

CLINICAL SUMMARY

Evaluation of Nutritional Support with Concentrated Microcrystalline Hydroxyapatite Concentrate (MCHC) and Vitamin D in Patients with Osteopenia and Osteoporosis: Summary of Clinical Experience

Introduction

Osteoporosis, a chronic progressive condition characterized by low bone mass and microarchitectural deterioration of bone tissue (resorption), is the most common metabolic bone condition in the U.S. Ten million Americans (80% women) are estimated to already have osteoporosis and almost 34 million more are estimated to have low bone mass or osteopenia, placing them at increased risk for osteoporosis.¹

Each year an estimated 7.2 million people in the U.S. are impacted by poor bone health—including emergency room visits, fractures, hospitalizations, and nursing home admissions. Office visits for osteoporosis have increased five-fold in the past 10 years, and according to a 2004 report from the Surgeon General, one in two Americans aged 50 years or older will be at risk for fractures from osteoporosis or low bone mass by the year 2020.^{1,2} A 2003 survey commissioned by the National Osteoporosis Foundation, however, revealed that 76% of all women aged 45 and older have never discussed osteoporosis with their healthcare practitioners.³ Furthermore, while 3.5 million American men are at risk of osteoporosis, only 4.5% are likely to be evaluated or receive treatment to address future bone loss *after a hip fracture*.⁴

Optimal Method of Diagnosing Osteopenia & Osteoporosis

Osteoporosis and osteopenia are identified by BMD tests, such as dual x-ray absorptiometry (DEXA), because a low BMD is known to contribute to increased fracture risk.^{1,5} To account for variations in different BMD testing equipment, the World Health Organization has set guidelines for diagnosing osteoporosis and osteopenia based on a T-score comparison to a population of young, healthy people of the same sex (see Table 1 for these guidelines).² While BMD tests represent the gold standard in identifying these conditions, they are less effective in rapidly measuring the success of anti-resorptive treatment and acute changes in bone. BMD represents a net balance between bone resorption and bone formation, which typically changes in response to therapy less than 2% per year or a maximum of < 1% in 3 to 6 months (changes of < 1% are difficult to measure due to precision limitations of BMD technologies).⁵

In complement to BMD measurement, biochemical bone resorption markers (though less precise than BMD scans) are advocated due to clinical trials that have established their utility in identifying patients with rapid bone loss, estimating rate of bone loss, aiding in therapeutic decision-making, and monitoring treatment efficacy. Elevated bone resorption markers have also been shown to be associated with increased risk of fracture in elderly women. These markers—breakdown products of type-I collagen and proteins secreted by osteoblasts and osteoclasts in blood and urine—offer a more effective tool for monitoring therapy, as most anti-resorptive agents act by rapidly reducing these markers.⁵ Research demonstrates that patients with rapid bone loss will show the greatest stabilizations and increases in bone density in response to anti-resorptive treatments.^{5,6} This is particularly of value in patients where osteoporosis is severe and the practitioner cannot wait for a year or longer to determine whether therapy has had a positive effect on BMD.⁵⁻⁷

Using select bone markers, the effectiveness of therapy may be detected as early as two to four weeks after initiation of therapy.^{5,7} Resorption markers also allow noninvasive assessment of bone turnover when compared to BMD, and are helpful in monitoring compliance in addition to therapy response.⁶

Selection of Biochemical Markers

The pyridinium cross-links—pyridinoline (PYD) and deoxypyridinoline (DPD)—have been suggested as the most sensitive and specific biochemical markers.^{6,8,9} Elevated pyridinium cross-link levels in the urine have been associated with excessive bone resorption and related observations, and have been shown to increase shortly after the onset of menopause.^{6,8}

Approximately 90% of the organic matrix of bone is Type I collagen, cross-linked to increase strength and rigidity.⁶ PYD and DPD are tripeptides that join adjacent collagen fibrils to strengthen and stabilize collagen fibers.⁹ They are found in significant amounts only in bone and cartilage collagen (not skin collagen or procollagen) and are released during collagen breakdown. Neither of these cross-links is influenced by dietary collagen or metabolized before excretion, and both remain stable in stored urine.^{6,8,9}

