

©Borgis

*Małgorzata Berwecka¹, Jarosław Amarowicz¹, Edward Czerwiński^{1, 2}

Vitamin D₃ and falls

Witamina D₃ a upadki

¹Department of Bone and Joint Diseases, Faculty of Health Sciences, Jagiellonian University Medical College, Kraków

Head of Department: Professor Edward Czerwiński, MD, PhD

Assistant: Małgorzata Berwecka, MSc; Jarosław Amarowicz, MSc

²Cracow Medical Center

Head of Center: Professor Edward Czerwiński, MD, PhD

Keywords

falls, vitamin D, elderly, prevention, muscle

Słowa kluczowe

upadki, witamina D, starzenie się, zapobieganie, mięsień

Conflict of interest

Konflikt interesów

None

Brak konfliktu interesów

Address/adres:

*Małgorzata Berwecka
Department of Bone and Joint Diseases
Faculty of Health Sciences
Jagiellonian University Medical College
ul. Kopernika 32, 31-501 Kraków
tel. +48 (12) 430-32-09
berwecka@kcm.pl

Summary

Falls are one of the major health and social issues among the elderly. They constitute one of the main causes of disability or death among people over the age of 75. Causes of falls are complex. Falls are almost always caused by the coexistence of a few factors – eliminating even one may be enough to prevent a fall. Vitamin D plays an important role in maintaining proper muscle function in the elderly, including prophylaxis of sarcopenia. Numerous studies present a correlation between the deficiency of 25(OH)D and increased risk of falls. Regardless of the reasons of falls, physical exercises are the most effective preventive measure, because they affect not only muscular system, but health in general. That is why today it is impossible to overestimate the impact of various types of exercise interventions, including: home, group, individual, power, balance exercises, Tai Chi, Nordic walking etc. in fall prophylaxis. Although exercises remain the most efficient way to prevent falls, a wide spectrum of vitamin D₃ benefits combined with its low cost gives enough evidence that prophylactic supplementation of vitamin D₃ is justified.

Streszczenie

Upadki są jednym z największych problemów medycznych i społecznych dotyczących osoby starsze. Należą one do głównych przyczyn niepełnosprawności i śmierci w grupie osób po 75. roku życia. Upadki są następstwem równoczesnego występowania czynników zewnętrznych i wewnętrznych w postaci niewydolności wielu układów i narządów.

Witamina D pełni istotną rolę w prawidłowym funkcjonowaniu aparatu mięśniowego u osób starszych. Jej znaczny niedobór jest jednym z istotnych czynników ryzyka upadku.

Nie podlega również wątpliwości, że niezależnie od przyczyn upadku ćwiczenia fizyczne są najbardziej skuteczne, bowiem wpływają nie tylko na sprawność mięśni, ale na ogólny stan zdrowia organizmu człowieka. Dlatego współcześnie nie można mówić o profilaktyce upadków z pominięciem wpływu różnego typu interwencji ruchowych, obejmujących ćwiczenia domowe, w grupach, indywidualne, siłowe, równoważne, wydolnościowe, Tai Chi, nordic walking i inne. Jednak biorąc pod uwagę rozpowszechnienie deficytów/niedoborów 25(OH)D w populacji osób starszych, szerokie spektrum jej korzystnego oddziaływania na organizm (układ immunologiczny, układ sercowo-naczyniowy, onkogenezę i funkcje poznawcze) oraz niski koszt, jej profilaktyczna suplementacja jest uzasadniona, zwłaszcza jako uzupełnienie różnych form aktywności ruchowej.

FALLS AS A MEDICAL AND SOCIAL ISSUE

“Population aging is a triumph of humanity, but is also a major challenge for the society” – falls among the elderly, both in medical and social context, are among these challenges (1). The problem with falls among the elderly will systematically increase with the following years as the population is aging. Falls are

one of the major causes of disability or death among people over 75. The frequency of injuries caused by falls has increased by 131% over the last three decades. The lack of undertaking proper prophylactic measures may result in further increase of fall-related injuries – as high as 100% until 2030. It is estimated that each year 1 out of 3 people over 65 experiences

a fall. After the age of 85 the number increases to 50% of the population. The highest risk can be observed among the inhabitants of Social Welfare Homes – 80% over 65 sustain a fall. Falls are also responsible for 50% of hospitalizations among people over 65. They are the cause of 40% of trauma-related deaths (2). Frequency of hospitalizations (due to a fall-related trauma) increases with age – the risk is two times greater for women. Fractures are the main reason for hospitalizations, usually fracture of the hip (3). Falls are not only a significant fracture risk factor in the elderly, but they also have an impact on the quality and length of life. Psychological and social results, such as the fear of a subsequent fall, are also crucial as they are a significant risk factor for subsequent falls. A fall, even without an injury, often results in self-restraint of physical activity, resulting in limited physical function and social interaction, even in isolation. It is a risk factor for dementia and also an independent predictive risk factor for institutional care (4). In 2007 WHO recognized falls as one of the major health and social issues (5).

