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Effect of Corticosteroid Injections on College Athletes' Bone Mineral Density and Biochemical Markers of Bone Turnover

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This cross-sectional study was performed to determine the effect of corticosteroid injections on athletes' bone mineral density (BMD). Fourteen collegiate athletes were pair-matched according to anthropometric measurements, gender and sport to minimize the effects of these confounding factors. Exclusionary criteria included, smoking, metabolic/hormonal disorders, oligo-or amenorrhea, use of hormonal medications or muscle-building formulas, and serious injuries. The experimental or cortisone group (C) was defined as athletes having received corticosteroid injections. The control or non-cortisone group (NC) was defined as athletes having never received corticosteroid injections. Total body and site-specific BMD and total body bone calcium were measured by Dual Energy X-ray Absorptiometry. Blood was collected to assess serum calcium and osteocalcin levels, and collected twenty-four hour urine was collected to assess urinary calcium excretion and N-telopeptide concentrations. Using Wilcoxon Signed Rank Test, lumbar BMD was significantly lower in C than NC ($p = 0.043$) (1.26 ± 0.10 vs. 1.37 ± 0.11 g cm^{-2}, respectively), while greater trochanter BMD tended to be lower in C than NC ($p = 0.063$) (0.92 ± 0.09 vs. 1.00 ± 0.06g cm^{-2}, respectively). No other significant changes were found in other bone and biochemical measurements. Despite the limited sample size, these preliminary results show a tendency toward a negative relationship between corticosteroid injections and lumbar and greater trochanter BMD.

Key words: Athletes, bone mineral density, corticosteroids, N-telopeptides, osteocalcin

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Introduction

Nutrition and exercise have strong positive influences on bone metabolism. Proper nutritional intake nurtures the mineralization process of bone, while physical activity enhances peak bone mass and bone mineral density (BMD); therefore, it seems unlikely that athletes could be at risk for impaired bone metabolism (Dook *et al.*, 1997; Dornemann *et al.*, 1997; Teegarden *et al.*, 1998). However, as competitive sports become increasingly popular, athletes are being exposed to various treatments for injuries that may ultimately be more harmful than beneficial.

Corticosteroids, which are commonly used in the treatment of inflammatory diseases, such as asthma and rheumatoid arthritis, have been correlated with decreased bone mass in supraphysiologic doses (Lukert and Kream, 1996). Glucocorticoids restrict the intestinal absorption and renal reabsorption of calcium, inhibit osteoblastic activity, and prevent the conversion of vitamin D to its active form, impairing bone metabolism (Lukert and Kream, 1996). Furthermore, corticosteroids inhibit the secretion of testosterone and estrogen leading to increased bone resorption (Lukert and Kream, 1996).

In addition to treating patients with inflammatory diseases, corticosteroids, in the form of injections, have become common in treating athletic-related injuries (Gagnon *et al.*, 1997; Lukert and Kream, 1996). Hill *et al.* (1989) reported that, of 200 orthopedic surgeons interviewed, greater than 90% were likely to treat an upper body inflammatory injury with a corticosteroid injection than with any other form of therapy. However, no research has been performed on the potential damaging effects corticosteroid injections may have on the BMD of athletes. Therefore, athletes, who are receiving corticosteroid treatments may be at risk for bone loss, and ultimately, corticosteroid-induced osteoporosis.

Because of the limited research in this area, the primary objective of this study was to examine if low dosages of past corticosteroid injections have any impact on healthy, collegiate athletes' BMD and biochemical markers of bone turnover. A secondary aim of this study was to assess if nutrition and exercise negate the impact of corticosteroid injections administered at lower doses.

Materials and Methods

Study design: This was a cross-sectional study composed of an experimental and a control group; the BMD of the two groups was compared at one point in time. This study was first approved by the University of Massachusetts Institutional Review Board for Human Subjects.

