EVALUATION OF OSTEOSARCOPENIA TREATMENT EFFECTIVENESS IN POSTMENOPAUSAL WOMEN

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Abstract

The aim: To assess the effectiveness of osteosarcopenia treatment with the use of systemic analysis methods. The results (criteria) developed allow to compare different methods of treatment effectiveness. The use of the multifunctional apparatus "Huber" in combination with osteotropic therapy (denosumab + Vit D metabolites) contributes to increase of musculoskeletal system functional capabilities: muscle strength, stability, coordination of movements. Besides it reduces functional limitations, promotes more effective treatment of structural and functional changes in bone tissue, increases bone tissue mineral density.

Key words: osteosarcopenia; postmenopause; therapy; system analysis.

Urgency. Osteosarcopenia (OSP) is a state that includes a combination of low muscle mass and reduced bone mineral density (BMD). This state is associated with aging and general pathogenesis [1-5]. The combination of sarcopenia (SP) and osteoporosis (OP) doubles the risk of fractures and premature death of patients [2]. OSP is often observed in postmenopausal (PM) women, reduces their physical capabilities, worsens the quality of life, contributes to increased frequency of falls and, consequently, the risk of OP fractures.

Therefore, the issues of timely treatment and rehabilitation of structural and functional changes in the musculoskeletal system (MSS) in PM women working under unfavorable factors of the working environment [6] are urgent.

The objective. To evaluate the effectiveness of OSP complex therapy schemes using system analysis methods.

Materials and methods. 298 PM women (mean age - 56.7 ± 2.3 years) were under examination. 278 of them had OSP and worked under unfavorable factors of the working environment. BMD study was performed by ultrasound densitometry on a Hologic Discovery apparatus (USA) before the start of treatment and in 12 months after the therapy end.

The level of 25 (OH) D in the blood serum was determined by the enzyme immunoassay on a EUROIMMUN analyzer (Germany). BT resorption, marker C-terminal telopeptide of the collagen type 1 degradation product (CTx) and BT formation marker osteocalcin (OC) were determined in blood serum by ECLIA immunochemiluminescent method on Cobas 6000 analyzer (Roche Diagnostics, Switzerland). The level of osteoprotegerin (OPG) in the blood serum was determined by the enzyme-linked immunosorbent assay using the AxsymSystem apparatus (Abbot, Germany). Dynamics of OC and OPG was studied in 6 and 12 months, CTx in 3 and 6 months.

The state of skeletal muscle tissue assessment was carried out using ultrasound examination of the main ultrasound parameters *m. quadriceps femoris* - pennation angle (°); echogenicity on the device "Toshibaaplio 300", linear sensor 7.5 MHz. Visualization was carried out in a patient's horizontal position.

The assessment of the functional state of BMS and risk of falls were studied using functional tests:

"tandem" test to assess the ability to maintain balance at rest, the test time is not less than 10 seconds);

"get up and go" test (10 seconds);

"sit-stand" test allows to assess muscle strength and the risk of falls (no more than 10 seconds). The strength of skeletal muscles was studied using a wrist dynamometer, (kg).

To assess the functional state of the BMS, we also used a complex for registration and processing of biosignals in vertebrology "Insight TM". The index of neurospinal function (NSF) and its components were determined: pain sensitivity (Algometry); spine flexibility (ROM, inclinometry). The parameters were assessed in accordance with the "Insight TM" scale. Coordination was assessed taking into account the time of maintaining balance on a movable opposing support platform of the "Huber" apparatus.

Measurement was made in seconds (sec) from the moment the platform started rotating until the first signs of uncoordinated movements appeared.

The patients undwer examination were divided into 3 clinical groups, depending on the method of treatment:

In the I group (Group I, n= 115) multifunctional apparatus "Huber" in combination with osteotropic therapy (denosumab + metabolite D) was used;

In the second group (Group II,n = 80) kinesiotherapy and denosumab (vitamin D metabolite) was used;

In the third group (Group III, n = 83) the patients took vitamin D metabolite.

Clinical course dynamics and the assessment of the therapy effectiveness was carried out in 3, 6 and 12 months.

Statistical processing of the data obtained was carried out with Microsoft Office Excel and Statistica 10.0 application programs. For mathematical processing, the methods of primary descriptive statistics were used: the mean value of the indicator, standard deviation, standard error, Student's t-test. The results were considered statistically significant at a value of $p < 0.05$.

To assess the treatment effectiveness system analysis methods were used and criteria of treatment effectiveness were developed, which allowed to compare objectively the therapeutical results of different methods treatment and assess their effectiveness.

The criteria can be based on the most important indicators of OSP patient's the health: 25 (OH) D, CTx, OPG, OC, BMD L1-L4, algometry, inclinometer, pennation angle, dynamometry, tandem-test, test "stand up and go", "sit-stand up" test, etc. To do this, it is necessary to assess the dynamics of changes in selected indicators. We choose as a criterion the ratio of the value of the indicator in the present period of the survey to the value of the indicator in the previous period, as well as the ratio of the value of the indicator in 12 months of treatment to the same value at the beginning of treatment. Such ratios are calculated for each group of patients separately on the basis of average values of the indicator. The efficiency of the system is the ratio between the set (target) indicator of the system functioning and the actually realized one. Typically, efficiency is measured as a percentage [7]

Results and discussion

The effectiveness of treatment with vitamin D metabolites in all groups in the first three months is extremely high - more than doubled ($p < 0.05$) the value of 25 (OH) D, because its drug correction is part of all three methods of treatment, but in each subsequent

period of observation, the growth rate of the value of 25 (OH) D slows down significantly. Characteristic changes in all groups are approximately the same (table 1).