While PYD—present in bone and cartilage—is more abundant, it is actually DPD that is more specific because it is found only in bone and dentin. Therefore, measurements, as ratios to creatinine (cr) in a timed specimen, of total pyridinium cross-links (both PYD and DPD) and/or DPD levels alone are primarily used when pyridinium cross-links are selected to evaluate treatment.^{6,8,9}

Natural, Anti-Resorptive Approaches for Bone Density

Microcrystalline hydroxyapatite concentrate (MCHC) is an all-natural, bovine-derived whole bone supplement that provides a full spectrum of highly absorbable macro-minerals (calcium, phosphorus) and trace minerals (boron, zinc, copper, magnesium) found naturally in bone. It also provides other factors that comprise healthy bone, such as type I collagen, bone amino acids, protein, organic factors, and growth factors.¹⁰ MCHC appears to provide calcium in an extremely bioavailable form, as demonstrated in a number of research studies on calcium balance and absorption. Many of these studies have indicated the superiority of MCHC over traditional calcium supplements—such as calcium carbonate—and it has been recommended for both the treatment and prevention of osteoporosis (see Published Research). In addition, MCHC is well-tolerated with an excellent safety profile.¹⁰

MCHC Processing Preserves Bioactivity

True MCHC is cold-processed to help preserve the raw bone constituent profile and delicate organic factors that heat processing and solvents can destroy. The processing of MCHC from bone requires no solvents or sterilization agents like

ethylene oxide or gamma irradiation to extract actives or control microbial overgrowth. Conversely, ossein-hydroxyapatite concentrate (OHC, an ashed bone extract) uses both.⁶ Differences in processing between the two materials may account for the presence of higher levels of bone growth factors in the protein matrix of MCHC; this intact matrix has been postulated as the therapeutic difference when compared to an ashed bone extract preparation and calcium supplements providing an identical amount of elemental calcium.¹¹⁻¹³ While the role of growth factors has not yet been determined, growth factor analysis of finished MCHC serves as a definitive marker for biological activity.¹⁴

Vitamin D Supplementation—More Than Just Calcium Absorption

Vitamin D is necessary for the absorption of calcium to form and maintain healthy bones, and supplementation is recommended to facilitate absorption when treating osteoporosis.^{12,15} A new study suggests that vitamin D sufficiency may even be more important than high calcium intake in regards to bone disease prevention, and research also shows that osteoporosis patients with higher vitamin D serum levels have increased muscle strength and a lower number of falls.^{16,17} A deficiency has been linked not only to bone conditions but also to obesity and an increased risk to cardiovascular disease and common cancers.¹⁸⁻²¹ Up to 40% of Americans, 32% of doctors, 42% of African American women of childbearing age, and 80% of nursing home patients may be deficient in the most prominent form of vitamin D in the body (25-hydroxyvitamin D), which is often overlooked in testing. While the current recommendations for daily intake of vitamin D are between 400 and 800 IU (based on age), more health organizations and health experts are questioning whether the daily minimums should be raised to 1,000 to 1,200 IU—as many healthcare providers are currently prescribing, particularly to those without regular exposure to sunlight.^{16,22,23}

Published Research

Over the last 30 years, studies comparing whole bone extracts (containing between 22% to 28% protein) to ashed hydroxyapatite powder (without protein), calcium carbonate, calcium gluconate, and other forms of calcium showed that whole bone extract has a superior effect on bone mineralization.^{11,12,15}

Whole bone extracts have also been shown to produce positive outcomes in maintaining bone health in at-risk postmenopausal women, as well as in women with an estrogen contraindication, those choosing an alternative to hormone replacement therapy, and those with surgical menopause.^{11,15,23} In addition, MCHC therapy has shown a dramatic reduction in skeletal pain in patients developing osteoporosis due to long-term corticosteroid therapy and age-related osteoporosis, and has been cited as the contributing factor to favorable biochemical and bone changes.^{10,15}

A variety of proteins are present in the bone matrix, specifically type I collagen, glycosaminoglycans, and growth factors. Properly processed whole bone extract will contain a quantifiable spectrum of these protein constituents. As the protein content and protein composition in the whole bone extract are denatured through heat and solvent exposure, the inorganic mineral portion

may increase but the overall bone health benefits of the material clearly declines.^{11,13} Furthermore, the most recent studies emphasize the link between measurable levels of bone-derived growth factors, such as insulin-like growth factors I and II (IGF-I and II), transforming growth factor beta I and II (TGFβ-I and II), and osteocalcin in the finished extract and positive effects on bone density.^{11,13-15,24}

Case Studies Overseen by the Functional Medicine Research CenterSM (FMRC)

Investigational case management studies conducted in a clinical setting at The Center for Women's Health in Darien, Connecticut by Joel Evans, MD confirmed the findings of third-party clinical research demonstrating the ability of MCHC to positively influence bone resorption markers. Six women ranging in ages from 47 to 62 and presenting with osteopenia or osteoporosis were given a combination of concentrated, purity-certified and bioactivity-verified MCHC and vitamin D in capsule form for varying periods of 12 to 33 weeks.

