Volume-4, Issue-8, August-2015 • ISSN No 2277 - 8160

Research Paper | Medical Science

Supplementation with Vitamin D3influence Better Outcome in Surgically Treated Hip Fractures

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ABSTRACT

Hip fractures represent the most frequent pathology in patients presenting to the traumatology department.

It's been well documented that adequatedoses of vitamin D are correlated with the better lower-extremities function in elderly people.

Aim of this study was to evaluate the influence of vitamin D3 supplementation on the reparation of hip fractures in elderly patients treated surgically at the University Clinic of Traumatology. This is the first study of this kind in our small country.

It was shown correlations between biochemical markers and age and gender, especially this of alkaline phosphatase.The study confirms the importance of vitamin D in the recovery of hip fractures.

Supplementation of vitamin D must start the day of hospitalization and it must be included in all protocols. All elderly people, especially postmenopausal women must take preventive dose of vitamin D for diminishing risk for fractures.

KEYWORDS : hip fractures, traumatology, vitamin D.

Introduction

Hip fractures and other non-vertebral fractures represent the most frequent pathology in patients presenting to the traumatology department.The increased fracture risk is associated with increased morbidity, mortality and, therefore, social and economic costs.

Recently it has been reported that in patients with a hip fracture, the 80% had secondary causes of bone loss, mainly related to disturbed calcium and vitamin D homeostasis. Despite this, only few patients receive evaluation and treatment for osteoporosis following a hip fracture.

It's been well documented that higher levels of vitamin D are correlated with the better lower-extremities function in subjects older than 60 years old, whether they are active or not (1,2,3,4,5).

Even the vitamin D hormone system is considered essential for calcium homeostasis there is no general consensus about vitamin D efficacy and safety in relation to bone health.

Vitamin D (both D2 and D3 forms) can be obtained through the intake of foods or dietary supplements. However, about 80% of human vitamin D is made through skin exposure to ultraviolet light that converts cutaneous provitamin D3 to previtamin D3, which isomerizes into vitamin D3 and translocates into the circulation. Vitamin D is biologically inert and must undergo two successive hydroxylations in the liver and kidney to become the biologically active 1,25-dihydroxyvitamin D [1,25(OH)2D] (1). Its main biological effect is to maintain the plasma calcium concentrations within the normal range.

In addition, 1,25(OH)2D is also capable of inhibiting the proliferation and inducing terminal differentiation of a variety of normal and cancer cells, modulating the immune system, enhancing insulin secretion, and down regulating the renin/angiotension system. Recently, it was shown that vitamin D deficiency can contribute to MRSA infection (6, 7, 8). It was confirmed that vitamin D plays an important role in mediating immune function via a number of pathways, including enhancing the release of antimicrobial peptides in the skin.

Aim of this study was to evaluate the influence of vitamin D3 supplementation on the reparation of hip (per trochanteric) fractures in elderly patients treated surgically at the University Clinic of Traumatology. This is the first study of this kind in our small country.

Sample and method:

We randomly selected 30 patients with hip fracture, all over 65 years old. The first 15 patients (8 females and 7 males) mean age 68, 34 ±6, 07 years represent experimental group which obtained vitamin D3 treatment together with operative correction of the fracture.

The second, control group, is also consisting of 15 patients (9 females and 6 males) mean age 72,93±6,19 years and they obtained only surgery treatment of the fracture, without D3 supplementation.

Inclusive criteria were: per trochanteric fractures, health condition of the patients which permit the operative treatment and the age over 65 years. Exclusive criteria were: hepatic, renal or thyroid/parathyroid diseases, patients' which obtained previous treatment for osteoporosis, as well as those with chronic thromboprophylaxis.

The experimental group obtained 5000 IE OH-D3 vitamin during six months, starting the day of hospitalization. All patients are operated and followed during 6 months period (clinical status, x-ray, biochemical analysis).

The results are presented in tables, figures and statistically evaluated using Statistics- 12 package. Descriptive data are presented as means and standard deviation (SD). Baseline data were compared according to treatment using one-way ANOVA. Analysis include Correlations as well as Student's t-test. The criterion for statistical significance was set at $p \leq 0.05$.

Results

Results for biochemical analysis of both groups are presented on Tables 1 and 2 respectively.

