Calcif Tissue Int (2000) 66:419–424

Calcified
Tissue
International

Hypovitaminosis D Myopathy Without Biochemical Signs of Osteomalacic Bone Involvement

H. Glerup,[1] K. Mikkelsen,[2] L. Poulsen,[2] E. Hass,[2] S. Overbeck,[2] H. Andersen,[3] P. Charles,[1] E. F. Eriksen[1]

[1]Department of Endocrinology and Metabolism C, Aarhus Amtssygehus, University Hospital of Aarhus, Tage Hansensgade 2, DK-8000 Aarhus C, Denmark
[2]Primary Health Care Centre, City Vest, Aarhus, Denmark
[3]Department of Neurology, Aarhus Kommunehospital, University Hospital of Aarhus, Denmark

Received: 10 September 1999 / Accepted: 11 January 2000

Abstract. The aims of this study were to investigate myopathy in relation to vitamin D status, and to study the muscular effects of vitamin D treatment on vitamin D-deficient individuals. Further, hypovitaminosis D myopathy was investigated in relation to alkaline phosphatase (ALP), the most commonly used marker for hypovitaminosis D osteopathy. Eight patients with osteomalacia had an isokinetic dynamometer test of all major muscle groups before and after 3 months of vitamin D treatment. The most pronounced improvements in muscle power were seen in the weight-bearing antigravity muscles of the lower limbs. A cross-sectional study was performed among 55 vitamin D-deficient veiled Arab women living in Denmark and 22 Danish controls. An isometric dynamometer model was used for determination of quadriceps muscle power. Both maximal voluntary contraction (MVC) and electrically stimulated values (single twitch, maximal production rate (MPR), and maximal relaxation rate (MRR)) were determined. The women underwent high-dose vitamin D treatment and were retested after 3 and 6 months. Prior to vitamin D treatment all parameters of muscle function in the group of vitamin D-deficient Arab women were significantly reduced compared with Danish controls. MVC: 259.4 ± 11.0 N (Newton) versus 392.6 ± 11.4 N ($P < 10^{-6}$), single twitch: 47.0 ± 1.8 N versus 74.6 ± 2.2 N ($P < 10^{-5}$), MPR 8.9 ± 0.3 N/10 ms versus 14.3 ± 0.4 N/10 ms ($P < 10^{-6}$), MRR 4.5 ± 0.2 N/10 ms versus 6.2 ± 0.2 N/10 ms ($P < 10^{-6}$). Muscle function was affected to a similar degree in women with and without bone involvement (as indicated by elevated ALP). After 3 months of vitamin D treatment all muscle-related parameters improved significantly. After 6 months only MVC was reduced compared with Danish controls (320.7 ± 14.3 N ($P < 0.02$)), whereas all other measurements were normalized. 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. Full normalization of hypovitaminosis D myopathy demands high-dose vitamin D treatment for 6 months or more. Our findings indicate that serum levels of ALP cannot be used in the screening for hypovitaminosis D myopathy. Assessment of s-25OHD is the only reliable test.

Correspondence to: H. Glerup

Key words: Myopathy — Vitamin D — Osteomalaci — Alkaline phosphatase — Hypovitaminosis D myopathy.

For many years myopathy has been known to be part of the osteomalacic symptom complex [1–7]. It is an unsolved question, however, whether hypovitaminosis D myopathy is a symptom occasionally seen in patients suffering from osteomalacic bone disease, or whether it precedes bone involvement. Skaria et al. [5] investigated 30 patients with biopsy-proven osteomalacia. Myopathy was the presenting symptom in 30% of the patients, but was clinically detectable in 96.7%. Thus, myopathy is a prominent symptom in osteomalacia, and it is obvious to ask if myopathy is seen in vitamin D-deficient individuals before bone involvement is detectable.