Methodology and Results

The patients selected for the investigational case studies were identified as having osteopenia or osteoporosis based on their T-scores from DEXA scans for BMD (see Table 1). To measure the effects of therapy with an MCHC and vitamin D formula, initial measurements of both total pyridinium cross-links and DPD levels were taken for later comparison. While initial doses were varied for some individuals, the average dose was four capsules daily, providing 4,048 mg of MCHC—which supplied 912 mg of elemental calcium and 476 mg of phosphorus—and 800 IU of vitamin D. Follow-up measurements of bone resorption markers were taken at the end of initial treatment.

All six patients moved into the normal reference range for total pyridinium cross-links, and all but one moved into the normal reference range for DPD levels, with the sixth being slightly above normal. These results (presented in Table 1) suggest a reduction in bone resorption, as well as a corresponding reduction in risk for osteoporotic fractures.

Conclusion

The results of these six clinical observations suggest that a targeted nutritional support program incorporating a concentrated MCHC and vitamin D supplement daily may help to improve bone resorption markers in patients with osteopenia and osteoporosis, thereby helping to protect bone density and reducing the risk to fracture.

Table 1. Nutritional supplementation featuring a combination of concentrated MCHC and vitamin D in capsule form showed improvement in bone resorption markers in patients with osteopenia and osteoporosis.

Decrease in Deoxypyridinoline and Pyridinium Crosslinks

Patient Data			Bone Mineral Density by DEXA	Deoxypyridinoline (DPD) Range: 3.0 – 7.4 nmol/mmol cr			Pyridinium Cross-Links (DPD & PYD) Range: 16.0 – 37.0 nmol/mmol cr		
Age	Condition	Therapy Length/ Dosage	T-Score Reference Range: -2.5 or less = Osteoporosis -1 to -2.5 = Osteopenia	Before Program (nmol/ mmol cr)	After Program (nmol/ mmol cr)	% Improve - ment	Before Program (nmol/ mmol cr)	After Program (nmol/ mmol cr)	% Improve - ment
62	Osteopenia	15 weeks 2 caps bid	-0.60 APS* -1.30 DFNB	15.7	4.2	73.2%	52.8	23.7	55.1%
47	Osteopenia	12 weeks 2 caps bid	-1.50 APS -1.50 BH	9.4	3.0	68.1%	49.0	14.5	70.4%
54	Osteopenia	33 weeks 1 cap am & 2 caps pm for 7 weeks then 2 caps bid	-0.90 APS -1.61 DFNB	5.3	3.2	39.6%	31.1	20.7	33.4%
53	Osteoporosis	31 weeks 2 caps bid	-2.60 APS -2.20 BH	6.9	5.2	24.6%	36.6	24.4	33.3%
55	Osteopenia	14 weeks 3 caps daily for 4 weeks then 2 caps bid	-2.40 APS -2.10 DFNB	7.4	6.0	18.9%	35.9	28.7	20.1%
59	Osteoporosis	12 weeks 2 caps bid	-2.10 APS -2.60 DFNB	9.6	8.7	9.4%	30.6	25.3	17.3%

* Anterior-Posterior Spine (APS), Dual Femur Neck Bone (DFNB), and Bilateral Hip (BH) bone mineral density values. The lowest value is used for diagnosis (in bold).

Case Study Highlight #1

A 62-year-old Caucasian female presented in February 2005 with concerns about osteopenia, as identified a month earlier by DEXA scan that revealed depressed dual femur neck T-score of -1.3. Surgical menopause had been induced by a hysterectomy 21 years prior to presentation. She was on a light exercise regimen (45 minutes walking/jogging per week).

