

EVALUATION OF THE EFFECT OF ANTIRESORPTIVE THERAPY ON THE DYNAMICS OF BONE METABOLISM MARKERS IN PATIENTS WITH DIABETIC CHARCOT OSTEOARTHROPATHY

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Abstract

Before treatment, there was a significant decrease in the values of total calcium, ionized calcium, creatinine, GFR, osteocalcin, Vit D, beta-cross laps, calcitonin, procalcitonin, which were significantly lower than in the control group against the background of high PTH values and the development of secondary hyperparathyroidism. Further, after 6 months of treatment, there is a significant improvement in such indicators of bone metabolism as the average levels of total calcium ($p < 0.001$), ionized calcium ($p < 0.001$), Vitamin D ($p < 0.001$), PTH ($p < 0.001$), ostase ($p < 0.001$), B-cross laps ($p < 0.001$) and calcitonin ($p < 0.001$) in groups 1 and 2 of patients.

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The purpose of the study was to study the dynamics of bone metabolism in patients with diabetic osteoarthropathy after 6 months of complex therapy.

Material and research methods: 65 patients (prospectively) with type 2 diabetes and Charcot foot were examined in the period 2021-2023 at the Russian Scientific and Practical Medical Center for Endocrinology, in the department of reconstructive plastic surgery for complications of diabetes mellitus.

All observed patients were divided into 2 groups: 1 g – patients with the acute stage of Charcot's foot with type 2 diabetes – 30 patients,

Group 2 - patients with subacute stage of Charcot foot - 35 patients.

Conclusions 1. Patients with Charcot's foot are at high risk of deficiency of 25-hydroxyvitamin D3 and total, ionized calcium.. 2. In order to achieve a significant increase in the values of total calcium, ionized calcium, creatinine, GFR, osteocalcin, Vit D, beta-cross laps, calcitonin, procalcitonin, long courses of antiresorptive therapy (vitamin D, calcium, bisphosphonates) are recommended for patients with Charcot's foot.

Relevance. Charcot diabetic foot syndrome is a serious and potentially limb-threatening complication

of diabetes. First described in 1883, this mysterious condition continues to challenge even the most experienced practitioners. Currently considered an inflammatory syndrome, Charcot diabetic foot is characterized by varying degrees of bone and joint disorganization secondary to underlying neuropathy, trauma, and disorders of bone metabolism. In January 2011, the American Diabetes Association and the American Podiatric Medical Association convened an international working group of experts to summarize the available data on the pathophysiology, natural history of the disease, presentations, and recommendations for the treatment of this disease [1].

Offloading during the acute active stage of Charcot foot is the most important treatment strategy and can stop the progression of the deformity. Ideally, the foot should be immobilized in a non-removable general contact cast (GCS), which is initially changed after 3 days and then checked every week. A reduction in swelling is often noticeable in the first few weeks of treatment. The cast should be changed frequently to avoid “pistoning” as swelling subsides. If possible, the patient should use crutches or a wheelchair and avoid putting weight on the affected side. The cast is continued until the swelling disappears and the temperature of the affected foot is within 2°C of the temperature of the contralateral foot [1]. An alternative device for offloading acute active CN is a prefabricated removable walking cast or the “instant NOP” technique, which converts a removable cast walker into a walker that is more difficult to remove [3, 4]. It is important to consider that PCC can actually have adverse effects on the non-Charcot limb and cause unnatural stress patterns causing ulceration and even fractures. In addition, patients with Charcot foot have an increased instability and risk of falls and fractures as a result of multiple comorbidities, including loss of proprioception and postural hypotension. However, it should be noted that complete immobility itself has disadvantages associated with loss of muscle tone, decreased bone density and loss of fitness.

The duration and aggressiveness of offloading (non-weight-bearing or weight-bearing, fixed or removable device) is determined by clinical assessment of Charcot foot healing based on swelling, erythema, and changes in skin temperature [2]. Evidence of healing on x-rays or MRI supports the clinical decision to switch the patient to footwear. To prevent recurrence or ulceration in subsequent deformities, various devices, including special shoes, boots, or other weight-bearing devices, are recommended after resolution of the acute or active episode. Frequent monitoring is required.

Treatment with antiresorptive drugs has been proposed due to excessive bone turnover in patients with active Charcot foot. However, there is little evidence to support their use, but both oral and intravenous bisphosphonates [5] have been studied in the treatment of Charcot foot in small randomized, double-blind, controlled trials [6, 7] or retrospective controlled studies [8]. Some patients cannot tolerate oral bisphosphonates but may benefit from intravenous pamidronate or zoledronic acid [9]. Intranasal calcitonin is another antiresorptive agent that has been studied in Charcot foot. This treatment was associated with significantly greater reductions in cross-linked carboxy-terminal telopeptide of type I collagen and bone-specific alkaline phosphatase than standard treatment in the control group, which received calcium supplementation and unloading only. Calcitonin has a safer profile in renal failure compared with bisphosphonate therapy [10–12]. However, a single intravenous administration of a bisphosphonate usually does not require correction of renal function. There is strong evidence for the effectiveness of bisphosphonates in active Charcot foot, and our understanding is evolving as new research is being conducted.

All of the above was the reason for this study.

The purpose of the study was to study the dynamics of bone metabolism in patients with diabetic osteoarthropathy after 6 months of complex therapy.

