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The Drug Alphakalcidol Effectiveness in Osteoporosis in Patients with Systemic Sclerodermia

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Abstract According to the WHO, this metabolic disease of the skeleton belongs to the leading non-infectious human pathologies after cardiovascular, oncological and diabetes mellitus. The article presents the results of studying the frequency of reducing bone mineral density and its relationship with traditional risk factors and clinical parameters, the effectiveness of the drug alfaphorcal (alfacalcidol) in complex treatment in 40 patients with systemic scleroderma with osteoporosis and osteopenia. According to ultrasound osteodensitometry, osteoporosis and osteopenia are a frequent complication of systemic scleroderma and are detected in 57.5% of patients. The incidence of osteoporosis in this disease is much higher with a long course of the disease and menopause. In patients with systemic scleroderma with osteoporosis, alfacalcidol at a dose of 0.5-1.0 μg per day leads to a significant reduction in bone pain, normalization of bone remodeling processes, and an increase in bone strength.

Key words: patients**,** osteoporosis, bone mineral density, vitamin D, drug alphacaltsidol, alkaline phosphatase (AF), improve

According to the data given by WHO, osteoporosis (OP), which is considered a metabolic disease of the skeleton, is among the leading diseases after cardiovascular diseases, oncological diseases and diabetes. The indicators of prevalence and disease prevalence with SS are relatively low: among the population of different countries, each population of 1 million is from 0.6 to 122 and 7 to 489, respectively [9]. Among patients with SS, the number of women aged 30-60 years, whose disease debut is detected, is 5-7 times higher than in men [6]. The interdependence of OP and rheumatic diseases has now been more fully studied in rheumatoid arthritis itself, which is also considered an independent risk factor for bone weight reduction and bone fractures associated with op. The study, described in the literature review of op and bone fractures in patients with SS, was carried out in non-large groups and differed in the diversity of MDB evaluation methods. Their results indicate that OP fractures range from 3.3% to 50%, and bone fractures range from 2% to 38% [8]. It is assumed that SS itself can be an independent risk factor of OP [3]. It is believed that the OP in SS may be associated with a violation of the process of absorption from the intestine and its deepening against the background of prolonged intake of proton pump inhibitors, as well as a decrease in physical activity. Constant intake of glucocsteroid even in small doses leads to OP-related bone fractures in the group of patients under 50 years of age, as in the group of patients in old age [7]. More than 640 regions of Russia 76% of of patients with SS received glucocsteroid drugs for a long time, according to the conducted study results of a GLUCOST [1, 5]. According to the results of studies devoted to the study of the level of vitamin D in SS, only in 13% of patients was found to be within the norm of 25 (OH)D index in the blood, while 11% had a deficiency expressed in vitamin D [Sampaio-Barros MM, Takayama L, Sampaio-Barros PD, et al. Low vitamin D serum levels in diffuse systemic sclerosis: a correlation with worst quality of life and severe capillaroscopic findings. *Rev Bras Reumatol Engl Ed.* 2016 Jul-Aug;56(4): 337-44. doi: 10.1016/j.rbre.2016.05.006. Epub 2016 Jun 2.]. In assessing vitamin D levels, most patients with SS (91%) had a low concentration of 25 (on) D in the blood serum and at the same time a severe deficiency of vitamin D (<10 ng/ml) was noted in 10% [3]. In addition, patients with SS are often diagnosed with lesions of the gastrointestinal tract. This condition can lead to malabsorption syndrome with a negative effect on the absorption of calcium, while skin lesions — a decrease in vitamin D synthesis, and eventually an increase in the risk of developing op [4].

Thus, in patients with SS, it is necessary to identify BMD and carry out anti-OP treatment measures more often than in real clinical practice.

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Purpose. To evaluate the prevalence and clinical significance of osteoporosis in patients with systemic sclerodermia, as well as the effectiveness of the drug alphacaltsidol in its treatment.