Hypovitaminosis D myopathy is often misdiagnosed [8] for several reasons. First, it is important to understand that the decrease in muscle strength is a continuous and gradual process, whereas the loss of functional ability is quantal. This means that the patients can have a considerable loss of muscle strength before complaining of muscle weakness. Their complaint would first be fatigue. Not until the patients are unable to walk or rise from a squatting position unaided will they complain of muscle weakness. Another reason for missing the diagnosis is that many of the symptoms are unspecific [4, 6, 8] (diffuse muscle pain, deep bone pain, arthralgia, paresthesia), which often leads to alternative diagnoses such as unspecific rheumatic disease, polymyalgia, psychoneurotic disorders, fibromyalgia, and malignant diseases, among others.

Only a few attempts have been made to estimate the progress in muscle strength during vitamin D treatment. In a prospective study, Young et al. [7, 9] followed the progress in muscle function of 12 osteomalacic patients during vitamin D treatment. They used an isometric dynamometer model for measurement of quadriceps muscle strength in combination with muscle biopsies from the lateral vastus muscle. In the biopsies prior to vitamin D treatment the most prominent finding was atrophy of the faster and more powerful type II fibers. A significant improvement in both muscle strength and muscle biopsies was demonstrated after 3 months of treatment, but full restitution of the muscles would need treatment for 6–12 months. When estimating the muscular effects of vitamin D treatment, it is therefore

important that the observation period should be at least 3 months or longer.

The aims of this study were to investigate myopathy in relation to vitamin D status and biochemical indices of hypovitaminosis D osteopathy, and to study the muscular effects of vitamin D treatment in vitamin D-deficient individuals. In order to find an ideal test muscle we performed a study, where we tested the muscular effects of vitamin D treatment in all major muscle groups (Study A). A cross-sectional study (Study B) with measurement of quadriceps muscle power and blood tests was performed among vitamin D-deficient Arab women living in Denmark and Danish controls. The Arab women were investigated during vitamin D treatment.

Subjects and Methods

Study Population

Study A. This group included eight patients (6 females, 2 males) with biopsy-proven osteomalacia, age 63.1 ± 5.3 years, mean s-25OHD 7.0 ± 0.7 nmol/liter.

Study B. Between December 1996 and June 1997, 55 veiled Arab women with vitamin D deficiency (s-25OHD < 20 nmol/liter) were included in the study. Controls were 22 Danish women living in the same area as the Arab women. Only individuals aged 18 years or more were included in the study. The mean age of the Arab women was 32.2 ± 1.4 years (mean ± SEM) compared with 36.1 ± 1.6 years (NS) for Danish controls. The weight of the two groups was 71.3 ± 0.9 kg versus 70.7 ± 1.9 kg (NS). The Arab women were slightly shorter [160.5 ± 0.7 cm versus 170.2 ± 0.9 cm ($P < 0.01$)] and had a slightly higher BMI 27.8 ± 0.7 kg/m^2 versus 24.4 ± 0.7 kg/m^2 ($P < 0.01$).

Laboratory Evaluations

s-25OHD was measured by a radioimmunoassay (RIA) with ^{125}I-labeled tracer [10]. Intraassay coefficient of variation (CV) was 6% and interassay CV 15%. s-1,25$(OH)_2$D was measured by radioreceptor assay with single cartridge extraction and purification [11]. Intra- and interassay CV was 10%.

s-Bone-specific alkaline phosphatase (BAP) was lectin-precipitated and the supernatant was analyzed spectrophotometrically [12]. Intraassay and interassay CV in the area investigated were 8–10%. s-PTH (1–84) was measured by a RIA [Immulite® intact PTH (DPC® Diagnostic Products Corporation, Los Angeles, CA, USA)]. The intraassay CV was 6% and the interassay CV was 6–12% [13]. s-calcium, s-phosphate, s-creatinine, and serum total alkaline phosphatase (TAP) were determined according to standard methods.

Muscle Function Tests

Study A. Maximal isokinetic muscle strength measurements were performed using an isokinetic dynamometer (Lido Active Multijoint II®, Loredan Biochemical Inc, CA, USA). The muscle strength was measured over several joints: hip (60°/s), knee (90 and 180°/s), ankle (60°/s), shoulder (90°/s), and elbow (60°/s) (angle velocity is given in parenthesis). The test—retest CV was 10%.

