DOI 10.29254/2077-4214-2022-1-163-119-122
UDC 616.71-007.23

Azizova G. I., Hasanova N. A., Dadashova A. R.

DYNAMICS OF OSTEOACTIVIN IN PATIENTS WITH OSTEOPOROTIC FRACTURES

Azerbaijan Medical University (Baku, Azerbaijan)

arzu26@mail.ru

The study examines the dynamics of a regulatory protein called osteoactivin in the blood serum of patients with osteoporosis and osteoporotic fractures. Patients applying to the Traumatology Department of the Azerbaijan Scientific Research Institute of Traumatology and Orthopedics were included in the research material. 68 people from 38 to 83 years of age who meet the admission criteria were selected and divided into 4 groups: Group I – control group – 14 practically healthy people, Group II – 14 patients with osteoporosis, Group III – 15 patients with non-osteoporotic fractures, Group IV patients with osteoporotic fractures. Patients were measured for serum osteoactivin 3 times on the first day, 10 days later, and 1 month later. According to the results, there was no statistically significant difference in the dynamics of osteoactivin in patients with osteoporotic fractures (p> 0,001). Following the dynamics for 1 month, it is impossible to think about the effectiveness of treatment during the recovery period. This requires more long-term and extensive research.

Key words: *Osteoporosis, fracture, osteoactivin, osteoblasts*

The connection of the publication with planned research work: This work is a fragment of the dissertation for the degree of Doctor of Philosophy in biology entitled “The role of protein and peptide regulators of bone and cartilage metabolism in osteoporotic patients with fractures”.

Introduction. The protein osteoactivin (OA) was discovered in bone tissue 10 years ago. Recently, a number of studies have indicated significant role of osteoactivin in the differentiation and functioning of various types of cells, including bone-forming osteoblasts and osteoclasts [1]. Osteoactivin/Glycoprotein NMB (OA/GPNMB) is a transmembrane, highly glycosylated glycoprotein produced by osteoblasts. Its expression is associated with accelerated differentiation of osteoblasts and matrix mineralization [2]. The initial identification of osteoactivin (OA) was first recorded in the course of studies on an animal model with osteoporosis [3]. Osteactivin protein and mRNA are localized in different tissues and cells: in Kupffer cells of the liver, myocytes in muscle, lymphoid tissue (where antigen-presenting cells (APCs) are expressed by melanocytes), bone marrow macrophages, dendritic cells, endothelial cells and bone, where they are secreted in osteoblasts, osteoclasts and osteocytes [4, 5, 6]. Studies conducted by Saffadi, Abdelmaged et al. involved a fracture model in rats: it was revealed that on 3rd and 10th days after fracture, the expression of OA mRNA in the bone marrow increased compared to the femur of healthy rats. Interestingly, the secreted OA protein was also found in the new matrix of cartilage and osteoid tissue [7, 8]. These results suggest that OA plays a positive regulatory role in bone formation and can be used in the treatment of fractures [4, 9].

The aim of the study. To investigate the role of osteoactivin as a more sensitive and modern diagnostic biomarker that has a prognostic value in metabolic and repair processes occurring in bone and cartilage tissue in osteoporosis and osteoporotic fractures.

Object and methods of research. Study involved the blood of 68 patients aged 38-83 years who were treated in the Traumatology Department of the Scientific-Research Institute of Traumatology and Orthopedics of the Republic of Azerbaijan in the period from 2018 to 2019. All patients were initially informed, afterwards blood samples were collected from patients in line with ethical rules (Protocol No. 07 dated 27.06.2019). Study included patients who had osteoporosis diagnosis in anamnesis and frequent osteoporotic fractures, as well as signs of osteoporosis and related complaints. The diagnosis was confirmed by densitometry and X-ray. The control group consisted of 14 people without a diagnosis of osteoporosis. All 68 patients were divided into 4 groups: I group– control group with 14 people; II group – 14 patients with osteoporosis; III group – 15 patients with non-steoporotic fractures; IV group – 25 patients with fractures associated with osteoporosis. To study the dynamics in all groups (with the exception of the control group), blood sampling for each patient was carried out in 3 stages: during the initial appeal, 10 days after the start of treatment and a month later. The concentration of OA in the blood serum was determined by ELISA method on the immunoassay analyzer “Mindray MR-96A” using a set of reagents from the company “Boster”.

Comparison of figures in the comparable groups was performed with the dispersion tests (ANOVA-test, Fisher’s criterion-F) and Kruskall-Wallis H, statistical accuracy of change in the dynamics – with the Wilcoxon test-W, statistical significance of the difference between the indicators – with Pearson’s chi-squared $\chi 2$ test with the use of SPSS 26 statistical package. The significance level of the difference between the indicators was considered statistically significant when it was at least $p < 0,05$.

