 1). Comparison of serum zinc levels of normal group (no prostatic disease) with all other patients finds out a correlation ('*P*' value) between them. In our study the '*P*' value was highly significant (0.0001), (Table 2 and Table 3).

We have correlated between serum zinc levels and prostate specific antigen (PSA) levels in prostate cancers patients.(Table 4) which showed the correlation

Table 1: Serum zinc levels in patients under study

Diagnosis	No. of cases	Min. (µg/dl)	Max (µg/dl)	Mean (µg/dl)	S.D. (±)
No disease	20	80	112	94.5	10.38
BPH	40	165	180	172.7	5.27
FM. Pr.	06	130	155	145.4	9.67
Ch. Pr.	04	160	165	162.4	2.22
Pr. Cancer	10	55	65	59.6	3.08

BPH = Benign Prostatic Hypertrophy FM. Pr. = Fibromuscular prostate; Ch. Pr. = Chronic prostatitis Pr. Cancer = Prostate Cancer.

Table 2: Comparative study of serum zinc levels of normal (no disease) cases with all other patient groups

Diagnosis	T (Test value)	P (Predictive value)
BPH	38.9	0.0001
FM. Pr.	10.7	0.0001
Ch. Pr.	12.8	0.0001
Pr. Cancer	10.3	0.0001

Table 3: Comparative study of serum zinc levels in benign prostate hypertrophy cases and prostate cancer cases under study

Diagnosis	No. of cases	Mean ± S.D.	T	*P*
Benign Prostatic hypertrophy	50	168.6±10.71	18.4	0.0001
Pr. Cancer	10	59.6±3.08		

Table 4: Correlation between serum zinc levels and psa levels in cases of prostate cancer

Diagnosis	No. of cases	Mean PSA (ng/ml)	Mean Zn (µg/dl)	t	*P*
Pr. Cancer	10	17.8	59.6	12.2	0.0001

between the two and this relationship is also significant (*P* value being 0.0001).

DISCUSSION

The study carried out by Elizabeth et al[1] emphasized serum zinc levels to the range between 94 – 186 µg/dl in benign prostatic hypertrophy. Similar studies were carrried by Schrodt et al[2] and Dhar et al[3] on prostatic tissue exhibiting comparative results. Lagiou et al[4] showed zinc (an element that is selectively concentrated in prostate) was significantly positively associated with benign prostatic hyperplasia risk. Liang et al[5] showed inhibitory effect of zinc on human prostatic carcinoma cell growth, possibly due to induction of cell cycle arrest and apoptosis. Costello et al[6] showed that zinc inhibits mitochondrial aconitase and exerts its importance in the citrate metabolism of prostatic epithelial cells. The intramitochondrial accumulation of high zinc levels inhibits m-aconitase activity which inhibits citrate oxidation. This essentially truncates the Kreb's cycle and markedly decreases ATP production (normally coupled to citrate oxidation). These relationships form the basis of a new concept of the role of zinc and citrate related energy metabolism in prostate malignancy. The inability of carcinoma cells to accumulate high zinc levels results in increased citrate oxidation and the coupled ATP products essential for progression of malignancy (Iguchi et al[7]).

Feng et al[8] showed similar effects of high intracellular accumulation levels of zinc in prostate cells inducing mitochondrial apoptogenesis. A human prostate cancer cell line, which is zinc accumulating, was exposed to a medium supplemented with physiological levels of zinc for approximately 24 hours. Zinc treatment resulted in the translocation of cytochrome-c from the mitochondria to cytosol, the activation of caspase-9 and caspase-3, and eventually, the cleavage of nuclear poly ADP ribose polymerase. (PARP). This represents a newly identified physiological effect of zinc in the regulation of prostate cell growth. All this has opened up new realms; as to whether supplements of zinc either via diet or locally into the prostate gland can help prevent prostate cancers from developing. Numerous researches and studies are underway for this.

