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# Changes in Urinary Bone Resorption Marker after Taking a Combination Nutrient Formula in Adults with Scoliosis: A Retrospective, Open-Label, Case-Controlled Series

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# **Abstract**

Background: Scoliosis is a common condition in adult patients, and often causes chronic back pain compared to non-scoliosis. It has also been identified that bone mineral density is very often compromised in patients with scoliosis, even occurring in adolescence. At this time, no study has looked at how bone mineral density and scoliosis incidence or severity may be connected with specific regard to treatment. This study presents data on the outcomes of a scoliosis-specific exercise therapy and its ability to correct scoliotic curvatures in adult patients alone and in combination with bone mineral density supplementation. Methods: The charts of 14 total patients were retrospectively selected based upon specific inclusion criteria. Outcome assessments included the radiographic Cobb angle of the primary curvature, as well as laboratory measures of urinary deoxypyridinoline cross links. These results were compared against 12 patients who did not take the bone density supplement during or after their exercise-based treatment. Results: Patients taking the bone density supplement achieved the same level of Cobb angle reduction as compared to the control group. However, they additionally achieved a significant reduction in urinary deoxypyridinoline cross links as compared to the control group at 6 months. Conclusion: Patients taking a multi-ingredient bone density supplement daily for 6 months after completing a scoliosis-specific exercise program reported statistically significant improvements in urinary deoxypyridinoline cross links as compared to controls. It is unknown if or how bone density loss may contribute to the onset or progression of scoliosis. Long-term follow-up of these patients will be ongoing to assess bone mineral density status and Cobb angle changes longitudinally.

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# **Keywords**

## Bone, Osteopenia, Osteoporosis, Scoliosis

#### 1. Introduction

The incidence of prevalence of scoliosis in adult populations may be as high as 68% or more in certain patient subsets [1]. This is an important statistic to consider, given that the largest growing segment of the US population is now over 60 years of age. Chronic pain is significantly more likely to occur in adults with scoliosis compared to age-matched non-scoliosis [2], and quality of life parameters tend to become a more primary objective of therapeutic intervention compared to radiographic Cobb angle correction. A review by Aebi [3] classified adult scoliosis into 3 main subgroups: 1) a primary "de novo" degenerative scoliosis; 2) a progressive idiopathic scoliosis and 3) scoliosis secondary to osteoporosis or arthritic disease. Aebi claims that types 1 and 3 are more common, with both being potentially worsened by osteoporosis [3].

Aebi is not the only author to observe and write about the effects of altered bone mineral density and bone metabolism associated with idiopathic scoliosis. Although this is thought to occur more in older adult patients, variations in bone mineral density have been reported in adolescents with idiopathic scoliosis. Suh *et al.* [4] studied 72 girls aging 11 - 14 and found lower levels of bone mineral density when compared with age-matched controls. A review by Li *et al.* [5] found that the incidence of osteoporosis in adolescent idiopathic scoliosis ranged from 20% - 38%.

Another concern is that post-menopausal women with existing scoliosis may see their curves deteriorate, given the natural decline of estrogen that follows menopause. In a study by Rogers *et al.* [6], 180 women aging 55 - 91 were evaluated for bone markers and estrogen levels. They found associations between estradiol levels, osteoprotegerin, and bone mineral density. Although chronic pain is becoming increasingly common across all age populations, it may be especially important in post-menopausal females to address the metabolic factors surrounding bone mineral density in the event which is shown to drive scoliosis progression in later adulthood.

Various nutrients have shown beneficial effects on bone mineral density. Among these, vitamin K [7], vitamin D [8], strontium [9], and calcium/magnesium [10] have been the most studied. However, no studies to date have reported on the effects that these nutrients may have in trying to reverse bone mineral density loss in patients with adult scoliosis. This study reports the results of patients who were recommended to take a proprietary bone nutrient supplement formula while participating in a scoliosis-specific exercise program.

## 2. Materials and Methods

We reviewed the charts of patients who took part in a one-week program of scoliosis-specific exercises between May 2013 and September 2014. All patients whose charts were selected presented with a history of adult scoliosis, scoliosis-related pain as determined by orthopedic physical assessment, as well as radiographic and laboratory evidence of osteopenia/osteoporosis, or increased osteoclast activity as measured by urinary deoxypyridinoline cross links. From this timeline, a total of 42 patient charts were selected. Patient charts were included in this study if they fulfilled the following inclusion criteria: 1) patient age at least 50 years old; 2) they did not have a history of neuromuscular, juvenile, or infantile scoliosis; 3) negative history of spinal fusion surgery and 4) patients could not be concurrently treated for other comorbid health conditions. Patient files were excluded if they did not perform follow-up laboratory analyses at 6 months. Based upon these inclusion and exclusion criteria, a total of 26 patient files were chosen.

At the initiation of therapy, patients opted to perform routine urinalysis, and were subsequently prescribed a multimineral supplement (Ossopan MD, Xymogen, Inc.) for the purpose of improving bone mineral density. All patients additionally began a one-week scoliosis-specific exercise program. All patients received the same types of exercises, which were adapted specifically to each patient's level of function as well as their particular curve patterns. Once the one-week therapy was completed, each patient was given a specifically prescribed set of home exercises to perform until the next follow-up. Following the conclusion of treatment, patients were instructed to report back to the clinic in 3 months for follow-up. At that time, all patients completed an updated urinalysis and follow-up scoliosis radiograph to evaluate curve correction from the exercises. This follow-up

routine was repeated at 6 months post-therapy also.

