Effect of vitamin D supplementation on bone and vitamin D status among Pakistani immigrants in Denmark

a randomised double-blinded placebo-controlled intervention study

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Published in:
British Journal of Nutrition

DOI:
doi:10.1017/S000711450789430X

Publication date:
2008

Document version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Effect of vitamin D supplementation on bone and vitamin D status among Pakistani immigrants in Denmark: a randomised double-blinded placebo-controlled intervention study

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(Received 3 April 2007 – Revised 8 November 2007 – Accepted 8 November 2007 – First published online 22 January 2008)

Severe vitamin D deficiency is common among Muslim immigrants. The dose necessary to correct the deficiency and its consequence for bone health are not known for immigrants. The aim was to assess the effect of relatively low dosages of supplemental vitamin D on vitamin D and bone status in Pakistani immigrants. This 1-year-long randomised double-blinded placebo-controlled intervention with vitamin D$_3$ (10 and 20 mg/d) included girls (10·1–14·7 years), women (18·1–52·7 years) and men (17·9–63·5 years) of Pakistani origin living in Denmark. The main endpoints were serum 25-hydroxyvitamin D (S-25OHD), parathyroid hormone, bone turnover markers and bone mass. The study showed that supplementation with 10 and 20 mg vitamin D$_3$ per day increased S-25OHD concentrations similarly in vitamin D-deficient Pakistani women (4-fold), and that 10 mg increased S-25OHD concentrations 2-fold and 20 mg 3-fold in Pakistani men. S-25OHD concentrations increased at 6 months and were stable thereafter. Baseline S-25OHD concentrations tended to be lower in girls and women than in men; females achieved about 46 nmol/l and men 55 nmol/l after supplementation. Serum intact parathyroid hormone concentrations decreased at 6 months, but there was no significant effect of the intervention on bone turnover markers and dual-energy X-ray absorptiometry measurements of the whole body and lumbar spine.

Randomised controlled trials: Vitamin D intervention: Pakistani immigrants: Bone turnover: Bone mass

The large population groups living in a traditional Islamic cultural pattern in Europe are at major risk of vitamin D deficiency due to insufficient sun exposure and low vitamin D intake. Previously, in the cross-sectional part of this study, we found median 25-hydroxyvitamin D (25OHD) concentrations between 10·9 and 20·7 nmol/l among adolescent girls, premenopausal women and men with Pakistani origin living in Denmark(1). Similar results have been reported in Norway(2–5) and in the UK(6).

Clinical trials investigating the effect of vitamin D supplementation on fracture risk have shown conflicting results(7–12). Several of the trials combined Ca with vitamin D, making it unclear which nutrient is responsible for an observed effect. However, trials with vitamin D supplementation alone (dosages 10–20 µg/d) also find conflicting results(10,11,13,14). A meta-analysis of seven randomised trials found that fracture risk was reduced among ambulatory or institutionalised elderly individuals at vitamin D supplemental dosages of 17·5–20 µg/d, but not at 10 µg/d(15). However, this differs from a Cochrane review, which found fracture reduction among elderly institutionalised individuals given vitamin D and Ca, but the effect of vitamin D alone was unclear(16). Bone mineral density (BMD) is a useful measure for predicting fracture risk(17,18), and BMD was increased with vitamin D and Ca supplementation in some studies among elderly Caucasians(7,9) and with vitamin D supplementation alone in other studies(19–21).

Case reports show improvement in vitamin D status (and reduced muscle pain) by vitamin D supplementation among immigrants(22,23); however, very few vitamin D intervention studies have been performed with ethnic groups other than Caucasians from Western countries. In a small group of vitamin D-depleted Asians in the UK, treatment with vitamin D increased their vitamin D status(24). Several surveys

Abbreviations: BA, bone area; BMC, bone mineral content; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; GLM, general linear model; MIXED, mixed linear model; 25OHD, 25-hydroxyvitamin D; S-25OHD, serum 25-hydroxyvitamin D; S-iPTH, serum intact parathyroid hormone.