Causes of falls are complex. Currently there are 400 known clinical risk factors for falls. Despite the fact that some of them cannot be eliminated, there is a great number of those which can be completely eradicated. They have been divided into external (associated with the environment) and internal (associated with health or increase of the disease symptoms). According to EBM among the most crucial factors are: muscle weakness, prevalent falls, balance disorder, gait disturbance, visual or cognitive function impairment, memory loss, depression and others (6). Many studies show that the fall risk is associated with ADL (Activities of Daily Living). Problems with performing even one ADL or IADL (Instrumental Activity of Daily Living) activity doubles the risk of falling (7). Correlation between prevalent falls and the use of orthopedic aids has also been reported (8). What is most important – falls are almost every time caused by the coexistence of a few factors – eliminating even one may be enough to prevent a fall from happening.

VITAMIN D AND FUNCTIONAL PERFORMANCE

Study results present a strong correlation between the efficiency of the musculoskeletal system and the risk of falling. Active form of vitamin D – 1,25(OH)₂D is a calcitropic hormone that plays an important role in the extracellular homeostasis of calcium and phosphorus between thin borderlines set as a standard required for proper functioning of nerves and muscles. Many studies proved that a higher concentration of vitamin D is associated with better balance, mobility and better self-reliance. Inversely, its deficiency results in lower muscle mass, decreased mobility, weakness of antigravity muscles, slower defense and balance reactions, muscle pains, paresthesia and joint pain (9, 10). It has been observed that people who have sustained a fall have a significantly lower level of 25(OH)D as compared to those who do not have a history of falls (11).

Cross-sectional studies (12-15) along with prospective observational surveys (16, 17) present an overview of effect of vit. D on muscle strength (upper and lower limb). It shows that it plays an important role in maintaining proper muscle function in the elderly, including the prophylaxis of sarcopenia.

Vitamin D influences muscles directly and indirectly. It affects the muscles indirectly by inducing changes in calcium absorption. Recent studies show that muscle weakness, detected in vitamin D deficits, may be partially explained by accompanying hypophosphatemia. It shows the effect of vitamin D on the functioning of muscle tissue by improving mitochondria's oxidative function (18). Another indirect mechanism by which vitamin D affects the skeletal muscles is the reduction of fat tissue (located in and between muscles). Studies indicate that the process of storing fat in muscles increases with age and it is a significant, independent prognostic factor for muscle function and physical performance among elderly. There is also a proof that higher physiological levels of 1,25(OH)₂D inhibits the growth of fat in muscles by decreasing transdifferentiation of myogenic stem cells into adipocytes (19).

Vitamin D affects the muscles by membrane receptors and nuclei receptor VDR (Vitamin D Receptor). Active vitamin D metabolite – 1,25(OH)₂D affects calcium transportation to the tissue by binding with the nuclei receptor VDR in the skeletal muscle tissue. Therefore, it directly influences the strength and time of a muscle contraction, stimulates protein biosynthesis – in consequence increasing amount of type II muscle cells which promotes the growth of muscle speed and strength.

The use of highly specific and sensitive VDR antibody lead to controversies regarding presence of VDR in skeletal muscles. Scientists were unable to identify them in skeletal muscles of adult mice, rats and humans (20, 21). Inconsistencies may be explained by different experimental conditions and also by differences in VDR expression in various groups of muscles – between species and stages of cell differentiation. It has been proven that during the proliferation and the differentiation phase of muscle cells – 1,25(OH)₂D may inhibit myoblast proliferation in muscle cell lines in mice, and at the same time it can increase the expression of fast myosin heavy chain isoform during the differentiation phase. This discovery may be a potential confirmation on the role of vitamin D in type 2 muscle fibers hypertrophy (22).

EFFICIENCY OF INTERVENTIONS IN FALLS PREVENTION

Taking under consideration positive effects of vitamin D on muscle mass and function – increasing risk of falls with age, the fact that 90% of fractures are caused by falls and common existence of vit. D deficiency (25-50 nmol/l 25(OH)D) or shortage (12.5-25 nmol/l 25(OH)D) among the elderly – vitamin D supplementation became a standard procedure

in some fields of geriatric medicine. Based on those facts it is expected that most of the randomized clinical trials should confirm its crucial role in fall prevention in the elderly. However, reports on vitamin D efficiency in fall prevention show that there is still a lot of controversies regarding the topic.

