Urol Res (1987) 15:161–163

Urological Research

Zinc, Cadmium and Selenium Concentrations in Separated Epithelium and Stroma from Prostatic Tissues of Different Histology

A. Feustel[1], R. Wennrich[2] and H. Dittrich[2]

[1] Department of Urology, Markkleeberg Hospital Leipzig
[2] Department of Chemistry, Karl-Marx-University Leipzig, German Democratic Republic

Accepted: January 12, 1987

Summary. The concentration of Zn, Cd and Se in unseparated tissues and epithelial and stromal fractions of normal prostate gland, BPH and prostatic carcinomas of different histological grading were determined by flameless AAS. There were distinct differences in the content of Zn, Cd and Se in the epithelial and stromal fractions depending on histology. In all cases the concentration of these elements in the epithelial fractions was higher than in stromal fractions. These differences are discussed.

Key words: Prostatic tissues, Epithelial and stromal fractions, Zn, Cd, Se concentrations

Introduction

Previous studies showed a distinct biological antagonistic effect with Zn and Cd in the prostatic gland. We found an increased content of Zn in BPH and a decrease of this element in prostatic cancer compared to normal prostatic tissues. We also found a continous increase of Cd concentration from normal prostate through BPH to carcinomas [3]. These results were confirmed by the identfication of these trace elements in the cellular fractions of the prostatic tissues of different histology [4]. The stroma – epithelial interaction in the prostate is important in the formation and accumulation of DHT [1, 8, 12]. Therefore it was interesting to analyze the concentration of Zn, Cd and Se, which may be protective in cancer, as suggested in bladder cancer [6, 14, 15]. We measured the three elements separated in epithelium and stroma, in comparison to the whole tissue, of normal human prostate, BPH and carcinoma of different histology.

Part of this paper was presented at the 5th Congress of the European Society for Urological Oncology and Endocrinology, 18–20 August 1986, Edinburgh, UK

Materials and Methods

Prostatic tissues of 10 BPH, 9 carcinomas of different grade and of 5 normal prostates taken at autopsy were examined. One part of each sample was taken for separation into epithelial and stromal portions and the other part was used as a control. Separation was effected by collagenase (SERVA) in a Krebs-Ringer-buffer at 37 °C for 1 h. The epithelial cells were separated from the stroma by centrifugation (15 min 800 *g*). The fractions were dried and washed in nitric acid (Suprapur, Merck). The sample solutions were analyzed by flameless atomic absorption. Cd and Zn were measured by graphite furnace technique, Se was analyzed with hydride generation. In all cases the standard addition technique was used.

Results

Zn Investigations

The Zn concentration in stroma and epithelial fractions of BPH was increased compared with those of normal prostate. In carcinoma the Zn concentration was decreased in the whole tissue in comparison to normal prostate and BPH as previously reported [3, 5]. The Zn level in epithelial fractions of BPH and also in carcinoma was higher than in the stroma. It was interesting that the Zn concentration in the stromal fractions of adenocarcinoma was similar to those of BPH. The poorly-differentiated carcinoma showed the lowest Zn-levels in the stromal fraction. In the prostates of healthy mean there was no difference in the Zn concentration between stroma and epithelium. Contrary to this the Zn values in BPH and carcinoma showed an increase in the epithelial fractions.

Cd Investigations

The Cd-investigations showed higher concentrations in the epithelial fraction than in the stroma in all cases. Though we had found the highest levels of Cd in the unseparated tissues

Table 1. Zn concentration in prostatic tissues (μg/g dried samples)

histology	*n*	unseparated tissues	stromal fraction	epithelial fractions
normal	5	488 ± 190	208 ± 128	181 ± 85
PBH	10	1,177 ± 485	394 ± 256	2,586 ± 1,429
Adenocarcinoma	7	440 ± 216	344 ± 216	936 ± 925
poorly-diff. Ca.	2	316 ± 86	61 ± 8	470 ± 86

Table 2. Cd-concentrations in prostatic tissue (μg/g dried samples)

histology	*n*	unseparated tissues	stromal fractions	epithelial fractions
normal	5	0.50 ± 0.26	0.47 ± 0.30	0.86 ± 0.55
BPH	10	0.65 ± 0.31	0.47 ± 0.24	1.06 ± 0.96
Adenocarcinoma	7	0.70 ± 0.17	0.37 ± 0.25	0.52 ± 0.11
poorly-diff. Ca.	2	0.80 ± 0.20	0.20 ± 0.10	1.10 ± 0.33

Table 3. Se-concentrations in prostatic tissues (μg/g dried samples)

histology	*n*	unseparated tissues	stromal fractions	epithelial fractions
normal	5	0.60 ± 0.21	0.74 ± 0.16	0.49 ± 0.02
BPH	10	0.76 ± 0.37	0.87 ± 0.77	1.89 ± 1.22
Adenocarcinoma	7	0.71 ± 0.32	0.80 ± 0.45	1.20 ± 0.71
poorly-diff. Ca.	2	0.38 ± 0.24	0.46 ± 0.16	0.60 ± 0.47

of prostatic carcinoma there were no significant differences between the stromal and epithelial fractions from normal prostate, as in BPH and carcinoma. This observation could be interpreted in connection with the results of Webber [15] who found that only a small change of the Cd concentration in presence of transferrin induced a decline in epithelial cell growth.