Research materials and methods. The study was attended by 40 women aged 23 to 62 with a clear diagnosis of SS, who were treated in the multidisciplinary clinic of the Tashkent Medical Academy in a stable condition and were on dispensary observation for 12 months. The diagnosis of SS was made using the diagnostic criteria proposed by (1982) [2] based on the working classification and nomenclature. The control group was made up of 20 women who had no RK in their anamnesis. The average age of the patients was 45,85±1,45 years. The duration of the disease was 8,31±0,81 on average. SS I-level activity was determined in 12 (30%), II — 24 (60%) and III-4 (10%) patients. A questionnaire was conducted using a questionnaire that included questions that made it possible to identify op risk factors among patients and to identify the causes of secondary OP. Ultrasound of the heel bone densitometry was performed in apparatus "Ostesys SONOST-300" (South Korea) to assess the bone tissue condition. Z and T, and BUA indicators were calculated. The diagnosis of OP was made in accordance with the recommendations of the WHO. The fact that the T-index was at the level of -1,0 do -2,5 SD was assessed as a characteristic decrease in smz as osteopenia, while the level of -2,5 SD and below was considered a diagnostic sign of OP, and this, according to most scientists, is a prognostic sign of bone fracture.

"T" - in -2,5 SD and Anamnesis there is a pathological fracture of the bones will be combed from heavy op. For the treatment of op in patients with SS, an active metabolite of vitamin D — alphacaltsidol (Alphaforkal, capsules with 0,25 mkg, Kusum, India) was used. From the software package for statistical analysis in the statistical processing of received data (Statistica for Windows version 10.0 (StatSoft Inc., USA)). When P<0,05, the differences were evaluated as significant.

Research findings and discussion. In general, in the groups, the normative indicators of BMD were determined in the patients with SS in the group with significantly fewer cases than in the control group (p<0.05). In 11 (27.5%) of the 40 patients examined, op was detected. The T-index was in the range of 1,74 -3,36. The results obtained from our studies correspond to the data in the literature [3]. According to other foreign scientists, OP were detected in 3-51% of patients with SSs [9]. As can be seen from Table 1,

Table 1.
The incidence of op and osteopenia in patients with TSD in relation to the control group

BMD condition	Patients with SS n=40	Control group n=40	The Reliability of P Values **(P)**
Osteoporosis n (%)	11 (27,5%)	1 (2,5%)	p<0,01
Osteopenia n (%)	12 (30%)	3 (7,5%)	
Norm n (%)	17 (42,5%)	36 (90%)	

the level of op development in women with SS was convincingly higher than in the control group (p<0,01).To study the effects of SS on BMD status, clinical and laboratory indicators were studied in patients. It was noted that OP and osteopenia are most common in high and moderate levels of activity (respectively 100% and 55%). In addition, there was an increase in the number of op encounters (41,7% and 100%, respectively) with SS escalation and spread from the initial stage and transition to the terminal stages (p<0,05). At the same time, it was determined that the OP is associated with the duration of the disease (p<0,05). Indicators of erythrocyte sedimentation rate (ESR) were also higher in patients with OP and osteopenia (28,15±0,42 and 21,54±0,19 in patients without op detection) (p<0.05). Considering the development of op against the background of GKS intake, we analyzed the results of treatment with GKS in patients with SS. Duration of glucocsteroid intake, average daily and cumulative doses were studied (Table 2).

Table 2.
Features of glucocorticosteroid therapy in patients with SS (M±t).

Treatment feature	Patients with SS		The Reliability of P Values (p)
	OP and osteopenia (n=9)	BMD normal (n=4)	
The average daily dose of glucosteroids is prednisolone (mg/milk)	12,13±1,17	6,15±1,35	p<0,05
Duration of reception of glucosteroids (months)	68,1±12,12	21,11±4,75	p<0,05

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Cumulative doses of glucosteroids prednisolone (g)	14,99±2,06	3,85±0,62	p<0,01

As can be seen from the table, in patients with OP and osteopenia, these indicators were significantly higher in patients with BMD norm (p<0.05, p<0.05 and p<0.01, respectively). The duration of treatment with GCS of BUA index (g = -0,75; p<0,001), as well as the inverse correlation correlation with daily and cumulative doses were recorded (g = -0,39; p<0,01 and g = -5353; p<0,01 respectively). These indicators are also consistent with the results obtained from the literature [4]. For the treatment of op in patients with SS, an active metabolite of vitamin D — alphacaltsidol (Alphaforkal, capsules with 0,25mkg, Kusum, India) was used. To assess the effectiveness of the drug, patients were divided into 2 groups. 1-Group op was determined 0.5-1.0 mkg/milk dose of alfacaltsidol and 10 patients with SS who received 1000 mg / day, 2-group was 6 patients who received 1000 mg / day.