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investigated the Asian community in Glasgow during the 1960–80s, and about 10 μg vitamin D/d seemed to prevent rickets and osteomalacia\textsuperscript{[25–29]}. Vitamin D-fortified chapatti flour was uniformly effective in increasing 25OHD concentrations as vitamin D capsules\textsuperscript{[20]}. In a study from Norway where Pakistani women were advised to take vitamin D supplements, no improvement in status was shown after 1 year, but whether the advice was followed was not known\textsuperscript{[39]}. A randomised controlled trial of vitamin D supplementation in Ca-replete African-American women did not observe an effect on bone loss or bone turnover markers\textsuperscript{[30]}

The purpose of the present study was to assess the effect of relatively low dosages of supplemental vitamin D on vitamin D status in an immigrant group where sun exposure and vitamin D intake is minimal, and to assess the effect of vitamin D supplementation on bone turnover and bone mass in this group. The main endpoints were serum 25-OHD (S-25OHD), serum intact parathyroid hormone (S-iPTH), and markers for bone turnover and bone mass. The relatively low dosages (the recommended daily intake and twice the recommended daily intake for this population group) used in the present study were chosen with a view to the possibility of fortification.

**Subjects and methods**

**Study design**

The study was a 1-year-long randomised double-blinded placebo-controlled intervention study with two doses of vitamin D\textsubscript{3} (10 and 20 μg/d). The subjects were seen three times during the year, at months 0, 6 and 12. The main endpoints were S-25OHD, S-iPTH, bone turnover markers and markers of bone mass (whole-body and lumbar spine bone area (BA), BMD and bone mineral content (BMC)).

The local ethics committee (registration no. KA01139gs) and the Danish Medicines Agency (a tablet containing 20 μg vitamin D\textsubscript{3} is considered as a drug and not a supplement in Denmark) (registration no. 2612-1805) approved the study protocol. The study was carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, as well as from the parents or guardians of the girls.

**Subjects**

Subjects were recruited through information meetings at schools, mosques, cricket clubs, private organisations, etc, adverts in local Pakistani newspapers, local Pakistani radio and television, and posters in relevant places, since the Danish National Central Offices of Civil Registrations do not contain information about ethnic origin. Consequently, the sample was not random and the representativeness of the sample could not be assessed due to lack of information about non-acceptors. The subjects were included from January 2002 to November 2002.

Subjects included were adolescent girls (median age 12.2 years; range 10.1–14.7 years), women (median age 36.2 years; range 18.1–52.7 years) and men (median age 38.3 years; range 17.9–63.5 years). All subjects were of Pakistani origin (immigrants or descendants with Pakistani parents) primarily living in the Copenhagen area, Denmark (latitude 55°N). About 87% of the 19,250 individuals with Pakistani origin (immigrants and descendants) in Denmark live in the Copenhagen area\textsuperscript{[31]}. The baseline S-25OHD status and the determinants of vitamin D status (for example, clothing, sun and smoking habits) were investigated earlier\textsuperscript{[32]}

Among the 247 subjects participating in the first visit, 199 (twenty-six girls, eighty-nine women and eighty-four men) were willing to be included in the intervention study (month 0). Twenty-two girls, sixty-five women and sixty-nine men participated in the second visit at month 6. Twenty-one girls, sixty-two women and sixty-five men were seen at month 12, and thus completed the study (the overall drop-out rate at the end of the study was 26%, and 19, 30 and 23% for girls, women and men, respectively).

The goal was to recruit sixty girls, sixty women, and sixty men, i.e. twenty girls, twenty women and twenty men in each of the three treatment groups (this number would be able to detect a change in BMD of the same size as the population standard deviation, 0.025 g/cm\textsuperscript{2}, i.e. a change of 1 SD (provided significance level 5%, power 85%)).

Exclusion criteria were medications known to affect bone metabolism or S-25OHD concentrations (anti-epileptics, active vitamin D metabolites, corticosteroids, thyroid hormones, bisphosphonates, oestrogens), serious illness (for example, cancer, or liver or kidney insufficiency), pregnancy, planning pregnancy within 1 year, breast-feeding, and serum ionised Ca concentrations >1.5 mmol/l.

