Use of ossein–hydroxyapatite complex in the prevention of bone loss: a review

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Key words: CALCIUM CARBONATE, OSSEIN-HYDROXYAPATITE COMPLEX, OSTEOPOROSIS, BONE REMODELING, BONE MASS, OSTEOPOROSIS PREVENTION

ABSTRACT

Background and objective The ossein–hydroxyapatite complex (OHC) is a microcrystalline form of calcium which provides a number of additional minerals (magnesium, phosphorus, potassium, zinc), and proteins (osteocalcin, type I collagen, type I insulin growth factor I and II, transforming growth factor beta) associated with bone metabolism. The objective of this review is to examine the role of OHC in preventing bone loss in different conditions.

Material and methods A review of clinical trials assessing the relationship between OHC and bone loss was made using the following data sources: Medline (from 1966 to December 2013), the Cochrane Controlled Clinical Trials Register, Embase (up to December 2013), contact with companies marketing the supplements studied, and reference lists.

Results Different randomized, clinical trials and meta-analysis suggest that OHC is more effective than calcium supplements in maintaining bone mass in postmenopausal women and in different conditions related to bone loss. In addition, OHC improves pain symptoms and accelerates fracture consolidation in patients with osteopenia or osteoporosis.

Conclusion The ossein–hydroxyapatite complex is significantly more effective in preventing bone loss than calcium carbonate.

INTRODUCTION

Calcium and vitamin D are crucial for bone health and essential in the prevention and treatment of osteoporosis. However, concerns have been raised about the risk–benefit ratio of the administration of total calcium and vitamin D in foods and supplements. The high intake of calcium supplements has been related in some, but not all studies to an increased risk of cardiovascular events. On the other hand, several studies have shown that low levels of 25-hydroxyl vitamin D, the main circulating metabolite of vitamin D, are associated with an increased risk of cardiovascular events and/or mortality by any cause. However, high levels of vitamin D have also been implicated in increased mortality in women but not in men. Conversely, an adequate intake of calcium and vitamin D is needed to maintain bone health and prevent the risk of fracture.

The ossein–hydroxyapatite complex (OHC) has been used to prevent and treat primary and secondary osteoporosis, to regulate the balance of calcium and phosphorus in conditions such as pregnancy and lactation, or as adjunct therapy to accelerate the healing of bone fractures, among others, with an excellent safety profile. OHC has shown greater bone regeneration than that observed with isolated hydroxyapatite or calcium salts. This complex also modulates bone turnover, particularly in cases of reduced osteoblast activity by stimulating osteoblast differentiation, proliferation and activity through ossein and decreasing bone resorption (Table 1). All these OHC properties have been corroborated by randomized trials and
meta-analyses suggesting that OHC is clinically more effective in maintaining bone mineral density (BMD) than calcium supplements\textsuperscript{1.5,6,8} (Tables 2–4).

In this review, an attempt is made to summarize the major published reports on the effectiveness of OHC in bone in different clinical situations as well as to evaluate the utility of OHC for bone health in women and emphasize the points that still need further clarification and additional research.

**METHODS**

**Information sources**

In January 2014, we searched Embase, Medline, and the Cochrane Library for all data up to and including December 2013 to identify potentially relevant publications. In order to maximize the number of publications meeting the selection criteria, the medical departments of companies marketing ossein–hydroxyapatite supplements were contacted to request publications that were not identified during the electronic search. Reference lists from studies initially selected and from existing reviews were also sought to identify any additional relevant studies not identified by the electronic searches.

**Search strategy**

To identify all the articles describing the use of the OHC in the treatment and prevention of bone loss, we designed the following search strategy including: osteoporosis or bone loss or bone fracture or BMD and hydroxyapatite or ossein–hydroxyapatite compound or Osteopor or Ossopan or Osteogenon and randomized, clinical trials. This strategy was adapted and applied to different Internet search engines, based on Medline and Cochrane Controlled Trials Register data. There were no language or date restrictions. Controlled and randomized studies evaluating the use of OHC in the treatment and prevention of osteoporosis were included.