Table 3 shows the dynamics of op indicators in patients with SS as a result of treatment with Alphacaltsidol and calcium and monotony with the drug calcium.

Table 3.
Changes in the dynamics of treatment of op clinical-laboratory indicators in patients receiving alphacaltsidol in patients with SS and in the control group (M±t)

Index	1 group (alfakaltsidol) n=10		2 Group (calcium preparations) n=6	
	Before treatment	After treatment	Before treatment	After treatment
Pain in the bones (points)	1,69±0,29	0,92±0,10*	0,64±0,20	0,91±0,24
Total alkaline phosphatase in the blood serum (norm: 0,90-2,3 mkkat / l.)	1,09±0,29	0,94±0,21	1,17±0,23	1,91±0,12*
General calcium in blood (norm in the blood:2,25-2,75 mmol/l)	1,94±0,09	2,35±0,01***	2,07±0,09	2,22±0,03

Note: P Values (*p<0,05; **p<0,01; *** p<0,001).

In Table 1, it is possible to see a convincing decrease in pain syndrome against the background of taking alphacaltsidol in Group patients (p<0.05). The total volume of calcium in the blood was convincingly higher than the pre-treatment indicators, and this was also confirmed by a decrease in the clinical signs of hypokalemia (p<0,001). A convincing discrepancy was not noted, even if the indicators of total alkaline phosphatase (AF) were somewhat close to the normative indicators (p>0,05). A convincing increase in the total AF level was noted in patients of the 2nd group who received calcium (r<0.05). During the time of the examination, no new bone fractures were observed in patients of both groups.

Table 4 shows the change in the dynamics of treatment of smz indicators in patients with SS.

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Table 4.
Changes in the dynamics of treatment of op densitometric indicators (M+t) in patients receiving alphacaltsidol in patients with SS in the control group.

Index	1 group (alfakaltsidol+calcium) n=10		2 Group (calcium preparations) n=6	
	Before treatment	After treatment	Before treatment	After treatment
BUA (dB/MHz)	55,46±1,32	59,23±0,61	60,50±0,57	60,12±1,1
Z-index (SD)	-1,42±0,18	-1,16±0,11	-0,61±0,30	-0,87±0,22
T-index (SD)	-1,97±0,22	-1,61±0,14	-1,12±0,17	-1,25±0,19

Note: P Values (*p<0,05; **p<0,01; *** p<0,001).

Data from the densitometry study (BUA, Z, T) reveal the positive dynamics of bone status indicators in patients of the 1st group who received alphacaltsidol. The 1-year growth of the BUA index averaged 4,5%. In the 2nd Group, a decrease in bone strength was noted -2,1%, indicating a decrease in the smz of BUA, Z-and T - indices.

No side effects of the drug were observed in patients taking alfacaltsidol.

Thus, in patients with SS, OP is characterized by a high bone exchange rate. The results of the application of the drug alphacaltsidol as a treatment for OP showed its effectiveness and safety in the treatment of OP in patients with SS. Having an impact on the underlying causes of OP pathogenesis in SS, alfacaltsidol allows for bone remodeling and normalization of calcium hemostasis, baratarization of pain syndrome, increase in movement activity and, at the same time, improve the quality of life of patients.

Conclusion.

1.In systemic scleroderma, osteoporosis often develops in patients with a high activity level, stage and duration of the disease, a low body weight index and a prolonged menopause. The intake of glucocorticosteroids in SS is a risk factor for the development of osteoporosis. The development of osteoporosis in patients taking steroids is associated with the duration of taking the drug, cumulative, and to a lesser extent daily dose.

2. Carrying out monotony with 1000 mg of the drug per day eliminates clinical-laboratory signs of hypocalcemia, but does not have a positive effect on laboratory indicators of BMD, pain syndrome and bone remodeling, does not stop the exacerbation of changes that lead to osteoporosis.

3. The use of the drug alphacaltsidol in the treatment of complex in patients with osteoporosis and osteopenia detected for 12 months at a daily dose of 0,5-1,0 mkg leads to a decrease in the pain syndrome in the bones, normalization of bone remodeling processes, an increase in bone strength according to ultrasound densitometry indicators, and can be recommended as a selecting drug

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