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Original article

A case-control study to evaluate alteration in manganese levels of prostate in benign prostatic hyperplasia

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Abstract:

Introduction-Levels of different elements have been assessed in benign prostatic hyperplasia to evaluate their role in the pathophysiology. The present study was conducted to assess the level of manganese in prostate gland to ascertain its significance.

Methods-Tissue from prostate was collected from 83 benign prostatic hyperplasia cases and 71 age and sex matched healthy controls and manganese levels were determined.

Observations and results-Manganese content of dry and wet specimens of prostatic tissue in benign prostatic hyperplasia cases was found to be highly significantly increased with respect to controls.

Conclusion-Altered levels of manganese in prostate in benign prostatic hyperplasia suggests a role of manganese in the pathophysiology, which should be elucidated by further research.

Keywords : Benign prostatic hyperplasia, manganese, hydrolase, decarboxylase, superoxide dismutase

Introduction

Benign prostatic hyperplasia poses a significant public health problem (1). BPH is first detectable around the fourth decade of life and affects nearly all men by the ninth decade. The resulting enlargement of the prostate gland can lead to urethral obstruction and even complete urinary retention (2). Symptoms from BPH are a major source of morbidity, if not mortality, especially in the older population in all countries. The natural progression of benign prostatic hyperplasia (BPH) has two phases. The first, or pathological phase of BPH, in turn, has two stages, termed microscopic and macroscopic BPH. Almost all men in the world will eventually develop microscopic BPH if they live long enough. But only approximately half of the men with microscopic BPH will ultimately progress to macroscopic enlargement of the gland (i. e., macroscopic BPH), implying that additional factors are involved in the conversion of microscopic to macroscopic BPH. Though several partially overlapping and complementary theories have been proposed to explain the etiology of the pathological phase of BPH, none have been able to unequivocally confirm the specific mechanism (3). And scientists are still a long way from clinching the exact mechanism of evolution of normal prostate gland into BPH; thus, the pathogenesis of BPH is still largely unresolved.

Many trace elements play important parts in various metabolic pathways in our body. Levels of different elements like zinc, cadmium, magnesium, etc have been evaluated in BPH to ascertain their significance (4, 5).

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Aims and objectives

So, the present study was conducted to assess the level of manganese (Mn) in prostate gland, to facilitate understanding the pathophysiology of BPH.

Materials and methods

The present research work was conducted in a tertiary care medical college and hospital for 1 year and 11 months. Samples were collected from 83 BPH cases and 71 age and sex matched healthy controls (without any prostate related problems). Informed consent and ethical committee clearance was taken from the appropriate authorities and persons.

Transrectal puncture biopsy of appropriate regions of the prostate of all cases was done. BPH was diagnosed by history, clinical examination and histopathological study of biopsy material. The controls had died due to problems not related to prostate or our study. Tissue samples were taken from the prostates of controls as soon as possible after death.

Samples from all cases and controls were coded and divided into two portions: for morphological study and for Mn analysis.

Samples for Mn analysis were weighed, freeze-dried and homogenized. Then these samples were sealed separately in clean polyethylene packets.

Then Mn analysis was done by UV-VIS molecular absorption spectrometry by the method of Mirea et al (6). All samples were assayed in a blind fashion by an investigator who was unaware of the participant's clinical status. Statistical analysis of data was performed using SPSS software version 20 (IBM, New York, USA), and inferences were drawn. A value of $p < 0.05$ was considered to be statistically significant and $p<0.001$ highly significant.

Observations and results

For dry weight

P value and statistical significance:

The two-tailed P value equals 0.0013

By conventional criteria, this difference is considered to be very statistically significant.

Confidence interval:

The mean of cases minus controls equals 0.1400

95% confidence interval of this difference: From 0.0556 to 0.2244

Intermediate values used in calculations:

t = 3.2779

df = 152

standard error of difference = 0.043

SEM= 0.0263 and 0.0344 for cases and controls respectively.

For wet weight

P value and statistical significance:

The two-tailed P value equals 0.0002

By conventional criteria, this difference is considered to be extremely statistically significant.

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Confidence interval:

The mean of cases minus controls equals 0.0900

95% confidence interval of this difference: From 0.0435 to 0.1365

Intermediate values used in calculations:

t = 3.8270

df = 152

standard error of difference = 0.024

SEM= 0.0187 and 0.0131 for cases and controls respectively.

Table 1. Prostate Mn levels, as Mean ± SD, in mg/kg, in cases and controls

	Dried weight	Wet weight	n
Cases	1.26±0.24	0.57±0.17	83
Controls	1.12±0.29	0.48±0.11	71

SD=Standard deviation, n=number of subjects

Discussion

In our body Mn has many roles- it is a cofactor for hydrolases, decarboxylases and transferases; it is important in glycoprotein and proteoglycan synthesis and it is a component of mitochondrial superoxide dismutase (SOD) (7). Superoxide dismutase in humans can have 3 forms: cytosolic and extracellular (containing copper-zinc), and mitochondrial (containing Mn). In literature, data about Mn concentration or role in BPH is sparse; still there is variation in opinion about the levels of Mn in prostate in BPH: Mn concentration was found to be decreased by Abul et al (8), but Kwiatek and workers found increased levels of Mn in BPH (9), whereas some researchers obtained unchanged levels of Mn (10). In the present study, Mn content of dry and wet specimens of prostatic tissue in BPH cases was found to be highly significantly increased with respect to controls (table 1).

Prostatic acid phosphatase is well known to be elevated in BPH (11). Ornithine decarboxylase activity is also raised in BPH (12). Prostatic acid phosphatase is a hydrolase and Ornithine decarboxylase is a decarboxylase, both of which require Mn as cofactor, as mentioned earlier. Total SOD levels are unchanged (13) and Cu-Zn SOD levels are decreased in BPH (14, 15); but we could not find any literature regarding levels of Mn-SOD in BPH. In our opinion, in BPH, Mn content of prostate is increased, which is reflected in elevated levels of Mn-containing enzymes like Prostatic acid phosphatase and Ornithine decarboxylase; Mn-SOD levels might also found to be increased if estimation is carried out, but this data will require further research.

This study has limitations that should be considered. To assess Mn, spectrophotometric method was used. Mn can be estimated by various methods, but the present method was employed as it is commonly used, time tested and simple. Also, number of patients in the study groups was not large. Thus, care must be taken in extrapolating the present findings to other populations. Patients were taking some medications for BPH. However, these drugs are

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characteristic of patients with BPH and do not affect serum Mn levels. We conducted the present study in a tertiary care hospital. However, in our country, most people visit district, subdivisional, and lower-tier hospitals for treatment. Hence, results of our study might not reflect the true picture of the population as a whole. Probably, a multicentric study on a larger population would be better in revealing the actual statistics. Despite these limitations, we believe that increased levels of Mn in prostate in our study point towards the importance of Mn in the pathophysiology of BPH.

Conclusions

Altered levels of Mn in prostate in BPH suggests a role of Mn in the pathophysiology, which should be elucidated by further research with a multicentric study on a larger population with evaluation of other elements.

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