Effect of a 6-week Cycle of Nordic Walking Training on Vitamin 25(OH)D₃ Calcium-phosphate Metabolism and Muscle Damage in Multiple Myeloma Patients

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Abstract

Introduction: Multiple myeloma (MM) is a hematological malignancy affecting older adults (median age 70 years). One of the most common myeloma defining events is the development of symptomatic lytic bone disease which leads to fractures and immobilization. It is caused by disturbances in bone metabolism affecting calcium-phosphate balance. Treatment of the bone disease and the underlying malignancy results in disease and symptom control.

Objectives: In this study, the impact of a 6-week Nordic walking (NW) exercise program on blood parameters related to calcium-phosphate metabolism and damage of skeletal muscles was assessed.

Patients and methods: 28 subjects with MM in remission stage, without cytostatic treatment were enrolled and completed the study: 15 in the training group (NW) and 13 in control group (CG). All patients were supplemented with vitamin D₃, calcium carbonate daily and received zoledronic acid every 4 weeks. Two venous blood samples were drawn – before and after the 6 weeks of training sessions – to assess the serum concentrations of vitamin 25(OH)D₃, inorganic phosphorus, total calcium, myoglobin, and lactate dehydrogenase (LDH).

Results: Patients from the NW group showed a statistically significant decrease in mean serum myoglobin concentration ($p=0.018$) and increase in 25(OH)D₃ ($p<0.001$) and total Ca ($p=0.001$) concentrations. In the NW group, there was a correlation between the changes in myoglobin, phosphorus, 25(OH)D₃ and Ca concentrations after 6 weeks.

Conclusions: NW training is a safe and beneficial form of physical exercise for patients with MM without inducing muscle damage. NW performed outside during Spring-Summer season improves serum vitamin 25(OH)D₃ concentration.

Introduction

Multiple myeloma (MM) is a plasma cell malignancy producing a monoclonal paraprotein either an intact immunoglobulin or its fragment which are detected by electrophoresis in the serum and/or urine [1]. The immunoglobulin isotype of the monoclonal protein, the heavy chain and light chain, is determined by immunofixation electrophoresis. Enumeration of the serum free light chain levels and the kappa/lambda ratio has provided a sensitive additional level of sophistication to paraprotein production at diagnosis and in response to treatment. In rare cases of non-secreting myeloma (approximately in < 2% of patients), no monoclonal protein is detected by these technologies [2].

MM accounts for 10-15% of all hematological malignancies and about 1-2% of all cancer cases [3]. It occurs predominantly in elderly people, the median age at diagnosis is 70 years, and 90% of patients are over 50 years old [1, 4]. Over the past 18 years, there have been 15 new drugs drugs have been approved for the treatment of MM resulting in almost doubling of the median survival to over 55% at 5 years [5]. The goal of anti-myeloma therapy is to achieve complete remission, to the level of minimal residual

disease. The frequency with which therapeutic strategies are utilized is dependent on the availability in individual countries [6]. The standard of care is induction with triplet therapy utilizing different mechanisms of action (e.g., proteasome inhibitors, immunomodulatory drugs, corticosteroids) to be followed by consolidative high dose therapy with autologous hematopoietic stem cell transplant (ASCT) for those patients who are eligible for HSCT. Slightly less aggressive therapy is often incorporated into the treatment of non-transplant eligible patients due to (age, frailty, and inadequate physiologic organ function) [1, 7, 8].

Bone involvement in multiple myeloma

Bone involvement in MM occurs in 80% of patients and is manifested as myeloma bone disease (MBD) [9]. It includes skeletal complications such as osteolytic lesions, bone pain, pathological fractures and osteoporosis [1]. The formation of osteolytic lesions is associated with the disturbance of the balance between osteoblasts and osteoclasts – it is shifted towards the osteoclastic destruction of bone tissue resulting from the interaction of neoplastic plasma cells and their cytokines within the bone marrow microenvironment [10]. Osteolytic lesions rarely heal, but the process of their formation can be slowed or stopped by administering bisphosphonates or rank-ligand inhibitors [9]. In addition, bisphosphonates/rank-ligand inhibitors are effective in the treatment and prevention of hypercalcemia [1]. The successful treatment of the MM by anti-myeloma agents also prevents the development of new MBD.