Table 1

Dynamics 25 (OH) D, ng / ml

	Initially	In 1 month	In 3 m-s	In 6 m-s	In 12 m-s
Gr I	11.91 ± 1.35	26.9 ± 1.8 *	30.9 ± 2.1 *	33.9 ± 2.21 *	34.9 ± 1.9 *
Gr II	11.8 ± 1.57	26.6 ± 1.54 *	30.5 ± 2.3 *	33.9 ± 2.21 *	34.4 ± 2.1 *
Gr III	12.57 ± 1.3	26.8 ± 1.62 *	30.5 ± 2.3 *	33.9 ± 1.8 *	33.9 ± 2.1 *

$p < 0.05$ compared to baseline

The ratio of the initial value of 25 (OH) D and its value in 12 months of treatment was accessed. There was a very significant increase in the value of 25 (OH) Din all groups: in Group I there was increase by 193.28%, in Group II - by 191.53%, while in Group III the value of this indicator in 12 months of treatment increased by only 169.69% (Fig. 1).
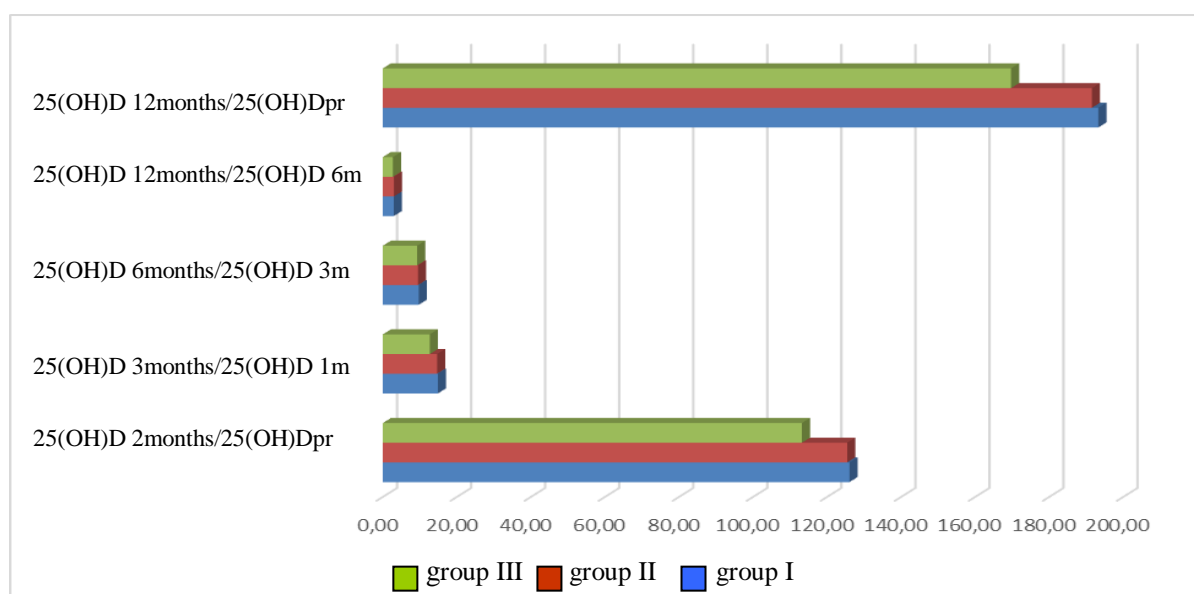

Fig. 1. The dynamics of the relative increase in the values of 25 (OH)D, %

Initially, CTx was elevated ($p < 0.05$) in all groups under study. The decrease in the value ($p < 0,05$) of CTx as a result of treatment in all groups indicates the effectiveness of therapy (Table 2).

The effectiveness of treatment in the first and second groups in the first three months of therapy is significantly higher than in the third group. In 6 months CTx decrease rate becomes approximately the same in all groups, but in the first group it is more noticeable than in the second and the third group of patients. Assessing the ratio of the initial value of CTx

and its value in 6 months of treatment, it was found that in the first and second groups of patients there was a significant decrease in the value of CTx. Thus, in the first group it was 34.98%, and in the second group - 24.76%, while in the third group this value in 6 months of treatment decreased by 17.23% (Fig. 2).

Table 2

Dynamics of CTx on the background of treatment, mmol / l

	initially	In 3 m-s	In 6 m-s
Group I	0.832 ± 0.139	0.624 ± 0.122 *	0.541 ± 0.124 *
Group II	0.828 ± 0.114	0.702 ± 0.121 *	0.623 ± 0.118 *
Group III	0.83 ± 0.137	0.765 ± 0.119	0.687 ± 0.125 *

p <0.05 compared to baseline
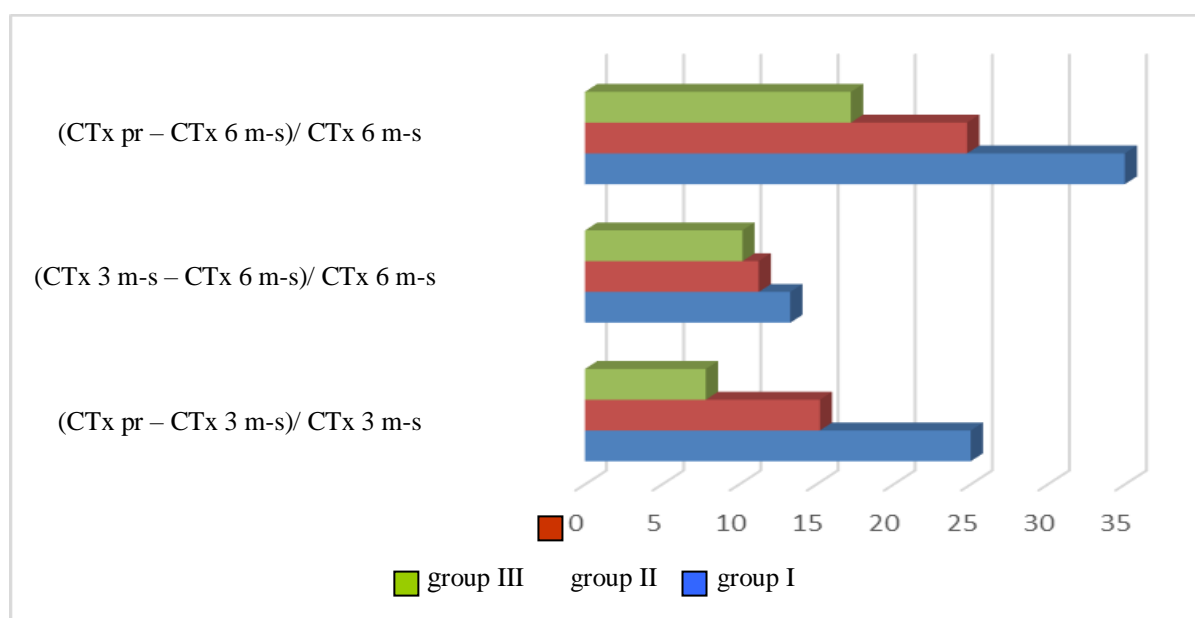

Fig. 2. Dynamics of relative decrease of CTx values, %.

