Serum 25 OH vitamin D concentrations and calcium intake are low in patients with prostate cancer

Mariela Varsavsky, Rebeca Reyes-García, María Cortés-Berdonces, Antonia García-Martin, Pedro Rozas-Moreno, Manuel Muñoz-Torres

Unidad de Metabolismo Óseo. Endocrinología. Hospital Universitario San Cecilio. Granada, Spain

Received 8 June 2011; accepted 12 July 2011
Available online 20 October 2011

Summary
Objective: To evaluate dietary calcium intake (DCI) and vitamin D serum concentrations in patients with prostate cancer.
Methods: We conducted a cross-sectional study including 91 subjects with prostate cancer. We determined DCI by a questionnaire, 25 OH vitamin D levels and bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA).
Results: According to current guidelines (1000 mg/day), calcium intake was low in patients with prostate cancer (394 ± 201 mg/day). Twenty percent (20) of patients had adequate levels of vitamin D, whereas 29.7% (27) of patients were vitamin D deficient and 48.3% (44) were classified as vitamin D insufficiency. Vitamin D levels were not different in patients with or without androgen-deprivation therapy. There were no correlation between DCI, 25 OH vitamin D and BMD.
Conclusions: In summary, in our group of prostate cancer patients DCI was low and vitamin D deficiency is highly prevalent. Although this is a common condition in other populations, in this group of patients especially prone to osteoporosis could have more relevance. Additional research is needed to establish the consequences of low calcium intake and vitamin D deficiency in prostate cancer patients.

© 2011 SEEN. Published by Elsevier España, S.L. All rights reserved.
Vitamin D deficiency remains a common condition. Serum vitamin D is not only a predictor of bone health but is also an independent predictor of risk for cancer and other chronic diseases. There are several data supporting the relationship between vitamin D deficiency and cancer prognosis. and numerous studies suggest that vitamin D deficiency is associated with an increased risk of medical complications to which patients with cancer are predisposed, i.e. infection, falls and immune dysfunction.

The effect of vitamin D in cancer processes has been demonstrated in experimental studies and may influence cancer incidence through mechanisms affecting cancer development and progression. Moreover, vitamin D deficiency has been proposed to be a risk factor for prostate cancer although increased risk of aggressive disease with higher circulating 25 OH vitamin D concentrations or no association had also been reported.

The mainstay of treatment for men with metastatic disease is androgen-deprivation therapy (ADT). Currently, ADT is increasingly prescribed to men with evidence of metastatic disease. Osteoporosis is the main complication of ADT, and the rate of osteoporosis is directly related to ADT duration. Numerous publications indicate the importance of calcium and vitamin D intake as risk factors for developing osteoporosis in men. In this population, especially prone to the development of osteoporosis, adequate calcium and vitamin D intake may be especially relevant. There are scarce data about calcium intake in prostate cancer. Previous studies had reported a calcium intake below the NIH recommendation, 1000 mg/day, in 90% of prostate cancer patients and calcium intake was an independent factor of osteoporosis. There are also a few studies reporting the frequency of vitamin D deficiency among patients with prostate cancer. There have been reported a 17% of vitamin D levels below 15 ng/ml and 75–80% of vitamin D deficient (<30 ng/ml) among patients with either clinically localized or recurrent prostate cancer.

Our aim was to evaluate calcium intake and vitamin D levels in patients with prostate cancer, and to determine the relationship between dietary calcium intake (DCI), 25 OH vitamin D and bone mineral density (BMD).
(FN: femoral neck and TH: total hip). The BMD was determined by Dual Energy X-Ray Absorptiometry (DXA; Hologic QDR 4500, Whatman, MA; variation coefficient <1%). We used the World Health Organization criteria for osteopenia and osteoporosis.

Biochemical measurements

Samples of venous blood were taken in the morning after fasting overnight. Samples were centrifuged immediately after collection at 4000 × g for 8 min. Biochemical parameters were measured by standard biochemical methods.

