Ossein-hydroxyapatite complex in the treatment of patients with pseudoarthrosis of the femur and shin bones, complicated by systemic osteoporosis

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Pseudoarthroses of long bones account for almost 25.4% of all injury-related disablement [1]. Most patients are of working-age and experience protracted periods of disablement [3]. Secondary immobilization osteoporosis is a complication of fracture treatment caused by prolonged immobilization of the affected extremity, reduced or absent bone loading and dynamics, and circulatory disorders. A deficit in functional loading is known to lead to bone demineralization within 4-6 weeks, even in the absence of a fracture [5]. In volunteers, it has been shown that the loss of bone tissue results in osteopenia 4 months after the onset of experimental hypokinesia [10-12]. An earlier study showed that reduced bone mineral density (BMD) occurred in 89.3% of patients (n=75) who had fractures of the femur and tibia which failed to heal; systemic change occurred in 70.6% of these subjects [21]. Osteoporosis adversely affects bone fracture healing [14, 17-19] and can lead to implants becoming loose [2, 9, 13]. Treatment of patients with pseudoarthrosis and concomitant osteoporosis lasts 1.5-2 times as long as treatment in patients with normal BMD who receive a prosthetic joint [4, 7, 14]. Pharmacological interventions which promote osteosynthesis in the presence of osteoporosis may therefore be extremely useful in these patients.

Ossein-hydroxyapatite complex (Osteogenon) has recently come to the attention of traumatic surgeons [8, 15, 16]. The product consists of organic (ossein) and inorganic (hydroxyapatite) components and has been shown to slow down bone resorption and stimulate ossification [8, 20]. In a number of studies [6, 15], Osteogenon was used as monotherapy in patients with isolated and multiple fractures and reduced the duration of treatment by 1-3 weeks. It also stimulated callus formation. Pain relief [8], activation of anabolic processes [7], and increased bone mass [16] have been associated with the use of Osteogenon to treat patients with bone fractures and impaired reparative osteogenesis. However, some aspects of Osteogenon therapy remain unclear, viz. optimal dosing and duration of treatment, and its efficacy in cases of immobilization osteoporosis associated with prosthetic joints.

The aim of this study was to evaluate the results of using Osteogenon as monotherapy to manage the surgical treatment of prosthetic joints of the femur and tibia after fractures related to systemic osteoporosis.

MATERIALS AND METHODS

Interosseous osteosynthesis was performed in 42 patients with osteporosis concomitant to hypoplastic diaphyseal pseudoarthrosis of the femur and tibia. Patient ages ranged from 20 to 58 years. There were 28 men and 14 women. Sixteen patients had femoral pseudoarthrosis and 26 had pseudoarthrosis of the tibia. All patients had bone fractures resulting from a high-energy injury. Exclusion criteria were diagnosis of diseases leading to secondary osteoporosis (endocrine and

rheumatic pathology, diseases of the blood, kidneys, digestive organs, etc.) and use of drugs which might affect bone mineral density.

Patients were admitted to our clinic within 5 months-4 years after injury. Over half (n=22) were hospitalized more than 1 year after injury. Thirty-three patients had received surgical treatment prior to hospitalization in our clinic (intramedullar osteosynthesis, plate osteosynthesis, and osteosynthesis with an apparatus for external fixation); eleven patients underwent these procedures two or more times (a total of 49 operations were performed on 33 patients). Seven patients had prosthetic joints complicated by chronic osteomyelitis. All patients used crutches to walk. Over 75% of patients did not load the affected leg at all after injury, and others loaded it only partially but with the affected segment fixed using plaster or orthosis. All patients showed pathological mobility at the junction of bone fragments. Femoral pseudoarthrosis was associated with knee joint contracture in all patients. The contracture was severe in the majority of cases (22), and the amplitude of motion in the knee joint did not exceed 30 degrees. Tibial pseudoarthrosis was also accompanied by contractures; one third of the patients suffered limited function of the knee joint (amplitude of motion up to 60 degrees), and the remainder had the same problem with the talocrural joint.
Bone mineral density was measured in all patients in the proximal parts of both femoral bones and the lumbar spine using a DPXA X-ray densitometer (LUNAR, USA). Patients were examined before treatment, after consolidation, and 1-3 years after surgery. All patients had osteoporosis of the affected leg prior to treatment (t-test up to –4.7 SD). Twenty seven patients had osteopenia of the contralateral (loaded) extremity, 11 had osteoporosis, and only 4 had normal BMD. BMD in the spine was generally consistent with the patients' age.

