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Comparison of the effects of calcium carbonate and ossein–hydroxyapatite complex on back and knee pain and quality of life in osteopenic perimenopausal women

Camil Castelo-Branco*, Jhery Dávila, Lina Alvarez, Juan Balasch

Institut Clínic of Gynecology, Obstetrics and Neonatology, Hospital Clínic-Institut dÍnvestigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Faculty of Medicine, University of Barcelona, Barcelona, Spain

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ABSTRACT

Background: Back and knee pain (BP; KP), which often accompanies osteoporosis, is a prevalent health problem affecting quality of life (QoL) in middle-aged women.
Aim: To compare the effects of calcium carbonate (CC) and ossein–hydroxyapatite complex (OHC) on BP and KP and QoL in perimenopausal osteopenic women.
Subjects: 74 perimenopausal women were randomized to receive 1200 mg/day of CC ($n = 38$) or 1660 mg/day of OHC ($n = 36$) for 6 months.
Methods: This was a randomized, open-label, parallel-group, controlled, prospective study. Back and knee basal pain was recorded using a visual analogue scale (VAS) at each control and exercise-induced pain was recorded using a visual rating system (VRS). Changes in QoL were evaluated using the SF-36 questionnaire.
Results: In patients treated with OHC, mean VAS and VRS pain scores decreased significantly after 5 and 6 months of treatment, indicating a significant analgesic effect. In the CC group, however, changes were minor and non-significant. Two-way analysis of variance using treatment group and time as independent variables revealed a significantly greater effect of OHC over CC on VAS and VRS scores. SF-36 showed significant improvement for OHC on the physical component summary score and no changes for CC. Responses to items assessing emotional and social aspects of QoL showed only a significant improvement in vitality for OHC and no significant changes for CC in any of the four dominions constituting the SF-36 mental component.
Conclusion: OHC has a significant analgesic effect and improves the physical component of QoL to a greater extent than CC.

1. Introduction

Women with osteopenia or osteoporosis can experience spontaneous and activity-induced pain that may be due to fractures, postural deformity, and stretching of ligaments [1]. Long-lasting pain, loss of height, and functional limitations can seriously affect their health-related quality of life [2] and they may also experience problems with activities of daily living and be less able to participate in social activities. Moreover, pain and reduced mobility can affect their mental health, eventually leading to depression and social isolation [3]. Consequently, quality of life (QoL) assessment has become an increasingly important outcome measure in these patients, with studies showing how pain, functional loss, social isolation, and emotional problems negatively affect patients' general well-being and QoL [4].

Randomized trials and meta-analysis have demonstrated that ossein–hydroxyapatite complex (OHC) plays a role in bone response in osteoporotic and osteopenic patients and that its effects are superior to those observed with calcium salts [5]. Formulations that include ossein–hydroxyapatite have also shown a significantly greater effect on bone than those with only a pure mineral supplement [6]. Moreover, several studies have suggested that OHC may have an analgesic effect [7,8] and that the use of OHC in patients with bone fractures and complications in regenerative osteogenesis is associated with pain relief and the activation of anabolic processes that result in an increase in bone mass [8,9].

* Corresponding author at: Institut Clínic of Gynecology and Obstetrics, Hospital Clínic, C/Villarroel 170, 08036 Barcelona, Spain. Tel.: +34 93 2275436; fax: +34 93 2279325.
E-mail address: castelobranco@ub.edu (C. Castelo-Branco).

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In the present study, we hypothesized that this analgesic effect of OHC would also be superior to that of calcium carbonate, one of the most frequently used calcium salts in the treatment of osteoporosis [10]. In addition, treatment effects on QoL were also analysed, which to the best of our knowledge has not been studied previously.

2. Materials and methods

To test this hypothesis, OHC and calcium carbonate products were administered to patients with low bone mass and back and knee pain, and their effects were compared based on pain assessment using VAS and VRS. A commonly used, generic measure of health status, the SF-36 [11,12], was used to evaluate the influence of pain on QoL. In studies in patients with low back problems, the SF-36 may be a sufficient measure of health status and patient function, without the need for additional condition-specific instruments [13].

