

## Efficiency of Ossein-Hydroxyapatite Complex in the Treatment of Patients with Non-Unions Complicated by Posttraumatic Osteoporosis

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### Abstract

Comparative analysis of the results of application of ossein-hydroxyapatite complex (OHC) and calcium with vitamin D3 together with surgical treatment of patients with hypoplastic non-unions of femur and shin, complicated by osteoporosis was performed. Patients were operated by open transosseous osteosynthesis with Ilizarov apparatus without the autobone plasty. After surgery one group of patients had received OHC for 6 months as it was recommended by authors (Patent RF № 2423983). Second group of patients had received calcium with vitamin D3 during the same period of time. Third group did not receive any medicaments. Non-unions of all patients were eliminated without repeated surgery. Analysis of union-time showed the use of OHC or calcium with vitamin D3 promoted significant reduction of the non-union consolidation time. OHC influenced also on bone mineral density of damaged leg positively. It contributed optimization to process of the bone remodeling and provided regression of osteoporosis even in time of the main pathology treatment and later; in 1.5 years of subsequent observation. Results of this investigations has shown high efficiency of OHC in treatment of non-unions complicated by posttraumatic (immobilized) osteoporosis. The use of OHC in treatment of this very difficult orthopaedical pathology is reasonable and efficient.

**Keywords:** Non-Union; Femur; Shin; Osteoporosis; Ilizarov Apparatus; Ossein-Hydroxyapatite Complex; Bone Mineral Density; Standard Deviation

### Introduction

Non-unions (NU) are heavy results of limbs long bones fractures which are leading to significant biomechanical disfunctions and reduce quality of life up to disability [1,2]. NU is a result of long-time absence or reducing of load on the damaged limb, as usual, immobilized osteoporosis is developing. In previously made investigations authors found lowering of the bone mineral density (BMD) in 91.7% of patients with NU of femur and shin bones. In 74.1% of patient's osteoporosis (OP) was revealed and only in 8.3% patients BMD corresponded to the norm [3].

Treatment of NU complicated by OP is one of significant problem of contemporary traumatology and orthopedics, because duration of the treatment of such patients on the background of OP in 1.5 - 2 times exceeds treatment time of NU in case of normal BMD [4]. Osteoporosis increases risk of the second fracture and insufficient fixation of already existing damage. Therefore, investigation of medicines for treatment of osteoporosis to step up of process of bone consolidation are relevant [5-9].

## **Materials and Methods**

Prospective open controlled randomized study was made in which patients with hypoplastic diaphyseal NU of femur and shin, complicated by immobilized osteoporosis were included.

Criteria of including into investigation were patients who did not received medicines which influenced on BMD and also those who didn't have diseases, leading to development of secondary osteoporosis. Patients who were elder 55 years and women in menopause, patients with osteoporotic fractures and NU of proximal part of femur were not included. In this investigation material of study was composed by 73 patients (56 men and 17 women) aged from 20 to 55 years (average age 41.3 years  $\pm$ 11.4 years) with NU of femur and shin complicated by regional osteoporosis (z-criterion from - 2.5 Standard Deviation to - 4.8 Standard Deviation). Remoteness of trauma was in general 17.410 months. 25 patients had NU of femur, 48 of them had NU of shin. NU of all patients was formed as a result of high-energetic fractures.

Clinically for all patients expressed pathological mobility in the zone of damage was defined, absence of pain in this area, impossibility of load of limb, necessity to use crutch during walking.

Diastasis between fragments of NU was clear seen on the X-rays. Ends of the fragments were thin, non-congruence, had abnormal shape, medullary canals were closed by compact layer of bone substance, thickness from 0.2 to 0.7 cm. X-ray indications of osteoporosis were noted at all patients: increased transparence of bone outline, increased diameter of bone medullar channel and thin cortical levels of both fragments and presence of positive sign of Kohler.

Investigation of bone mineral density (BMD) was provided by double-energetic x-ray absorptiometry (DXA) on densitometer DPX-A (LUNAR USA). BMD in loins part of spine (L1-L4) and proximal parts of femur (total hip) also were investigated. BMD was valued both in absolute values g/cm<sup>2</sup> as well as in values of standard deviation (SD) on Z-criteria. BMD analysis was provided before operation and after it 6, 12 and 18 months after consolidation of bone fragments.