On comparing, a significant value ($P<0.01$) is obtained very similar to studies carried out earlier. Kristal et al,[9] Lagiou et al,[10] Brys et al,[11] Fuestal et al,[12] Zaichick et al.[13] This clearly indicates that both these diseases signify the opposite ends of the wide spectrum with regards to serum zinc levels; and that it can prove as an evaluation tool for the diagnosis / screening of prostate diseases; if raised pointing to a benign pathology; and it lowered, malignancy. Thus, it clearly reinforces the claims of serum zinc levels as a means of diagnosing prostatic disease.

CONCLUSION

The plasma zinc levels (as compared to normal individuals) were markedly raised in cases of benign prostatic disease and were dramatically lowered in patients with carcinoma prostate. This clearly indicates that both these diseases signify the opposite ends of the wide spectrum with regards to serum zinc levels; and that it can prove as an evaluation tool for the diagnosis / screening of prostate diseases; if raised pointing to a benign pathology; and if lowered, malignancy. Thus, it clearly reinforces the claims of serum zinc levels as a means of diagnosing prostatic disease.

Another aspect which was found was that the mean plasma zinc level in cases of carcinoma prostate with dissemination was not very diverse from those without metastasis. This indicated that metastasis in cases of carcinoma prostate had practically no effect on plasma zinc levels, though more study into this aspect is warranted.

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Forthcoming Events

EVENT	The 64th Annual Conference of the Association of Surgeons of India
DATE, VENUE	*December 26th to 30th, 2004*
CONTACT	Dr Mohan Gupta, Organising Secretary, ASICON 2004 Aarogya Hospital, Twin City Market, 5-4-183 to 199, Moazam Jahi Market. Hyderabad - 500001, India. Tel: 0091-40-30903994, 55624687, Tele/Fax:0091-40-24744223, E-mail: asicon_2004@yahoo.com / asicon20004@rediffmail.com
EVENT	IAGES Mid Term Conference Laparo Link : 2005
DATE, VENUE	*January 28th - 30th, 2005,* Coonoor: Nilgiris, Tamilnadu
CONTACT	Dr. V. Venkatesh, Organizing Chairman IAGES Mid Term Conference, Indian Institute of Laparoscopic Surgery, Research and Training Centre, V.G. Hospital, Mettupalayam Road, Coimbatore - 641 034, Tamil Nadu, India. Tel: 2642772, 2642071. Mobile: 98430 64045. E-mail: vghospital@eth.net
EVENT	National CME of Indian Association of Surgical Gastroenterology
DATE, VENUE	*February 6th 2005, Silver Okas Hospital, Mohali*
CONTACT	Prof. S. P. Kaushik, Silver Okas Hospital, Phase IX, Sector 63, SAS Nagar, Mohali - 160 063, India. Tel.: +91-172-2211303 / 2211308 / 2211309.
EVENT	ENDOSURGERY'05
DATE, VENUE	*February 24th / 25th / 26th, 2005, Ayushman, New Delhi*
CONTACT	Dr. Pradeep Chowbey, Organizing Chairman, Ayushman, Double Storey Market, R-Block, New Rajinder Nagar, New Delhi - 110 060, India. Tel.: +91-11-25821768 / 25748085 / 28741188 / 28742929. Fax.: +91-11-26519935/25748085. E-mail: info@endosurgery05.com /chowbey1@vsnl.com
EVENT	8th Annual Conference of Indian Society of Wound Management WOUNDCON?2005 and CME Programme on Wound Care
DATE, VENUE	*March 5th & 6th, 2005, Science City, Kolkata*
CONTACT	Dr. Tuhin Kanti Biswas, Organising Secretaray, WOUNDCON - 2005, J. B. Roy State Ayurvedic Medical College and Hospital, 170-172, Raja Dinendra Street, Kolkata - 700004, India. Tel.: +91-33-28730842 (Off) / (0)9433173272 (Mobile). Tele Fax : +91-33-22233260. E-mail: biswastuhin@rediffmail.com