Table 1: Results for the experimental group (basic, after the 1, 3, and 6 months)

Gender	age	Ca	P	Alk. Phosph.
F = 8 M = 7	68,34 ±6, 07	2,08 ±0,29	1,19 ±0,62	70,8 ±16,11
	I	2,24 ±0,19	1,11 ±0,37	83,91 ±25,50

	II	2,17 ±0,16	1,27 ±0,28	122,73 ±17,10
	III	2,37 ±0,17	1,008 ±0,29	60,53 ±12,56

Table 2: Results for the control group (basic, after the 1, 3, and 6 months)

Gender	age	Ca	P	Alk. Phosph.
F=9 M=6	72,93 ±6,19	2,24 ±0,25	1,22 ±0,55	79,33 ±18,67
	I	2,24 ±0,25	1,23 ±0,59	81,46 ±9,87
	II	2,21 ±0,21	1,02 ±0,35	77,06 ±10,29
	III	2,23 ±0,17	1,11 0,38	77,06 ±9,94

Referent values in our laboratory for Calcium are 2.10-2.75 mmol/l; for Phosphorus 0.80-1.40 mmol/l,and for alkaline phosphatase 38-126 U/L.

Groups are matched for age (t- test 1, 2; p= 0, 251) and gender (t-test 0, 91; p = 0, 362).

Fig. 1 shows the levels of Calcium in both groups at the beginning, after the first, third and sixth months. Ca1 is for experimental, and Ca 2 for control group.

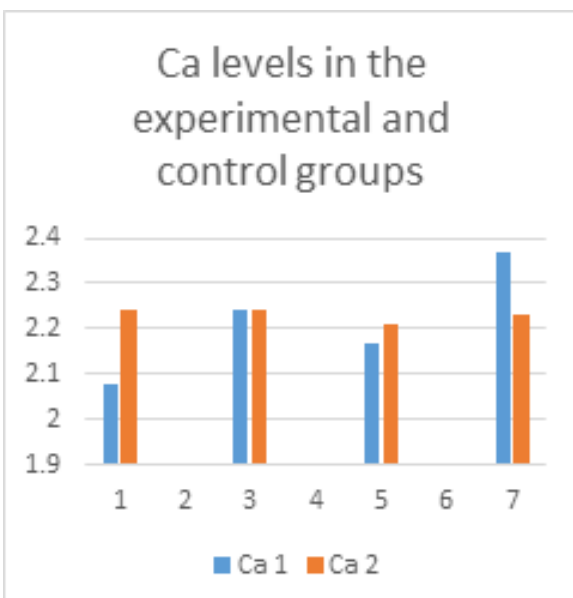


Fig 1. Levels of Calcium (mean values in mmol/l) in both groups (basic and after 1, 3, and 6 months period)

As can be seen the levels of Calcium in all samples are in normal range.

The levels of Phosphorus are presented on Fig. 2; P1 is for experimental and P2 for control group.

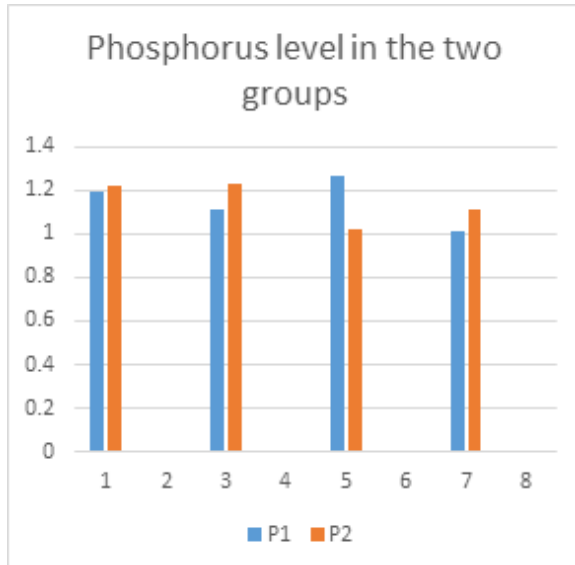
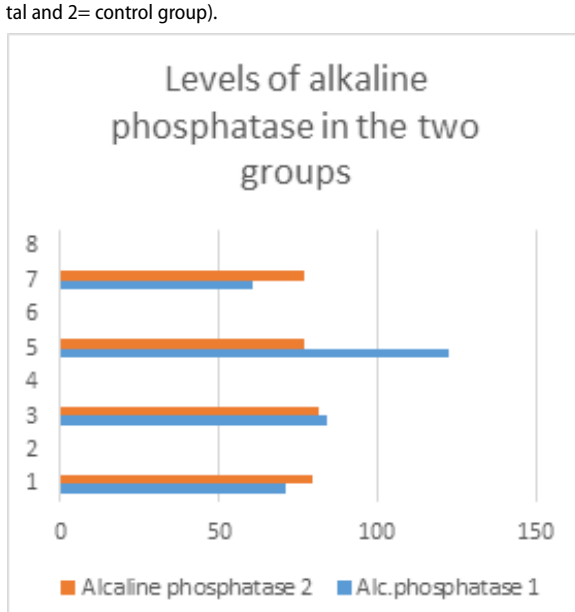


Fig 2. Levels of Phosphorus (mean values in mmol/l) in both groups (basic and during 1, 3 and 6 months period) The level of Phosphorus in all samples is normal, too.