Study B. Isometric muscle strength measurements were performed in a strain gauge dynamometer together with equipment for electrical stimulation. The methods described by Edwards et al. [14] were used with some modifications. Measurements were only performed on the knee extensors of the dominant leg with the knee in 90° flexion. To ensure low skin resistance, pads of 9 × 13 cm were used. The pads were placed at the lateral vastus muscle approximately 10 cm above the knee and 10 cm distal from the trochanter major, respectively. All measurement data were collected via an A/D-converter and analyzed with a software package ("In Good Shape", Meititur Ltd, Finland). Maximal voluntary contraction (MVC) was estimated as the best of three measurements given in Newton (N). Single twitch stimulation (twitch) was estimated by measuring the maximal force during a well-defined electrical stimulation (400 V, 240 mA, 200 μs). Maximal production rate (MPR) was estimated as the steepest increase in the force development in 5 minutes. Maximal relaxation rate (MRR) was estimated as the steepest decrease in the force over a period of 5 minutes. Both parameters are expressed as N/10 minutes.

At 40 Hz, 400 V, 200 μs the electrical stimulation was adjusted to stimulate approximately 25% of the MVC (resulting in electrical currents of 80–120 mA). Stimulations were given at 1, 10, 20, 40, and 50 Hz for 3 seconds and intervals of 1 minute.

To test the CV of the method, 12 individuals were tested twice on two different days. The test—retest CV was 5% for MVC and 9.1% for twitch.

Protocol

Study A. Muscle strength was measured over several joints (hip, knee, ankle, shoulder) before and after 3 months of treatment with 0.5 μg alfacalcidol per day in combination with 400 IU ergocalciferol and 1 g calcium per day.

Study B. All participants had a blood test and a muscle function test immediately after inclusion. The 55 vitamin D-deficient Arab women were treated with a high dose vitamin D regimen consisting of intramuscular injections of ergocalciferol 100,000 IU per week for 1 month followed by one injection per month for the following 5 months. Additionally, an oral supplementation of 800–1200 mg calcium carbonate in combination with 400–600 IU ergocalciferol per day was given. After 3 months of treatment, all 55 Arab women were retested with blood tests and muscle function. After 6 months, 10 Arab women underwent another retest.

Prior to treatment, 88% of the vitamin D-depleted Arab women reported muscle pain, 36% had deep bone pain, 26% had experienced a change in gait, and 32% experienced difficulties in raising from a chair or ascending a staircase. Thus, we did not consider including a placebo group for ethical reasons. The study was approved by the local ethical committee, and was performed in accordance with the Helsinki Declaration II.

Statistical Analysis

The software packages Microsoft Excel 7.0 and SPSS 6.1.3 were used for the statistical analysis. Data were analyzed for normality distribution by means of a normality plot. *T*-tests were used for analysis of paired and unpaired data as appropriate. *P*-values <0.05 were considered significant. Correlation analyses were performed by Pearson's correlation and multivariate analysis.

Results

Study A. Increases in muscle power were seen in all muscle groups tested (Fig. 1). The most significant increases were in the knee extensors and flexors, the dorsal flexors of the ankle, and the hip extensors. The mean improvement in all muscle groups was 24.8 ± 8.0% ($P < 0.03$). S-25OHD increased during treatment from 7.0 ± 0.7 nmol/liters to 48.3 ± 8.3 liters ($P < 0.001$).

Study B. The pretreatment s-25OHD levels were very low among the Arab women (6.7 ± 0.6 nmol/liter) compared with 47.1 ± 4.6 nmol/liter in Danish controls (Table 1).