The women were tested for pregnancy before dual-energy X-ray absorptiometry (DXA) scanning. Subjects with incomplete data in one or more of the explanatory variables were excluded in the multiple regression analyses, and they did not differ significantly from the study population with respect to S-25OHD and the available explanatory variables.

**Tablets**

Scanpharm A/S (Birkerød, Denmark) produced the placebo (cellulose microcrystallium) and vitamin D\textsubscript{3} (10 and 20 μg) tablets especially for the present study without using any pig-containing substances. Scanpharm A/S delivered the three kinds of tablets in coded boxes. The subjects (girls, women and men separately) were randomised (by an impartial scientist) in blocks of six using random numbers.

At the first visit, 3 months’ consumption of tablets were handed out, the next 3 months’ consumption were sent by mail to the subjects, and at the second visit the remaining 6 months’ consumption of tablets were handed out. The subjects were instructed to bring back any remaining tablets at the second and third visit, and the compliance was calculated by tablet counting. The median compliance was 85 (range 43–100), 92 (42–115) and 93 (33–105) % for girls, women and men, respectively.

**Sampling and analyses of biochemical parameters**

Blood samples were taken between 07.30 and 10.30 hours at all three visits (months 0, 6 and 12) by venepuncture after an overnight fast. Local anaesthetic patches were offered to the girls to reduce the discomfort of venepuncture. Blood samples were centrifuged (about 3000 g for 10 min) within 2 h of sampling, and serum was frozen and stored at −80°C. Morning second
void urine samples were collected after an overnight fast. Urine samples were frozen and stored at −20°C. S-25OHD concentrations (vitamin D$_3$ plus D$_2$ are used here) were analysed by HPLC using a diode array detector for detection and an absorbance detector for quantification. The inter-assay CV was 6.3 % and the intra-assay CV was 4.3 %. S-25OHD was analysed at the National Food Institute, Denmark. Participation in the Vitamin D External Quality Assessment Scheme (Charing Cross Hospital, London, UK) ensured that the HPLC method was in agreement with commercially available assays.

S-iPTH concentrations were analysed by an immunoradiometric method using a commercial assay (IDS, Bolton, Lancs, UK). The inter-assay CV was 4.0 % and the intra-assay CV was 2.3 %. Urinary Ca was analysed by an absorptiometry method using a KoneLab spectrophotometer (Thermo Clinical Labsystems Ltd, Espoo, Finland). The inter- and intra-assay CV were less than 5 %. S-iPTH and urinary Ca were analysed at the University of Helsinki, Finland.

Serum osteocalcin was analysed by an ELISA (BRI-Diagnostics, Dublin, Republic of Ireland). The inter-assay CV was 11 % and the intra-assay CV was 8 %.

Urinary pyridinoline and deoxypyridinoline were measured by HPLC with fluorescence detection and quantified by external standardisation using a commercially available pyridinoline/deoxypyridinoline HPLC calibrator (Metra Biosystems Ltd, Wheatley, Oxon, UK). The inter-assay CV was 9 and 11 %, respectively and the intra-assay CV was 6 and 7 %, respectively.

Urinary creatinine was analysed by a colorimetric method using a diagnostic kit (catalogue no. 124; Boehringer Mannheim GmbH, Mannheim, Germany). The inter-assay CV was 6.7 % and the intra-assay CV was 3.2 %.

Serum osteocalcin, urinary pyridinoline and urinary deoxypyridinoline were analysed at University College Cork (Republic of Ireland).

Serum ionised Ca was analysed by a Ca++/pH Analyser Ciba Corning 634 with ion-selective electrodes. The inter-assay CV was 2.4 % on level 1.23 mmol/l and the intra-assay CV was 0.8 % on level 1.16 mmol/l (external quality control: DEKS (Danish Institute for External Quality Assurance for Laboratories in Health Care)). Ionised Ca was analysed at the Department of Clinical Biochemistry (Hvidovre Hospital, University of Copenhagen, Denmark). Serum ionised Ca and urine Ca were measured to check for developing hypercalcaemia.