Se Investigations

The results of Se levels were similar to the Cd levels in all fractions and in the unseparated tissue. The unseparated tissues from prostatic carcinoma revealed decreased amounts of Se compared with normal prostate and with BPH. This is similar to the results of previous investigations in bladder cancer [6]. We also found higher values of Se in the epithelial fraction than in the stroma. It was interesting that the concentration of Se in the epithelial fraction of BPH was higher than in the epithelial fraction from normal prostate. The molar relation of Se to Cd in the epithelium was equal, in normal tissues and in poorly-differentiated carcinoma. In contrast to this we found that Se was more evident in the epithelium of BPH and of adeno-carcinoma.

Conclusions

In agreement with the results obtained by Habib and other authors [7, 8, 9, 11] we confirm the general decrease of the Zn concentration from BPH through normal to poorly-differentiated carcinoma. In our investigations it seemed that the relationship of the Zn-concentration between the stromal and epithelial fractions is strongly diminished in poorly-differentiated carcinoma in comparison to normal prostate. These results indicate the possible role of disturbed enzyme biosynthesis and protein metabolism which depend upon Zn concentration in carcinomatous tissues.

We generally found higher Zn levels in epithelium than in stroma as a possible expression of the RNA and DNA synthesis and the action of the carboanhydrases and other enzymes.

The role of Cd in the carcinogenesis and its interactions with Zn inside the prostate is complicated [10, 13]. The higher amount of Cd found in the epithelium compared with stroma in normal tissues and in prostatic cancer could be due to the higher amount of specific metal-binding protein in the prostatic epithelium.

The role of Se as a possible inhibitor for chemical carcinogenesis was discussed by several investigators [2, 6, 14,

Table 4. Conclusion

Zn:	– epithelial concentration > stromal – lowest Zn-levels in stromal fractions of cancer
Cd:	– unseparated tissues: Concentration in cancer increased – epithelial concentration > stromal
Se:	– lowest Se-levels in prostatic cancer

15]. Se shows a strong tendency to form complexes with metals. Investigations suggest that Se may play a role in inhibition of both the initiation and promotion stages of carcinogenesis. It can inhibit the activation of carcinogens requiring metabolic interaction and accelerate their detoxification [15]. Se also has the ability to abolish the growth, stimulatory effect of Cd which may be important in prostatic carcinogenesis. In agreement with this statement we found the lowest Se concentration in the whole tissues of prostate cancer. We could not find any significant differences of Se-levels in the stromal fractions of BPH, normal prostates and adenocarcinoma. The Se concentration in the stroma of poorly-differentiated carcinoma was decreased.

In the epithelial fraction of both BPH and of adenocarcinoma selenium was promiment as was zinc. This may confirm an interaction of Zn and Se in the cellular growth.

References

1. Cowan RA, Cowan SK, Grant JK, Elder HY (1977) Biochemical investigations of separated epithelium and stroma from benign hyperplastic prostatic tissue. J Endocrinol 74:111–120
2. Dürre P, Andreesen JR (1986) Die biologische Bedeutung von Selen. Biologie in unserer Zeit 16:12–23
3. Feustel A, Wennrich R, Steiniger D, Klauß P (1982) Zinc and cadmium concentration in prostatic carcinoma of different grading in comparison to normal prostate tissue and adenofibromyomatosis (BPH). Urol Res 10:301
4. Feustel A, Wennrich R (1984) Zinc and cadmium in cell fractions of prostatic cancer tissue of different histological grading in comparison to BPH and normal prostate. Urol Res 12: 147
5. Feustel A, Wennrich R (1984) Determination of the distribution of zinc and cadmium in cellular fractions of BPH, normal prostate and prostatic cancer of different histology by atomic and laser absorption spectrometry in tissue slices. Urol Res 12: 253–256
6. Feustel A, Wennrich R, Vorberg B (1986) Schwermetallgehalte in Zellfrationen menschlicher Harnblasentumoren und normaler Harnblase. 8th Symp Exp Urol Mainz, July 1986
7. Habib FK, Mason MK, Smith PH, Stitch SR (1979) Cancer of the prostate: early diagnosis by zinc and hormone analysis. Br J Cancer 39:700–704
8. Habib FK, Tesdale AL, Chisholm GD, Busuttil A (1980) Androgen metabolism in the epithelial and stromal components of the human hyperplastic prostate. J Endocrinol 91:23–32
9. Habib FK, Leake A, Beynon L, Chisholm GD (1984) Studies on the relationship between zinc and androgens in the human prostate. Adv Urol Oncol Endocrinol, Rome, pp 143–150
10. Hoffmann L, Putzke HP, Kampehl HJ, Russbult R, Gase P, Simon C, Erdmann T, Huckstorf C (1985) Carcinogenic effects of cadmium on the prostate of the rat. J Cancer Res Clin Oncol 109:193–199
11. Lathonen R (1985) Zinc and cadmium concentrations in whole tissue and in separated epithelium and stroma from human benign prostatic hyperplastic glands. Prostate 6:177–183
12. McLoughlin MG, Bruchowsky N (1983) Stromal – epithelial interaction. In: Hinman F Jr (ed) Benign prostatic hypertrophy. Springer, New York
13. Piscator M (1981) Role of cadmium in carcinogenesis with special reference to cancer of the prostate. Environ Health Perspect 40:107–120
14. Salonen JT, Salonen R, Lappeteläinen R, Mäenpää PH, Alfthan G, Puska P (1985) Risk of cancer in relation to serum concentration of selenium and vitamines A and E: matched case control analysis of prospective data. Br Med J 290:417–420
15. Webber MM (1985) Selenium prevents the growth stimulatory effects of cadmium on human prostatic epithelium. Biochem Biophys Res Commun 127:871–877

Prof. A. Feustel
Department of Urology
Markkleeberg Hospital
Leipzig
GDR