**Study selection**

One reviewer (C.C.B.) independently evaluated the eligibility of the trials. Articles reviewed that did not establish the indication of administration, literature reviews or those whose purpose was not to demonstrate a therapeutic impact were not considered. In the final selection of articles, only those using diagnostic techniques currently recognized to diagnose systemic bone loss were included.

**Eligibility criteria**

Publications were included if the full text of the article was available. All types of clinical studies were included. Publications were included only if they contained information on the treatment administered together with the dose, duration and reason for treatment, participant characteristics, and study design and duration.

**Data extraction**

For each study included, one author extracted the data and a second author confirmed the data selected. Any potential discrepancies were resolved by consensus.
RESULTS

After crossing-clearing the reference lists, a total of 326 studies relating to OHC and bone were identified. Of these, 38 were considered selectable and were allocated to one of the following topics according to the objective of the study for further review: OHC and bone metabolism, prevention of postmenopausal osteoporosis, treatment of postmenopausal osteoporosis, treatment and prevention of secondary osteoporosis, treatment and healing fractures, and OHC use during pregnancy.

The usefulness of OHC in different pathologies with decreased bone mass, which may determine both primary or secondary osteoporosis, was evaluated in the different studies summarized in Tables 2–4. Early in the 1970s, the first results of the clinical use of OHC in osteoporotic patients were published, demonstrating better calcium absorption than most other calcium salts. Subsequent studies demonstrated that OHC was a safe and effective drug in the treatment of patients with metabolic bone diseases.

Table 2 Ossein–hydroxyapatite compounds (OHC) in the prevention of postmenopausal osteoporosis. Summary of the included clinical trials

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Follow-up</th>
<th>Sample</th>
<th>Treatment groups</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castelo-Branco</td>
<td>controlled open study, prospective randomized</td>
<td>12 months</td>
<td>118 surgically menopausal women</td>
<td>1. HT (n = 28) 2. OHC (n = 28) 3. HT + OHC (n = 32) 4. No treatment control group (n = 30)</td>
<td>change in spine BMD</td>
<td>+2.2% HT (p &lt; 0.01) vs. +0.3% OHC vs. +4.7% HT + OHC (p &lt; 0.01) vs. −1.1% control (p &lt; 0.05) (intergroups, p &lt; 0.01)</td>
</tr>
<tr>
<td>Castelo-Branco</td>
<td>controlled open study, prospective randomized</td>
<td>2 years</td>
<td>60 postmenopausal women</td>
<td>1. OHC (n = 19) 2. Calcium carbonate (n = 21) 3. No treatment (n = 20)</td>
<td>change in spine BMD</td>
<td>1st year: −0.2% OHC vs. −1.0% CC vs. −3.5% control (p &lt; 0.05) 2nd year: −0.4% OHC vs. −3.7% CC vs. −5.6% control (p &lt; 0.01)</td>
</tr>
<tr>
<td>Castelo-Branco</td>
<td>meta-analysis of RCTs</td>
<td>1–3 years</td>
<td>614 subjects in 6 RCTs</td>
<td>1. OHC 2. Calcium carbonate</td>
<td>change in spine BMD</td>
<td>+1.34% OHC vs. no changes in CC (p &lt; 0.0001) Cortexal BMD: −2.4% OHC vs. −6.94% control†</td>
</tr>
<tr>
<td>Stepan</td>
<td>controlled open study, prospective randomized</td>
<td>3 years</td>
<td>48 women with bilateral oophorectomy</td>
<td>1. OHC (n = 28) 2. Control (n = 20)</td>
<td>change in bone markers and bone density</td>
<td>Cortical BMD: −2.4% OHC vs. −6.94% control† Hydroxyproline: −30.3% OHC vs. −8.86% control† TRAP: −18.9% OHC vs. +2.1% control† Alkaline phosphatase: −30.1% OHC vs. −10.7% control†</td>
</tr>
<tr>
<td>Lorenc</td>
<td>controlled open study, prospective randomized</td>
<td>12 months</td>
<td>125 postmenopausal women with osteopenia or osteoporosis</td>
<td>1. OHC (n = 84) 2. Calcium carbonate (n = 41)</td>
<td>change in BMD</td>
<td>+3.28% OHC vs. −1.9% CC†</td>
</tr>
<tr>
<td>Fernández-Pareja</td>
<td>retrospective observational study</td>
<td>4 years</td>
<td>237 postmenopausal women</td>
<td>1. OHC (n = 112) 2. Control (n = 125)</td>
<td>change in spine BMD</td>
<td>+3.2% OHC vs. −7.3% control†</td>
</tr>
</tbody>
</table>