Estimation of the received data static significance was provided with using program BIOSTAT (version 4.03). For analysis of consolidation periods non-parametric criterions were used: for comparison 3 groups criteria Kruskal-Wallis was used, in case of founding distinctions between groups we ascertained nature of them using Danna criteria, distinctions were valued significant if  $p < 0,05$ .

In order to distribute patients by groups method of stratified randomization was used. Between patients of three groups there was no distinctions on sex, age, localization, type of non-unions, remoteness of trauma, existence of osteoporosis.

All patients received treatment in one clinic of Ural Institute of Traumatology and Orthopaedics. Patients were operated by open transosseous osteosynthesis. NU zone was uncovered, cicatrix between fragments were removed, then economical resection of fragments ends was made adapting them to each other. Bone autoplasty was not used. Firm contact of fragment ends was provided with Ilizarov apparatus during all period of treatment until consolidation.

In post-operation time patients of the main group (n = 17) had received OHC: 2 tablets three times daily during 3 initial months, and 1 tablet three times daily for the next 3 months [10]. Patients of the comparison group (n = 23) during first 3 months received Ca carbonate (1000 mg) and vitamin D<sub>3</sub> (400 IU) daily. Next 3 months the dose was reduced by two times. Such medical regimen provided identical quantity of daily acceptance of elementary calcium for patients of main and comparison groups. Patients of the control group (n = 33) had not received any medicine.

Postoperative treatment of patients for all groups did not distinguish, except the above-mentioned medicinal therapy. Since first-second days after surgery patients got permission to stand up, on 2 - 3 days they began active movement in joints. Load on the operated

leg with crutch patients began by the end of the first week after operation and they increased it gradually. In such case at osteosynthesis of shin bone in three weeks after operation load of the limb was not less than 50% of body weight and at osteosynthesis of femur it was about 30%. In 2 - 3 months after operation patients loaded legs fully and after osteosynthesis of shin - later - in 4 - 5 months after operation. After completion of the hospital treatment patients were dynamically observed in the institute once in 1.5 - 2 months during all period of bones fixation by Ilizarov apparatus and after its dismantling - to 1.5 years.

Results

As a result of provided treatment NU of patients of all groups were abolished with restoration of bone segment integrity, support ability and function of the damaged limbs without of the repeated operations. Analysis of the consolidation time of patients of different groups revealed their authentic differences. Diagnosis was provided by two independent specialists: traumatologist and radiologist on the bases of clinical and x-ray information. On condition of osteoporosis standard x-ray indications of fragments joining, typical for fracture, in patients with NU practically were absent. On patients of control group during 4 - 5 months after operation there was slit between fragments ends, washing away of the fragments ends outline, osteoporosis was in progress, transparence of bone and cortical layer were increasing. Slit between fragments on the x-ray of patients after femur osteosynthesis was not discovered in 8 - 12 months and 7.5 - 10.5 months after operation of shin. The ends of NU were united by common cortical bone plate to this time. This x-ray symptom is the main sign of presence of the bone fragments firm consolidation. In connection with difficulty estimation of the mechanical strength of bone consolidation at osteoporosis before removal the apparatus off to all patients "clinical test" was carried on. For this internal nut on the screw rods of Ilizarov apparatus on the level of fragments consolidation were untwisted on 2 - 4 mm for increasing of axis load on the bone. In case of absence of swelling and/or pain in the zone of fragments consolidation apparatus was kept in addition for 3 - 4 weeks. After dismantling the apparatus additional fixation of limbs was not used.

Analysis of the consolidation time in groups has shown that it was for sure shorter on patients who after operation took OHC or Ca carbonate with vitamin D<sub>3</sub> in comparison with patients of control group. Formation of common united cortical plate, connected both fragments, marked by 6 - 7 months on patients with femur NU who got OHC, by 7 - 8 months on patients who got Ca carbonate with vitamin D<sub>3</sub>, and only in 9 - 10 months in patients of control group. Similar X-ray indications were discovered in all groups at treatment shin NU, but they were studied in general on 4 - 8 weeks earlier than in case of femur NU.