Physical activity in multiple myeloma patients

Patients with MM are candidates, even with MBD, for physical activities of low and moderate intensity [11]. In Poland, patients with MM do not have ready access to rehabilitation centers or private physical therapists [12]. A number of research studies have shown the beneficial effect of regular physical activity in patients with MM, with improvement in functional and psychological aspects [13–15] even if applied during MM therapy [16, 17]. However, there are no reports assessing the impact of physical training on biochemical parameters in MM patients.

Patients And Methods

The aim of this study was to assess the effect of a 6-week Nordic walking training cycles on the blood concentrations of the active metabolite of calcidiol (25(OH)D₃), total calcium (Ca), inorganic phosphorus (P), myoglobin (Mb) and lactate dehydrogenase (LDH) activity in MM patients in remission.

Study group

Thirty-three MM patients in the Department of Hematology of Jagiellonian University Medical College in Krakow were recruited to participate in this study. Participants were randomly assigned to one of 2 groups: Nordic walking (NW; n = 17) and the control group (CG; n = 16). The NW group underwent a 6-week health walking training cycle; the CG did not have any formal planned physical activity. All patients

were supplemented with 2000 U of vitamin D3 and 1000-1500 mg calcium carbonate daily and received 4 mg zoledronic acid i.v. every 4 weeks. The inclusion criteria were: MM in remission, ECOG scale: 0-1, no contraindications to participate in health training, and no chronic respiratory diseases. The exclusion criteria were: hypercalcemia, active infection requiring treatment, and any pre-existing injury of the limbs or trunk which would limit participation in the study.

The patients were informed that participation in this study was voluntary and were acquainted with the details of the project. The study protocol was constructed according to the Declaration of Helsinki, and all participants gave their written consent. The procedures of this study were approved by the Bioethical Committee at the District Medical Chamber in Krakow (166/KBL/OIL/2018).

Study protocol

Blood samples were obtained pre-study and at the completion of the study at 6 weeks. The determination of the concentrations of biochemical indices in the serum was performed in the medical diagnostic laboratory with use of Cobas 6000/8000 analyzer (Roche Diagnostics, USA). The concentrations of P and total Ca were determined using the colorimetric method. LDH activity was determined according to the UV test methodology. Vitamin 25(OH)D₃ concentration was determined with use of electrochemiluminescence (ECLIA) method and myoglobin concentration – with use of chemiluminescence method.

Nordic walking training

Nordic walking training sessions were performed 3 mornings a week during Spring-Summer at the Academy of Physical Education in Krakow by a qualified instructor for 6 weeks. The Nordic walking pole lengths were adjusted for each participant individually. The subjects were instructed to the correct Nordic walking technique, which was individually monitored and adjusted for each participant during the training.

Each session consisted of a 10-minute warm-up, including limb, general development and dynamic stretching exercises. The planned duration of the Nordic walking was 45 minutes. The walking time, and thus, the distance, was extended with each training session, until it reached a maximum of 45 minutes. At the end, a 5-minute cooling period was performed, during which the patients were performing breathing and stretching exercises.

Statistical analysis

Descriptive statistics (mean, standard deviation) were calculated for all variables, the normality of the distribution was assessed (Saphiro-Wilk test) and the homogeneity of the variance for variables with a normal distribution was verified (Levene's test) [24]. The results $p < 0.05$ were considered statistically significant. Student's t-test for dependent groups was used to compare the results of the blood biochemical analyses in each group. Pearson's r correlations were also calculated for all tested

parameters. Statistical analyses were performed using JASP 0.14.1 software (University of Amsterdam, Netherlands).

Results

The 6-week NW cycle was completed by 15 patients (8 women and 7 men, mean age: 62.3 ± 8.5 years). Thirteen patients (5 women and 8 men, mean age: 63.7 ± 3.7 years) completed the study as control group (CG). 5 patients (5 from NW, 3 from CG) did not complete the study due to personal reasons (3) or meeting the exclusion criteria during their participation in this research project (2).