**Bone mineral assessment**

At the first and third visit (months 0 and 12) whole-body and lumbar (L2–L4) BMC measured in g hydroxyapatite, bone size expressed as anterior–posterior projected BA measured in cm$^2$, and BMD measured in g/cm$^2$ (BMD = BMC/BA) were determined by DXA scan using a Hologic 1000/W scanner (Hologic, Inc., Waltham, MA, USA). The method is described elsewhere$^{1)}$.

**Dietary intake and background information**

At the first and third visit (months 0 and 12) the subjects answered an FFQ that ascertained the food groups contributing to 95 % of the vitamin D intake and 75 % of the Ca intake determined from the Danish national dietary survey, which, however, does not contain intake data from Pakistani immigrants$^{32)}$. The intake calculations were performed using the General Intake Estimation System described elsewhere$^{33,34)}$.

At the first visit (month 0) the subjects answered a detailed questionnaire that ascertained demographic characteristics, chronic diseases, use of medication and other lifestyle variables. At the second and third visit (months 6 and 12) the subjects answered a questionnaire ascertaining changes in disease or use of medication. Weight and height were recorded without shoes at all three visits. The age of the subjects at months 0 and 12 was the age on the date of blood sampling and interview. The median age difference between month 12 and 0 is 1.04 (range 0.99–1.12), 1.05 (range 0.92–1.32) and 1.05 (range 0.92–1.25) years for girls, women and men, respectively (drop-outs excluded).

**Statistical analysis**

All statistical analyses were performed for girls, women and men separately. Analyses included standard descriptive statistics. The significance level was chosen at 0.05. SAS version 8.02 (SAS Institute, Inc., Cary, NC, USA) was used for all statistical analyses.

Non-parametric ANOVA was performed in order to compare the three treatment groups at baseline (month 0) in age, anthropometrics, vitamin D dietary intake, Ca dietary intake, biochemical markers and bone mass. Non-parametric ANOVA was also performed in order to compare the three treatment groups at the end of the study (month 12) in age, anthropometrics, vitamin D dietary intake and Ca dietary intake.

Age- and baseline-corrected multiple regression (general linear model; GLM) was performed in order to quantify the effect of tablet dose (0, 10 or 20 μg vitamin D$_3$/d) on various outcomes at endpoint (12 month) as an intention-to-treat analysis. Outcomes were biochemical markers and markers for bone mass, all logarithmically transformed in order to meet the requirements of the statistical model. Likewise, the corresponding baseline measurements (month 0) were also logarithmically transformed, whereas age was included as a quantitative covariate without transformation. Pair-wise comparisons between the three dose groups were performed using Tukey adjustment, and effects are stated as estimated ratios between a high-dose individual compared with a low-dose individual.

In order to investigate further the dose–time interaction, we included all three time points in a repeated-measurement analysis (mixed linear model; MIXED), including subject as a random factor (compound symmetry correlation structure). Age was included as a quantitative covariate, dose and time as fixed factors, the latter described by two dummy variables. At the second and third visit (months 6 and 12) the subjects answered a questionnaire ascertaining changes in disease or use of medication. Weight and height were recorded without shoes at all three visits. The age of the subjects at months 0 and 12 was the age on the date of blood sampling and interview. The median age difference between month 12 and 0 is 1.04 (range 0.99–1.12), 1.05 (range 0.92–1.32) and 1.05 (range 0.92–1.25) years for girls, women and men, respectively (drop-outs excluded).

**Results**

The baseline subject characteristics of the three treatment groups are shown in Table 1. There were no significant
differences ($P>0.05$; non-parametric ANOVA) between the three treatment groups in subject characteristics either at baseline (month 0) (Table 1) or at the end of the study (month 12) (data not shown). There was also no significant difference between the three treatment groups at baseline in S-25OHD concentrations (logarithmically transformed) for girls and women (Table 2). Serum ionised Ca and urinary Ca were measured at all three visits. No subjects developed hypercalcaemia (serum ionised Ca was below 1·5 mmol/l for all subjects at all visits). There was no significant difference ($P>0.05$; non-parametric ANOVA) between the three treatment groups in serum and urinary Ca either at baseline (month 0) or at the end of the study (month 12) (data not shown).