Fig. 3 shows obtained values for alkaline phosphatase (1= experimental and 2= control group).



Alkaline phosphatase measures the metabolic activity of bone and in all samples is in normal range. Maximal values of alkaline phosphatase are obtained in experimental group after one month's treatment with vitamin D3

Fig. 3. Levels of alkaline phosphatase (mean values in U/l) in both groups (basic and after 1, 3 and 6 months period)

Statistical evaluation for the data of the**experimental group** are presented on Table 3.

Table 3. Correlations obtained for biochemical results (experimental group)

Correlation gender/Calcium	0,108718
Correlation age/Calcium	-0,028912
Correlation gender/Phosphorus	-0,318954*
Correlation age/Phosphorus	-0,186451
Correlation gender/alkaline phosphatase	-0,212403

Correlation age/alkaline phosphatase	-0,070426

Calculated correlations between gender and age and the level of Ca (r= 0,108) and (r= -0,028) respectively, are not significant. Only significant is the negative correlation between gender and the level of phosphorus (r= -0,318).

ANOVA for Ca level for both genderis not significant (F (1, 58) p=0, 40).

Statistics for **the control group** shows significant correlation between gender and the level of Calcium (r=0, 29), gender and phosphorus level (r= 0,29) as well as gender and alkaline phosphatase (r=-0,3790).

Table 4. Calculation obtained for biochemical results (control group)

Correlation gender/Calcium	0, 29
Correlation age/calcium	-0,3317*
Correlation gender/Phosphorus	0,2918*
Correlation age/Phosphorus	-0,1910
Correlation gender/alk.phosphatase	-0,3790*
Correlation age/alk. phosphatase	- 0,3790

Fig.4 shows correlation between gender and the level of alkaline phosphatase.

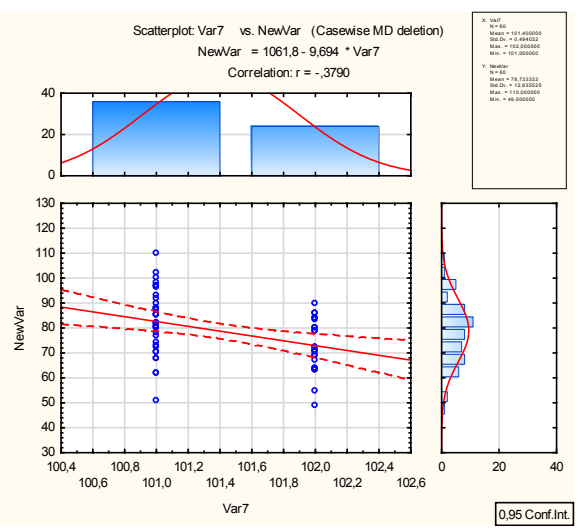


Fig. 4 Correlation obtained between gender and the level of alkaline phosphatase Concerning the level of alkaline phosphatase in different age we obtained ANOVA which is significant [F (34, 25)= 3,0017, p = 0,0028] (Fig.5).

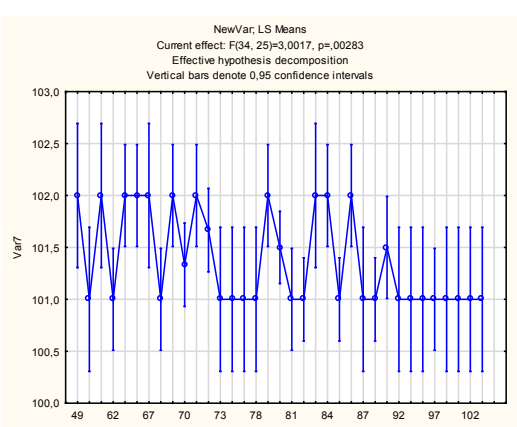


Fig. 5. ANOVA for alkalinePhosphatasein different age

In addition, we calculated Student t-test for the differences in Calcium and Phosphorus during the follow up period for the control and experimental groups and obtained results are not significant: for Ca (t-test 0,524 p = 0,60) and for Phosphorus (t-test= - 0,038; p = 0,969).

Opposite, Student t-test for differences in alkaline phosphatase during the treatment period shows high significant results (t= 2, 467; p= 0, 015).

It is clear that the main biochemical parameter for the metabolism of vitamin D is alkaline phosphatase.

The group which obtained 5000 IE Cholecalciferol shows on X ray imaging callus formation in 7/15 for the first months period; while the control group shows only partially formed callus in 5/15 patients.