Subjects: A total of 14 subjects, ranging between the ages of 18 to 25 years, were recruited for this study. The subject pool consisted of ten Caucasian and two Asian female volunteers and two Caucasian male volunteers. The sports represented were as follows: two female rowers, two female divers, six female gymnasts and two male gymnasts. One group (n = 7) consisted of the experimental group: athletes who have been treated with corticosteroid injections in the past (C). The frequency of corticosteroid injections ranged from one to eight injections within the past two to ten years. In addition, the amount of corticosteroid in each injection most likely differed; however, subjects were not able to recall the dosage they received. Another group (n = 7) comprised the control group: athletes who never had corticosteroid treatments (NC). Subjects from the experimental group and the control group were pair-matched according to gender, height, body weight, body mass index (BMI [kg m^{-2}]) and sport to minimize the effects of these confounding factors. To further control for confounding factors, subjects were excluded if they smoked, had any metabolic or hormonal disorders, were oligo- or amenorrheic (present or past), were taking any hormonal medications, used any muscle-building formulas, such as creatine monohydrate and anabolic steroids, and/or had serious injuries (e.g., use of crutches). Each subject read and signed an informed consent form before initiation of the study.

Anthropometric measurements: Height, body weight and percent body fat were collected for demographic purposes and to assign subjects to pairs. Height was measured to the nearest 0.5 cm using a stadiometer. Body weight was measured to the nearest 0.5 kg on a calibrated balance-beam scale. Percent body fat was measured via the Lunar Dual Energy X-ray Absorptiometer (DEXA) [DPX computer software, Version 3.63. Lunar Corporation, Madison, WI: 1993].

Three-day dietary records: Each subject was asked to maintain a three-day dietary record recording all foods/beverages/supplements they consumed during that time. The dietary record included two weekdays and one weekend day. The three-day dietary records were analyzed using Nutritionist V [computer software, Version 1.7. The Hearst Corporation, San Bruno, CA: 1998]. Three-day dietary records were collected to compare recent dietary intakes to the biochemical indices because biochemical indices tend to reflect more recent physiological changes.

Food frequency questionnaires: Food frequency questionnaires (FFQ's) were also collected (Block, 1987). The FFQ consisted of questions regarding typical food consumption (e.g., portion size, frequency of consumption, preparation methods, supplement use). FFQ's were analyzed using Dietsys [computer software, Version Full 1987. National Cancer Institute, Bethesda, MD: 1987]. FFQ's were collected to compare long-term dietary intakes with direct measures of bone, because bone turnover typically represents changes over an extended period of time.

Direct measurement of bone: BMD was measured using a Lunar DEXA [DPX computer software, Version 3.63. Lunar Corporation, Madison, WI: 1993] at one point in time. In addition to total body BMD (TBBMD), lumbar spine, femoral neck, Ward's triangle and greater trochanter BMD (g cm^{-2}) and total body bone calcium (TBCA) (g) were assessed. All BMD measurements were performed at Canyon Ranch Health Resort in Lenox, Massachusetts.

Blood collection and storage: Subjects fasted for 12 hours before giving 15mL of blood, which was drawn into Monovette mineral-free tubes (Sarstedt, Inc., Germany). After the blood draw, serum was allowed to clot for one hour on ice and then centrifuged for 15 minutes at 1500 x g. Serum was then removed using mineral-free transfer pipettes and placed into 1.5mL Eppendorf tubes (Outpatient Services, Inc., Petaluma, CA). All serum was stored in a -80 oC freezer for future analyses. All blood samples were assessed in duplicate.

Serum calcium: A 1% nitric acid (HNO_3)/lanthanum solution was prepared. Serum samples were diluted in a 1:50 ratio, then analyzed by an Atomic Absorption Spectrophotometer (AAS) Model #2380 (Perkin-Elmer, Norwalk, CT). The AAS was set at 422.7nm, 6 milliamps and a 3.00 second reading, which is required for calcium analysis.

Serum osteocalcin: Serum osteocalcin levels were analyzed by radioimmunoassay kits provided by Nichols Diagnostics Institute (San Clemente, CA). Samples were assessed on a Beckman Gamma 4000 gamma counter (Beckman Instruments, Inc., Irvine, CA).

Urine collection and storage: Urine was collected in acid-washed containers in 24-hour pools. Total weight of the urine was measured, then aliquotted into 50 mL mineral-free conical tubes. Urine was stored in a -80 oC freezer until analyses were performed. All urine samples were assessed in duplicate.