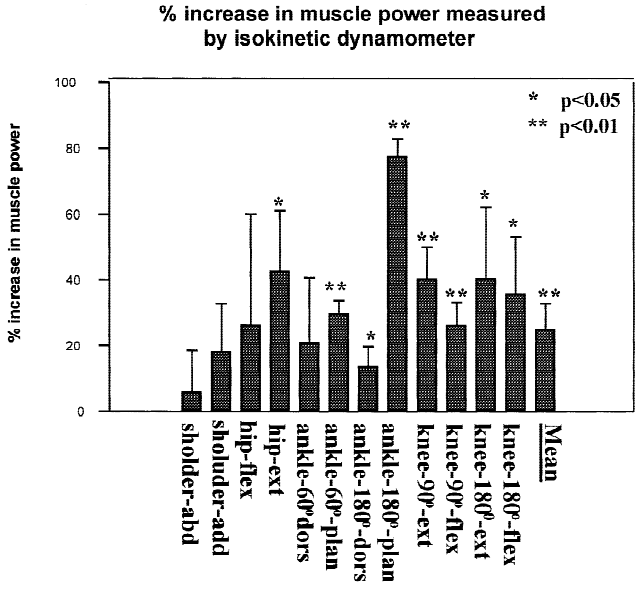

Fig. 1. The effect of treatment with vitamin D on muscle function in different muscle groups (mean ± SEM). The muscle strength was measured with the following angle velocities: hip (60°/s), knee (90 and 180°/s), ankle (60°/s), shoulder (90°/s). s-25OHD increased during treatment from 7.0 ± 0.7 nmol/liter to 48.3 ± 8.3 nmol/liter ($P < 0.001$).

After 3 months of treatment, 25OHD increased to 34.4 ± 2.0 nmol/liter, but it was still significantly lower than the values obtained in Danish controls. No further improvement in s-25OHD was seen from 3 to 6 months of treatment (data not shown). There was no significant difference in s-1,25$(OH)_2$D levels between Danish controls and pretreatment Arab women, but a significant increase was seen during treatment (Table 1). s-PTH was significantly increased to 19.7 ± 2.0 pmol/liter (normal range 1.3–7.6 pmol/liter) in the Arab women, and was normalized during the first 3 months of treatment 6.8 ± 0.8 pmol/liter ($P < 10^{-6}$), but it was still higher than in Danish controls [2.7 ± 0.3 pmol/liter ($P < 0.01$)].

Serum calcium was below the normal range in only 6% of the pretreatment Arab women. Three months of vitamin D treatment normalized s-calcium (Table 1). In order to control for hypercalcemic episodes, a blood test was taken after 1 month of treatment; no episodes were seen.

The average serum levels of BAP and TAP were increased in Arab women. The values decreased during the first 3 months of vitamin D treatment, but remained elevated compared with Danish controls (Table 1). After 6 months of treatment, elevated serum values of PTH and ALP values were only detectable in one patient. Within the group of vitamin D-deficient Arab women, 20 had serum levels of BAP and TAP above the normal range, whereas the remaining 35 had serum levels inside the normal range (Table 2).

The muscle function test data of the Danish controls (Table 1) were all in agreement with the normal data given by Edwards et al. [14].

During vitamin D treatment, improvement in serum levels of 25OHD was paralleled by a significant reduction in muscle and bone discomfort complaints. Severe bone pain tended to last longer than muscle pain. Most individuals had reduced subjective complaints of muscle discomfort within 1–1½ months after initiation of vitamin D treatment, but in some individuals the complaints could last longer than 3–6 months.

The MVC measurements revealed very low values among Arab women (259.4 ± 11.0 N) compared with Danish controls [392.6 ± 11.4 N ($P < 10^{-8}$)]. After 3 months of vitamin D treatment, significant improvement was seen [294.6 ± 12.9 N ($P < 0.005$)], and after 6 months, further improvement occurred (320.7 ± 14.3 N), but MVC was still significantly lower than in Danish controls ($P < 0.02$) (see Table 1 and Fig. 2).

For single twitch the results were similar: Danish controls 74.6 ± 2.2 N versus Arab women 47.0 ± 1.8 N ($P < 10^{-8}$); after 3 months treatment, single twitch had increased to 56.3 ± 2.3 N ($P < 10^{-4}$). After 6 months the difference in Danish controls was no longer significant (Table 1 and Fig. 3).

MPR and MRR improved in exactly the same way. After 6 months of treatment, both were no longer significantly different from Danish controls (Table 1).

In the frequency-stimulated protocol, all measurements (both muscle force and relaxation rates) were significantly decreased in pretreatment of Arab women compared with Danish controls. After 6 months of vitamin D treatment, no significant difference was seen anymore (Fig. 4).