The increase (p <0,05) in the value of OC as a result of treatment indicates positive changes in the process of bone formation (Table 3).

Table 3

Dynamics of osteocalcin on the background of treatment, ng / ml

	initially	In 3 m-s	In 6 m-s
Group I	13.79±0.39	16.1±0.42*	18.45±0.42*
Group II	13.77±0.31	15.3±0.51*	17,15±0,53*
Group III	13.81±0.25	14.1±0.62	15,1±0,67*

* p <0.05 compared to baseline

In the first six months, the increase in the value of OC in the first and second groups is significantly higher than in the third group (almost 8 times higher in the first group and more than 5 times in the second). In the next six months, the growth rate in the first group was slightly lower (but still the highest compared to the second and third groups), in the second group there was a slight acceleration of growth, in the third group growth is almost 3.4 times higher than in previous 6 months (but significantly lower than in the first and second groups). After 12 months of treatment, the growth rate of OC was 33.79%, which is almost 1.4 times better than in the second group and 3.6 times better than in the third group (Fig. 3).
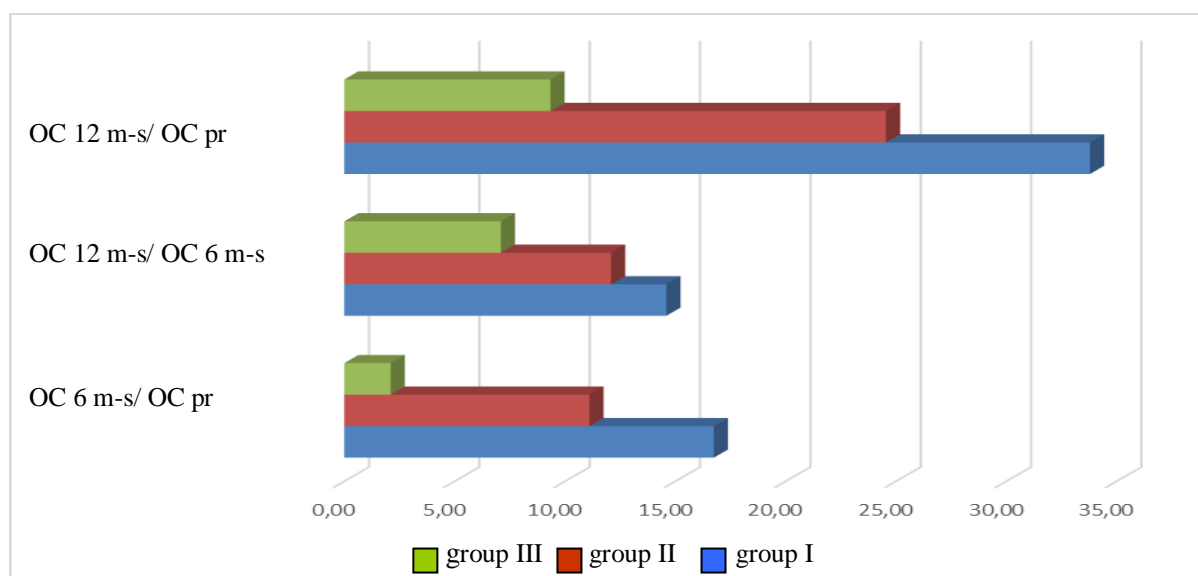

Fig. 3. The dynamics of the relative increase in OC values, %

The increase ($p < 0.05$) in the value of OPG as a result of treatment indicates positive changes in bone remodeling (Table 4)

Table 4

Dynamics of OPG against the background of treatment, pmol / l

	Initially	In 6 m-s	In 12 m-s
Group I	1.14 ± 0.12	1.79 ± 0.15 *	1.92 ± 0.13 *
Group II	1.16 ± 0.14	1.64 ± 0.16 *	1.75 ± 0.12 *
Group III	1.18 ± 0.13	1.42 ± 0.12 *	1.49 ± 0.15 *

* $p < 0.05$ compared to baseline

In the first six months the effectiveness of treatment in the first and second groups of patients is significantly higher than in the third group, in the next 6 months of treatment there

is a slowdown in OPG growth in all groups, but in the first group the growth rate is the highest. The ratio of OPG initial value and its value in 12 months of treatment, was 68.3% higher in the first group, in the second group it increased by 62.70%, and in the third group in 12 months of it treatment increased by 38.25% (Fig. 4).
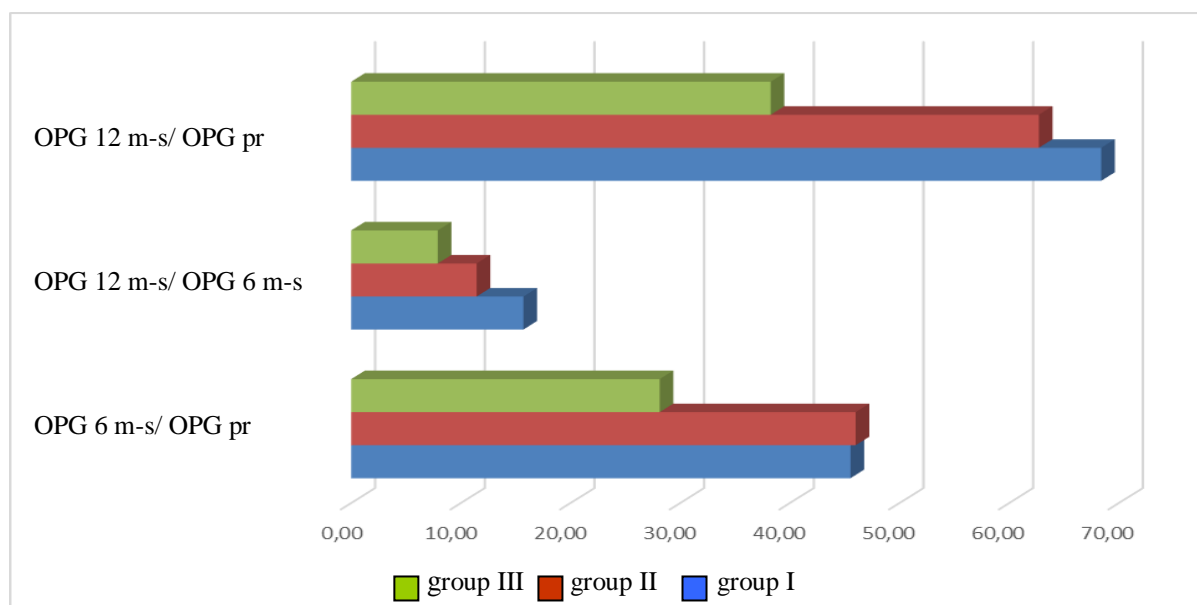