Urinary calcium: A 0.125 N HNO_3/lanthanum solution was first prepared. The urine samples were diluted in a 1:40 ratio then analyzed by AAS Model #2380 (Perkin-Elmer, Norwalk, CT). The

AAS was set at 422.7nm, 6 milliamps and a 3.00 second reading, which is required for calcium analysis.

Urinary N-Telopeptide Cross-Links: Urinary N-Telopeptide Cross-Links (NTx) were analyzed using enzyme-linked immunoassay (ELISA) by Ostex International Incorporated (Seattle, WA).

Urinary creatinine: Urinary creatinine excretion was analyzed by Ostex International Incorporated (Seattle, WA).

Statistical analyses: Non-parametric Wilcoxon Signed Rank Tests were performed comparing the two groups for each of the aforementioned measures. Non-parametric Spearman Correlation analyses were also conducted on both groups combined for all measurements. The p-value was set *a priori* at 0.05. Statistical Program for the Social Sciences (SPSS) [computer software, Version 9.0. SPSS, Chicago, IL: 1993] was used for all analyses.

Results

Anthropometric measurements: There were no significant differences between C and NC in anthropometric measurements (Table 1).

Three-day dietary records and food frequency questionnaires: There were no significant differences between the three-day dietary records and FFQ's (Table 2). The majority of the nutrient intakes were within the Dietary Reference Intakes (DRI's) (Food and Nutrition Board, 1997 and 2001). However, protein intake was greater than the DRI of 58 grams for men and 46 grams for women, and phosphorus intake was above the DRI of 700 mg for both genders (Food and Nutrition Board, 1997).

Direct measurement of bone: Bone mineral density

Bone mineral density and frequency of corticosteroid injections: A negative trend was observed between the frequency of corticosteroid injections and lumbar spine BMD (LBMD) ($r = -0.515$, $p = 0.059$) and femoral neck BMD (FBMD) ($r = -0.4936$, $p = 0.071$). Furthermore, the frequency of corticosteroid injections was found to be significantly negatively correlated with greater trochanter BMD (GBMD) ($r = -0.659$, $p = 0.01$). In addition, there was a significant negative correlation between LBMD ($r = -0.585$, $p = 0.028$) and GBMD ($r = -0.549$, $p = 0.042$) and increased time that had lapsed since the administration of corticosteroid shots.

Bone mineral density for corticosteroid and non-corticosteroid groups: Normal values range from 0.97 to 1.13g cm^{-2} for TBBMD for both adult males and females (Gagnon *et al.*, 1997). No significant differences were observed in TBBMD, FBMD, Ward's triangle BMD (WBMD) and TBCA between C and NC (Table 3). However, LBMD was significantly lower ($p = 0.043$) in C compared to NC. Furthermore, there was a trend ($p = 0.063$) for GBMD to be lower in C versus NC.

Bone mineral density and biochemical indices: There were no significant correlations found between serum osteocalcin, serum calcium and urinary calcium levels and BMD. However, a negative trend ($r = -0.465$, $p = 0.094$) was observed between urinary NTx levels and TBBMD. No other relationships were observed between urinary NTx levels and other measurements of BMD and TBCA.

Bone mineral density and nutrient intake according to food frequency questionnaire for all subjects combined: Many nutrients were found to be positively correlated with various BMD sites, while fiber was shown to have a negative association with LBMD (Table 4). FFQ's were selected to assess BMD and long-term nutrient intake because bone turnover typically reflects changes over an extended period of time.

Biochemical indices

Biochemical indices and corticosteroid use: No significant differences were observed between C and NC in any of the biochemical indices measured (Table 5). Serum calcium values and urinary calcium excretion were within the normal ranges for all subjects and female subjects. Serum osteocalcin levels tended to be lower than the reference values in all subjects and female subjects. In addition, one male subject in NC and one female subject from C had NTx values of 182 and 169 nM/mM of creatinine, respectively, which were above normal values.

Biochemical indices and nutrient intake according to three-day dietary records for all subjects combined: When the complete subject pool ($n = 14$) was included in the assessment, urinary calcium excretion was found to be positively associated with calcium intake ($r = 0.600$, $p = 0.023$) as assessed by three-day dietary records. Furthermore, a positive trend was observed between urinary calcium excretion and protein ($r = 0.512$, $p = 0.061$) and vitamin D ($r = 0.486$, $p = 0.078$) intakes. No significant associations were observed between other biochemical indices and dietary intake. Three-day dietary records were selected to assess biochemical indices and current nutrient intake because biochemical indices reflect recent physiological changes.