CC, calcium carbonate; HT, hormone therapy at menopause; BMD, bone mineral density; RCT, randomized, controlled trial; TRAP, tartrate resistant acid phosphatase
* Changes vs. baseline; †, p < 0.01; ‡, p < 0.0001

Results

After crossing-clearing the reference lists, a total of 326 studies relating to OHC and bone were identified. Of these, 38 were considered selectable and were allocated to one of the following topics according to the objective of the study for further review: OHC and bone metabolism, prevention of postmenopausal osteoporosis, treatment of postmenopausal osteoporosis, treatment and prevention of secondary osteoporosis, treatment and healing fractures, and OHC use during pregnancy.

The usefulness of OHC in different pathologies with decreased bone mass, which may determine both primary or secondary osteoporosis, was evaluated in the different studies summarized in Tables 2–4. Early in the 1970s, the first results of the clinical use of OHC in osteoporotic patients were published, demonstrating better calcium absorption than most other calcium salts. Subsequent studies demonstrated that OHC was a safe and effective drug in the treatment of patients with metabolic bone diseases.
### Table 3
Ossein–hydroxyapatite compounds (OHC) in the treatment of postmenopausal osteoporosis and healing fractures

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Follow-up</th>
<th>Sample</th>
<th>Treatment groups</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
</table>
| Ciria**4**      | open, parallel groups, controlled, prospective randomized | 2 years   | 115 subjects with senile osteoporosis | 1. OHC ($n=55$)  
2. CC ($n=65$) | BMD femoral neck, bone turnover markers: osteocalcin, TRAP | BMD: 2.5% OHC vs. 1.2% CC; osteocalcin: 1.86% OHC vs. 0.31% CC; TRAP: 2.3% OHC vs. -1.1 CC |
| Pelayo**4**     | open, parallel groups, controlled, prospective randomized | 3 years   | 90 women with osteoporosis     | 1. RLX + OHC  
2. RLX + CC | BMD by ultrasound measurement of ADSoS | ADSoS: -18.72 m/s from baseline to year 3 in RLX + OHC group and -63.64 m/s in RLX + CC group

Reduction of back pain, increased serum calcium, increased X-ray metacarpal cortical thickness. Increased serum calcium and not significant changes in cortical thickness. No differences between groups

Loss of trabecular bone: 0.8 ± 0.5% OHC vs. 1.8 ± 0.7% CC group. OHC more effective than CC in slowing peripheral trabecular bone loss in patients with manifest osteoporosis

Non-fractured women: FS BMD (%): 0.6 ± 0.5 OHC + CC vs. -1.2 ± 0.7 placebo*. No difference between OHC and CC. FN BMD (%): 0.7 ± 0.8 OHC + CC vs. -1.7 ± 1.6 placebo (not significant)