Fig. 4. The dynamics of the relative increase in OPG values, %

The increase ($p < 0.05$) in the value of BMD L1-L4 as a result of treatment indicates positive changes in bone mass set (Table 5).

Table 5

Dynamics of BMDL1-L4 (g / cm^2) against the background of treatment

	Initially	In 12 m-s
Group I	0.601 ± 0.043	0.651 ± 0.043 **
Group II	0.598 ± 0.042	0.642 ± 0.039 *
Group III	0.602 ± 0.038	0.619 ± 0.038

* $p < 0.05$ compared to baseline

For 12 months of treatment, the increase in BMD L1-L4 in the first group of patients was 8.32%, slightly lower was the increase of this indicator in the second group (7.36%), and in the third group of patients BMD L1-L4 increase was less than 3% (Fig. 5).

Similarly, as it was done above, we construct a criterion of treatment quality on the basis of value of pennation angle (°) (Tab. 6).
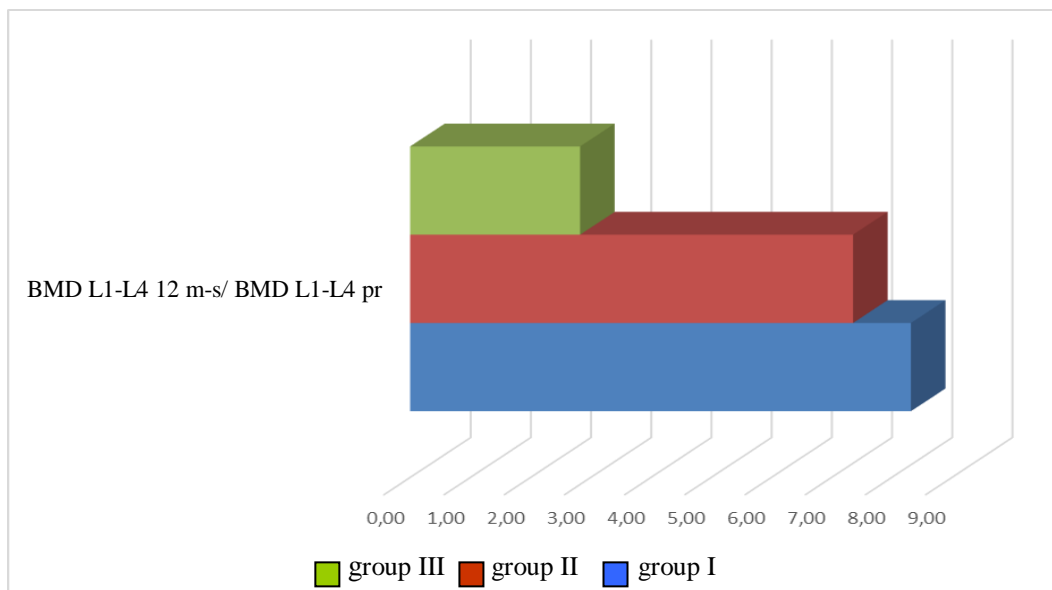
Fig. 5. The dynamics of the relative increase in the values of BMD L1-L, %

Table 6

Dynamics of the pennation angle (°)

	initially	In 6 m-s	In 12 m-s
Group I	11.56 ± 0.45	14.6 ± 0.38 *	18.5 ± 0.41 *
Group II	11.35 ± 0.38	12.4 ± 0.39	13.5 ± 0.38 *
Group III	11.42 ± 0.43	12.0 ± 0.41	12.5 ± 0.42

* $p < 0.05$ compared to baseline

In the first six months, the effectiveness of treatment according to this criterion is much higher in the first group than in the second group (almost three times higher) and is almost five times higher if compared with the third group. In the next 6 months the same tendency was observed. The ratio of the penneation angle initial value and its value in 12 months of treatment, had a significant increase in the first group (60.03%), in the second group it was 18.94%, which is twice better than in the third group (Fig. 6).

We assessed ratio of the initial algometry index and its value in 12 months.