**Serum 25-hydroxyvitamin D**

There was a significant difference (Table 2; GLM) between the three treatment groups at the end of the study (month 12) in S-25OHD for girls, women and men. Vitamin D supplementation elevated median S-25OHD concentrations in all groups; for women concentration increased by 31–32 nmol/l with both 10 and 20 μg/d, and for the men S-25OHD increased 16·5 nmol/l with 10 μg/d and 35·8 nmol/l with 20 μg/d (the baseline and final values are shown in Table 2). Vitamin D status of the women increased about three times by 20 μg/d (Table 2; MIXED). However, there were individuals with increased S-25OHD during months 6 to 12, as seen in Fig. 1, which shows the S-25OHD raw data and illustrates the entire course of the intervention.

Figure 2 shows the relationship between the outcome and baseline S-25OHD concentrations (logarithmically transformed) for women and men (not shown for girls due to the low number of subjects). As seen in Fig. 2, the outcome concentrations depend on baseline values both for intake of 10 and 20 μg/d for women, and the slope is similar for both treatment groups ($α = 0.3$ and 0.2 for doses 10 and 20 μg/d, respectively). For men the endpoint concentrations depend on baseline values only for intake of 10 μg/d ($α = 0.3$), whereas for the 20 μg/d treatment group the slope was close to zero ($α = −0.004$) and thus independent of the baseline value. This illustrates an interaction between dose and baseline value, which is confirmed by including this interaction term in the GLM analysis; the interaction is significant for men ($P=0.0045$), but not for women.

**Serum intact parathyroid hormone**

Vitamin D supplementation decreased S-iPTH significantly between months 0 and 6 for girls, women and men, but not between months 6 and 12 (Table 2; MIXED). There was a significant difference between the three treatment groups at the end of the study (month 12) for women, but not for girls and men (Table 2; GLM). There was no significant difference in S-iPTH between dose 10 and 20 μg/d for girls, women and men (data not shown).

**Bone turnover (serum osteocalcin, urinary pyridinoline and urinary deoxypyridinoline)**

There was no significant difference (GLM) between the three treatment groups at the end of the study (month 12) and there...
Table 2. Serum 25-hydroxy vitamin D (S-25OHD) and serum intact parathyroid hormone (S-iPTH) in the three treatment groups at month 0, 6 and 12, and *P* values from the two statistical tests performed (general linear model (GLM) and mixed linear model (MIXED))

(Medians with 25th and 75th percentiles)

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</table>

**P** values indicate statistical significance. NS, non-significant (*P* > 0.05).

* No significant difference between treatment groups at baseline (month 0) (*P* > 0.05; non-parametric ANOVA).

† n = 19.

‡ n = 6.

§ n = 22.

¶ Ratio of change (CI) over 12 months for dose 20 μg/d as compared with placebo for subjects completing the study.

** Effects are stated as estimated ratios between a high-dose individual compared with a low-dose individual.
Table 3. Serum osteocalcin (S-Osteo), urine pyridinoline (U-Pyr) and urine deoxypyridinoline (U-dPyr) in the three treatment groups at months 0, 6 and 12 (Medians with 25th and 75th percentiles)

<table>
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<th>Men</th>
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<td>S-Osteo (ng/ml)</td>
<td>U-Pyr (nmol/mmol creatinine)</td>
<td>U-dPyr (nmol/mmol creatinine)</td>
<td>S-Osteo (ng/ml)</td>
<td>U-Pyr (nmol/mmol creatinine)</td>
<td>U-dPyr (nmol/mmol creatinine)</td>
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<td>Median 25th, 75th percentiles</td>
<td>Median 25th, 75th percentiles</td>
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<td>Median 25th, 75th percentiles</td>
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<tr>
<td></td>
<td>Subjects month 6 (n)</td>
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<td>22</td>
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<td>Subjects month 12 (n)</td>
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<td>19</td>
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<tr>
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<td>37·3</td>
<td>25·8, 41·7</td>
<td>37·9†</td>
<td>20·7, 45·6</td>
<td>20·3†</td>
</tr>
<tr>
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<td>32·6</td>
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<td>32·9†</td>
<td>16·3, 50·8</td>
<td>23·2†</td>
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<td>23·4, 124·2</td>
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<td>57·6, 85·7</td>
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<td>1·55</td>
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<td>1·14</td>
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</table>