Table 1: Subject characteristics of corticosteroid (C) and non-corticosteroid (NC) groups

Parameters	C	NC
Age (years)	20.57 ± 2.37	19.57 ± 1.51
Height (cm)	160.94 ± 12.35	160.39 ± 11.58
Body weight (kg)	57.79 ± 14.73	57.34 ± 12.33
BMI (kg m^{-2})	21.96 ± 2.26	22.03 ± 1.73
Percent body fat	18.17 ± 6.75	23.37 ± 7.75
LBM (kg)	45.35 ± 10.86	43.66 ± 9.49
Fat mass (kg)	10.69 ± 7.21	13.62 ± 6.15

Values represent means ± standard deviation
BMI = Body Mass Index; LBM = Lean Body Mass

Table 2: Dietary intakes assessed by three-day dietary records and food frequency questionnaires (FFQ's) for All subjects combined

Parameters	Three-day dietary record	FFQ
Energy (kilocalories)	2,002.2 ± 830.9	2,031.0 ± 1,040.2
CHO (g)	307.9 ± 130.7	265.5 ± 144.0
Prot (g)	71.3 ± 35.0	82.5 ± 42.3
Fat(g)	57.7 ± 37.3	70.5 ± 40.7
Ca (mg)	938.9 ± 575.5	1,139.9 ± 650.9
Na (mg)	2,770.9 ± 1,566.4	3,491.1 ± 1,986.2
P (mg)	1,295.3 ± 572.5	1,525.0 ± 790.7
Zn (mg)	9.0 ± 4.2	15.1 ± 11.1
Mg (mg)	288.0 ± 127.9	342.2 ± 151.0
Fiber (g)	20.6 ± 11.4	15.89 ± 6.96

Values represent means ± standard deviation
CHO= Carbohydrate; Prot= Protein; Ca = Calcium
Na = Sodium; P = Phosphorus; Zn = Zinc; Mg = Magnesium

Table 3: Total body and site-specific bone mineral density and total body bone calcium for corticosteroid (C) and non-corticosteroid (NC) groups

Parameters	C	NC
TBBMD (g cm^{-2})	1.19 ± 0.07	1.22 ± 0.06
LBMD (g cm^{-2})	1.26 ± 0.10*	1.37 ± 0.11
FBMD (g cm^{-2})	1.17 ± 0.13	1.22 ± 0.10
WBMD (g cm^{-2})	1.16 ± 0.14	1.21 ± 0.10
GBMD(g cm^{-2})	0.92 ± 0.09+	1.00 ± 0.06
TBCA (g)	1,026.6 ± 173.2	1,038.5 ± 187.3

Values represent means ± standard deviation
TBBMD = Total body bone mineral density; LBMD = Lumbar spine bone mineral density; FBMD = Femoral neck bone mineral density; WBMD = Ward's triangle bone mineral density; GBMD = Greater trochanter bone mineral density; TBCA = Total body bone calcium; *= LBMD was significantly lower in C versus NC ($p = 0.043$); + = GBMD was lower in C versus NC ($p = 0.063$)

Table 4: Significant correlations between bone mineral density, total body bone calcium and nutrient intake according to food frequency questionnaire (FFQ) for all subjects combined

Parameters	TBBMD	LBMD	FBMD	WBMD	TBCA
Energy (kilocalories)	r= 0.695			r= 0.609	r= 0.577
	p= 0.006			p= 0.021	p= 0.039
Carbohydrate	r= 0.581			r= 0.587	
	p= 0.021			p= 0.027	
Protein	r= 0.711			r= 0.559	
	p= 0.04			p= 0.038	
Fat	r= 0.744				r= 0.571
	p= 0.002				p= 0.041
Calcium	r= 0.667		r= 0.616	r= 0.639	
	p= 0.009		p= 0.019	p= 0.014	
Sodium	r= 0.656				
	p= 0.011				
Phosphorus	r= 0.656				
	p= 0.011				
Zinc	r= 0.655				
	p= 0.011				
Magnesium				r= 0.625	
				p= 0.017	
Fiber		r= -0.560			
		p= 0.037			
Vitamin A	r= 0.561				
	p= 0.037				