Further observation of patients had shown that osteoporosis gradually underwent a slow regression: thickness of the cortical plate was growing, transparence of bone picture reduced, medullary canal had restored.

Analysis of the consolidation time at patients with femur NU has shown reduction of union time both in group, which got OHC, and group which got Ca preparations with vitamin D<sub>3</sub> (p < 0.05). However, in patients, who got OHC, consolidation came in general by 34.3% earlier than in control group In patients, who got Ca carbonate with vitamin D<sub>3</sub>, time of consolidation was shorter and came to only 15,3% in comparison with control group (Table 1).

Group	N	Time of Union, Days
Control	9	326 ± 58
OHC	7	214 ± 42*
Ca preparations with vitamin D	9	276 ± 43.7*

Table 1: Union time of the femur NU complicated by osteoporosis.

\*p < 0.05 in comparison with control group.

Consolidation time of shin NU(Non-Union), complicated by osteoporosis, in patients who got OHC (Ossein-Hydroxyapatite Complex) or Ca with vitamin D<sub>3</sub>, also reduced by 28.6 - 31.8% for sure being different from reduction time in patients of control group (p<0.05) (Table 2).

Group	N	Time of Union, Days
Control	24	280 ± 45
OHC	10	200 ± 44*
Ca carbonate with vitamin D <sub>3</sub>	14	191 ± 32*

**Table 2:** Union time of the shin NU complicated by osteoporosis.

\*p<0.05 in comparison with control group.

So, application in post-operation period OHC and Ca with vitamin D<sub>3</sub> in patients with NU of femur and shin complicated by osteoporosis, aloud to shorten their time of consolidation and general duration of treatment.

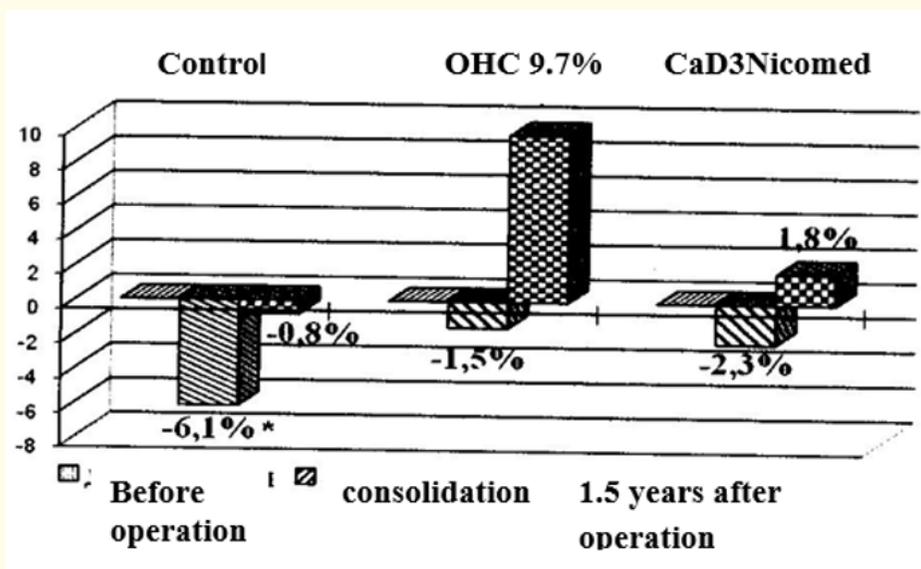
Change of the BMD inside groups as well as in patients with femur NU and with shin NU had the same character. This allowed consolidate got results on dynamic of BMD in patients with different NU localization.

BMD healthy lower limb and loin section of spine in all patients authentically did not change in treatment process and 1.5 years of observation after eliminated of NU. BMD dynamic of damaged limb had principal difference in patients of various groups.

In patients of control group in treatment process loss of BMD in operated limb by the moment of consolidation showed progress: reduction of BMD (total hip) was 6.1% in comparison with preoperative values (p<0.05).

In 1.5 years after consolidation the BMD of the damaged legs had increased a little for these patients under the full functional load, but it had reached only the preoperative values.