In the first six months, the effectiveness of treatment in the first and second groups is approximately the same, but significantly higher than in the third group, in the next 6 months of treatment there is a significant slowdown in algometry in all groups of patients (Table 7).
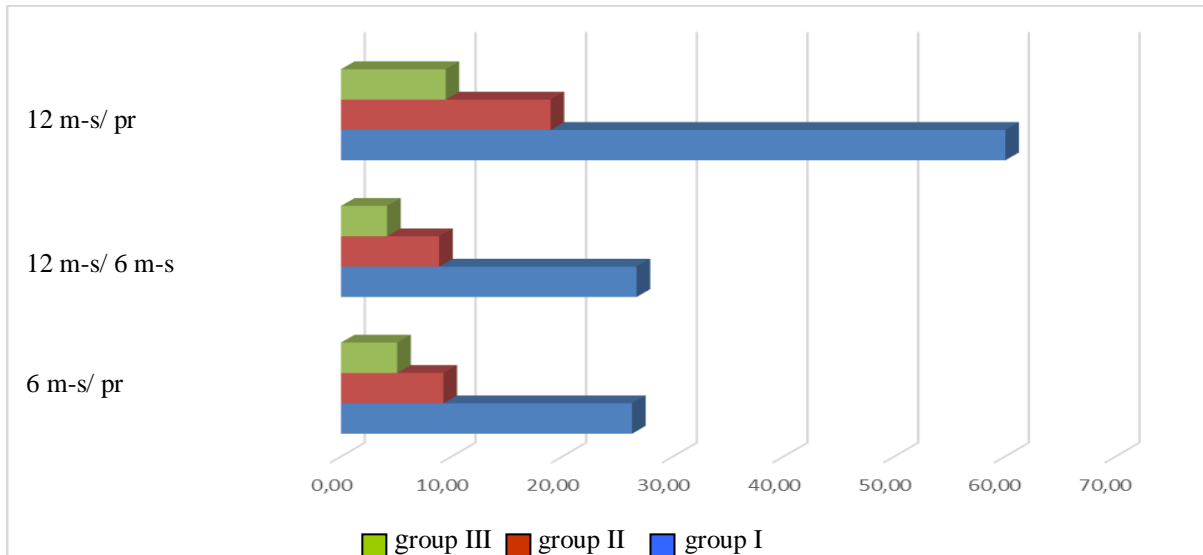
Fig. 6. Dynamics of the relative increase in the values of the pennation angle, %

	Initially	In 6 m-s	In 12 m-s
Group I	57.31±2.8	83.4±2.7*	96.5±3.1*
Group II	56.3±2.56	82.2±2.5*	91.6±3.5*
Group III	58.3±2.71	74.7±3.1*	84.6±2.9*

* p <0.05 compared to baseline

We assessed the ratio of the initial value of algometry and its value in 12 months.

There was an increase in algometry by 68.38% in the first group, and by 62.70% in the second one, in the third group this indicator increased by 38.25% in 12 months of treatment (Fig. 7).
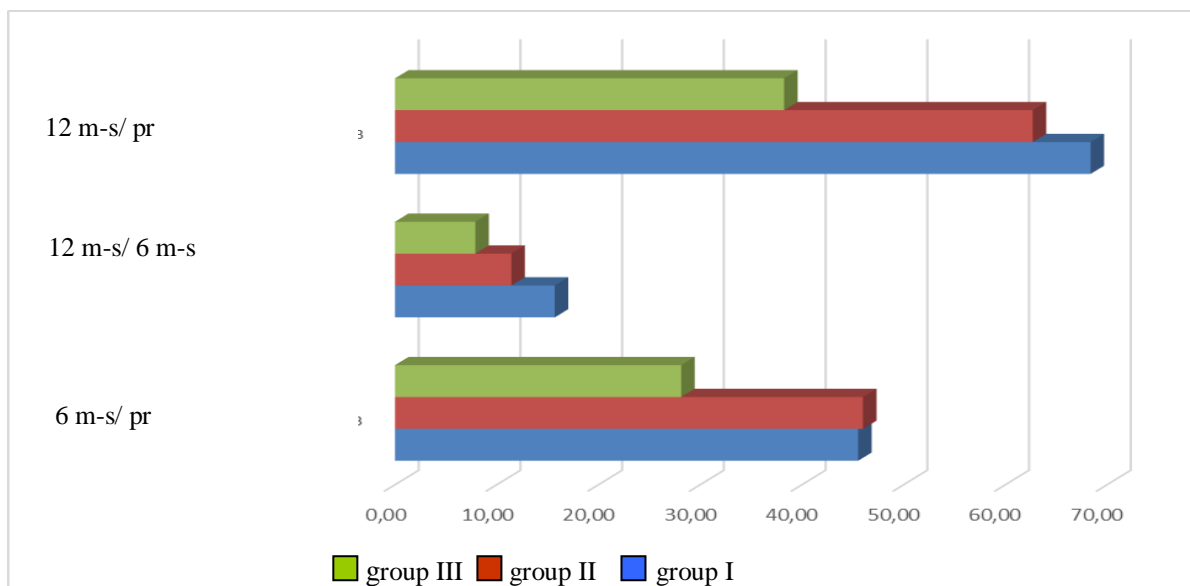

Fig. 7. Dynamics of the relative increase in the values of algometry, %

Inclinometry allows to set the limits of joint mobility, so it is also an important indicator of patient's quality of life. The increase of inclinometry value as a result of treatment indicates an increase in the volume of movement of the spine (Table 8).

Table 8

Dynamics of inclinometry against the background of treatment, points

	Initially	In 6 m-s	In 12 m-s
Group I	60.07 ± 1.92	76.8 ± 2.1	91.3 ± 2.51
Group II	60.3 ± 1.87	71.2 ± 2.5	82.8 ± 2.6
Group III	62.1 ± 2.05	67.9 ± 1.9	70.8 ± 2.48