Serum Mb concentration after 6 weeks in the NW group decreased significantly from the initial level by an average of $6.1 \mu\text{g/l}$ ($t=2.687$, $p=0.018$). No statistically significant changes were observed in the CG group for this parameter. Between the groups, statistically significant changes were observed only in the Mb concentration ($t=2.150$, $p=0.041$). No significant differences in groups and between groups were noted for LDH activity in both timepoints. The concentration of $25(\text{OH})\text{D}_3$ (calcidiol) in the NW group at baseline was within the normal range in 6 patients (between $30\text{--}80 \text{ ng/ml}$, mean: $37.75 \pm 6.3 \text{ ng/ml}$), low (between $20\text{--}30 \text{ ng/ml}$, mean: $25.4 \pm 2.5 \text{ ng/ml}$) in 4 patients, and the severely low in 5 patients ($<20 \text{ ng/ml}$, mean: NW, the concentration of calcidiol increased significantly in all subjects ($t=-5.809$, $p<0.001$) in average by 9.9 ng/ml (mean: $26.7 \pm 3.8 \text{ ng/ml}$). In 10 subjects, the calcidiol either remained in the normal range ($n=6$) or improved from low or severely low ($4/9$) (mean: $41.3 \pm 9.8 \text{ ng/ml}$). Even after the NW training, 5 patients remained in the low range but none in the severely low range (mean: $26.7 \pm 3.8 \text{ ng/ml}$). There were statistically significant changes between the groups in vitamin $25(\text{OH})\text{D}_3$ concentration ($t=-4.389$, $p<0.001$) (Figure 1). Concomitantly, an increase in serum total Ca concentration was observed by an average of 0.08 mmol/l ($t=-3.990$, $p=0.001$). There was a trend toward improvement in the total Ca concentration between groups ($t=-1.917$, $p=0.066$). In contrast, there was not a significant change in P concentrations in either group. The concentrations of P and Ca in all subjects from both groups were within the reference values. In the control group, no statistically significant changes in $25(\text{OH})\text{D}_3$, Ca, P, Mb serum concentrations and LDH serum activity were found.

Correlations

In the NW group, correlation was found for changes in the concentration of Mb and P with the concentration of Ca after 6 weeks ($r=-0.773$, $p=0.003$, and $r=0.527$, $p=0.043$, respectively) and changes in the concentration of Ca with the concentration of $25(\text{OH})\text{D}_3$ after 6 weeks of training ($r=-0.560$, $p=0.030$). For the remaining parameters, no statistically significant correlations were found. In the control group, no statistically significant correlation was found between the studied indices. There was no correlation of age and any of the parameters. Graphs showing statistically significant correlations are shown in Figure 1.

Discussion

Biochemical parameters of skeletal muscle damage

Lactate dehydrogenase (LDH)

Lactate dehydrogenase is an enzyme present in all cells, but its highest activity is observed in the cells characterized by a high level of energy metabolism: in skeletal and heart muscles, liver cells, neurons and erythrocytes. Elevated LDH activity in MM patients, after excluding other causes, may be associated with extensive disease or with presence of extramedullary plasmacytoma(s) [1]. Teke et al. [18] presented a case of MM patient in which LDH activity was within the reference range at the diagnosis but increased 27 times during progression and occurrence of extramedullary plasmocytomas. LDH activity level is a useful prognostic parameter in MM patients and is included in revised international MM staging system (R-ISS) [1]. Gu et al. reported that both progression-free survival (PFS) (12.0 months versus 24 months, $p < 0.001$) and overall survival (OS; 15.5 months versus 52.5 months, $p = 0.030$) was shorter compared to those with its normal LDH levels [19].