Fractured patients: LS BMD (%): 5.0 ± 1.6 OHC vs. 1.2 ± 1.7 CC; FN BMD (%): 5 ± 2.6 OHC vs. -0.9 ± 1.8 CC

| Durance**23**   | open, parallel groups, comparative, randomized, prospective | 9 months  | 14 subjects with severe osteoporosis | 1. OHC tablets ($n=7$)  
2. OHC powder ($n=7$) | Bone turnover markers: calcium, phosphate, proteins, total hydroxyproline; Rx metacarpal thickness, cortical bone biopsies | Increased X-ray metacarpal cortical thickness. Increased serum calcium and not significant changes in cortical thickness. No differences between groups

| Ruegsegger**13** | randomized, placebo-controlled double-masked study | 20 months | 40 women with postmenopausal osteoporosis | 1. OHC ($n=20$)  
2. CC ($n=20$) | BMD of radius and tibia BMD in 4-month intervals using pQCT | Loss of trabecular bone: 0.8 ± 0.5% OHC vs. 1.8 ± 0.7% CC group. OHC more effective than CC in slowing peripheral trabecular bone loss in patients with manifest osteoporosis

Non-fractured women: FS BMD (%): 0.6 ± 0.5 OHC + CC vs. -1.2 ± 0.7 placebo*. No difference between OHC and CC. FN BMD (%): 0.7 ± 0.8 OHC + CC vs. -1.7 ± 1.6 placebo (not significant)

| Chevalley**5**  | randomized, placebo-controlled double-masked study | 18 months | 93 healthy subjects; 63 subjects with recent hip fracture | 1. OHC ($n=31$)  
2. CC ($n=62$)  
3. Placebo ($n=31$)  
4. OHC ($n=31$)  
5. CC ($n=32$) | % changes in FS, FN and LS BMD | Non-fractured women: FS BMD (%): 0.6 ± 0.5 OHC + CC vs. -1.2 ± 0.7 placebo*. No difference between OHC and CC. FN BMD (%): 0.7 ± 0.8 OHC + CC vs. -1.7 ± 1.6 placebo (not significant)

Fractured patients: LS BMD (%): 5.0 ± 1.6 OHC vs. 1.2 ± 1.7 CC; FN BMD (%): 5 ± 2.6 OHC vs. -0.9 ± 1.8 CC

| Gyr`nazarova**44** | open, parallel groups, comparative, prospective | healing fractures, 6 months | 42 osteoporotic patients with femoral or tibia fracture | 1. OHC ($n=15$)  
2. CC + VIt D3 ($n=12$)  
3. Control ($n=15$) | Time to heal fracture | Femur: 285 control vs. 220 OHC vs. 247.5 CC Tibia: 273 control vs. 180 OHC vs. 180 CC

Fracture consolidation: non-operative group: 11.3 weeks OHC vs. 14.03 weeks placebo; surgical group: 10 weeks OHC vs. 14 weeks placebo

| Gupta**50**     | open, parallel groups, comparative, prospective | healing fractures, 14 weeks | 60 patients with long-bone fracture | A. Non-operative group  
1. OHC ($n=15$)  
2. Placebo ($n=15$)  
B. Surgical group  
1. OHC ($n=15$)  
2. Placebo ($n=15$) | Time to heal fracture | Fracture consolidation: non-operative group: 11.3 weeks OHC vs. 14.03 weeks placebo; surgical group: 10 weeks OHC vs. 14 weeks placebo

| Mills**25**     | randomized, placebo-controlled double-masked study | healing fractures, 10 months | 85 patients with tibial shaft fracture (26 ± 55 years, 59 < 55 years) | A. ≥ 55 years  
1. OHC ($n=13$)  
2. Placebo ($n=13$)  
B. < 55 years  
1. OHC ($n=29$)  
2. Placebo ($n=30$) | Time to heal fracture | Fracture consolidation: ≥ 55 years: 11 weeks OHC vs. 14.2 weeks placebo; < 55 years: 11.5 weeks OHC vs. 12.5 weeks placebo