When comparing muscle function tests of pretreatment Arab women with raised serum levels of ALP with those with normal values, no difference in MVC and twitch (Table 2) could be demonstrated. Both groups of vitamin D-deficient Arab women had equally reduced muscle power when compared with Danish controls.

Correlation analysis revealed that muscle power was significantly correlated to serum levels of 25OHD (MVC: $r = 0.34$, $P < 0.001$; twitch: $r = 0.42$, $P < 0.001$) but not to 1,25(OH_2)D (MVC: $r = -0.14$, NS; twitch: $r = 0.02$, NS). Further muscle power was inversely correlated to serum levels of PTH (MVC: $r = -0.33$, $P < 0.001$; twitch: $r = -0.36$, $P < 0.001$). Correlation between muscle power and s-BAP and s-TAP did not reach significance. When multivariate regression analysis between MVC and 25OHD, 1,25(OH_2)D, and PTH were applied, only 25OHD reached significance ($P = 0.02$; $P = 0.08$, and $P = 0.07$ respectively). In single twitch measurements the trend was exactly the same (25OHD ($P = 0.02$), 1,25(OH_2)D ($P = 0.09$), and PTH ($P = 0.09$)).

Discussion

In study A we demonstrated that primarily the weight-bearing antigravity muscles of the lower limb are affected by vitamin D deficiency. This finding may explain the increased number of falls seen in vitamin D-deficient elderly. Further, it is obvious that studies on the muscular effect of vitamin D treatment should be made with measurements of muscle strength on one of the large muscles of the lower limb, which plays an important role for balance and postural stability. Consequently, we decided to use the quadriceps muscle for measurements in study B.

Our results clearly indicate that significant myopathy is a common feature in vitamin D-deficient individuals (defined as s-25OHD <20 nmol/liter). Maximal voluntary knee extension (MVC) was reduced by 34% in vitamin D-deficient Arab women compared with Danish controls. A 14% increase in MVC was seen after 3 months of vitamin D treatment, and after 6 months, MVC was further improved but still not equal to Danish controls. The difference in

Table 1. Effects of vitamin D treatment on blood tests and muscle-function measurements. The results at baseline and after 3 and 6 months of treatment are compared with the Danish controls group

	Arab women baseline n = 55	Paired T-test *P*-value	Arab women after 3 months of treatment n = 55	Unpaired T-test *P*-value	Danish controls n = 22	Unpaired T-test *P*-value	Arabs after 6-months of treatment n = 10
25OHD (nmol/liter)	6.7 ± 0.6	10^{-17}	34.4 ± 2.0	<0.003	47.1 ± 4.6	<0.003	34.0 ± 3.8
1,25(OH_2)D (pmol/l)	108.3 ± 5.6	<0.01	122.6 ± 8.4	<0.05	99.9 ± 8.0	<0.05	121.1 ± 6.1
PTH (pmol/l)	19.7 ± 2.0	10^{-6}	6.8 ± 0.8	<0.01	2.7 ± 0.3	<0.05	6.1 ± 1.6
Ca^{2+} (corr) (mmol/l)	2.29 ± 0.01	10^{-4}	2.37 ± 0.01	NS	2.40 ± 0.02	NS	2.39 ± 0.01
BAP (U/l)	218.4 ± 65.7	0.05	99.0 ± 12.3	0.05	56.2 ± 3.5	NS	70.6 ± 7.5
TAP (U/l)	349.3 ± 72.1	0.05	204.1 ± 13.5	<0.01	146.9 ± 6.0	<0.05	181.1 ± 7.2
MVC (N)	259.4 ± 11.0	<0.005	294.6 ± 12.9	$<10^{-6}$	392.6 ± 11.4	<0.02	320.7 ± 14.3
Twitch (N)	47.0 ± 1.8	$<10^{-4}$	56.3 ± 2.3	$<10^{-5}$	74.6 ± 2.2	NS	69.7 ± 9.1
MPR-twitch (N/10 ms)	8.9 ± 0.3	$<10^{-3}$	10.6 ± 0.4	$<10^{-6}$	14.3 ± 0.4	NS	13.3 ± 1.9
MRR-twitch (N/10 ms)	4.5 ± 0.2	<0.02	5.0 ± 0.3	$<10^{-6}$	6.2 ± 0.2	NS	6.5 ± 0.6

