Study of Parathyroid hormone, Cortisol and Calcium in the Serum of Non-metastatic Prostate Cancer Patients Cohorts in Iraq

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Abstract: The causes of prostate cancer (PCa) are not well understood (1). There is an endogenous and exogenous factor that affects PCa incidence (2). Calcium (Ca) regarded as an endogenous factor and it has been shown to be a principle factor for increasing proliferation cell of the prostate (3). Parathyroid hormone (PTH) functions to increase calcium uptake in the elementary tract and to mobilize calcium from bone. Parathyroid hormone PTH is now understood to have mitogenic effects for prostate cancer cells (4). Cortisol is the active form of glucocorticoids, produced and secreted by the adrenal cortex (5). Results have showed there is no significant difference (p>0.05) in calcium level between PCa patients and control respectively (8.89 ± 1.50, 9.24±0.34 mg/dl) and cortisol level in PCa patients with control respectively (325.08±12.3, 319.33±15.1 nm/l). There is no significant differences (p>0.05) in PTH level between PCa patients than control group respectively (56.62±11.54, 56.15±10.12 pg/ml). Conclusion: These findings may be important to get new promising treatment or new biomarker for PCa. More studies should be achieved in Iraq.

Keywords: Prostate, cancer, PTH, Calcium, Cortisol.

Introduction

Prostate cancer (PCa) ranks the 10th among leading cancers in male in Iraq (Iraqi Tumor Registry, 2009). There is 473 new cases which constitute 2.78 per 10^5 in 2011(6), and it is the second leading death from cancer in USA(7).

Many exogenous and endogenous factors affect prostate cancer incidence(3). Calcium (Ca) can activate or inhibit cellular signaling to get response like muscle contraction, synaptic transmission, cellular proliferation and apoptosis(8). A high intake of calcium is considered to be cause of prostate cancer(9). Prevention of the excess calcium flow to cancer cells due to stimulation of mitochondria and cytoplasmic pathways stopped proapoptotic steps and made the cell immortal(10). The calcium-sensing receptor (CaSR) plays a central role in calcium homeostasis and regulating parathyroid hormone (PTH) secretion and renal calcium excretion to normalize Ca(11). Parathyroid glands are four small glands located on the posterior side of the thyroid to regulate calcium serum (Tfelt-Hansen et al., 2003). Parathyroid hormone (PTH) implicated in bony metastases with (CaSR) by modulation of parathyroid hormone related peptide (PTHrP) secretion from cancer cells(11). Cancer-induced hypercalcemia (CIH) occurs in Lung cancer, breast cancer and myeloma while rarely occurs in patients with colorectal and prostate cancer(12). Hypocalcemia of severe degree is not common in patients with malignant disease(13). There is inverse relationship between secondary PTH elevation and calcium level(4). Elevated serum PTH in men associated with advanced prostate cancer(14). Cortisol produced in humans from adrenal gland cortex by the zonafasciculata. Cortisol regulates many biological processes including metabolism, behavior,
growth and cellular apoptosis via glucocorticoid receptor GR activation. Cortisol has mixed glucocorticoid and mineralocorticoid effects. Cortisol affects mutant androgen receptors AR and made it responsive to low level of cortisol which converted to cortisol by 11b-Hydroxysteroid dehydrogenase (11b-HSD) type I, which would then drive the growth of prostate cancer that related with obesity cancer. Studies on experimental animals have shown that corticosteroids could stimulate tumor growth and increased metastasis of pulmonary and mammary tumors. Obese subject have high level of serum cortisol as a result of increased rate of the synthesis due to systemic stress induced by obesity that lead to abnormal production of adipokines from adipose tissue and high level of tumor necrotic factor-alpha (TNF-α) in turn may activate tumor progression.

Material and methods

Blood samples were collected from ten (10) prostate cancer patients from AL-AMAL general hospital in Iraq/Baghdad and ten (10) healthy subjects, age matched. Blood samples were centrifuged (2000 rpm for 10 minutes), the serum immediately stored in -20°C until analysis. Serum calcium, parathyroid hormone and cortisol hormone measured by Cobas e 411 (GERMANY) using (ROSCH) kits for detection according to the manufacturer's instructions.