All patients underwent open interosseous osteosynthesis using external pin and pin-nail fixators. Patients with pseudoarthrosis complicated by chronic osteomyelitis were operated on during the remission phase. Patients were given osteotropic antibiotics, analgesics, and non-steroidal anti-inflammatory drugs in the immediate postoperative period (supplemented by prophylaxis of thrombotic complications). They started to load the affected extremity during the first week after the intervention, and upon resolution of oedema. Wound healing was by primary intention. Exacerbation of chronic poliomyelitis in two patients (4 and 5 months after surgery) was managed conservatively. Three patients who developed deep vein thrombosis in the affected leg 1-1.5 months after surgery received a course of conservative therapy including confinement to bed.

Patients were allocated to three groups which were comparable in terms of age and gender, duration of the period between the injury and hospitalization in our clinic, and frequency of osteoporosis. Patients in group 1 (control, n = 15) were treated only surgically. Patients in group 2 (main group, n = 15) received both surgical treatment and anti-osteoporosis therapy with Osteogenon starting on day 21 after the operation (6 tablets daily for the first 3 months and 3 tablets/day for the following 3 months). Patients in group 3 (comparison group, n = 12) were given Ca-D3 Nycomed from day 21 after similar surgical treatment (2 tablets daily for the first 3 months and 1 tablet/day for the following 3 months). Patients in groups 2 and 3 consumed virtually identical daily amounts of calcium: six Osteogenon tablets ingested daily during the first 3 months contained a total of 1068 mg calcium as compared with 1000 mg in 2 tablets of Ca-D3 Nycomed; calcium consumption in groups 2 and 3 decreased to 534 mg and 500 mg respectively in the final 3 months .

The size of the study samples meant that data were non-normally distributed. Analyses were therefore performed using non-parametric tests. Medians and interquartile ranges were calculated and between-group differences were determined using the Kruskal-Wallis (H), Dunn (Q), and Mann-Whitney (T) tests.

RESULTS AND DISCUSSION

Consolidation of pseudoarthrosis without repeated surgical interventions was achieved in all patients included in the study. The supporting function of the affected leg was also restored. Eight patients experienced resorption of bone tissue around fixators in the femur (t-test –3.2 SD and below). This was resolved by stepwise substitution of the fixing elements.

Time to consolidation in the femur or tibia was significantly lower in the group treated with Osteogenon (see table). Osteogenon therapy reduced time to consolidation in the femur and tibia by 2 and 3 months, respectively, compared to the control group. Time to consolidation with Ca-D3 Nycomed was only significantly different from controls in patients with pseudoarthrosis of the tibia. Time to consolidation was not significantly different between groups 2 (Osteogenon) and 3 (Ca-D3 Nycomed). This was probably due to the small number of patients with pseudoarthrosis of the femur and a small mean difference in the consolidation velocity. Notably, three of the 9 patients with tibial prosthetic joints treated with Osteogenon had deep vein thrombosis and two experienced exacerbation of chronic osteomyelitis. These problems may have led to a longer time to consolidation in these patients.

Comparison of BMD dynamics in the three groups showed that BMD either decreased by 0.3-0.7 SD or remained unaltered by the time consolidation occurred in groups 1 and 3. An increase in BMD of 0.3-1.7 SD was observed only in patients treated with Osteogenon, though BMD remained unchanged in six patients in this group. The absence of effect in these patients may be attributed to the fact that 3 patients did not load the affected extremity because of concomitant severe foot pathology and 3 others, who were bed-ridden for 3-6 weeks due to deep vein thrombosis, were only able to partially load the affected leg. Patients with pseudoarthrosis in which consolidation was achieved and the supportive function completely restored in the affected leg were followed up for a period of 6 months to 3 years. X-ray densitometry was performed every 6 months and showed an increase in BMD from the moment of consolidation in practically all patients in the three study groups.

This study has confirmed that Osteogenon is an effective treatment when systemic osteoporosis associated with artificial joints of long bones in the lower extremities is present. Osteogenon appeared to facilitate the activation of bone-forming processes and significantly accelerated time to consolidation in comparison with patients who only received surgery. Time to consolidation was reduced by 2 – 3 months, with a corresponding reduction in the overall time required for rehabilitation. Ingestion of Osteogenon at a daily dose of 6 tablets in the first 3 months (to activate post-surgical reparation) and 3 tablets during the following 3 months improved treatment outcomes; it has also been shown to be a cost-effective option in comparison with other therapeutic alternatives [17]. The between-group comparison performed here showed that Osteogenon had produced an increase in BMD by the time consolidation occurred. A return to normal functioning in the affected extremity during the following 1-3 years was accompanied by a gradual increase in BMD from pretreatment values and those observed after consolidation. However, none of the patients had achieved normal BMD 1-3 years after surgery. The irreversibility of immobilization systemic osteoporosis after the loss of large bone mass is therefore still as much of a problem as it was 10 years ago [5].

To conclude, using Osteogenon after the surgical treatment of prosthetic joints of long bones complicated by osteoporosis significantly accelerates consolidation and improves clinical outcomes. The results of the present study demonstrate the possibility of new indications for the product in traumatology and particularly in managing the consequences deriving from serious skeletal injuries.

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