In the first six months, the growth rate of inclinometry in the first group of patients is the highest (1.5 times better than in the second group and almost 3 times better than in the third group), in the second group is almost 2 times higher than with the third group, in the next 6 months of treatment the growth rate of the indicator decreases in all groups, but in the first and second groups of patients the increase is 4-4.5 times higher than in the third group. In general, for 12 months of treatment we see that the increase in the value of the inclinometry in the first group of patients was 51.99%, lower was the increase in this indicator in the second group (37.31%), and in the third group of patients the increase in the value of the inclinometry was only 14, 01%. Thus, the use of Huber in complex treatment provides significant advantages in the development of spinal movements (Fig. 8).
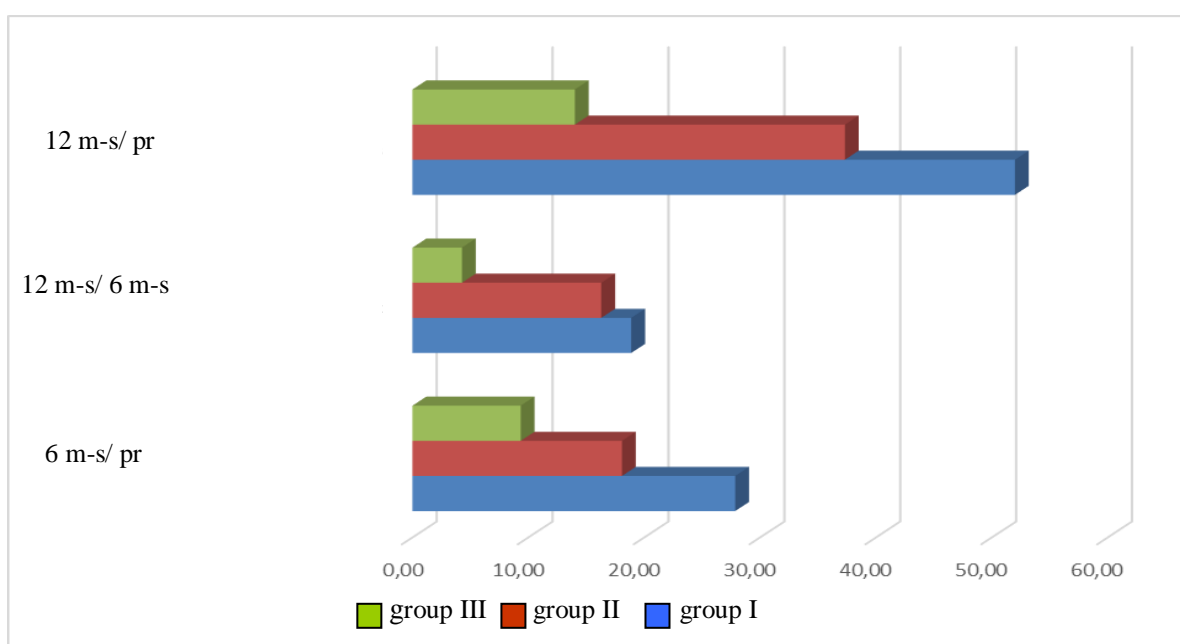

Fig. 8. Dynamics of relative increase of inclinometry values, %

Table 9

Dynamics of dynamometry, kg

	Initially	In 6 m-s	In 12 m-s
Group I	10.1 ± 0.68	18.3 ± 0.7 *	22.5 ± 0.68 *
Group II	11.3 ± 0.57	16.5 ± 0.65 *	19.8 ± 0.57 *
Group III	11.4 ± 0.75	14.5 ± 0.54	15.3 ± 0.62

* p <0.05 compared to baseline

In the first six months the growth rate of dynamometry in the first group was significant and almost twice as high as the growth rate of dynamometer in the second group, and if compared to the third group it was thrice higher. In the next 6 months of treatment the growth rate of dynamometry slowed in all groups, and in the first and second groups these values were close, while in the third group the growth rate of dynamometry was almost four times lower than in the first and second groups. In general, for 12 months of treatment the increase in the value of the dynamometry in the first group of patients was 122.77%, the increase in this indicator in the second group was lower -75.22%, and in the third group it amounted to 34.21% (Fig. 9).
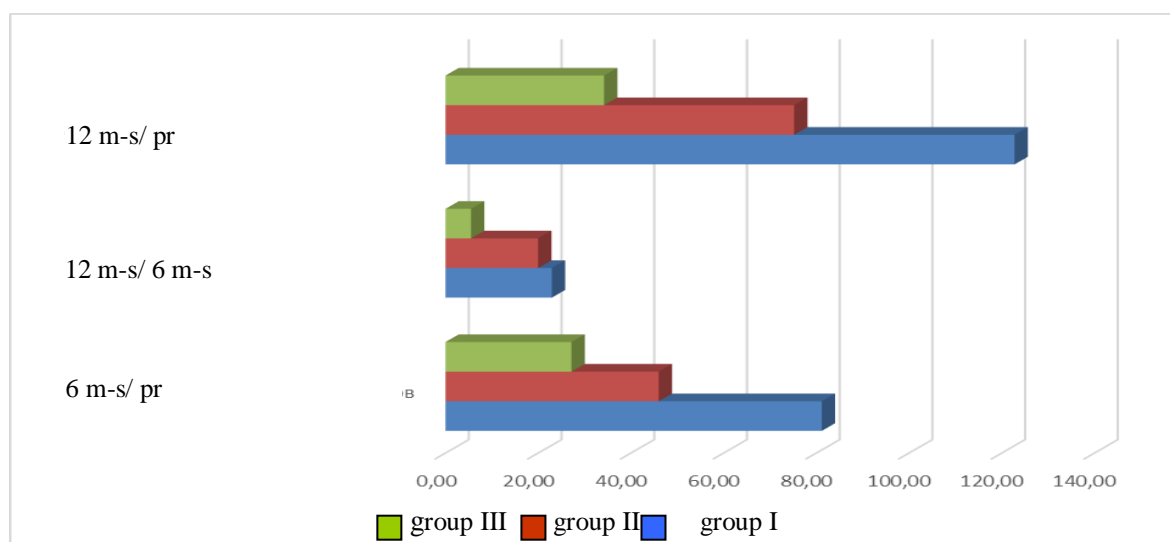

Fig. 9. Dynamics of the relative increase in the values of the dynamometry index, %

Table 10

Dynamics of the "tandem test", sec

	Initially	In 6 m-s	In 12 m-s
Group I	8.34 ± 0.45	11.5 ± 0.51	15.3 ± 0.54 *
Group II	8.37 ± 0.42	9.38 ± 0.65 *	12.2 ± 0.51 *
Group III	8.28 ± 0.38	9.05 ± 0.45	10.2 ± 0.43