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All observed patients were divided into 2 groups:

1 g – patients with the acute stage of Charcot's foot with type 2 diabetes – 30 patients,

Group 2 - patients with subacute stage of Charcot foot - 35 patients.

Of the 65 patients, there were 40 men and 25 women. Average age: men were 69.12 years, women - 68.15 years. The duration of type 2 diabetes ranged from 17 to 25 years.

Research methods included: biochemical (bilirubin, direct, indirect, lipid spectrum, ALT, AST, PTI, coagulogram, blood sugar, glycated hemoglobin, urea, creatinine, GFR, total calcium, ionized calcium, bone coenzyme alkaline phosphatase, beta cross laps, osteocalcin, vitamin D, PTH, calcitonin, blood procalcitonin and instrumental: ECG, MRI of the feet, Dopplerography of the great vessels of the legs, ultrasound of the internal organs, DEHA, fundus.

Patients of all groups received, after a complete examination and distribution into groups, a single regimen of drugs: calcium, vitamin D3 and bisphosphonates for 6 months against the background of glucose-lowering therapy with monitoring of carbohydrate metabolism until compensation was achieved.

Statistical calculations were carried out in the Microsoft Windows software environment using the Microsoft Excel-2007 and Statistica version 6.0, 2003 software packages. The obtained data are reflected in the form $M \pm m$, where M is the average value of the variation series, m is the standard error of the mean value. The significance of differences between independent samples was determined using the Mann-Whitney and Student methods.

Research results. Table 1 shows the distribution of patients by gender and age.

Table 1. Distribution of patients by gender and age

Age, years	Number of men		Number of women	
	1 g	2 g	1 g	2 g
30-44	-	-	-	-
45-59	5	7	3	3
60-74	10	13	10	9
75 and older	-	-	-	-
Total: n = 65	15	20	13	12

As can be seen from Table 1, the majority of patients were aged from 60 to 74 years - 40 (62.7%), while the number of men was greater: 40 men and 25 women.

The next step in our research was to study carbohydrate metabolism indicators. The patients had significant disturbances in carbohydrate metabolism in all groups, which shows the state of decompensation in these patients before treatment.

Our main task was to study the biochemical and hormonal parameters of bone metabolism in the compared groups of patients with Charcot's foot over time after 6 months of antiresorptive therapy (Table 2).

Table 2. Comparative characteristics of biochemical and hormonal parameters of patients by group before and after 6 months of treatment

N ^o	Indicators	1g up to (n=30)	1g after (n=30)	2g up to (n=35)	2g after (n=35)
1	Age, years	58.3±8.23	58.3±8.23	56.9±9.3	56.9±9.3
2	Total calcium, mmol/l	1.23±0.08	1.78±0.33*	1.33±0.21	1.72±0.18*
3	Ionized calcium, mmol/l	0.77±0.03	1.08±0.09*	0.76±0.08	1.34±0.01*
4	blood urea, mmol/l	5.87±0.86	5.43±1.12	6.87±0.09	5.23±0.08
5	blood creatinine, mmol/l	76.9±8.9	89.3±7.9	78.6±4.32	83.3±6.22
6	GFR, ml/min	65.3±9.1	81.2±8.2	71.2±6.3	88.2±5.9
7	blood osteocalcin, ng/ml	12.2±2.12*	15.83±3.5	12.8±3.7	15.3±4.78*
8	vitamin D	18.3±5.17*	26.8±8.8	12.8±6.33	25.7±8.76*
9	PTH, pg/ml 15 – 65 pg/ml	80.5±9.87	67.8±7.56*	77.8±6.98	60.6±5.32*
10	Blood stasis 0.7 – 85.8 µg/l	112.9±12.8	95.8±25.3*	3.87±1.8	33.9±6.9*
11	B-cross laps, ng/ml.	0.68±0.08	0.76±0.09*	0.65±0.03	0.72±0.02*
12	calcitonin, pg/ml	11.8±0.80	14.8±7.76*	7.88±2.64	9.76±2.07*
13	procalcitonin, ng/ml.	0.36±0.03	0.32±0.05	0.17±0.08	0.14±0.08

Note: PTT – parathyroid hormone – significance of differences between groups in comparison with control. At the same time, *p<0.05 **p<0.001

As can be seen from Table 2, before treatment there was a significant decrease in the values of total calcium, ionized calcium, creatinine, GFR, osteocalcin, Vit D, beta-cros laps, calcitonin, procalcitonin were significantly lower than in the control group against the background of high PTH values and development secondary hyperparathyroidism. Further, after 6 months of treatment, there is a significant improvement in such indicators of bone metabolism as the average levels of total calcium (p<0.001), ionized calcium (p<0.001), Vitamin D (p<0.001), PTH (p<0.001), ostase (p <0.001), B-cross laps (p<0.001) and calcitonin (p<0.001) in groups 1 and 2 of patients.

Conclusions

1. Patients with Charcot's foot are at high risk of deficiency of 25-hydroxyvitamin D3 and total, ionized calcium.
2. In order to achieve a significant increase in the values of total calcium, ionized calcium, creatinine, GFR, osteocalcin, Vit D, beta-cross laps , calcitonin, procalcitonin, long courses of antiresorptive therapy (vitamin D, calcium, bisphosphonates) are recommended for patients with Charcot's foot.

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