* No significant difference between treatment groups at baseline (month 0) (P > 0·05; non-parametric ANOVA).
† No significant difference between treatment groups (P > 0·05; general linear model and mixed linear model).
‡ n 6.
§ n 25.
‖ n 5.
¶ n 19.
** n 18.
†† n 23.
‡‡ n 21.
§§ n 27.
*** n 24.
††† Ratio of change (CI) over 12 months for dose 20 μg/d as compared with placebo for subjects completing the study.
was no significant dose–time interaction for any of the bone turnover markers for girls, women and men (MIXED) (Table 3). Based on the confidence limits (Table 3), we cannot rule out the possibility of a clinically relevant effect; an effect might have been found if we had studied more subjects.

**Bone mass (whole-body and lumbar spine bone mineral content, bone area and bone mineral density)**

There was no significant difference (non-parametric ANOVA) between the three treatment groups at baseline in whole-body and lumbar spine BMC, BA and BMD for women and girls.
Table 4. Whole-body and lumbar spine bone mineral content (BMC), bone area (BA) and bone mineral density (BMD) in the three treatment groups at months 0 and 12 (Medians with 25th and 75th percentiles)

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<th>Men</th>
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<td>1.02</td>
<td>0.96, 1.07</td>
<td>1.01</td>
<td>0.98, 1.03</td>
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</tbody>
</table>

*No significant difference between treatment groups at baseline (month 0) (P > 0.05; non-parametric ANOVA).
† Significant difference between treatment groups at baseline for men: whole-body BMC P = 0.04 and BA P = 0.007; lumbar spine BMC P = 0.02 and BA P = 0.009 (non-parametric ANOVA).
‡ No significant difference between treatment groups (P > 0.05; GLM). For the exceptions (whole-body BMC for men, BMD and BA for women), please refer to the text.
§ Ratio of change (CI) over 12 months for dose 20 µg/d as compared with placebo for subjects completing the study.
Discussion

The present study showed that supplementation with 10 and 20 μg vitamin D₃ per d increased S-25OHD concentrations similarly in vitamin D-deficient Pakistani women (4-fold), and that 10 μg increased S-25OHD concentrations 2-fold and 20 μg 3-fold in Pakistani men. S-25OHD concentrations increased at 6 months and were stable thereafter. Baseline S-25OHD concentrations tended to be lower in girls and women than in men; females achieved about 46 nmol/l and men 55 nmol/l after supplementation. S-iPTH concentrations decreased at 6 months, and there was no significant difference in S-iPTH between the 10 and 20 μg/d treatment groups.

The other main finding of the present study was the lack of significant effect of the vitamin D intervention on bone turnover markers and on markers of bone mass (BMC, BMD, BA).

For girls, the lack of significant effects could be due to lack of statistical power, since fewer than the scheduled sixty subjects were recruited. For women, the different directions of the estimated ratios (0·99 and 1·02) weaken the significant differences found (whole-body BMC and BA), and for men, the only significant P value (whole-body BMC; 0·049) was close to 0·05, and it cannot be concluded that vitamin D supplementations had an effect on bone mass. One could discuss whether the S-25OHD values are high enough to affect the bone parameters; the S-25OHD concentrations did not reach 70–80 nmol/l, which is often considered the optimal concentration for bone health(35); at least among elderly Caucasians. However, in the present study there was no significant difference in S-iPTH between the 10 and 20 μg/d treatment groups. Further studies in different ethnic population groups are needed to clarify whether doses above 20 μg/d and study durations longer than 1 year would increase S-25OHD and decrease S-iPTH further and thereby improve bone health.