* p <0.05 compared to baseline

In the first six months, the growth rate of the "tandem test" in the first group was thrice higher than in the second group and four times higher than in the third group. In the next 6 months of treatment, there was a slowdown in the growth rate of the tandem test in the first group with its increase in the second and a slight increase in the third group. In general, after 12 months of treatment, in the first group there was a significant increase in the tandem test (83.45%), in the second group by 45.76%, and this was almost twice higher than in the third group (Fig. 10).
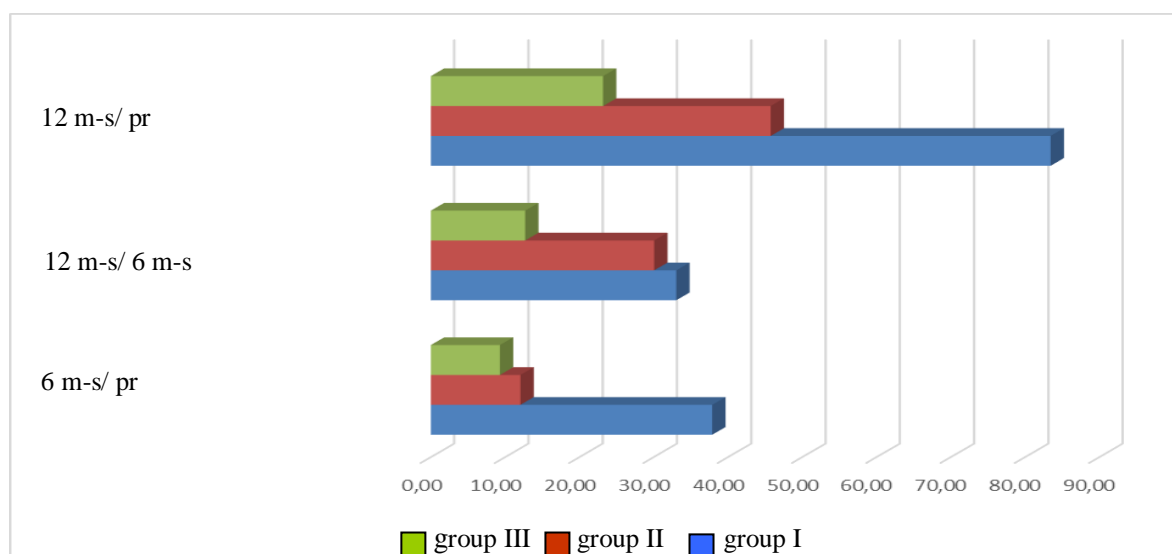

Fig. 10. Dynamics of relative growth of tandem test results in, %.

Test "get up and go" is one of the main methods of assessing the stability of the patient's movement. The decrease in the value of this test results "get up and go" as a result of treatment indicates a positive change in the BMS (Table 11).

Table 11

Dynamics of "get up and go", sec

	Initially	In 6 m-s	In 12 m-s
Group I	13.3 ± 0.42	10.3 ± 0.38 *	8.65 ± 0.37 *
Group II	13.2 ± 0.57	11.8 ± 0.34	10.5 ± 0.38 *
Group III	13.6 ± 0.48	12.9 ± 0.38	12.1 ± 0.41

* $p < 0.05$ compared to baseline

According to this criterion, we see that the best results were in the first group of patients during first six months of treatment, in the second group the value of the criterion was twice less, and in the third it was 4 times less than in the first. Similar to the criterion based on the tandem test, there was a decrease in the value of the criterion in the first group in

the next 6 months of treatment and its slight increase in the second and third groups. According to the results of treatment for 12 months, the value of this criterion was 34.96%, 22.35% and 11.03% in each group, respectively (Fig. 11).
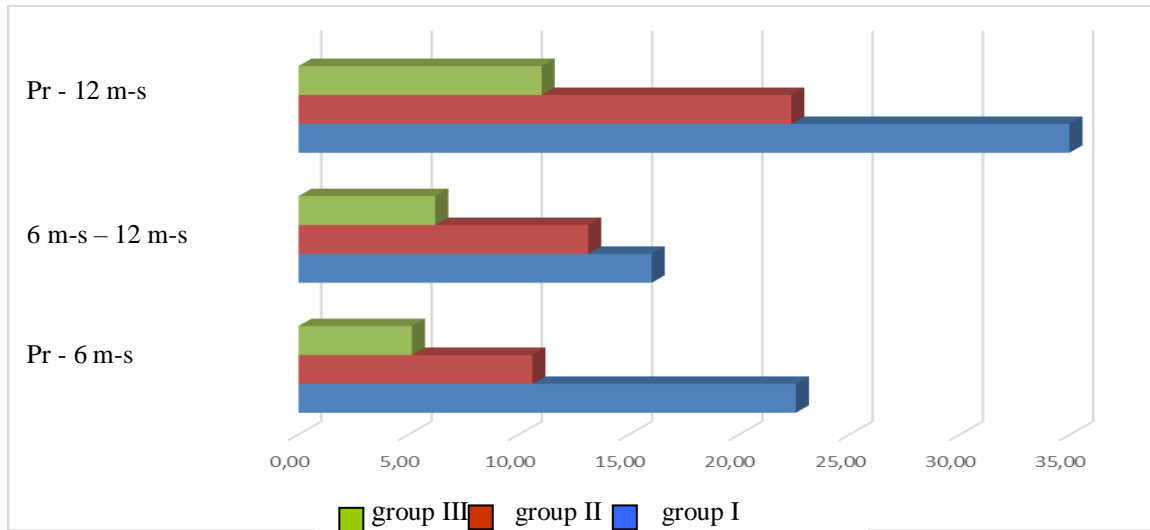

Fig. 11. Dynamics of relative decrease of values of test results "get up and go", %

The decrease in the value of the results of "sit-up" test under the influence of the treatment indicates positive changes in the BMS (Table 12).

Table 12

Dynamics of "sit-up" test, sec

	Initially	In 6 m-s	In 12 m-s
Group I	13.5 ± 0.61	11.5 ± 0.51 *	8.1 ± 0.62 *
Group II	13.43 ± 0.54	12.1 ± 0.53	9.3 ± 0.56 *
Group III	13.57 ± 0.62	13.1 ± 0.6	11.5 ± 0.53

$p < 0.05$ compared to baseline

During the first six months, the results of "sit-up" test in the first group decreased by 14.81%, which is 1.5 times better than in the second group and 4.3 times better than in the third group. In the next 6 months, this test rate of decrease changed significantly and were the best in the first group. In general, in 12 months of treatment the results of "sit-up" test in patients of the first group were 40%, which is 1.3 times better than in the second group and more than 2.6 times better than in the third group (Fig. 12).