Values represent correlation coefficients and p-values

Table 5: Biochemical indices of corticosteroid (C) and non-corticosteroid (NC) groups for all subjects and females

Parameters	C	NC	Females only C	Females only NC
Serum Ca (mg dl-1)	009.78± 0.43	009.46± 0.66	009.74± 0.46	009.41± 0.70
Urinary Ca (mg/24 hours)	248.40± 117.85	229.84± 154.45	227.65± 114.22	231.01± 169.16
Serum Osteo. (ng ml-1)	009.74± 8.55	010.80± 5.97	008.30± 8.39	011.19± 6.44
Urine Ntx. (nM/mM of creatinine)	066.71± 46.78	067.57± 50.61	071.67± 49.20	048.50± 4.23

Values represent means ± standard deviation Serum Ca= Serum calcium levels; Urinary Ca= Urinary calcium excretion
Serum Osteo= Serum osteocalcin levels; Urine Ntx= Urinary N-Telopeptide levels (express per nM/mM of creatinine)

of each subject were within, or exceeded, the reference ranges for a young adult population (Nichols *et al.*, 1994). The athletes' high BMD, compared to the general population, supports the findings of others (Dook *et al.*, 1997; Dornemann *et al.*, 1997).

Bone mineral density and frequency of corticosteroid injections: The results of this study demonstrate that increased frequency of corticosteroid injections were significantly negatively correlated with a lower GBMD, while a negative trend was observed with LBMD and FBMD. Corticosteroids impair the intestinal absorption and renal reabsorption of calcium, inhibit osteoblastic activity, and prevent the conversion of vitamin D to its active form, ultimately impairing bone metabolism (Lukert and Kream, 1996), which could explain the decrease in BMD observed in this study.

Numerous studies have reported that oral and inhaled corticosteroid use impairs bone metabolism, resulting in decreased hip and lumbar BMD in patients diagnosed with rheumatoid arthritis or asthma (Buckley *et al.*, 1995; Ebeling *et al.*, 1998; Hanania *et al.*, 1995). In addition, others have shown that short-term inhaled corticosteroid therapy affects healthy adult individuals (Ali *et al.*, 1991; Teelucksingh *et al.*, 1991). Teelucksingh *et al.* (1991) found a decrease in osteocalcin levels, while Ali *et al.* (1991) observed an increase in urinary hydroxyproline levels, after healthy adults were given high dosages of beclomethasone dipropionate. Although previous studies differed in the form of corticosteroid treatment administered and the subject population utilized compared to our study, it is interesting to observe the similar decreases in site-specific BMD. It is also of interest to note that a healthy adult population can be susceptible to corticosteroids' negative impacts, even over a short period of time.

Bone mineral density for corticosteroid and non-corticosteroid groups: The differences that were exhibited in LBMD and GBMD between C and NC, not observed at other sites, could be due to the type of bone that is present in these regions. The lumbar spine and hip are sensitive areas because they are primarily composed of trabecular bone, which is more porous in nature than cortical bone. Therefore, the lumbar spine and hip tend to be more susceptible to corticosteroid therapy compared to other sites (Heaney, 1996). In addition, the correlation between decreased LBMD and GBMD and prolonged duration of time since administration of injections may imply that corticosteroid injections have a metabolic residual effect within the skeletal structure.

Bone mineral density and nutrient intake according to Food Frequency Questionnaire for all subjects combined: Energy, carbohydrate, protein and fat intakes were significantly positively correlated with TBBMD, which supports findings from previous studies (Dyson *et al.*, 1997; Einhorn, 1990). Furthermore, dietary intake of vitamin A was positively correlated with TBBMD (Table 4). This vitamin is, in part, responsible for the formation of collagen and bone Gla proteins; therefore, the significant positive correlation was as expected (Faridi *et al.*, 1984; Root, 1990), because our subjects' vitamin A consumption was within the DRI (Food and Nutrition Board, 2001). However, more recent research has shown that excessive amounts of vitamin A can be linked with bone degradation. Melhus *et al.* (1998) reported that increased dietary vitamin A intake was correlated with decreased BMD and increased risk of hip fracture in women between the ages of 28 and 74 years.