Changes in serum LDH activity depend on the type of training and the level of adaptation to training; it increases significantly when muscle damage occurs. Callegari et al. [20] compared changes in LDH activity after aerobic training with the intensity of 60%VO₂max and 80%VO₂max and aerobic training combined with resistance exercises. LDH activity measurements before and after training showed a statistically significant increase in all groups. Participation in NW may also affect LDH levels. Hagner-Derengowska et al. [21] reported on 32 post-menopausal women showed that LDH activity in its participants decreased significantly after a cycle of 10-week NW trainings (184.3 vs 175.7 IU/l).

In our study, LDH activity increased slightly in the NW group, while in the control group there was a minimal decrease in the activity of this enzyme. These changes, however, were not statistically significant, which allows us to conclude that the NW training stimulus was not strenuous enough to affect LDH activity.

Myoglobin (Mb)

Myoglobin is a protein present in heart and skeletal muscle cells with corresponding increases in Mb level with muscle damage. Mb functions in the storage of oxygen in the muscle – it releases oxygen molecules when the partial pressure in the cell decreases. In cases of massive muscle damage e.g. rhabdomyolysis, Mb may also appear in the urine. In addition, serum Mb concentration may be associated with deteriorating renal function with age [22]. The concentration of Mb in skeletal muscle cells increases as a result of regular exercise in an adaptive mechanism, which leads to an increase of the efficiency of oxygen delivery during exercise. Serum Mb levels rise in case of muscle damage, which leads to leakage of this protein from the cells. Physical exercise affects serum Mb concentration, which increases after a single exercise in proportion to its intensity [23]. Cornish et al. [23] reported on Mb concentration in 11 men over 65 years demonstrated that Mb levels after a single session of resistance exercise returns to the baseline values after 48 hours, regardless of exercise intensity. A significant increase in serum Mb

concentration was found after 3 hours. in the case of low exercise intensity, it returned to the baseline value after 24 hours, and in the case of moderate and high intensity – after 48 hours.

Initial Mb concentration in MM patients participating in our study was similar to the concentrations reported previously by Anesi et al. for healthy elderly subjects [22] – the mean Mb concentration in this population was 53,7 µg/l in men and 44.9 µg/l in women. In subjects taking part in our study, we observed a statistically significant decrease in the mean serum Mb concentration in the NW group as a result of participation in the NW (from 50.5 to 44.4 µg/l) while in the CG a slight increase was observed (from 52.8 to 53.6 µg/l). Statistically significant differences were shown between the study groups after 6 weeks – serum concentration in subjects from NW group was significantly lower than in CG.

Bone metabolism indicators: calcium-phosphate metabolism, vitamin 25-(OH)D₃

Calcium (Ca) and phosphorus (P)

MM affects the calcium-phosphate balance, hypercalcemia may occur in approximately 15-20% of patients at diagnosis and is one of CRAB diagnostic criteria [1]. Patients with MM may also develop hyperphosphatemia associated with renal failure and pseudohyphosphatemia associated with the interference of monoclonal protein in the IgG class with the method of determination of serum inorganic P [24, 25]. Renal-related hypophosphatemia in patients with MM may be associated with acquired Fanconi syndrome which is rare complication of MM. It is caused by a reabsorption dysfunction in the proximal tubules [26].

The calcium-phosphate metabolism is regulated by vitamin D₃, calcitonin and parathyroid hormone. The decrease in blood Ca concentration stimulates the release of Ca from the mineralized osteoid within minutes by the action of parathyroid hormone and vitamin 1,25(OH)₂D (calcitriol), which activates the release of Ca and P from the bone. In the kidney, there is an increase in the production of 1,25(OH)₂D, leading to increased reabsorption of Ca ions and inorganic P in the renal tubules. Additionally, the intestinal absorption of Ca, P, and magnesium increases.

Exercise affects the body's ionic balance, including blood levels of Ca and P. Acute physical exercise causes a decrease in Ca concentration and an increase in serum inorganic P concentration. In a study of Karakukcu et al. [27] 32 healthy adolescent men rigorously undergoing boxing training a statistically significant increase in serum Ca concentration at 4 weeks in the from 9.62 mg/dl to 9.90 mg/dl ($p < 0.001$) and a slight increase in inorganic P from 4.56 mg/dl to 4.70 mg/dl was observed. In contrast, Kałużny et al. [28] in which 32 obese postmenopausal women underwent a 10-week cycle of NW trainings (30 sessions, 60 minutes each) a statistically significant decrease in serum total Ca concentration and a non-significant decrease in inorganic P concentration were shown.