Results given as mean ± SEM
Abbreviations: BAP – bone specific alkaline phosphatase, TAP – total alkaline phosphatase, MVC – maximal voluntary knee extension, twitch – single twitch electrical stimulation, MPR – maximal production rate, MRR – maximal relaxation rate

Table 2. Muscle power in vitamin D-deficient Arab women with normal or elevated levels of TAP and BAP

	Normal levels of TAP and BAP n = 35	Unpaired T-test *P*-value	Elevated levels of TAP and BAP n = 20	Danish controls n = 22	ANOVA *P*-value
TAP	190.8 ± 7.7	$<10^{-8}$	449.8 ± 46.2	146.9 ± 6.0	<0.01
BAP	80.7 ± 6.4	$<10^{-8}$	192.7 ± 43.1	56.2 ± 3.5	<0.01
MVC	269.6 ± 12.9	0.75	261.9 ± 23.3	392.6 ± 11.4	<0.001
Twitch	47.7 ± 2.3	0.77	46.5 ± 4.0	74.6 ± 2.2	<0.001

Mean ± SEM. TAP and BAP given in U/liter. MVC and twitch given in Newtons

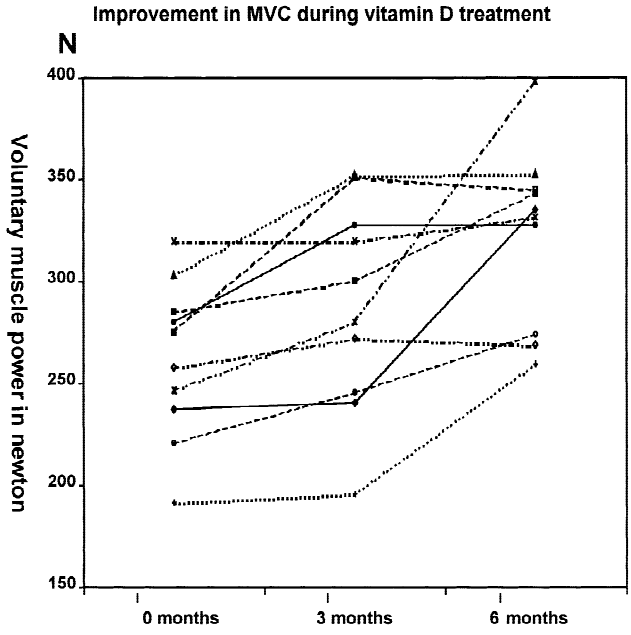

Fig. 2. Maximal voluntary knee extension after 0, 3, and 6 months of treatment.

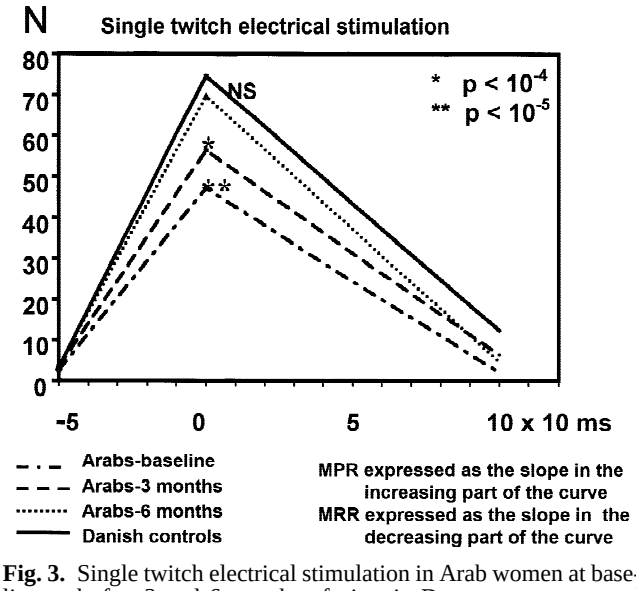

Fig. 3. Single twitch electrical stimulation in Arab women at baseline and after 3 and 6 months of vitamin D treatment compared with Danish controls.