The results of the research and their discussion. Figure shows the levels of osteoactivin in the studied groups during 1 month. The concentration of osteoactivin was higher in all groups compared with the control. The highest content of OA was recorded in group of patients with fractures associated with osteoporosis. The median was approximately the same in groups II and IV. The obtained data are provided in the **table**.

The **table** shows the minimum and maximum levels of GPNMB, the mean value (M±m), as well as the comparison of the initial indicators for each group with indi-

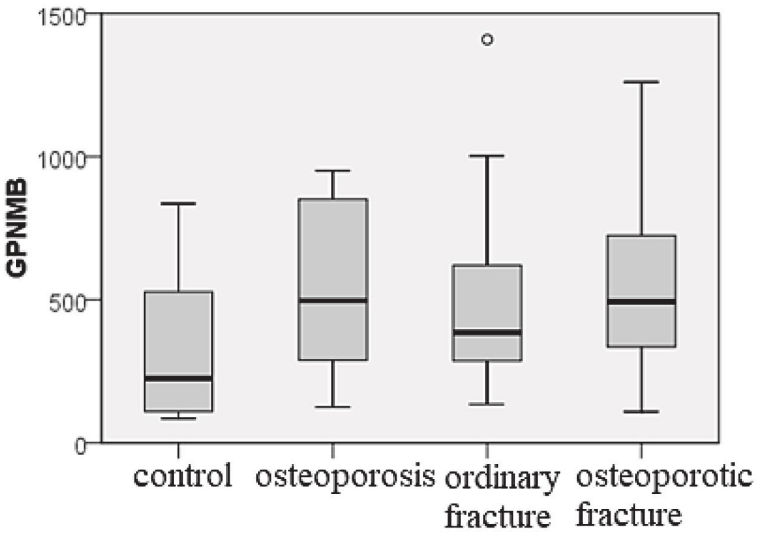

Figure – Osteoactivin level (GPNMB) in the studied groups.

Table – Dynamics of osteoactivin (GPNMB) indicators in groups

Indicator (pg/ml)	Groups	N	M±m	Min.	Max.	P_H	P_w
GPNMB(1)	I	14	323,4±66,8	84,9	836,3		
	II	14	537,6±80,9	125,3	951,6		
	III	15	498,5±87,1	135,2	1409,5		
	IV	25	582,8±71,9	109,0	1581,5		
GPNMB(2)	I	14	323,4±66,8	84,9	836,3	0.005	
	II	14	806,5±266,1	145,3	4059,5		0,011
	III	15	766,7±113,2	331,4	2063,5		0,001
	IV	25	613,0±58,2	201,5	1162,2		0,716
GPNMB(3)	I	14	323,4±66,8	84,9	836,3	0.000	
	II	14	794,0±214,0	162,5	3325,4		0,026
	III	15	902,6±109,9	298,2	2133,3		0,001
	IV	25	633,7±75,1	144,8	1726,5		0.840

Note: Statistical significance of differences is indicated in the p_w-dynamics of intragroup indicators within the Wilcoxon test, p_H – according to the Kruskell-Wallis test. I group – control group, II group – patients with osteoporosis, III group – patients with non-osteoporotic fractures, IV group – patients with osteoporotic fractures. GPNMB(1) refers to the first sample, GPNMB(2) – sample in 10 days, GPNMB(3) – sample collected in 1 month.

cators after 10 days and over 1 month. Thereby, when comparing GPNMB indicators in the group of patients with osteoporosis in the first days and after 10 days of treatment, it was revealed that in 13 out of 14 patients there was a growth in indicator, whereas in one patient there was a decline (p_w=0,011). Throughout 1 month, 12 out of 14 patients showed growth in comparison with initial levels, whilst the remaining two patients had a decrease in this indicator (p_w=0,026, p<0,05).

In group of patients with fractures associated with osteoporosis, the comparison of concentration of GPNMB in the first and subsequent 10 days showed a decline in 12 out of 25 patients and an increase in 13 patients (p_w=0,716). Comparison of initial concentrations with concentrations after 1 month revealed the same result (p_w=0,840, p<0,05).

In group of patients with fractures not associated with osteoporosis, the content of GPNMB in the first and subsequent 10 days changed by a statistically significant value. An increase in this indicator was observed in 15 patients (p_w=0,001). Collation of GPNMB concentrations in blood serum in the first day and after 1 month returned a similar result (p_w=0,001, p<0,05).