In our study, similar relationships were observed – a statistically significant increase in serum total Ca concentration and a non-significant increase in inorganic P concentration after 6 weeks of NW training. However, the initial mean serum concentration values (Ca – 2.33 mmol/l, P – 0.99 mmol/l) of both groups in our study were lower than in one by Karakucuk et al. [27], which may be related to age of the participants in our study. In the elderly, Ca absorption from the gastrointestinal tract is often deteriorated and reabsorption in the renal tubules is impaired. In the study by Markiewicz-Żukowska [29] conducted on the population of 99 Polish seniors (mean age: 76 years) the mean serum total Ca concentration was (2.07 mmol/l), there were no gender differences for this parameter. Whereas our results are consistent with that reported by Karakucuk et al. [27], we do not know why Kaluzny et al. [28] reported the opposite results.

Vitamin 25(OH)D₃

Vitamin D is a fat-soluble vitamin. The serum concentration of vitamin D serum concentration is dependent on the oral intake and skin synthesis [30]. The ingested inactive form of vitamin D is metabolized in the liver to 25(OH)D₃ (calcidiol) as a result of hydroxylation, then in the proximal tubules in the kidneys another OH group is added leading to the formation of 1,25(OH)₂D (calcitriol). The transformation of vitamin D in the body and the nature of its active metabolites on target tissues allows for the classification of vitamin D as a pleiotrophic hormone [31]. Its reduced concentration is associated with the development of noncommunicable diseases (NCD) and various types of cancers [30]. It was also shown that the optimal serum level of vitamin D may contribute to lower post-exercise concentrations of biochemical indicators of muscle damage compared to subjects with its suboptimal concentration [32].

Serum 25(OH)D₃ concentrations are seasonal dependent-higher in the Spring/Summer due to sunlight ultraviolet light exposure. Pilch et al. [33] indicated a statistically significant increase in calcidiol concentration of women in NW training for a period of 12 weeks from March to May. The mean change in 25(OH)D₃ concentration was +3.5 ng/ml and was lower than in this study (+9.9 ng/ml). Pilch et al. [34] also reported a decrease in 25(OH)D₃ concentration in a 6-week cycle of NW training taking place in late Autumn. The difference in the results are probably a reflection of the timing of the studies: May-July in our study versus Autumn in the Pilch et al. study. The total solar irradiation time during our research period was longer than in the other studies. A significant increase in the concentration of 25(OH)D₃, which was statistically significant, which took place in our study was most likely associated with an increase in exposure to UV radiation [30]. Increased exposure to UV radiation intensifies skin synthesis, which is the main source of vitamin D, apart from that taken with food [31].

Vitamin 25(OH)D₃ concentration is also related to BMI. In obese individuals, the bioavailability of vitamin D is reduced due to its accumulation in adipose tissue: Wortsman et al. reported lower 25(OH)D₃ levels in individuals with a BMI above 30 kg/m² compared to the control group with a BMI below 25 kg/m² [35]. In obese people, the bioavailability of vitamin D is reduced due to its accumulation in adipose tissue, which was demonstrated in people with a BMI above 30 kg/m² compared to the control group with a BMI below

25 kg/m² [35]. In our study, the vitamin 25(OH)D₃ level in the NW group was an average of 29.3±3.5 kg/m² compared to 23.4±2.5 kg/m² reported by Pilch et al. [33].

Conclusions

Nordic walking training was associated with a significant decrease in serum Mb concentration, with no significant changes in LDH activity, the lat. The concentration of 25(OH)D₃ increased significantly in all patients in the NW group without a change in the CG group. In patients who took part in trainings, the serum Ca concentration increased significantly, but remained within the normal range. PP concentrations did not change significantly. Nordic walking performed outdoors in the Spring-Summer period resulted in an increase in the serum concentration of vitamin 25(OH)D₃ which was not observed in the CG group who did not have the same UV light exposure. In summary, individually adapted moderate-intensity Nordic walking for 6 weeks, adjusted to the patient's capacity, did not cause muscle damage assessed. by Mb or LDH determinations yet has a positive effect on the vitamin D serum concentration, we conclude that NW training can be considered as a safe and beneficial form of physical activity for patients with MM.