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CC, calcium carbonate; BMD, bone mineral density; TRAP, tartrate resistant acid phosphatase; ADSoS, amplitude-dependent speed of sound; pQCT, peripheral quantitative computed tomography; FS, femoral shaft; FN, femoral neck; LS, lumbar spine; RLX, raloxifene

*<sup>p</sup> < 0.05; †<sup>p</sup> < 0.01; ‡<sup>p</sup> = 0.006
### Table 4  Ossein–hydroxyapatite compounds (OHC) in the treatment and prevention of secondary osteoporosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Follow-up</th>
<th>Sample</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nilsen²⁶</td>
<td>controlled clinical trials</td>
<td>72 patients with rheumatoid arthritis</td>
<td>1st Group: OHC 2nd Group: Control</td>
<td>OHC group: decreased loss in size; increased BMD radio; decreased bone pain. Control group: decreased BMD radio; increased bone pain</td>
<td></td>
<td></td>
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<tr>
<td>Pines³⁷</td>
<td>open RCT</td>
<td>1 year</td>
<td>40 subjects with respiratory disease treated with prednisone (dose ≥ 5 mg/day)</td>
<td>1. OHC (n = 32) 2. Control (n = 8)</td>
<td>mean cortical thickness; mean metacarpal index; back pain</td>
<td>mean cortical thickness and mean metacarpal index showed insignificant decreases (&lt;0.05 mm) in OHC group but much more marked decreases (0.03 mm) in control group. OHC group showed significant (p &lt; 0.001) reduction in pain during trial, almost to point of its disappearance. Control group showed a back pain severity increase during trial in 3 patients and was unchanged in 4th</td>
</tr>
<tr>
<td>Stellon³⁸</td>
<td>open RCT</td>
<td>2 years</td>
<td>36 corticosteroid-treated patients with chronic hepatitis</td>
<td>1. OHC (n = 18) 2. Control (n = 18)</td>
<td>Changes in: BMD radius; mean metacarpal index; TBV</td>
<td>BMD radius: 0% OHC vs. 4.06% Control; mean metacarpal index: −22.2% OHC vs. −38.8% control; TBV: +9.13% OHC vs. −4.06% Control</td>
</tr>
<tr>
<td>Epstein³⁹</td>
<td>open RCT</td>
<td>14 months</td>
<td>64 postmenopausal women with primary biliary cirrhosis</td>
<td>1. control (C, no supplements) 2. OHC 3. Calcium gluconate (CG)</td>
<td>All patients received parenteral vitamin D2 (100 000 IU monthly)</td>
<td>changes in metacarpal cortical thickness; T, M, CT, CA, PCA</td>
</tr>
<tr>
<td>Varga⁴⁸</td>
<td>Open, parallel groups, comparative, prospective Healing fractures, 6 months</td>
<td>28 osteoporotic premenopausal women (13 rheumatoid arthritis, 15 chronic renal failure)</td>
<td>1. OHC (n = 15) (7 rheumatoid arthritis, 8 chronic renal failure) 2. Control (n = 13) (6 rheumatoid arthritis, 7 chronic renal failure)</td>
<td>Pain relief (VAS); time to heal fracture</td>
<td>Fracture consolidation: 26 days OHC vs. 32 days control Pain relief: VAS basal 80 mm to VAS 20 mm; 21 days OHC vs. 35 days control</td>
<td></td>
</tr>
</tbody>
</table>

CC, calcium carbonate; BMD, bone mineral density; RCT, randomized, controlled trial; TBV, trabecular bone volume; T, total metacarpal width; M, medullary cavity width; CT, cortical thickness; CA, cortical area; PCA, % cortical area; VAS, visual analog scale * p < 0.005; † p < 0.01; ‡ p < 0.025
OHC in the prevention of postmenopausal osteoporosis

Castelo-Branco and colleagues\(^{15}\) evaluated the effects of OHC on bone loss in healthy women receiving hormone therapy (HT) for climacteric complaints. The group receiving HT plus adjuvant OHC showed a greater increase in bone mineral content than those who only received HT, and the effect of OHC was greater than that observed in women on calcium carbonate (Table 2). In a subsequent study, the same authors assessed the effect of OHC in postmenopausal women who did not wish to take HT, demonstrating that continuous administration of OHC was more effective in preventing bone loss in postmenopausal women than calcium carbonate\(^{16,46}\) (Table 2).