25 OH vitamin D was measured using a competitive radioimmunoassay (RIA) (Diasorin, Stillwater, MN, USA). The RIA is a combined measure of 25-hydroxyvitamin D$_3$ and 25-hydroxyvitamin D$_1$ which have similar biological activities. The total analytical coefficient of variation was 10%, and interassay CV was 8.6%. Vitamin D status was defined as follows: vitamin D deficiency was defined as a 25 OH vitamin D level <15 ng/ml, and insufficiency 15–30 ng/ml. Patients with 25 OH vitamin D levels above 31 ng/ml were considered as vitamin D sufficiency.

PTHrP was measured by ELISA (Roche Diagnostics SL, Barcelona, Spain). The normal values are 15–65 pg/ml. The analytical and inter assay coefficient of variation were 3%.

Other parameters

Height and weight were measured at baseline according to standard procedures. Weight was measured to the nearest 100 g using digital electronic scales. Height was measured to the nearest 1 mm using a stadiometer and a metal anthropometric tape, respectively. Body mass index (BMI) in Kg/m$^2$ was calculated as weight divided by the square of height in meters.

Statistical analysis

Data were recorded and analyzed with SPSS version 15.0 (SPSS Inc., Chicago, IL). Descriptive statistics, including means, frequencies and percentages, were used to describe the study population and look at differences between groups. Data were expressed as mean ± standard deviation (SD). A p value <0.05 was considered to be significant. The normal distribution of variables was determined by Kolmogorov–Smirnov test.

Mean values in groups were compared by parametric statistics (Student’s t-test, ANOVA) or nonparametric statistics (Mann–Whitney, Kruskal–Wallis) depending on the distribution of the variable of interest. Correlations between the variables were evaluated using Pearson’s simple and partial correlation coefficient. The association among qualitative variables was realized by means of the Chi-square test or Fisher’s exact test in case the conditions of the first one were not fulfilled.

Results

The baseline characteristics of study subjects are shown in Table 1. Patients in ADT group were older and had higher serum phosphate levels than no-ADT patients. There were no differences in other baseline characteristics according to the presence of bone metastases or ADT treatment.

PTH and 25 OH vitamin D showed an inverse correlation, but it did not reach statistical significance ($r = −0.181$, $p = 0.09$). i-PTH levels and serum calcium were negatively correlated ($r = −0.210$, $p < 0.05$). There was no correlation between i-PTH or 25 OH vitamin D and other analyzed variables (age, weight, renal function, BMI, BMD, calcium intake, prostatic specific antigen).

DCI was low in prostate cancer patients (394 ± 201 mg) according to current recommendations. Only two patients (2.2%) had a DCI of 1000 mg/day. There was no difference in calcium intake according to ADT treatment (ADT 343 ± 172 mg/day vs. no ADT 454 ± 218 mg/day, $p = 0.08$) (Table 1). Medium vitamin D levels showed no differences in patients with or without ADT (ADT 20.92 ± 12.1 ng/dl vs. no ADT 22.58 ± 10.96 ng/dl, $p = 0.51$) (Table 1). There was no correlation between DCI, 25 OH vitamin D levels and BMD.

Vitamin D deficiency and insufficiency were highly prevalent. In the entire cohort, only 22% (20 patients) of patients had adequate levels of vitamin D, whereas 29.7% (27) of patients were vitamin D deficient and 48.3% (44) were classified as vitamin D insufficiency.

Discussion

In our study a high proportion of prostate cancer patients (98%) had a DCI below the NIH recommendations (more than 1000 mg/day). Two previous studies in prostate cancer patients showed a high proportion of patients (about 90%) with a low DCI, but our data show an insufficient DCI in almost all patients. In this population, especially prone to the development of osteoporosis because of age and ADT treatment, dietary counselling and probably treatment with calcium supplements are warranted.

In our study, vitamin D deficiency was highly prevalent in patients with prostate cancer. Our data showed a higher percentage of patients with vitamin D deficiency and insufficiency than previous reports in prostate cancer patients. There have been proposed many factors contributing to low vitamin D levels: the infrequent use of vitamin D as a part of treatment, the use of inadequate doses as a result of the conservative level of vitamin D supplementation usually recommended, the limited availability of vitamin D in foods, and the use of sun screens and limited outside activity. The known consequences of vitamin D deficiency in prostate cancer, i.e. increased risk of medical complications, a possible effect in cancer progression and prognosis, and the importance of vitamin D in the development of osteoporosis confirms the relevancy of this condition.