2.1. Sample

Osteopenic perimenopausal women consulting at the Gynaecological Endocrinology Unit at the Hospital Clínic (Barcelona) were included in this randomized, open-label, parallel-group, controlled, prospective study if they complained of back pain, were under 55 years of age, and absorptiometry showed T scores between −1.0 and −2.0 SD T (DEXA: Lunar DPX-L system, Lunar Radiation Corporation, Madison, WI). Women with endocrine, metabolic, and/or rheumatic disease, which could also cause pain, and those who were receiving estrogens, progestogens or bone anti-resorptive drugs were excluded from the study. An intra-individual coefficient of variation of L1–L4 BMD over 10% [14,15] (indicative of spinal osteoarthritis) and spinal or knee osteoarthritis of grade 2 or higher on the Kellgren–Lawrence (KL) scale [16,17] were considered abnormalities associated with osteoarthritis. Eligible patients were allocated into one of two groups for 6 months of treatment consisting of either daily administration of 1660 mg of OHC (Osteopor®, Pierre Fabre, Castres, France) (OHC group) or daily oral administration of 1200 mg of calcium (CC group) in the form of calcium carbonate (Natecal®, Italfarmaco, Madrid, Spain). The OHC dose contained 150 mg no-collagen proteins, 432 mg collagen, 356 mg calcium, and 164 mg phosphorus. Each participant was assigned a number following the chronological enrolment sequence and treatments were allocated using a computer generated randomization table. All subjects, having given their informed consent, participated voluntarily in the study, which was approved by the Ethics Committee.

No other treatments for osteoporosis or osteoarthritis, such as oestrogen derivatives, selective oestrogen receptor modifiers, vitamin D derivatives, vitamin K derivatives, or non-steroidal anti-inflammatory drugs were used from 3 months prior to study enrolment until end of follow-up.

Sample size and study design were decided arbitrarily but in keeping with previous studies on the subject [7,18,19].

2.2. Pain measurement

Basal pain: patients were asked to rate their daytime pain during the previous week on 10 cm VAS where 0 represented no basal pain at all and 10 represented the most severe pain the patient has ever had. Induced pain: pain was induced by lying down supine on a bed from a standing position and standing up again (spine loading – SL), standing up from a sitting position (knee loading – KL) and walking horizontally and up and down stairs (spine and knee loading – SKL).

Induced pain was presented as a percentage in comparison with the most unbearable pain (100%) on a VRS scale. For analysis, increase in VRS scores by exercise loading was determined in comparison with a preloading level set at 0 to estimate the severity of pain induced by exercise. The VRS value at each time point indicates pain expressed as an increase from the pre-loading baseline towards unbearable pain set at 100%.

2.3. QoL

The Medical Outcome Study Short Form-36 (SF-36) is a generic QoL questionnaire that has been adapted for the Spanish speaking general population and which has been shown to have good reproducibility and validity [20,21]. The SF-36 questionnaire consists of 36 self-administered questions which measure health status in eight domains, covering both physical and mental health. The physical component summary (PCS) includes four domains: physical functioning (PF, 10 questions), role physical functioning (RP, four questions), bodily pain (BP, two questions), and general health (GH, five questions). The mental component summary (MCS) includes four domains: vitality (VT, four questions), role emotional functioning (RE, three questions), social functioning (SF, two questions), and mental health (MH, five questions). Domain scores range from 0 to 100, with higher scores indicating better health status. SF-36 summary health scores were calculated using standard and country-specific algorithms for Spain, according to the results from the IQOLA Project [22,23]. Mean scores were calculated for each domain and then normalized by subtracting the average of the Spanish population and dividing by the standard deviation.

2.4. Statistical analysis

The Student t-test was used to compare characteristics between treatment groups, and means and standard deviations were used to summarize those characteristics. A two-way repeated measures ANOVA was performed to compare the evolution between treatment groups during the follow-up period (0–6 months); treatment was included as a between-subjects factor and time (months) as a within-subject factor. To take baseline pain (or other additional baseline characteristics) into account, a two-way ANCOVA was performed in which baseline characteristics were introduced as covariates. The statistical software R (version 3.1.1) [24] was used for all analyses. More specifically, the ANOVA and ANCOVA models were performed using the ez R-package [25]. A value of $p < 0.05$ was considered statistically significant.

3. Results

A total of 74 subjects were enrolled ($n = 38$ in the CC group and $n = 36$ in the OHC group). Two patients in the OHC group and four in the CC group dropped out during the early stages of treatment due to dyspepsia or non-specific abdominal pain. One additional patient per group withdrew from the study later in the study period because of the inconvenience of monthly visits. A total of 66 patients (33 in each group) therefore completed the 6 months of treatment.

Clinical characteristics including age and the results of metabolic, radiologic, and bone absorptiometry tests are summarized in Table 1. No significant differences were found between the two groups in terms of age, or anthropometric, and clinical characteristics, or on parameters for bone and joint metabolism, based on measured values and frequency of abnormalities. There was no significant difference in the number of severe osteopenic ($T < -1.5$) patients between the two groups. Metabolic and radiographic bone parameters were obtained only once, at the start of the study.

As shown in Table 1, bone metabolic parameters were in the normal or close to normal range in the majority of subjects in both