Dietary fiber intake was significantly negatively correlated with LBMD. Dietary fiber from various types of bran has been shown to inhibit intestinal calcium absorption due to the existence of the calcium chelator, phytate (Christakos, 1996). Although dietary fiber intakes were within normal limits, fiber-related compounds (e.g., pectin, uronic acid) may have impaired calcium absorption leading to the significant inverse relationship between dietary fiber

and LBMD (Gallaher *et al.*, 1996; Kerstetter *et al.*, 1998). No negative correlations were found between dietary fiber and other bone measurements in the present study.

Biochemical indices: Serum calcium values and urinary calcium excretion were within the reference ranges of 8.5 to 11mg dL^{-1} and < 250 mg/24 hours, respectively (Krall *et al.*, 1997; Zeman and Ney, 1996). Meanwhile, serum osteocalcin levels tended to be lower for females and all subjects combined compared to the normal value of 18.7ng mL^{-1} for women and 21.5ng mL^{-1} for men (Nichols Diagnostics Institute, 1999). Osteocalcin contains a vitamin K-dependent amino acid, y-carboxyglutamic acid (Root, 1990). During vitamin K deficiency, levels of serum osteocalcin may be disrupted (Vermeer *et al.*, 1996). According to the three-day diet record, 11 out of the 14 subjects were below the vitamin K DRI of 90µg day^{-1} for women and 120µg day^{-1} for men (Food and Nutrition Board, 2001). Therefore, the limited vitamin K intake could have resulted in the lower than normal osteocalcin values.

Biochemical indices and corticosteroid use: No significant differences were found between C and NC in females and in all subjects combined in the biochemical indices of bone, suggesting that the corticosteroid levels present in injections may not impact bone, as do excessive oral and inhaled doses in patients suffering from rheumatoid arthritis and asthma, as well as healthy individuals (Ali *et al.*, 1991; Gagnon *et al.*, 1997; Sambrook *et al.*, 1993). Jeffries (1981) noted that the half-life of pharmacological corticosteroids is approximately 200 hours in the blood, possibly explaining why no changes were detected in the biochemical indices in this study. The anticipated differences in biochemical indices between groups may have occurred immediately after corticosteroid treatment. Unfortunately, no data were collected at that time point. In addition, our subjects received injections of varying amounts of corticosteroids from two to ten years prior to the study.

Urinary NTx values were all within the normal ranges of 5 to 65 nM/mM of creatinine for women and 3 to 51 nM/mM of creatinine for men (Ostex International, Incorporated, 1999), except for one male subject in NC and one female subject in C. These two subjects were 18 years of age, which was the minimum age of the entire subject pool; therefore, their bone development may not have been complete at the time of data collection. Their high NTx levels could possibly be a result of skeletal immaturity.

Biochemical indices and nutrient intake according to three-day dietary records for all subjects combined: Dietary protein and calcium were correlated with elevated urinary calcium excretion. Previous studies have shown that excessive dietary protein leads to an increase in urinary calcium excretion, which is due to the enhanced absorption rate of calcium and increased glomerular filtration rate, ultimately resulting in hypercalciuria (Kerstetter *et al.*, 1996; Linkswiler *et al.*, 1974). Excessive calcium intake will be excreted in the urine in order to maintain the homeostatic balance within the body; supporting the observation that calcium intake was positively correlated with elevated urinary calcium excretion (Arnaud *et al.*, 1996).

The inverse association between protein and urinary NTx levels could have been due to the impact of low dietary protein on calcium absorption. Kerstetter *et al.* (1996) demonstrated that decreased dietary protein results in a reduction in intestinal calcium absorption. Thus, the low intake of protein could have led to an imbalance in calcium levels, resulting in a stimulation of bone resorption, marked by elevated urinary NTx levels.

Limitations of the study: The following limitations could have affected the outcome of this investigation: limited sample size, the exact dosages of corticosteroid injections could not be reported, the number of injections varied among subjects, the site of injections differed among subjects and corticosteroid treatments ranged between two to ten years prior to the study. The results cannot be generalized for a large population due to these limitations, however, these results should stimulate further research in this area.