A statistically significant difference in the level of osteoactivin was observed in the group of patients with osteoporosis and in the group of patients with non-osteoporotic fractures (p<0,05). An increase in osteoactivin level was observed in 90% of patients with osteoporosis and in 100% of patients with non-osteoporotic fractures. However, in individuals with osteoporotic fractures, an increase in GPNMB concentration in blood serum was observed in 52% of patients within 1 month of recovery, yet the result was not statistically significant (p>0,05).

Conclusions. It is possible to monitor the metabolic process in bones and cartilage during the recovery period of patients with osteoporosis and non-osteoporotic fractures by monitoring the serum dynamics of GPNMB. However, a more extensive and long-term research is required to monitor the dynamics of GPNMB during the full recovery of osteoporotic fractures.

Prospects for further research. Further research in this direction will make it possible to prevent complications in the prescription of treatment and contribute to the prevention of long-term complications of osteoporosis.

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ДИНАМІКА ОСТЕОАКТИВІНУ У ПАЦІЄНТІВ ІЗ ОСТЕОПОРОТИЧНИМИ ПЕРЕЛОМАМИ

Азізова Г. І., Гасанова Н. А., Дадашова А. Р.

Резюме. У проведеному нами дослідженні було досліджено динаміку регуляторного білка, який називається остеоактивіном у сироватці крові пацієнтів з остеопорозом та остеопоротичними переломами. До дослідження були включені пацієнти, які зверталися до відділення травматології Азербайджанського науково-дослідного інституту травматології та ортопедії. Пацієнти цього дослідженні мали діагноз остеопорозу в анамнезі та часті остеопоротичні переломи, а також ознаки остеопорозу та супутні скарги. Діагноз було підтверджено денситометрією та рентгенографією. Було відібрано 68 осіб віком від 38 до 83 років, які відповідають критеріям госпіталізації та розподілені на 4 групи: I група – контрольна група – 14 практично здорових людей, II група – 14 хворих на остеопороз, III група – 15 пацієнтів з переломами не пов'язаних. з остеопорозом, IV група – 25 хворих з остеопоротичними переломами. У пацієнтів вимірювали сироватковий остеоактивін у три прийоми: у перший день, через 10 днів і через 1 місяць.

Згідно з нашими результатами, протягом перших і наступних 10 днів у 13 із 14 хворих на остеопороз спостерігалося підвищення концентрації ГПНМБ, у решти одного пацієнта спостерігалося зниження цього показника. Через 1 місяць у 12 з 14 пацієнтів спостерігалося підвищення порівняно з початковими рівнями. У всіх пацієнтів із переломами, не пов'язаними з остеопорозом, вміст ГПНМБ у першу та через 10 днів підвищився на статистично значущу величину. У той же час порівняння концентрацій ГПНМБ у сироватці крові в першу добу та через 1 місяць дало подібний результат. Проте статистично достовірної різниці в динаміці остеоактивіну у пацієнтів з остеопоротичними переломами не було (p>0,001). За динамікою протягом 1 місяця не можна думати про ефективність лікування в період відновлення. Це вимагає більш тривалих і масштабних досліджень для моніторингу динаміки ГПНБМ під час повного відновлення остеопоротичних переломів.

Ключові слова: остеопороз, переломи, остеоактивін, остеобласти.

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Results. According to the results, in the first and subsequent 10 days in 13 out of 14 patients with osteoporosis, there was an increase in concentration of GPNMB, while remaining one patient witnessed a decline in this indicator. After 1 month, 12 out of 14 patients showed an increase relative to initial levels. In all patients with fractures not associated with osteoporosis, the content of GPNMB in the first and in 10 days increased by a statistically significant value. At the same time, comparison of GPNMB concentrations in blood serum in the first day and after 1 month yielded a similar result. Nevertheless, there was no statistically significant difference in the dynamics of osteoactivin in patients with osteoporotic fractures (p>0,001). Following the dynamics for 1 month, it is impossible to think about the effectiveness of treatment during the recovery period. This requires more long-term and extensive research to monitor the dynamics of GPNBM during the full recovery of osteoporotic fractures.

Key words: osteoporosis, fracture, osteoactivin, osteoblasts.

ORCID and author's contribution:
Azizova G. I.: 0000-0001-8758-2573 [EF]
Hasanova N. A.: 0000-0002-1342-7981 [ABD]
Dadashova A. R.: 0000-0003-4666-9087 [AC]

Conflict of interest:
The authors have no conflicts of interest to declare.

Corresponding author
Dadashova Arzu Ramiz kizi
Azerbaijan Medical University
Azerbaijan, AZ1022, Baku, Nasimi district, 167 Samad Vurgun street
Email: arzu26@mail.ru

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article.

Рецензент – доц. Пелипенко О. В.
Стаття надійшла 17.08.2021 року
Стаття прийнята до друку 16.02.2022 року