In patients who got Ca carbonate with vitamin D<sub>3</sub> reliable of BMD were not noted both during treatment and followed period of observation. Only patients received OHC, demonstrated reliable BMD increasing by 5.5% (p = 0.011) in 6 months after bone union, in 12 months - by 7.1% (p = 0.01), in 1.5 years BMD of damaged leg increased in comparison with preoperative value by 9.7% (p<0.05) (Figure 1).



**Figure 1:** BMD dynamic of damaged legs (total hip) in operated patients.

\*(p < 0.05) in comparison with starting level. Axis X - % in comparison with starting level.

## Discussion

It is known that fracture is a cause of the post-traumatic development of osteopenia and osteoporosis [11,12]. In order estimate efficiency of OHC at surgery treatment of NU, complicated by OP, group of comparison was organized, which after operation received Ca in dose 1000 mg with vitamin D<sub>3</sub>. It conformed daily dose of Ca, which patients of the main group got (1068 mg). Comparative analysis had shown that OHC receiving was more effective in relation of bone fractures consolidation time in comparison with Ca carbonate. Consolidation time on patients with femur NU was on 1/3 shorter and a bit less (28.6 - 31.8%) in patients with shin NU. Dynamic of BMD in the investigated groups revealed its increasing only on patients received OHC. In 1.5 years in this group after completion of the consolidation increasing of BMD was 9.7%. Results of provided investigation were close to the meta-analysis data [13], which was carried out for the comparison of receiving efficiency of OHC and carbonate Ca in treatment of OP and osteopenia. In this investigation it was found that in patients with reduced BMD OHC was for sure more effective than Ca preparations. By present time there is positive experience of OHC application in the treatment of pathological fractures on background of OP coupled with noninvasive osteosynthesis [14-16], in the treatment of acute traumas with isolated and plural fractures [1,17,18]. Favorable results of treatment with using OHC were got also on patients with disruption of bone reparative regeneration [19-21]. It was expressed in bone fragments consolidation by 2 - 3 weeks earlier than usual time, increasing of bone mass in damaged leg. Moreover, receiving of OHC promoted to reduction of the time when patients are in the hospital and acceleration of damaged leg restoration. One of investigations [22] was devoted to the OHC application at the fracture treatment in young and middle-aged patients (in average 39.6 years), who did not have bone tissue pathology. These patients with insulated fractures of femur and tibia got operations of osteosynthesis with application of the plates or intramedullary nails and after operation patients got OHC for 1 month 2 tablets 3 times daily. Consolidation of bone fractures was in 3 months in patients with shin fractures and in 5 months on patients with femur fractures. Thanks to exceptional composition of OHC bone remodeling is optimized by presents of growth factors and sufficient receiving of bioreasonable Ca [18,20,22,23]. Adequate osteosynthesis of fracture in combination with OHC receiving normalizes time of consolidation [18,20,22]. Analyses of efficiency of the OHC application in treatment of fresh fractures, delayed consolidation and results of our own investigation about NU [24-27] allows recommend OHC for the active application for patients of any age in practice of traumatologists and orthopedics.

## Conclusion

Present investigation has shown that patients with hypoplastic non- unions of lower bones complicated by osteoporosis in the process of surgical treatment continuous to lose bone mass which makes time of consolidation longer. Normalization of the union time can be reached by combination of surgery treatment and medicinal correction of osteoporosis. The use of the ossein-hydroxyapatite complex with surgery in treatment of hypoplastic NU of long bones complicated by osteoporosis provides significant reduction of the consolidation time of the bone's fragments and regression of osteoporosis. It is demonstrated by reduction of consolidation time in comparison with control group by 28.6 - 34.3%. Besides this OHC positively influences on the mineral bone density of the operated leg which gradually increases in conditions of complete functional load and in 1.5 years after consolidation it came to 9.7% in comparison with initial indicators. It allows believe that OHC promotes optimization of bone remodeling and osteoporosis regress. Therefore, the use of OHC in treatment of very difficult pathology - hypoplastic NU complicated by OP is reasonable and efficient on our opinion.

## Conflict of Interests

The authors do not have conflict of interests.

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