In conclusion, it appears that low dosages of corticosteroid injections may have a systemic impact on bone. The significant difference in LBMD and the trend for lower GBMD in C compared to NC may imply that, although the injections were localized at the site of injury, the effects may be observed systemically. The biochemical measurements do not support the decrease in BMD measurements; however, the half-life of pharmacological corticosteroids is only 200 hours in the blood, thus possibly explaining why no significant changes were detected in the biochemical indices (Jeffries, 1981). The lower LBMD and GBMD observed in C may represent a residual effect that occurs several years after receiving corticosteroid therapy, which could not be detected by the biochemical markers. Longitudinal studies are necessary to assess potential long-term consequences of corticosteroid injections on the BMD of athletes. In addition, research should target an at-risk population, such as post-menopausal women or young athletes, who may be receiving corticosteroid treatments during a crucial stage of bone metabolism and development.

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References

Ali, N.J., S. Capewell and M.J. Ward, 1991. Bone turnover during high dose inhaled corticosteroid treatment. Thorax, 46: 160-164.

Arnaud, D.A. and S.D. Sanchez, 1996. Calcium and phosphorus. In: Ziegler, E.E., Filer, L.J. (Eds.), Present Knowledge in Nutrition, 7th ed. International Life Sciences Institute Press, Washington, DC., pp: 245-255.

Block, G., 1987. Health Habits and History Questionnaire. National Cancer Institute, Bethesda, MD.

Buckley, L.M., E.S. Leib, K.S. Cartularo, P.M. Vacek and S.M. Cooper, 1995. Effects of low dose corticosteroids on the bone mineral density of patients with rheumatoid arthritis. J. Rheumatol., 22: 1055-1059.

Christakos, S., 1996. Bone formation assays. In: Bilezikian, J.P., Raisz, L.G., Rodan, G.A. (Eds.), Principles of Bone Biology. Academic Press, Boston, pp: 435-446.

Dook, J.E., D. James, N.K. Henderson and R.I. Price, 1997. Exercise and bone mineral density in mature female athletes. Med. Sci. Sports. Exerc., 23: 291-297.

Dornemann, T.M., R.G. McMurray, J.B. Renner and J.J. Anderson, 1997. Effects of high-intensity resistance exercise on bone mineral density and muscle strength of 40 to 50 year old women. J. Sports. Med. Phys. Fitness, 37: 246-251.

Dyson, K., C.J.R. Blinkie, K.S. Davison, C.E. Webber and J.D. Adachi, 1997. Gymnastics training and bone density in pre-adolescent females. Med. Sci. Sports. Exerc., 29: 443-450.

Ebeling, P.R., B. Erbas, J.L. Hopper, J.D. Wark and A.R. Rubinfeld, 1998. Bone mineral density and bone turnover in asthmatics treated with long-term inhaled or oral glucocorticoids. J. Bone. Miner. Res., 3: 1283-1289.

Einhorn, T.A., 1990. Dietary protein and bone calcium metabolism. In: Simmons, D.J. (Ed.), Nutrition and Bone Development. Oxford University Press, New York, pp: 223-236.

Faridi, M.M., Z. Ansari and S.K. Bhargava, 1984. Imprints of protein energy malnutrition on the skeleton of children. J. Trop. Pediatr. Abs., 30: 150-153.

Food and Nutrition Board, 1997. Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D and Fluoride. National Academy Press, Washington, DC.

Food and Nutrition Board, 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc. National Academy Press, Washington, DC.

Gagnon, L., L. Boulet, J. Brown and T. Desrosiers, 1997. Influence of inhaled corticosteroids and dietary intake on bone density and metabolism in patients with moderate to severe asthma. J. Am. Diet. Assoc., 97: 1401-1406.

Gallaher, D.D. and B.O. Schneeman, 1996. Dietary fiber. In: Ziegler, E.E., Filer, L.J. (Eds.), Present Knowledge in Nutrition, 7th ed. International Life Sciences Institute Press, Washington DC, pp: 87-97.

Hanania, N.A., K.R. Chapman, W.C. Sturtridge, J.P. Szalai and S. Kesten, 1995. Dose-related decrease in bone density among asthmatic patients treated with inhaled corticosteroids. J. Allergy. Clin. Immunol., 95:571-579.