Thus, to assess the effectiveness of treatment, the methods of system analysis were used.
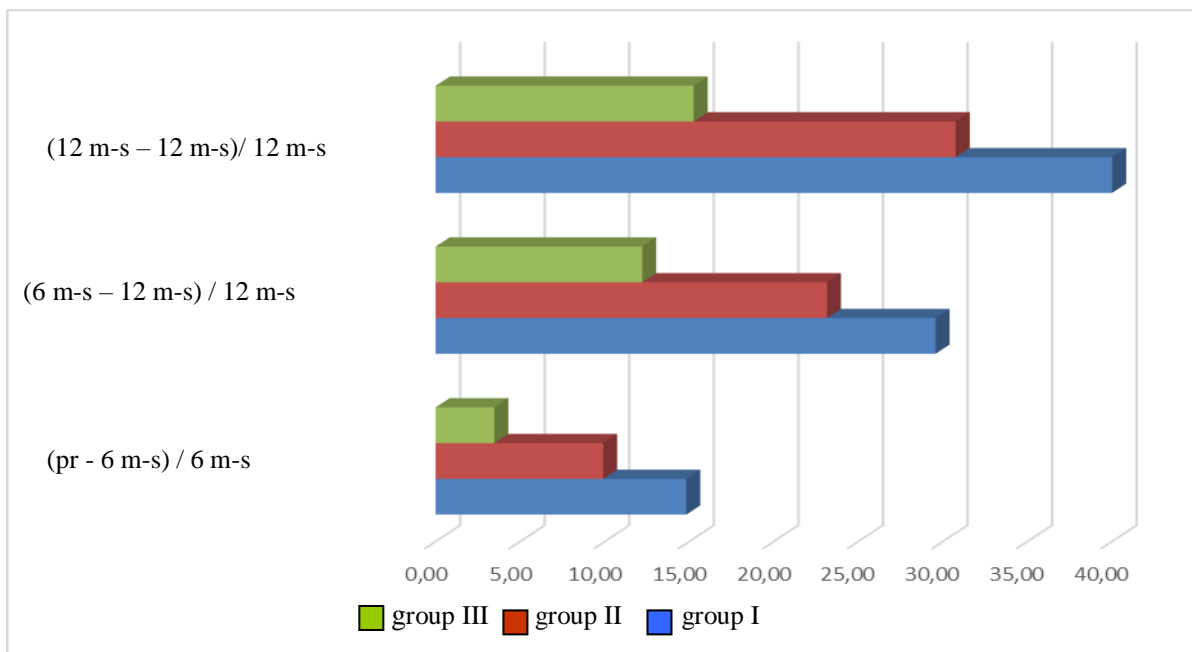
Fig. 12. Dynamics of relative decrease in the values of the test results "sit-stand", %

The criteria of treatment effectiveness worked out allow to compare objectively different methods (schemes) used and assess the progress of therapy.

The use of the multifunctional apparatus "Huber" in combination with osteotropic therapy (denosumab + Vitamin D metabolites) promotes effective increase in the functional capabilities of the BMS: muscle strength, stability, coordination of movements, reduces functional limitations, promotes more successful treatment of structural and functional changes in BT, increases BTMD (Fig. 13).
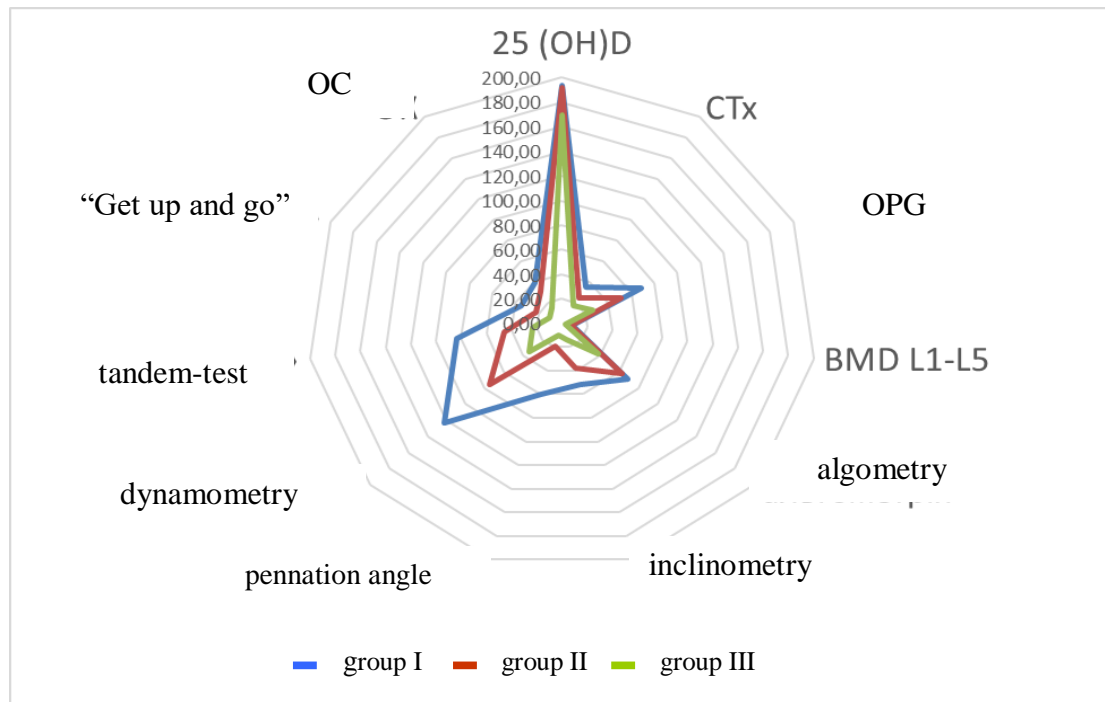
Figure 13. Evaluation of the effectiveness of treatment according to the set of selected criteria

Conclusions: Complex use of physical rehabilitation (multifunctional HUBER simulator) in combination with drug therapy (vitamin D metabolites and denosumab) effectively enhances the functional capabilities of the musculoskeletal system: muscle strength, stability, coordination of movements, reduces functional limitations, promotes more effective treatment structurally - functional changes in BT, increase in BTMD.

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