#### 3. Results

The average age at baseline was 50 years in both the intervention and control groups. All of the patients in both groups were female. There were a total of 14 patients placed in the intervention group since they took the bone density supplement, while the remaining 12 served as the control group. Since weight bearing exercise is thought to increase bone density, or at least prevent its loss, urinary deoxypyridinoline is an easy way to obtain clinical information on osteoclastic activity. The average starting Cobb angle for patients in both groups was  $38^{\circ}$ . Baseline values for urinary deoxypyridinoline cross-links were 9.65 for the treatment group and 9.74 for the control group. Cobb angle improvements were observed in both groups and both groups' improvements reached statistical significance in student t-tests (P < 0.001). The intervention group had an average Cobb angle change of  $8^{\circ}$ , while those in the control group had an average change of  $10^{\circ}$ . The urinary output of deoxypyridinoline cross-links decreased in the intervention group by 2.43 (P < 0.001), while the average output in the control group did not significantly change (reduction of 0.3, P value = 0.015). A 99% confidence interval was selected due to the small sample sizes in the study. All statistical analysis was completed in Microsoft Excel 2010. **Table 1** and **Table 2** show the data of both groups.

#### 4. Discussion

Because of the financial cost of more traditional bone density measurement and tracking methods, such as dual energy x-ray absorptiometry (DEXA), it is clinically desirable for providers to use more cost-efficient, easily collected information that can serve as reasonable complements or replacements for more conventional diagnostics. Urinary deoxypyridinoline cross-links have been used for this purpose for quite some time [11], due primarily to its specificity of type 1 bone collagen status [12]. It has been shown to be a reliable indicator for testing the effectiveness of prescription osteoporosis medications [13]. Demir *et al.* [14] found a sensitivity of 67% and a specificity of 68% when using urinary deoxypyridinoline as a screening tool for osteoporosis. In our study, however, the purpose was not to diagnose osteoporosis, but to evaluate whether scoliosis-specific exercises and/or a bone density supplement could improve bone metabolism as evidenced by reduced urinary deoxypyridinoline levels.

Although strength training in geriatric patients has been shown to improve bone turnover markers [15], our data did not show any improvement in the control group who only performed the scoliosis-specific exercises. It

4	Age	Cobb1	Cobb2	UA1	UA2
1	37	42	34	11.2	7.1
2	48	31	25	15.1	8.1
3	55	33	25	10.4	6.6
4	61	45	32	8.8	8
5	43	42	37	7.7	7.1
6	60	29	20	8.4	7.4
7	53	24	18	9.1	7.3
8	44	33	20	7.9	6.4
9	41	37	25	6.8	5.5
10	49	40	30	7.3	5.1
11	54	52	44	9.5	7.8
12	63	38	36	11.4	7.6
13	50	46	41	12.2	8.7
14	47	40	35	9.3	7
AVG	50.3	38	30.14	9.65	7.12

a. Statistically significant at 99% confidence interval.

Table 2. Control group values.									
Patient	Age	Cobb1	Cobb2	UA1	UA2				
15	55	45	40	10.3	9.9				
16	49	41	35	11.6	10.4				
17	47	36	33	8.7	8.8				
18	57	25	17	7.3	6.9				
19	64	27	18	9.6	9.4				
20	39	35	22	10.7	10.9				
21	44	29	20	12	11.8				
22	36	41	26	9.2	8.9				
23	48	46	33	7.7	7.6				
24	50	51	27	6.9	6.9				
25	61	60	48	7.8	7.7				
26	58	30	20	11.7	10.4				
27	53	38	29	13.1	13				
AVG	50.8	38.77	28.31	9.7	9.4				
		P value = $6$ .	.10738E-06 <sup>a</sup>	P value = $0.015418^{b}$					

a. Statistically significant at 99% confidence interval; b. Not statistically significant.

is possible that these exercises do not provide enough resistance or weight bearing to improve urinary deoxypyridinoline. However, this was not the intended goal of these exercises either. From this data, it would appear that bone density status is not related to scoliosis, as both of our patient groups faired about the same in terms of radiographic Cobb angle outcome. However, it is possible, given the known linear rate at which adult scoliosis progresses throughout the lifespan [16], that bone mineral density loss may play a role in the continued progression. Future studies should attempt to select patients in various stages of the menopause spectrum, so that other associations may be possibly identified.

## Limitations

Our study did have a control group. However, it was retrospective in design, so it cannot exclude selection and examiner bias. We took several precautions to minimize these biases. We selected inclusion criteria before selecting any patient charts. We then consecutively selected any and all charts that fit those criteria. From this total pool of charts we were able to subcategorize based upon each patient's decision to take the bone density supplement.

We do acknowledge that the control group did not take, nor were they offered, any placebo supplement. This is mainly due to the fact that it was retrospective, and therefore we were limited by past treatment protocols. It is possible that at least some of these patients may have demonstrated bigger placebo improvements had they taken a placebo capsule. Finally, with a small sample size, and no power analysis, it is unknown for sure what degree of improvement would be required to reach clinically and statistically significant change. We did, however, attempt to account for this by using a 99% confidence interval instead of the usual 95%.

#### 5. Conclusion

Two groups of adult scoliosis patients participated in a short term scoliosis-specific exercise program, after which their radiographic Cobb angles and a urinary bone resorption marker were obtained. The group who took an oral proprietary bone density supplement saw their urinary bone resorption marker significantly decreased, while the group performing exercises only had unchanged urinary markers after 6 months. An important step next in following these patients is to monitor changes in any future bone mineral density scans for more direct measurement and correlation.

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