Heaney, R.P., 1996. Osteoporosis. In: Krummel, D.A., Kris-Etherton, P.M. (Eds.), Nutrition in Women's Health. Aspen Publishers, Inc., Gaithersburg, pp: 418-439.

Hill, J.J., R.G. Trapp and J.A. Colliver, 1989. Survey on the use of corticosteroid injections by orthopaedists. Contemp. Orthop., 18: 39-45.

Jeffries, W., 1981. Safe Uses of Corticosteroid. Charles C. Thomas Publishers, Springfield.

Kerstetter, J.E., D.M. Caseria, M.E. Mitnick, A.F. Ellison, L.F. Gay, T.A. Liskov, T.O. Carpenter and K.L. Insogna, 1996. Increased circulating concentrations of parathyroid hormone in healthy, young women consuming a protein-restricted diet. Am. J. Clin. Nutr., 66: 1188-1196.

Kerstetter, J.E., K.O. O'Brien and K.L. Insogna, 1998. Dietary protein affects intestinal calcium absorption. Am. J. Clin. Nutr., 68: 859-865.

Krall, E., B. Dawson-Hughes, K. Hirst, J.C. Gallagher, S. Sherman and G. Dalsky, 1997. Bone mineral density and biochemical markers of bone turnover in healthy elderly men and women. J. Gerontol., 52: M61-M67.

Linkswiler, H.M., C.L. Joyce and C.R. Anand, 1974. Dietary Protein and Bone Calcium Metabolism. New York Academy of Science, New York.

Lukert, B.P. and B.E. Kream, 1996. Clinical and basic aspects of glucocorticoid action in bone. In: Bilezikian, J.P., Raisz, L.G., Rodan, G.A. (Eds.), Principles of Bone Biology. Academic Press, Boston, pp: 533-548.

Melhus, H., K. Michaelsson, A. Kindmark, R. Bergstrom, L. Holmberg, H. Mallmin, A. Wolk and S. Ljunghall, 1998. Excessive dietary intake of vitamin A is associated with reduced bone mineral density and increased risk for hip fracture. Ann. Intern. Med., 129: 770-778.

Nichols, D.L., C.F. Sanborn, S.L. Bonnick, V. Ben-Ezra, B. Gench and N.M. DiMarco, 1994. The effects of gymnastics training on bone mineral density. Med. Sci. Sports. Exerc., 26: 1220-1225.

Nichols Diagnostics, Institute, 1999. Human osteocalcin instruction kit. San Clemente, CA.

Ostex International, Incorporated, 1999. Osteomark Instruction Kit. Seattle, WA.

Root, A.W., 1990. Effects of undernutrition on skeletal development, maturation and growth. In: Simmons, D.J. (Ed.), Nutrition and Bone Development. Oxford University Press, New York, pp: 114-130.

Sambrook, P., J. Birmingham, P. Kelly, S. Kempler, T. Nguyen, N. Pocock and J. Eisman, 1993. Prevention of corticosteroid osteoporosis. A comparison of calcium, calcitriol and calcitonin. New. Engl. J. Med., 328: 1782-1792.

Teegarden, D., R.M. Lyle, G.P. McCabe, W.R. Proulx, K. Michon, A.P. Knight, C.C. Johnston and C.M. Weaver, 1998. Dietary calcium, protein and phosphorus are related to bone mineral density and content in young women. Am. J. Clin. Nutr., 68: 749-754.

Teelucksingh, S., P.L. Padfield, L. Tibi, K.J. Gough and P.R. Holt, 1991. Inhaled corticosteroids, bone formation and osteocalcin. Lancet., 338.

Vermeer, C., L.M. Birgit, B.L. Gijsbers, A.M. Craciun, M.M. Groenen-Van Dooren and M.H. Knapen, 1996. Effects of vitamin K on bone mass and bone metabolism. J. Nutr., 126: 1187S-1191S.

Zeman, F.J. and D.M. Ney, 1996. Clinical Laboratory Values. In: Applications in Medical Nutrition Therapy. Prentice Hall, Englewood Cliffs, pp: 373-389.

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