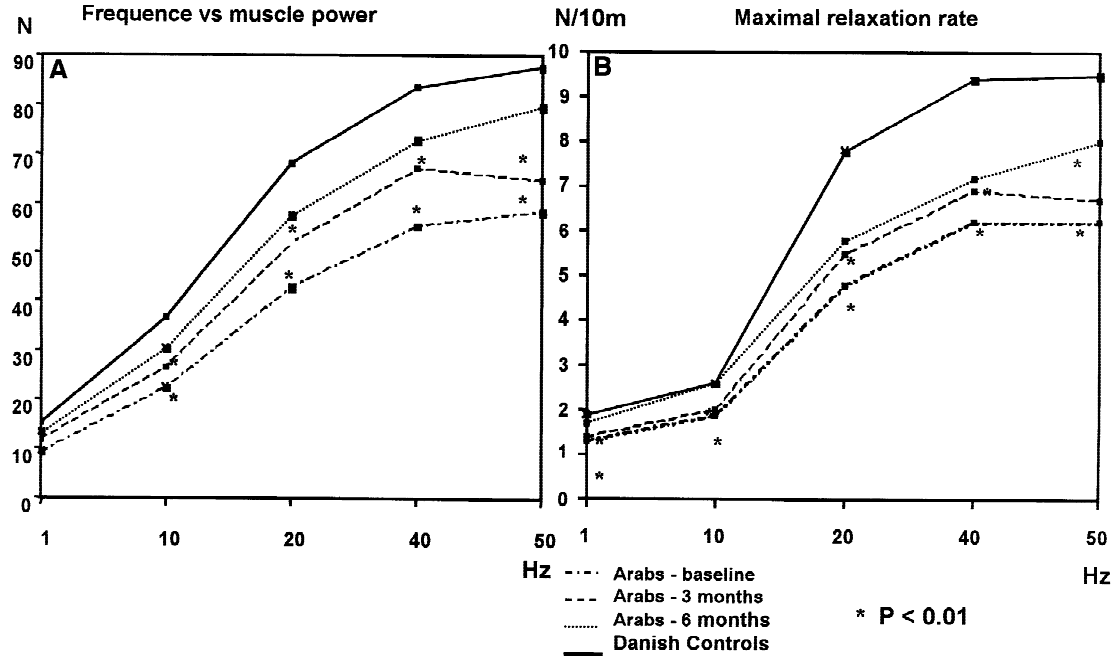

Fig. 4. Electrically stimulated force development in Arab women at baseline and after 3 and 6 months of vitamin D treatment compared with Danish controls. Electrical stimulation was given at 1, 10, 20, 40, and 50 Hz. Maximal forces are given in **(A)** and maximal relaxation rates are given in **(B).**

MVC could be a question of different body size between the groups, but the fact that MVC was nearly normalized during 6 months of vitamin D treatment also supports the fact that myopathy was caused by vitamin D deficiency. In the observation period, no other treatment that could influence muscle power was given. Especially, no muscle training was given. The vitamin D doses given in the study could from the latest recommendations be argued to be suboptimal [15], and it is possible that the improvement in muscle power would have been even more significant if larger doses of vitamin D had been given. An alternative explanation of the difference in MVC could be that complete normalization takes 6–12 months, as suggested by Young et al. [17].

The results could also be biased due to racial differences. Newham et al. [7] previously demonstrated the absence of racial differences in muscle strength between Asians and Caucasians, but we have not been able to find any data on Arabs versus Caucasians. An ideal control group would have been Arab women with a documented normal vitamin D status for 6 months or more. We were, however, not able to identify a sufficient number of Arab women fulfilling this criteria.

Results, based only on measurements of voluntary contractions, may be dependent on the motivation of the participants. It can further be claimed that the participants can learn how to perform "a good test" and thus make a better result in the retest. However, we demonstrated a high reproducibility for test—retest MVC measurements (CV 5%). MVC might also be dependent on the pain relief of the patients. Participants in pain would probably not be able to make a maximal contraction. In osteomalacia, pain is an integral part of the symptom complex. We therefore believe that our protocol with electrical stimulation is an important supplementation to the MVC measurements. The electrical stimulation is independent of the motivation and the pain relief of the participants. In addition, electrically stimulated contractions cannot be "learned" by the participants and the measurements have an acceptable reproducibility (CV 9.1%).