The use of OHC in the prevention of postmenopausal bone loss has also been studied in women with surgically induced menopause. In a series of 48 patients with prior bilateral oophorectomy (1–5 years), Stěpáň and colleagues\(^{17}\) found that the administration of OHC led to a reduction in the loss of BMD and biochemical markers of bone turnover (Table 2). Fernández-Pareja and colleagues, in a retrospective study, analyzed 237 postmenopausal women and found similar results\(^{47}\).

Another comparative study involving osteopenic women was performed by Lorenc and colleagues\(^{18}\) who compared the efficacy of OHC versus calcium carbonate in natural and surgically induced menopausal women older than 55 years with more than 5 years since the beginning of menopause. These authors observed a significant reduction of bone resorption in the OHC group.

OHC in the treatment of postmenopausal osteoporosis

Some evidence suggests that the organic component of OHC plays an important role in bone response in osteoporotic patients. The formulations that include ossein–hydroxyapatite show a significantly greater effect in bone than those with only a pure mineral supplement. In patients with severe osteoporosis, an increase has been observed in metacarpal and phalangeal bone density as well as a significantly higher decrease of pain than that observed with calcium\(^{14,48}\) (Table 3).

This superior efficacy has also been observed in patients who already have osteoporotic vertebral\(^{19,49}\) and hip\(^{49}\) fractures. In a comparative study, OHC was more effective in preventing the loss of trabecular bone in patients with osteoporosis and at least one vertebral fracture due to fragility than calcium carbonate\(^{19}\). Additionally, the lack of adverse events in this study suggests the possibility of safe long-term treatment (Table 3).

It is noteworthy that anabolic actions on bone have recently been attributed to OHC. Ciria-Recasens and colleagues\(^{50}\) conducted a comparative study with calcium carbonate on bone metabolism in women with senile osteoporosis and detected a higher increase in BMD and higher levels of osteocalcin in the group receiving OHC (Table 3). Similarly, Stamp and colleagues\(^{21}\) suggested that the intake of sodium fluoride with OHC stimulates osteoblasts and induces new bone formation, increasing trabecular and osteoid bone volume (Table 3). Furthermore, the association of sodium fluoride with hydroxyapatite provides better absorption of calcium\(^{50}\).

OHC in the treatment and prevention of secondary osteoporosis

An emerging concern is the prevention of bone loss in patients with chronic diseases treated with corticosteroids. Nilsen and colleagues\(^{39}\) showed that, after 1 year of treatment, patients with rheumatoid arthritis receiving OHC showed significantly less loss of height and bone density at the radius and that bone pain also significantly improved (Table 4). Similarly, Varga and colleagues\(^{51}\) found, in patients with rheumatoid arthritis and chronic renal failure treated with OHC, an analgesic effect and an improvement of well-being.

OHC has also been studied in other situations requiring chronic treatment with corticosteroids such as chronic obstructive pulmonary disease or autoimmune processes. Pines and colleagues\(^{52}\) showed an increase in bone mineralization, a decrease in the progression of osteoporosis and a great reduction in skeletal pain in asthmatic patients with corticosteroid-induced osteoporosis receiving OHC (Table 4). This study demonstrated the excellent tolerability and safety of the drug.

