

Alpha₁-Antitrypsin, Alpha₂-Macroglobulin and Complement C4 in Human Benign Prostatic Hyperplasia

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Summary. The concentrations of the globulins α_1 -antitrypsin, α_2 -macroglobulin and complement C4 have been determined in tissue samples of benign prostatic hyperplasia, from patients with and without prior treatment before open surgery. Globulins have been determined by means of radial immunodiffusion. Results obtained show that α_1 -antitrypsin is present in high concentrations in human prostate. Treatment with anti-androgens influences the α_2 -macroglobulin concentration in the different prostatic lobes. Complement C4 concentration is not influenced by the treatment.

Key words: BPH, α_1 -antitrypsin, α_2 -macroglobulin, Complement C4, Radial immunodiffusion.

Introduction

Agargel electrophoresis of prostate homogenates showed an important α_1 -globulin, which could be identified as α_1 -antitrypsin (α_1 -AT) by means of immunoelectrophoresis. Alpha₂-macroglobulin (α_2 -M) is also present. These two proteins play a role in the inhibition of proteolytic enzymes. Complement C4 has been studied by Grayhack [3] in prostatic fluid and its level is increased in prostatic carcinoma.

The aim of the present study was to quantify these three globulins in the prostatic tissue of treated and untreated patients with benign prostatic hyperplasia (BPH).

Material and Methods

44 BPH tissues (32 from untreated patients and 12 from patients treated with anti-androgens), obtained after open surgery, were brought to the laboratory in liquid nitrogen. The samples were treated immediately or stored at -87°C . Homogenates of the tissues were made following the technique of Van Camp [8]. Total protein was measured by the biuret method [2].

Normal prostates were not available. Autopsy material is unsuitable for the study of proteins, due to the high proteolytic activity of prostatic tissue [9].

The globulins α_1 -AT, α_2 -M and C4 were determined by the method of Mancini et al. [4], in commercially available plates (Behringwerke, Marburg, FRG).

Results obtained are expressed in mg globulin per g protein in the homogenate. The values obtained from treated and untreated patients were analysed statistically, using a non parametric test [6], $P < 0.05$ is considered as significant.

Results

The results obtained for α_1 -AT are represented in Table 1.

Statistical examination of the results obtained shows no significant difference when comparing the mean values of all the untreated and treated patients ($0.10 < P < 0.20$). For the mean value of the lateral and median lobes of the untreated patients: $0.60 < P < 0.70$; for the treated patients (test of Wilcoxon) no significant difference between lateral and median lobes has been found.

α_2 -M is present in much lower concentrations in human prostate. The values obtained are represented in Table 2.

Statistical Analysis: There is no difference between the means of the treated and untreated patients ($0.70 < P < 0.80$). Also, the mean values for the lateral and median lobes are not different ($0.40 < P < 0.50$).

However, there exists a significant difference of the α_2 -M-concentration between the mean and lateral lobes of the treated patients: $0.02 < P < 0.025$. That means that the α_2 -M-concentration in the median lobe is significantly higher than in the lateral lobes. It should be noted that there is no significant difference between the α_2 -M-levels of the median lobe in treated and untreated patients ($0.40 < P < 0.50$). C4 is present in rather low concentrations in prostate homogenates. Our results obtained are represented in Table 3.

Statistical analysis of the results did not show any significant difference: Treated patients/untreated patients:

Table 1. Alpha 1-antitrypsin concentrations in 48 homogenates of treated and untreated BPH

	<i>n</i>	M	SEM
Untreated patients	36	16.38	1.27
Lateral lobes	26	15.96	1.50
Median lobes	10	14.45	2.35
Treated patients	12	12.34	2.11
Lateral lobes	6	11.70	—
Median lobes	6	12.77	—

Results in mg/g protein

n = number of cases; M = mean value; SEM: standard error of the mean**Table 2.** Alpha-2-macroglobulin concentration in 44 homogenates of treated and untreated BPH

	<i>n</i>	M	SEM
Untreated patients	32	2.83	0.11
Lateral lobes	24	2.76	0.12
Median lobes	8	2.95	0.25
Treated patients	12	3.00	0.23
Lateral lobes	6	2.63	0.27
Median lobes	6	3.73	0.23

Results in mg α_2 M/g protein*n* = number of cases; M = mean value; SEM: standard error of mean**Table 3.** C4 concentration in 33 homogenates of treated and untreated BPH

	<i>n</i>	M	SEM
Untreated patients	32	2.68	0.64
Lateral lobes	24	2.50	0.35
Median lobes	8	3.22	0.97
Treated patients	12	2.96	0.57
Lateral lobes	6	2.67	0.80
Median lobes	6	3.25	0.86

Results in mg C4/g protein

n = number of cases; M = mean value; SEM = standard error of the mean

$0.60 < P < 0.70$; Untreated lateral lobes/untreated median lobes: $0.30 < P < 0.40$; Treated cases: lateral lobes/median lobes: $0.60 < P < 0.70$.

Discussion

α_1 AT is a 50,000 molecular weight glycoprotein. It is present in serum as the major α_1 -globulin, comprising approximately 4% of the total serum protein level. This protein has been found to possess inhibitory activity against a

broad spectrum of proteolytic enzymes. It is the major inhibitor of chymotrypsin and is also an effective inhibitor of trypsin. One mol of antitrypsin inactivates 2 mol of trypsin, so that 1 g of antitrypsin is equivalent to 0.91 g of trypsin [1]. Other authors describe that 1 mg α_1 AT inhibits 0.20–0.50 mg trypsin [5]. Anyhow, the relative small size of α_1 AT allows it to enter in a wide variety of body fluids and tissues where it is assumed that a broad-spectrum protein inhibitor might be useful in counteracting the tissue-damaging effects of enzymes [7].

α_2 M appears to be the most effective collagenase inhibitor. Furthermore, α_1 AT can complex with an enzyme, e.g. chymotrypsin, and then transfer this enzyme to α_2 M.

For α_1 AT, it has been demonstrated that the serum level increases during the administration of oestrogens; this way it might be assumed that this protein is hormone dependent.

Our results obtained on α_1 AT on prostatic tissue show:

a) that it is quantitatively the most important α -globulin in prostatic tissue;

b) that anti-androgens have no influence on its level in the prostate.

For α_2 M, which has a much lower concentration in prostatic tissue, it could only be demonstrated that anti-androgen therapy does not change the total level of this protein in the prostate, but that in the treated cases the concentration increases significantly in the middle lobe, compared with the lateral lobes.

Grayhack et al. [3] have found a significantly higher value of C4 in the prostatic fluid of adenocarcinomatous patients, compared with BPH-patients. However, the authors did not study the influence of anti-androgen therapy on the C4-levels in BPH-prostatic fluids. Our results indicate that C4 is unchanged in prostatic tissue by anti-androgen medication. Studies on the precursor of C4, i.e. complement C3, could perhaps give further information. Our results obtained for untreated BPH can serve as a reference for comparison with those obtained in prostatic cancer tissue.

In summary, our results indicate that:

a) α_1 -antitrypsin is the major α -globulin in BPH tissue. Its level is not influenced by anti-androgen therapy.

b) α_2 -macroglobulin has a rather low concentration in BPH tissue. During treatment with anti-androgen, the total concentration does not change, but in the treated patients, the ratio of the concentration of the median and lateral lobes changes.

c) The complement C4 in BPH-tissue is not influenced by anti-androgen therapy.

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