Declarations

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Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Availability of data and material

Data available on request from the authors.

Code availability

Not applicable

Author Contributions

All authors were responsible for study concept and its design. AJ and OCzL performed patients' recruitment. OCzL and JG were involved in data collection. OCzL performed statistical analysis of obtained data. DV, WP, AJ and OCzL contributed in data interpretation. The draft manuscript was prepared by OCzL. All authors revised and approved the final version of the manuscript.

Ethical approval

The procedures of this study were approved by the Bioethical Committee at the District Medical Chamber in Krakow (166/KBL/OIL/2018).

Consent to participate

The patients were informed that participation in this study was voluntary and were acquainted with the details of the project. The study protocol was constructed according to the Declaration of Helsinki, and all participants gave their written consent.

Consent for publication

No personal data is published, we provided a complete anonymity of participants.

References

1. Giannopoulos K, Jamroziak K, Usnarska-Zubkiewicz L, et al (2020) Zalecenia Polskiej Grupy Szpiczakowej dotyczące rozpoznawania i leczenia szpiczaka plazmocytoowego oraz innych dyskracji plazmocytoowych na rok 2021. Polska Grupa Szpiczakowa
2. Chawla SS, Kumar SK, Dispenzieri A, et al (2015) Clinical course and prognosis of non-secretory multiple myeloma. *European Journal of Haematology* 95:57–64. <https://doi.org/10.1111/ejh.12478>
3. Wojciechowska U, Czaderny K, Ciuba A, et al (2018) Cancer in Poland - 2016
4. Rajkumar SV (2020) Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. *American Journal of Hematology* 95:548–567. <https://doi.org/10.1002/ajh.25791>
5. Institute NC (2019) Cancer Stat Facts: Myeloma. NIH Surveillance, Epidemiology, and End Results Program
6. Coriu D, Dytfeld D, Niepel D, et al (2018) Real-world multiple myeloma management practice patterns and outcomes in selected Central and Eastern European countries. *Polish Archives of Internal Medicine* 128:500–511
7. Mikhael J, Ismaila N, Cheung MC, et al (2019) Treatment of multiple myeloma: ASCO and CCO joint clinical practice guideline. *Journal of Clinical Oncology* 37:1228–1263. <https://doi.org/10.1200/JCO.18.02096>
8. Palumbo A, Rajkumar SV, San Miguel JF, et al (2014) International Myeloma Working Group consensus statement for the management, treatment, and supportive care of patients with myeloma not eligible for standard autologous stem-cell transplantation. *Journal of Clinical Oncology* 32:587–600. <https://doi.org/10.1200/JCO.2013.48.7934>
9. Terpos E, Zamagni E, Lentzsch S, et al (2021) Treatment of multiple myeloma-related bone disease: recommendations from the Bone Working Group of the International Myeloma Working Group. *The Lancet Oncology* 22:e119–e130. [https://doi.org/10.1016/S1470-2045\(20\)30559-3](https://doi.org/10.1016/S1470-2045(20)30559-3)