At her initial visit, laboratory tests revealed elevated urinary bone resorption markers, indicating an increased rate of bone

resorption and an increased risk of further bone loss and bone fracture (see Figures 1 and 2).

In late April 2005, she was instructed to begin the concentrated MCHC and vitamin D supplement at 2 capsules bid. At her 15-week visit in August 2005, both measurements of pyridinium cross-links and DPD levels revealed that they were both in normal range.

Figure 1. The patient's deoxypyridinoline levels decreased substantially from 15.7 to 4.2 nmol/mmol cr (reference range: 3.0 – 7.4 nmol/mmol cr) in 15 weeks. This result suggests substantial reduction in bone resorption.

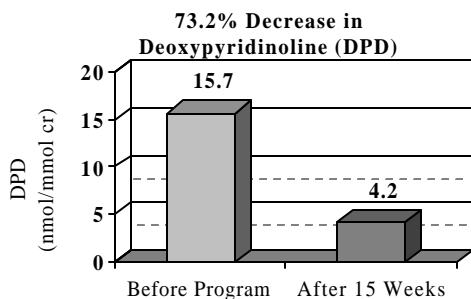
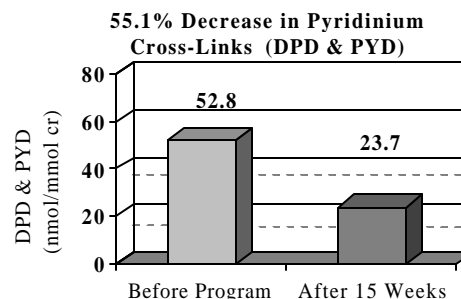


Figure 2. After 15 weeks, the patient's level of pyridinium cross-links had normalized by decreasing from 52.8 to 23.7 nmol/mmol cr (reference range: 16.0 – 37.0 nmol/mmol cr), also suggesting substantial reduction in bone resorption.

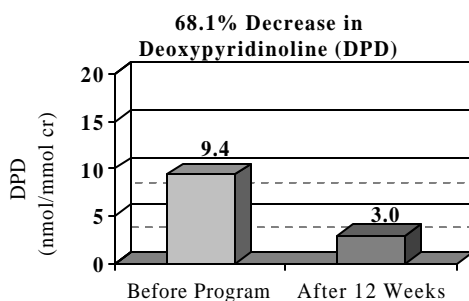


Case Study Highlight #2

A 47-year-old Caucasian female presented in December 2004 with concerns about osteopenia, as identified 6.5 months prior by DEXA scan that revealed depressed anterior-posterior spine and dual femur neck bone, both with a T-score of -1.5.

Laboratory tests at her initial visit indicated elevated levels urinary bone resorption markers, suggesting an increased rate of bone resorption and an increased risk of further bone loss and bone fracture (see Figures 3 and 4). She was currently on hormone replacement therapy for hypothyroidism, and her family

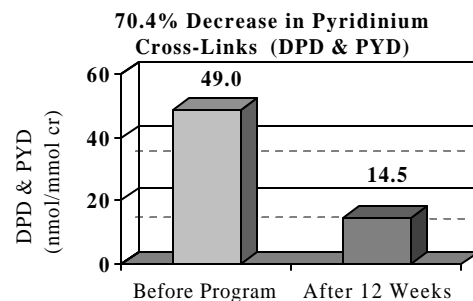
Figure 3. After 12 weeks, the patient's deoxypyridinoline (DPD) levels noticeably decreased 9.4 to 3.0 nmol/mmol cr (reference range: 3.0 – 7.4 nmol/mmol cr), suggesting substantial reduction in bone resorption.



history included macular degeneration and Parkinson's disease (maternal), as well as osteoporosis (paternal). She reported a combination of aerobic exercise and stretching for more than 45 minutes per week.

She was immediately instructed to begin the concentrated MCHC and vitamin D supplement at 2 capsules bid. At her 12-week visit in March 2005, laboratory tests revealed normalized levels of pyridinium cross-links and DPD.

Figure 4. The patient's level of pyridinium cross-links decreased from 49.0 to 14.5 nmol/mmol cr (reference range: 16.0 – 37.0 nmol/mmol cr) in 12 weeks. This result also suggests a substantial reduction in bone resorption.



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Note

The information provided in each of these case studies describes the results of one patient under the care of a licensed healthcare practitioner and may not be a typical response.

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