After the period of three months with D3 vitamin treatment practically all patients (14/15) showed callus formation, which is strongly confirmedafter six month of the treatment with D3 vitamin (15/15).

In the control group after three months period 8/15 patients manifested partial callus on X-ray imaging, in 4/15 the callus was probable, while in two (2/15) was not yet present.

After the period of six months in this group callus was visible in 5/15; partially visible in 8/15 patients while in 2/15 was not visible.

The motoric function (walking, staying, and setting) was as follows: In the group which obtained D3 vitamin after six months 11/15 of patients could walk alone, and 4 of them needed some minimal orthopedic help.In the control group after six months period only 8/15 could walk alone, the others needed orthopedic help.

Discussion

Many years ago, Lips (1985) alarmed that vitamin D deficiency is common in the elderly people, especially in patients with hip fracture. Elderly people infrequently stay outside in the sunshine, and nutrition is also deficient in vitamin D. In addition, the hydroxylation of vitamin D into active metabolites decreases with age. Vitamin D deficiency ultimately leads to osteomalacia, but in an earlier stage it causes secondary hyperparathyroidism, which is accompanied by increased bone turnover and cortical bone loss. Along these pathways vitamin D deficiency may contribute to the pathogenesis of hip fractures. In a survey of a population in Amsterdam vitamin D deficiency was observed in more than 60% of the patients with hip fracture. The elderly which are institutionalized carry an increased risk. It was concluded that prevention of vitamin D deficiency is possible by adequate exposure to ultraviolet light. When sunshine exposure is negligible, as in many disabled and institutionalized elderly, a daily supplement of vitamin D3 400 IU should be given.

However, in the following period many surgeons forgot to give vitamin D supplementation after hip fractures which are mainly treated surgically. The recent study of Maier (2013) showed that only about 20% of seniors receive vitamin D at the time of their fracture and after the event. This is despite the documented 81% prevalence of vitamin D deficiency. Interdisciplinary efforts may be warranted to improve vitamin D supplementation in seniors both before a hip fracture occurs and after.

In the study of Iolascon *at all* (2009) the data suggest that vitamin D is important to reach a good functional outcome and to reduce the risks of new fractures. After orthopedic surgery, vitamin D and calcium supplementation in a correct nutrition, physical exercise, can ensure the optimal recovery and survival, especially in hip fractured patients.

As conclusion of the large study of Chapuy*at all*.(1992) published in the prestigious New England Journal of Medicine,it was suggested that 18 months of daily supplementation with 1.2 g. of elemental calcium and 800 IU of vitamin D_3 was safe and decreased the incidence of hip fractures and other nonvertebral fractures among elderly women. As these results demonstrate, it may never be too late to prevent hip fracture.

There remains uncertainty regarding the appropriate therapeutic management of hip fracture patients. The primary aim of the study of Papaioannou*et all* (2011) was to examine whether large loading doses in addition to daily vitamin D offered any advantage over a simple daily low-dose vitamin D regimen for increasing vitamin D levels. Their findings suggest that starting with a lower daily dose of Vitamin D_3 achieved similar results as providing an additional large loading dose of Vitamin D_2.

In many studies concerned the hip fractures it was confirmed that about 87% happened over the age of 65, and 82% of these are women. As it is well known, risk factors for osteoporosis are many, and include: genetic predisposition, poor nutrition in childhood and adolescence, early age of onset of menopause, decreased exposure to sunshine and low vitamin D intake, low dietary calcium, alcohol and cigarette use, caffeine consumption, low weight, lack of regular exercise.

An adequate vitamin D intake is associated with a lower risk of osteoporotic hip fractures in postmenopausal women. Neither milk nor a high-calcium diet appears to reduce risk. Because women commonly consume less than the recommended intake of vitamin D, supplement use or dark fish consumption may be prudent (Feskanich, 2003).

The cost of a broken hip has been estimated at 5,000sterling (strictly hospital medical costs), but some others have suggested much higher figures. Prophylactic treatment of high-risk patients would be worthwhile if the cost of prophylaxis was about the same or less than the cost of treating a fractured hip (**Bandolier** conference on osteoporosis **25**, March 1996).

The results of our study confirm the beneficial effect of D3 supplementation after hip fractures even it was given after the fracture. So, in all surgical protocols for hip fractures treatment D3 vitamin supplementation must be proposed.

Conclusion

- This study confirm the importance of vitamin D in the recovery of hip fractures.
- It was shown correlations between biochemical markers and age/ gender, especially this for alkaline phosphatase.
- Supplementation of vitamin D must start the day of hospitalization (if it is not the case in earlier pre hospital period). All elderly people, especially postmenopausal women must take preventive dose of vitamin D for diminishing risk for fractures. It is not enough sunlight exposure and nutritive regiment for normal needs of vitamin D daily.

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