10. Jurczyszyn A, Gdula-Argasińska J, Kosmaczewska A, Skotnicki A (2015) Rola mikrośrodowiska szpiku kostnego w patogenezie szpiczaka plazmocytoowego. *Postepy Hig Med Dosw* 69:521–533. <https://doi.org/10.5604/17322693.1150216>
11. Craike M, Hose K, Courneya KS, et al (2017) Physical Activity Preferences for People Living with Multiple Myeloma. *Cancer Nursing* 40:E1–E8. <https://doi.org/10.1097/NCC.0000000000000425>
12. Czerwińska-Ledwig O, Szaporów T, Majcher P, Jurczyszyn A (2018) Problemy rehabilitacji pacjentów ze szpiczakiem plazmocytoowym. *Przegląd Lekarski* 75:131–135
13. Coleman EA, Goodwin JA, Coon SK, et al (2011) Fatigue, sleep, pain, mood, and performance status in patients with multiple myeloma. *Cancer Nurs* 34:219–27. <https://doi.org/10.1097/NCC.0b013e3181f9904d>
14. Coleman EA, Goodwin JA, Kennedy R, et al (2012) Effects of exercise on fatigue, sleep, and performance: a randomized trial. *Oncology nursing forum* 39:468–477. <https://doi.org/10.1188/12.ONF.468-477>
15. Craike MJ, Hose K, Courneya KS, et al (2013) Perceived benefits and barriers to exercise for recently treated patients with multiple myeloma: a qualitative study. *BMC Cancer* 13:1. <https://doi.org/10.1186/1471-2407-13-319>
16. Coleman EA, Coon S, Hall-Barrow J, et al (2003) Feasibility of exercise during treatment for multiple myeloma. *Cancer Nurs* 26:410–419. <https://doi.org/10.1097/00002820-200310000-00012>
17. Coon SK, Coleman EA (2004) Exercise decisions within the context of multiple myeloma, transplant, and fatigue. *Cancer nursing* 27:108–118
18. Teke HÜ, Başak M, Teke D, Kanbay M (2014) Serum Level of Lactate Dehydrogenase is a Useful Clinical Marker to Monitor Progressive Multiple Myeloma Diseases: A Case Report. *Turkish Journal of Hematology* 31:2012–2015. <https://doi.org/10.4274/tjh.2013.0044>
19. Gu Y, Yuan YH, Xu J, et al (2017) High serum lactate dehydrogenase predicts an unfavorable outcome in Chinese elderly patients with multiple myeloma. *Oncotarget* 8:48350–48361. <https://doi.org/10.18632/oncotarget.16237>
20. Callegari GA, Novaes JS, Neto GR, et al (2017) Creatine Kinase and Lactate Dehydrogenase Responses after Different Resistance and Aerobic Exercise Protocols. *Journal of Human Kinetics* 58:65–72. <https://doi.org/10.1515/hukin-2017-0071>
21. Hagner-Derengowska M, Kałużny K, Hagner W, et al (2015) The effect of a 10-week Nordic walking training program on the level of GH and LH in elderly women. *Climacteric* 18:835–840. <https://doi.org/10.3109/13697137.2015.1058354>
22. Anesi A, Rondanelli M, Trotti R, Melzi d'Eril G V. (2000) Biological variability of myoglobin in healthy elderly and younger subjects. *Aging Clinical and Experimental Research* 12:168–172. <https://doi.org/10.1007/BF03339834>
23. Cornish SM, Chase JE, Bugera EM, Giesbrecht GG (2018) Systemic IL-6 and myoglobin response to three different resistance exercise intensities in older men. *Journal of Aging and Physical Activity* 26:451–456. <https://doi.org/10.1123/japa.2017-0167>