Results presented in systematic reviews which examine various fall prevention therapies seem to deny the efficiency of vitamin D supplementation. Some studies did not show any statistically significant differences between groups receiving vitamin D and control groups – neither in reference to the frequency or risk of falls (23). There was no confirmation of the fact that vitamin D₃ supplementation may decrease the risk of falling by 15%. Furthermore, the authors claimed that the current knowledge is insufficient to prove the sense of prescribing vitamin D supplements as a fall preventing measure (24). Probably the main reason for such discrepancies might be incomparable study groups and the fact the many of the studies did not take under consideration 25(OH)D level at the baseline.

There are many studies which confirm the efficiency of vitamin D on preventing falls which underline its high efficiency among specific subgroups, such as: community-dwellers, age over 80, patients receiving calcium supplements, patients with no prevalent falls and patients on supplemental vitamin D intake of more than 6 months (25). Dosage and achieved concentration of 25(OH)D in plasma also proved to be significant in the matter. Reduction of falls risk was noticed with doses of 700 IU and higher as well as 25(OH)D concentration at 60 nmol/l (26). In the studies where vitamin D₃ deficiency was among the inclusion criteria, its efficiency was proven without a doubt (27-30).

Interesting results were found in a study on the efficiency of falls prevention when combining vitamin D and exercises. In this 2-year, double-blind, randomized study, involving 409 female subjects aged 70-80, participants were divided into 4 groups: placebo without exercises, vitamin D₃ (800 IU), exercises, exercises and vitamin D₃ (800 IU/day). Intent-to-treat analysis showed that neither vitamin D₃ nor exercises, nor both interventions combined decreased the frequency of falls. However, the frequency of falls with recurring trauma as well as relative risk of falling with trauma proved to

be significantly lower in groups with exercises or exercises + vitamin D₃. Reduction in frequency was nonetheless associated mainly with balance exercises and strength training – as the biggest difference (~50%) was noticed in a group with exercises alone. Relative risk in a group with vitamin D₃ alone was similar to the placebo group without exercises (31). Observation is consistent with the results from other meta-analysis in which the efficiency of various falls prevention interventions was under scrutiny – proving that the most efficient way to reduce the risk of falling is to use complex physical exercise. Exercises were responsible for the reduction of frequency and risk of falling and, what is most important, decreasing the frequency of fall related fractures (23, 32).

CONCLUSIONS

Falls are a result of a simultaneous coexistence of many factors (internal and external), presenting in a form of dysfunctions of many systems and organs. There is no universal medicament which could be used in order to “heal” all of them. Therefore, it would be a mistake to believe that vitamin D might be a universal solution. On the other hand it has been proven that eliminating just one of the factors is often enough to prevent a fall. Due to its effect on the function of musculoskeletal system – vitamin D deficiency may prove to be that single factor. There is a lot of evidence showing that there is a relation between low level of 25(OH)D and increased risk of falls. We can state without any doubt that exercises remain the most efficient way to prevent falls – due its effect on muscle performance and human condition. This is why we cannot debate fall prevention without including different types of physical activities (such as exercises at home, in groups, individual, balance, focused on muscle power and endurance, Tai Chi, Nordic Walking, etc.). Taking under consideration common deficits/shortages of 25(OH)D among the elderly along with a wide spectrum of this vitamin's benefits (on immune system, cardiovascular system as well as on oncogenesis and cognitive functioning) and low price, its prophylactic supplementation is highly justified, especially as an addition to various types of physical activity.

BIBLIOGRAPHY

- Kalache A, Gatti A: Active ageing: a policy framework. *Adv Gerontol* 2003; 11: 7-18.
- British Orthopaedic Association: Blue Book. September 2007.
- Peel NM, Kassulke DJ, McClure RJ: Population based study of hospitalised fall related injuries in older people. *Inj Prev* 2002; 8(4): 280-283.
- Yardley L, Smith H: A prospective study of the relationship between feared consequences of falling and avoidance of activity in community-living older people. *Gerontologist* 2002; 42(1): 17-23.
- WHO global report on falls prevention in older age. WHO, Genova 2007; www.who.int/ageing/publications/Falls_prevention7March.pdf (accessed: 14 July 2016).
- Todd C, Skelton D: What are the main risk factors for falls amongst older people and what are the most effective interventions to prevent these falls? WHO, Health Evidence Network (HEN) 2004; www.euro.who.int (accessed: 14 July 2016).
- Bloch F, Thibaud M, Dugué B et al.: Episodes of falling among elderly people: a systematic review and meta-analysis of social and demographic pre-disposing characteristics. *Clinics (Sao Paulo)* 2010; 65(9): 895-903.
- Deandrea S, Lucenteforte E, Bravi F et al.: Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiology* 2010; 21(5): 658-668.