We did not find differences in vitamin D deficiency levels according to ADT. Our results are in agreement with previous reports evaluating vitamin D levels in patients with prostate cancer that showed similar levels of vitamin D deficiency and insufficiency independently of stage of disease. However, the cross-sectional design and the low number of patients with bone metastasis do not allow to establish definite conclusions.
The determination of serum 25 OH vitamin D levels and the use of vitamin D supplements in patients with prostate cancer is low despite the likelihood that vitamin D deficiency would predispose to osteoporosis and may impair bone quality in this group of patients predisposed to bone loss. The present study shows a high frequency of low vitamin D levels among patients with prostate cancer that warrants attention to vitamin D levels determination and careful repletion in this group of patients.

This study has some limitations. The cross-sectional design does not allow to determine a relationship between serum vitamin D levels and the progression of disease. Strengths of the study are the well characterized cohort of prostate patients, the evaluation of DCI by a validated questionnaire, the determination of 25 OH vitamin D levels in all patients, and the evaluation of BMD in all patients by DXA.

In summary, in prostate cancer patients dietary calcium intake is low according to current recommendations and vitamin D deficiency is highly prevalent. Additional research is needed to establish the consequences of low calcium intake and vitamin D deficiency in prostate cancer patients. Dietary counselling and adequate treatment with calcium and vitamin D supplements could improve bone health in this group of patients.

### Conflict of interest
The authors declare that they have no conflict of interest.

### References


### Table 1  Baseline characteristics of study subjects. Data expressed as n, n (%), or mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>No ADT</th>
<th>ADT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>91</td>
<td>42</td>
<td>49</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70.4 ± 6.2</td>
<td>67 ± 5</td>
<td>73 ± 5†</td>
</tr>
<tr>
<td>Body weight</td>
<td>81.5 ± 12.7</td>
<td>82.29 ± 13.71</td>
<td>80.9 ± 11.93</td>
</tr>
<tr>
<td>BMI</td>
<td>29.5 ± 3.9</td>
<td>29.52 ± 4</td>
<td>29.51 ± 3.8</td>
</tr>
<tr>
<td>Physical activity (hours/week)</td>
<td>5.4 ± 3.2</td>
<td>5.0 ± 3.2</td>
<td>5.8 ± 3.14</td>
</tr>
<tr>
<td>Calcium intake (mg/day)</td>
<td>394 ± 201</td>
<td>454 ± 218</td>
<td>343 ± 172</td>
</tr>
<tr>
<td>LS BMD (g/cm²)</td>
<td>948 ± 177</td>
<td>953 ± 156</td>
<td>942 ± 200</td>
</tr>
<tr>
<td>FN BMD (g/cm²)</td>
<td>775 ± 139</td>
<td>793 ± 138</td>
<td>753 ± 141</td>
</tr>
<tr>
<td>TH BMD (g/cm²)</td>
<td>920 ± 153</td>
<td>937 ± 141</td>
<td>902 ± 117</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>9.35 ± 0.40</td>
<td>9.27 ± 0.39</td>
<td>9.41 ± 0.37</td>
</tr>
<tr>
<td>Phosphate (mg/dl)</td>
<td>3.30 ± 0.48</td>
<td>3.09 ± 0.38</td>
<td>3.51 ± 0.47†</td>
</tr>
<tr>
<td>PTH i (pg/ml)</td>
<td>54.1 ± 22.6</td>
<td>52.3 ± 21.1</td>
<td>51.4 ± 18.5</td>
</tr>
<tr>
<td>25 (OH) vitamin D (ng/ml)</td>
<td>21.8 ± 11.5</td>
<td>22.6 ± 11.0</td>
<td>20.9 ± 12.1</td>
</tr>
</tbody>
</table>

BMD, bone mineral density; LS, lumbar spine; FN, femoral neck; TH, total hip; ADT, androgen-deprivation therapy; BMI, body mass index.

* Unpaired t-test: p < 0.05 between groups.