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CHANGES IN BIOCHEMICAL MARKERS OF HYPERPLASTIC AND MALIGNANT PROSTATIC TISSUES

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Some biochemical markers were evaluated in human prostatic tissue obtained from patients with benign hyperplasia. There was an almost threefold increase in the activity of acid phosphatase of these patients as compared to that of normal men. The changes in the acid phosphatase activity were directly correlated with citric acid concentration. Significant ($p < 0.001$) increases in the content of citric acid, zinc, and calcium in benign hyperplastic prostates was found. There was no change in the activity of aminopeptidase. The activities of both enzymes were lower in malignant prostatic tissues.

Key Words: Hyperplasia; Markers; Cancer; Prostatic.

INTRODUCTION

Certain biochemical parameters are useful in the diagnosis of malignancy and the progression of tumors [1, 5, 21]. Prostatic acid phosphatase occurs in its highest concentrations in seminal plasma and shows androgen dependence [17, 19]; this is a possible diagnostic indicator for the development of prostatic carcinomas [2, 23]. In human prostatic carcinoma and benign prostatic hyperplasia, nuclear androgen receptor levels change in comparison to the normal prostate [6, 11]. The concentration of Zn, which exhibits very high levels in the human prostate, is correlated with prostatic carcinoma, showing reduced values during malignancy [8, 10] and relatively higher levels in benign prostatic hyperplasia [20].

The present study was undertaken to evaluate the possible changes in the biochemical markers of the prostate in normal, benign prostatic hyperplasia and malignant human prostates.

MATERIALS AND METHODS

Human benign prostatic hyperplastic and cancerous tissues were obtained from Calcutta National Medical College and Hospital (Calcutta, 700 014, India) and the Institute for Post-Graduate Medical Education and Research (Calcutta, India). The tissues were obtained from open prostate surgery. Normal human prostates were obtained from the morgue of Calcutta Medical College Hospitals within 4 to 6 hr

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TABLE 1 Variation in the Levels of Some Marker Components of Normal, Benign Hyperplastic, and Malignant Prostat Tissues

Cases (number of patients)	Acid phosphatase (mg PNP/ml/min)	Citric acid (μg/ml)	Zinc (μg/ml)	Calcium (μg/ml)	Aminopeptidase (μg β-naphthylamine/ml/min)	Protein (mg/ml)
Normal (7)	2.45 ± 0.4	37 ± 4.4	4.2 ± 1.1	28 ± 1.7	31.7 ± 3.7	5.3 ± 0.3
Benign (7)	6.96 ± 0.1	104 ± 7.9	33.1 ± 4.6	50 ± 4.5	30.3 ± 2.2	5.2 ± 0.1
Malignant (2)	1.00 ± 0.2	23 ± 5.5	9.4 ± 3.2	38 ± 7.5	18.9 ± 6.9	5.2 ± 0.8
p values between normal and benign	$p < 0.005$	$p < 0.001$	$p < 0.001$	$p < 0.001$	Insignificant	Insignificar

Values are mean ± SEM.

after the accidental death of normal men between 42 and 63 years of age. Copland et al. [3] stated that acid phosphatase activity in prostatic tissues of patients with benign hyperplasia or carcinoma has no correlation with the age of the patient. Postmortem stabilities of the enzymes were checked.

Prostatic tissues were immediately placed on crushed ice, minced, and homogenized in 0.025 mol/L sodium acetate buffer, pH 5. The homogenates were centrifuged at 10,000 × g for 15 min. All steps were carried out at 0° to 4°C. Supernatants were collected and were used to assay enzymatic and nonenzymatic parameters. Only two cancerous samples could be obtained during a period of 15 months, and therefore statistical evaluations were not performed with values obtained from malignant prostates. Acid phosphatase activity was measured [9] using p-nitrophenylphosphate as a substrate and 100 mmol/L acetate buffer, pH 5. Aminopeptidase activity was estimated [13] using L-leucine-β-napthylamide HCl as a substrate. Zine and calcium concentrations were measured [4, 7], and citric acid concentration and total protein were estimated [15, 18].

RESULTS

Table 1 shows the changes in the levels of several enzymatic and nonenzymatic constituents of the normal, benign prostatic hyperplastic and cancerous prostatic tissue homogenates. A statistically significant ($p < 0.005$) increase in the activity of acid phosphatase was observed in benign prostatic hyperplasia as compared to that of the normal prostate tissue. There was a decrease in the activity of cancerous prostate tissue. The level of aminopeptidase activity remained the same when compared with benign hyperplastic tissue and the control; however, a decrease was demonstrated in malignant tissues. Among the nonenzymatic parameters, a highly significant ($p < 0.001$) increase in concentrations of zinc and calcium was observed in benign prostatic hyperplasia when compared to normal prostate tissue. In carcinoma, however, there was only a twofold increase in the zinc level. Citric acid also showed a highly significant ($p < 0.001$) increase in concentration in the benign hyperplastic prostates. In cancerous prostates, the concentration was decreased, whereas total protein content was unchanged.

DISCUSSION

A direct relationship was found between the prostatic acid phosphatase activity and citric acid concentration, with a parallel threefold increase in benign prostatic hyperplastic tissues in comparison to normal prostate tissue. The result is of significance for the early detection and screening of benign prostatic growth. However, malignant prostate tissue appears to

have less enzymes and citric acid, when measured on a wet-weight basis. Copland et al. [3] also showed that the specific activity of acid phosphatase in tissues with benign prostatic hyperplasia was significantly higher than that in prostatic tissues with carcinoma. Lad et al. [12] stated that prostatic acid phosphatase activity is elevated as a result of the increase in the number of cells rather than the enhanced secretion during prostatic cancer. The present results do not support the results of Lad et al. [12] and show significantly higher contents of the enzyme with concomitant significant increases in citric acid and zinc levels in benign prostatic hyperplasia. However, the decrease in malignant cases could not be explained at this stage, although Woodard [22] reported lower activities of acid phosphatase in carcinomatous prostates. Among the cations, zinc and calcium contents showed significant increases in benign prostatic hyperplasia as a result of the high levels of these components in citric acid in primary tumors.

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