9. Menant JC, Close JC, Delbaere K et al.: Relationships between serum vitamin D levels, neuromuscular and neuropsychological function and falls in older men and women. *Osteoporos Int* 2012; 23(3): 981-989.
10. Czerwiński E, Kumorek A: Upadki, witamina D i złamania. *Postępy Nauk Medycznych* 2012; 3: 226-231.
11. Annweiler C, Beauchet O: Questioning vitamin D status of elderly fallers and nonfallers: a meta-analysis to address a 'forgotten step'. *J Intern Med* 2015; 277: 16-44.
12. Gerdhem P, Ringsberg KAM, Obrant KJ, Akesson K: Association between 25-hydroxy vitamin D levels, physical activity, muscle strength and fractures in the prospective population-based OPRA Study of Elderly Women. *Osteoporos Int* 2005; 16(11): 1425-1431.
13. Houston DK, Cesari M, Ferrucci L et al.: Association between vitamin D status and physical performance: The InCHIANTI Study. *J Gerontol A Biol Sci Med Sci* 2007; 62(4): 440-446.
14. Tieland M, Brouwer-Brolsma E, Nienaber-Rousseau C et al.: Low vitamin D status is associated with reduced muscle mass and impaired physical performance in frail elderly people. *Eur J Clin Nutr* 2013; 67(10): 1050-1055.
15. Janssen HC, Emmelot-Vonk MH, Verhaar HJ, Schouw YT: Vitamin D and muscle function: is there a threshold in the relation? *JAMDA* 2013; 14(8): 27.
16. Scott D, Bizzard L, Fell J et al.: A prospective study of the associations between 25-hydroxyvitamin D, sarcopenia progression, and physical activity in older adults. *Clin Endocrinol* 2010; 73(5): 581-587.
17. Houston DK, Tooze JA, Neiberg RH et al.: 25-Hydroxyvitamin D status and change in physical performance and strength in older adults the health, aging, and body composition study. *Am J Epidemiol* 2012; 176(11): 1025-1034.
18. Sinha A, Hollingsworth KG, Ball S, Cheetham T: Improving the vitamin D status of vitamin D deficient adults is associated with improved mitochondrial oxidative function in skeletal muscle. *J Clin Endocrinol Metabol* 2013; 98(3): E509-513.
19. Ryan KJ, Daniel ZC, Craggs LJ et al.: Dose-dependent effects of vitamin D on transdifferentiation of skeletal muscle cells to adipose cells. *J Endocrinol* 2013; 217(1): 45-58.
20. Czerwiński E, Borowy P, Kumorek A: Witamina D a układ mięśniowo-szkieletowy. *Stand Med* 2012; 9: 649-654.
21. Wang Y, DeLuca HF: Is the vitamin D receptor found in muscle? *Endocrinology* 2011; 152(2): 354-363.
22. Okuno H, Kishimoto KN, Hatori M, Itoi E: $1\alpha,25$ -dihydroxyvitamin D₃ enhances fast-myosin heavy chain expression in differentiated C2C12 myoblasts. *Cell Biol Int* 2012; 36(5): 441-447.
23. Gillespie LD, Robertson MC, Gillespie WJ et al.: Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012; 12(9): CD007146.
24. Bolland MJ, Grey A, Gamble GD, Reid IR: Vitamin D supplementation and falls: a trial sequential meta-analysis. *Lancet Diabetes Endocrinol* 2014; 2(7): 573-580.
25. Kalyani RR, Stein B, Valiylil R et al.: Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis; *J Am Geriatr Soc* 2010; 58(7): 1299-1310.
26. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB et al.: Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ* 2009; 339: b3692.
27. Pfeifer M, Begerow B, Minne HW et al.: Effects of a long-term vitamin D and calcium supplementation on falls and parameters of muscle function in community-dwelling older individuals. *Osteoporos Int* 2009; 20(2): 315-322.
28. Prince RL, Austin N, Devine A et al.: Effects of ergocalciferol added to calcium on the risk of falls in elderly high-risk women. *Arch Intern Med* 2008; 168(1): 103-108.
29. Dhesei JK, Jackson SH, Bearne LM et al.: Vitamin D supplementation improves neuromuscular function in older people who fall. *Age Ageing* 2004; 33(6): 589-595.
30. Pfeifer M, Begerow B, Minne HW et al.: Effects of a short-term vitamin D and calcium supplementation on body sway and secondary hyperparathyroidism in elderly women. *J Bone Miner Res* 2000; 15(6): 1113-1118.
31. Uusi-Rasi K, Patil R, Karinkanta S et al.: Exercise and vitamin D in fall prevention among older women: a randomized clinical trial. *JAMA Intern Med* 2015; 175(5): 703-711.
32. Stubbs B, Breda S, Denkiner MD: What Works to Prevent Falls in Community-Dwelling Older Adults? Umbrella Review of Meta-analyses of Randomized Controlled Trials. *Phys Ther* 2015 Aug; 95(8): 1095-1110.

received/otrzymano: 01.09.2016
accepted/zaakceptowano: 22.09.2016