Statistical analysis

SPSS 20.0 programs used for least significant difference (LSD ≤0.05). Analysis of variance test (ANOVA) between sites and different studies parameters.

Results

There is slight reduction but not significant (p> 0.05) between serum calcium level of prostate cancer patients than healthy group respectively (8.89 ± 1.50, 9.24±0.34 mg/dl), (Table-1).

There is slight elevation but not significant (p> 0.05) in serum cortisol level of prostate cancer patients than healthy group (325.08±12.3, 319.33±15.1 nm/l) respectively. (Table-1)

Table -1: levels of calcium, cortisol and parathyroid hormone in prostate cancer patients and control (Mean ± SD)

<table>
<thead>
<tr>
<th>Test</th>
<th>Prostate cancer</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>serum calcium mg/dl</td>
<td>8.89 ± 1.50</td>
<td>9.24±0.34</td>
</tr>
<tr>
<td>cortisol hormone nm/l</td>
<td>325.08±12.3</td>
<td>319.33±15.1</td>
</tr>
<tr>
<td>parathyroid hormone pg/ml</td>
<td>56.62±11.54</td>
<td>56.15±10.12</td>
</tr>
</tbody>
</table>

There is no significant difference reduction in serum parathyroid hormone level of prostate cancer patients compare to healthy group (56.62±11.54, 56.15± 10.12 pg/ml) respectively, (p> 0.05) (Table-1).

Discussion

Although many experimental and clinical studies enrolled calcium and parathyroid hormone (PTH) in the development of prostate cancer, the epidemiologic data are sparse.

Calcium (Ca) homeostasis controls many cellular processes mediated signaling pathways including tumorigenesis (angiogenesis, tumors progression, invasion and metastasis). Hypocalcaemia occur when total calcium level lower than (8.5 mg/dl). This study found a slight reduction in the serum level of Calcium in the prostate cancer (PCa) patients, and this finding may be related to the low serum albumin level that bound calcium. And/or low level of vitamin D (Vit D) in the serum of prostate cancer (PCa) patients decrease the serum calcium level.

In a prospective study in Sweden, no significant association between serum calcium and fatal prostate cancer was found. Although a significant positive association was found between albumin-adjusted serum
calcium and the risk of “aggressive prostate cancers”). Authors gave a conclusion of a time-dependent association between serum calcium and the risk of fatal prostate cancer. As well bone metastases from prostate cancer are mainly blastic (bone-forming) and commonly cause increased serum levels of PTH, and subsequently hypocalcemia (calcium ions are transferred from serum into blastic bone). Cortisol considered as glucocorticoids family and it receptors (GR) closely related with androgen receptors (AR) and may have to substitute its action in case of castrated resistance prostate cancer (CRPC). Cortisol and (GR) has tumor suppresser action but less than production of androgen. Ectopic adrenocorticotropic hormone (ACTH) and/or corticotropin-releasing hormone (CRH) are associated with a growing list of tumors. High level of cortisol in CRPC is worst prognosis. This study demonstrated that rising of cortisol level in PCa patients in early stages was not significantly palpable. Resistance exercise does not appear to compromise testosterone suppression, and acute elevations in serum GH and DHEA may partly underlie improvements observed in physical function. A study by Galvão reported significantly higher PTH-rp expression in high-grade versus low-grade prostate cancers. Suggesting that an increased sensitivity of prostate cancers to PTH may contribute to bone metastasis. This study show there is no detectable elevation in (PTH) in PCa patients for two reasons, the first; all the patients are newly diagnosed with prostate cancer and have no metastasis, and the second; most middle east population (patients and control) suffer from vitamin D insufficiency and this may affect the result. Skinner& Schwartz found that serum PTH and calcium were correlated significantly with free PSA. Their findings support the hypothesis that both variables (serum calcium and PTH) stimulate prostate growth in men.

Abbreviation

Calcium -sensing receptor /CaSR , parathyroid hormone related peptide/ PTHrPPProstate cancer /PCa , parathyroid hormone /PTH, Cancer-induced hypercalcemia /CIHGlucocorticoid receptor /GR, 11b-Hydroxysteroid dehydrogenase/ (11b-HSD), castrated resistance prostate cancer (CRPC), androgen receptor (AR)

References


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