Electrical stimulation gave exactly the same results as the MVC measurements. Normalization was seen after 6 months of vitamin D treatment. The tests also provided information about muscle kinetics. In vitamin D-deficient individuals the force development was slower and weaker, and the relaxation rate was slower than in normal controls. This is in agreement with the atrophy of the stronger and faster type II fibers described by several researchers in muscle biopsies from vitamin D-deficient individuals [4, 5, 16–19]. After 6 months of vitamin D treatment, muscle kinetics were normalized. This finding again corresponds with the normalization of type II fibers after vitamin D treatment for 6–12 months, demonstrated by Young et al. [7].

Correlation analysis showed that muscle power correlated inversely to s-PTH and positively to s-25OHD, but was not correlated to s-1,25(OH_2)D. In multivariate regression analysis only 25OHD was significant. Our results therefore strongly suggest that normal serum levels of 25OHD are essential for maintaining a normal muscle function, whereas we could demonstrate only minor importance of PTH and no effect of 1,25(OH_2)D. Other researchers have previously suggested a direct effect of 25OHD on striated muscle. Birge and Haddad [20] found that 25OHD stimulated protein synthesis and increased intracellular ATP content in striated muscle more efficiently than did 1,25(OH_2)D. Furthermore, Pointon et al. [21] and de Boland et al. [22] demonstrated a stimulation of the synthesis of troponin-C, actin, and proteins of the sarcoplasmatic reticulum that seemed most likely to be an action of 25OHD rather than 1,25(OH_2)D. On the other hand, muscular effects of 1,25(OH_2)D are well documented in several *in vitro*

studies [23], but we believe that our study strongly suggests that *in vivo* 25OHD is by far the most important effector in striated muscle. Additional research is needed to clarify how 25OHD's muscular effect are mediated. Our conclusion, that 25OHD is the most important *in vivo* effector in striated muscle, is supported by the findings of Grady et al. [24]. In an *in vivo* study, they failed to demonstrate any muscular effects of treatment with 0.5 μg calcitriol daily. Serum levels of 25OHD among the participants were, however, above >60 nmol/liter. If 25OHD is the primary *in vivo* effector, no hypovitaminosis D myopathy could be expected among these participants, and consequently no effect of treatment with calcitriol should be expected.

Previously it has been described [1] that muscle weakness is pronounced when bone involvement is marked. However, we could demonstrate no significant correlation between muscle power and the most common used markers of bone involvement, TAP and BAP. In agreement with this finding we demonstrated no difference in muscle power between individuals with elevated serum levels of BAP and TAP and individuals with normal levels (Table 2). The muscle power was equally decreased in both groups compared with healthy Danish controls.

In conclusion, muscle weakness is common among vitamin D-deficient individuals (s-25OHD <20 nmol/liter) with normal serum levels of TAP and BAP. The finding of equally decreased muscle power among vitamin D-deficient individuals with and without biochemical signs of bone involvement indicate that myopathy precedes bone disease. s-25OHD and probably intact s-PTH are the only qualified tests in screening for hypovitaminosis D myopathy. Our study clearly indicates that more focus should be put on muscle symptoms in population groups known to have an increased risk for vitamin D deficiency (elderly, individuals with limited sunlight exposure). If vitamin D deficiency-related myopathy is to be avoided, as 25OHD serum level of at least 20 nmol/liter should be maintained. It seems reasonable to suggest that vitamin D deficiency seen among the elderly could also result in hypovitaminosis D myopathy. Reduced function of the faster and stronger type II fibers could result in increased frequency of falls, leading to increased incidence of hip fracture. This mechanism could have a satisfactory explanation for the reduced incidence of falls [25] and hip fractures [26] seen in elderly who take vitamin D prophylactics. Probably the best solution to the problem would be increased recommended doses for daily vitamin D intake [27] for risk groups [28].

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