OHC has been also administered in patients with autoimmune chronic active hepatitis undergoing corticosteroid therapy for long periods of time who developed corticosteroid-induced osteoporosis. In a group of 36 patients with corticosteroid-induced osteoporosis, Stellon and colleagues\(^{53}\) showed that bone pain, plasma calcium and creatinine values decreased in the treated group and, contrary to what was observed in the control group, new vertebral fractures were not detected in the group receiving OHC (Table 4).

The role that cortical bone may play in bone quality and fracture risk is increasingly considered. Pathological cortical bone resorption is characteristic of malabsorption syndromes, chronic renal tubular acidosis, physical inactivity and primary biliary cirrhosis. In this way, Epstein and colleagues\(^{43}\) demonstrated the positive effect of OHC in the prevention of cortical bone thinning in postmenopausal women with primary biliary cirrhosis. These authors also showed that vitamin D alone did not prevent the loss of cortical bone, and that the absorption of calcium was greater when OHC was administered instead of calcium carbonate. An additional advantage of OHC in situations with salt retention such as cirrhosis is the low sodium content of this complex compared to other calcium salts\(^{43}\). The effects of OHC on cortical bone are not related to the stimulation of bone formation but rather to a reduction in bone resorption. However, the exact mechanism of action is unknown\(^{52,43}\).

OHC has also been studied in congenital defects of bone formation. Dent and Davies\(^{46}\) evaluated the effect of the combination of OHC microcrystals and dihydrotachysterol in patients with imperfect osteogenesis. The positive calcium
balance observed was probably related to a better mineral absorption because of the presence of amino acids such as proline in the composition of OHC (Table 4).

OHC in the treatment and healing of fractures

Bone fractures are one of the most common causes of prolonged disability and loss of work for young people and of mortality in older patients. Fracture healing inevitably takes time, and therefore the speed of healing and functional recovery are of great clinical and economic importance. It is well known that the bone matrix contains substances that may regulate bone formation in vitro by controlling precursors of mitosis and stimulating osteoblastic activity, and experimental studies have shown that treatment with OHC results in accelerated fracture healing. However, this beneficial effect of OHC on the healing process of bone is lost when the organic components of the compound are destroyed or when OHC is replaced by pure calcium carbonate. These data strongly suggest that the organic components of OHC have osteogenic effects.

New indications for the use of OHC in trauma lesions have recently been suggested, particularly in the treatment of severe skeletal lesions. OHC has been demonstrated to reduce the rate of bone resorption and to stimulate ossification when OHC is replaced by pure calcium carbonate. These data strongly suggest that the organic components of OHC have osteogenic effects.

Use of OHC during pregnancy

OHC has also been used in pregnant women, proving to be effective in different complaints and safe. In one study, OHC was given to 170 women with abdominal, pelvic, back and lumbosacral pain, paresthesias, alopecia, onychorrhexis and odontopathies throughout the pregnancy and postpartum period. Most of the women receiving OHC showed a reduction or elimination of bone pain, with no further alopecia and onychorrhexis.

OHC was used in another study for a period of 1 month in 20 pregnant women at 28–40 weeks’ gestation with pain syndrome in the long bones, lumbosacral region and disturbed dental status, with a considerable clinical improvement of pain syndrome and dental status at the end of the treatment.

Finally, an improvement in muscular complaints has been observed in up to 77% of patients with functional muscle disorders related to pregnancy. The positive therapeutic effect, easy way of administration, its good tolerance and lack of side-effects make it convenient for treatment of disturbances in calcium-phosphorus balance in pregnant women.

CONCLUSIONS

OHC has been demonstrated to be useful in different clinical situations in which bone metabolism is compromised such as in primary and secondary osteoporosis and osteogenesis imperfecta, mineral deficiency and increased mineral requirements (pregnancy, lactation, elderly patients), and fractures in the elderly. Finally, it is of note that OHC has been shown to be more effective than calcium carbonate in maintaining bone mineral density in postmenopausal women and that, when used with other antiresorptive agents, treatment outcomes improve.

Conflict of interest The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

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