The non-random recruitment of the sample is a limitation of the present study. The drop-out rate was high; however, we expected this problem and mitigated it by recruiting more subjects to start with (except for the girls, since parents were not very willing to let their daughters participate). The compliance was calculated by tablet counting, but we could obviously not control the actual tablet intake. It was not within the scope of this project to measure muscle strength; however, it could have been interesting to do so. We did ask questions about muscle pain (duration and degree). However, the questions were compounded by language difficulties; consequently the questions were not included in the analyses. In the discussion of optimal vitamin D status one must keep in mind the difficulties in comparing S-25OHD concentrations in different studies due to large inter-laboratory variations(36–38).

The clinical trials evaluating the effect of vitamin D supplementation on bone mass and/or fracture risk are mainly performed among Caucasians elderly women, some even frail or institutionalised(7,11), and the trials have produced conflicting results(7–12). The specific benefit to be gained from increasing vitamin D intake remains to be defined for other ethnic groups. It has been suggested that vitamin D supplementation is likely to have favourable effects on the skeleton among black subjects(79); however, a 3-year randomised controlled trial of vitamin D supplementation (20–50 μg/d) in Ca-replete postmenopausal African-American women did not find an effect on bone loss or bone turnover markers(90). Whether the lack of effect on bone turnover and bone density is due to ethnic differences or other reasons, we do not know. Studies from Norway found similar BMD and bone turnover markers among Pakistanis and Norwegians in spite of different S-25OHD(D90,43).

Even though we did not find a beneficial effect of vitamin D supplementation on bone parameters, the improved vitamin D status among immigrants might affect muscle strength and the risk of other diseases beneficially. Hypovitaminosis D myopathy is a prominent symptom of vitamin D deficiency, and severely impaired muscle function may be present even before biochemical signs of bone disease develop(72). Besides, vitamin D deficiency may increase the risk of several other diseases, for example, autoimmune diseases, some types of cancers, and diabetes(42).

Convincing immigrants to consume supplemental vitamin D every day for a longer period of time would certainly represent a major challenge. Food fortification could be a more realistic solution. The relatively low dosages used in the present study were chosen with a view to the possibility of fortification. Presently in Denmark margarine can voluntarily be fortified with 7.5–10 μg vitamin D per 100 g. Fortification of chapatti flour, which could be a way to reach Pakistani immigrants, was tested in the 1970s in the UK, but it was not recommended, since the age consumption pattern was not favourable to the aims of fortification and not all Asians eat chapatti(24,43). Muslim immigrants in Denmark are now recommended through information leaflets to take 10 μg vitamin D supplements/d.

The present study on one hand clearly demonstrates that the vitamin D status of severely vitamin D-deficient Pakistani immigrants in Denmark increases two to four times with relatively small dosages of supplemental vitamin D, and that S-iPTH decreases at the same time. On the other hand, this improvement in vitamin D and PTH status did not benefit bone mass and bone turnover parameters. The optimal vitamin D nutrition for skeletal health in different ethnic groups should be further investigated.

Acknowledgements

We thank Karin Hess Ygil, Dorte Strange and Nighat Kwajada for interviewing the participants; Nighat Kwajada for the blood sampling and the interpretation into Urdu when necessary; Dorte Strange for the DXA scannings; Birgitte
Hermansen et al. for assisting the DXA scannings and assisting designing the FFQ; Karin Hess Ygil, Tue Christensen and Anders Møller for the dietary intake calculations. The study is part of the OPTIFORD project ‘Towards a strategy for optimal vitamin D fortification’, financed by the EU, the 5th Framework Programme (QLK1-CT-2000-00623).

The work was carried out from the Danish Institute for Food and Veterinary Research (now National Food Institute, Technical University of Denmark), Department of Nutrition, Mørkhøj Bygade 19, DK-2860 Søborg, Denmark.

R. A. collected the data, wrote the manuscript and undertook the statistical analyses with L. T. S., C. M. and L. O. providing advice. R. A., C. B., K. D. C., C. L.-A., C. M. and L. O. designed the study. J. J. undertook the measurements of S-25OHD, K. D. C. the measurements of bone turnover markers, and C. L.-A. the measurements of iPTH. All contributed to the manuscript. None of the authors had conflicts of interest.

References