24. Barutçuoğlu B, Parildar Z, Mutaf I, et al (2003) Spuriously elevated inorganic phosphate level in a multiple myeloma patient. *Clinical and Laboratory Haematology* 25:271–274.
<https://doi.org/10.1046/j.1365-2257.2003.00524.x>
25. Vaidya GN, Bhattad VB, Aggarwal A (2014) Pseudohyperphosphatemia in Multiple Myeloma: a Commonly Misdiagnosed Phenomenon. *Science Postprint* 1:.
<https://doi.org/10.14340/spp.2014.12c0002>
26. Sy-Go JPT, Dingli D, Gertz MA, et al (2021) Acute Acquired Fanconi Syndrome in Multiple Myeloma After Hematopoietic Stem Cell Transplantation. *Kidney International Reports* 6:857–864.
<https://doi.org/10.1016/j.ekir.2020.12.007>
27. Karakukcu C, Polat Y, Torun YA, Aysenur Kisaarslan PAC (2013) The effects of acute and regular exercise on calcium, phosphorus and trace elements in young amateur boxers. *Clinical Laboratory* 59:557–562. <https://doi.org/10.7754/Clin.Lab.2012.120505>
28. Kałużny K, Kałużna A, Budzyński J, et al (2016) Effect of a ten-week Nordic Walking exercise program on serum electrolyte concentration and plasma acid-base balance in postmenopausal women with overweight or obesity. *Journal of Education, Health and Sport* 6:353–364
29. Markiewicz-Żukowska R (2012) Stężenie wapnia w surowicy krwi osób starszych. *Bromatologia i Chemia Toksykologiczna* 3:771–774
30. Mason RS, Sequeira VB, Gordon-Thomson C (2011) Vitamin D: The light side of sunshine. *European Journal of Clinical Nutrition* 65:986–993. <https://doi.org/10.1038/ejcn.2011.105>
31. Piotrowska AM, Czerwińska-Ledwig O, Podhorecki A, Pilch W (2019) Aktywne formy witaminy D a zdrowie. *Polski Przegląd Nauk o Zdrowiu* 4:343–351
32. Pilch W, Kita B, Piotrowska A, et al (2020) The effect of vitamin D supplementation on the muscle damage after eccentric exercise in young men: a randomized, control trial. *Journal of the International Society of Sports Nutrition* 17:53. <https://doi.org/10.1186/s12970-020-00386-1>
33. Pilch W, Tota L, Piotrowska A, et al (2018) Effects of nordic walking on oxidant and antioxidant status: Levels of calcidiol and proinflammatory cytokines in middle-aged women. *Oxidative Medicine and Cellular Longevity* 2018:.
<https://doi.org/10.1155/2018/6468234>
34. Pilch W, Tyka A, Cebula A, et al (2017) Effects of a 6-week Nordic walking training on changes in 25(OH)D blood concentration in women aged over 55. *Journal of Sports Medicine and Physical Fitness* 57:124–129. <https://doi.org/10.23736/S0022-4707.16.05964-X>
35. Wortsman J, Matsuoka LY, Chen TC, et al (2000) Decreased bioavailability of vitamin D in obesity. *American Journal of Clinical Nutrition* 72:690–693. <https://doi.org/10.1093/ajcn/72.3.690>

Table

Table 1 Changes in average concentrations of biochemical indices in multiple myeloma patients after a cycle of 6-weeks of Nordic walking training

	NW (n=15)		CG (n=13)	
	Baseline	After 6 weeks	Baseline	After 6 weeks
Mb [$\mu\text{g/l}$]	50,5 $\pm$ 22,6*	44,4 $\pm$ 16,5* [#]	52,8 $\pm$ 21,3	53,6 $\pm$ 20,7 [#]
LDH [U/l]	200,8 $\pm$ 34,0	204,3 $\pm$ 36,8	200,3 $\pm$ 39,9	198,3 $\pm$ 35,8
Ca [mmol/l]	2,33 $\pm$ 0,07*	2,40 $\pm$ 0,07*	2,37 $\pm$ 0,14	2,39 $\pm$ 0,10
P [mmol/l]	0,99 $\pm$ 0,22	1,02 $\pm$ 0,17	0,97 $\pm$ 0,21	0,98 $\pm$ 0,20
25(OH)D ₃ [ng/ml]	26,3 $\pm$ 11,6*	36,4 $\pm$ 10,8* [#]	30,2 $\pm$ 11,3	31,6 $\pm$ 11,5 [#]

Results shown as arithmetic mean $\pm$ standard deviation (SD). Abbreviations: NW, group participating in Nordic walking trainings; CG, control group; Mb, myoglobin; LDH, lactate dehydrogenase; Ca, total calcium; P, phosphorus; 25(OH)D₃, calcidiol

*Results statistically significant for $p > 0.05$, * – statistically significant differences in a group, # – statistically significant differences between the NW and GK groups*

Figures

Figure 1

Correlations of statistically significant biochemical indices in the NW group

Figure 2

Correlation plot for 25(OH)D₃ concentrations in patients from NW group at baseline (before) and after 6 weeks of trainings (after)