

*The role of calcium and vitamin D in the prevention
of low bone density and Adolescent Idiopathic
Scoliosis (AIS) in prepubertal women*

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Abstract

Generalized low bone mass has been well documented in patients with Adolescent Idiopathic Scoliosis (AIS). However, there is a lack of research linking calcium and Vitamin D deficiency to bone mass development and AIS in adolescent girls. In addition, no large-scale cross-sectional or longitudinal study has been conducted to determine factors contributing to low bone-mineral-density (BMD) and the impact of calcium and Vitamin D supplementation on prepubertal girls, i.e., the age most vulnerable to developing bone deformities like scoliosis and generalized osteopenia.

Adolescent Idiopathic Scoliosis (AIS) is a pathological lateral curvature of the spine of the idiopathic or familial variety. Nearly 80% of the patients happen to be female (Rogala, Drummond, & Gurr, 1978). It generally becomes noticeable between the age of 10 and 15 -- an age, when an adolescent is acutely image conscious. In all its degrees of severity, scoliosis affects approximately 2%-4% of the adolescent population (Kane, 1977). In approximately 7% of those affected (2% of the general population), idiopathic scoliosis will produce a truncal deformity which progresses throughout the rapid growth period of adolescence (Rogala, Drummond, & Gurr, 1978).

This thesis presents a literature review of how, if at all, calcium and vitamin D deficiency in prepubertal women may be related to the development of AIS. It is the most common type of spinal deformity confronting orthopedic surgeons (Lonstein, 1995). Although AIS has been studied since Hippocrates' time, it remains a disputed subject in orthopedic discipline, mainly because of its several varieties, unknown causes, and unpredictable outcome.

Introduction

Several studies of adolescent girls show that poor nutritional intake during the pre-pubertal age could have a significant impact on their bone health. (Lee et al, 2006).

Calcium in particular is needed for the growth of bones in both length and mass. (Lloyd, Martel, Rollings, Andon, Kulin, Demers, Eggi, Kieselhorst, Chinchilli, 1996; Bonjour, Theintz, Buchs, Slosman, Rizzoli, 1997). This thesis studies the impact of calcium and Vitamin D deficiency on bone development in prepubertal women. Although peak bone mass is not achieved until the age of 30, diets providing adequate calcium intake before and during adolescence are known to ensure peak rates of gain in bone mass (Barr & McKay, 1998).

Thereafter, the impact of calcium supplementation may not be very significant. (Winzenberg, Shaw, Fryer, Jones, 2006). Winzenberg and his associates (2006) did the largest ever meta analysis of 19 previous studies involving 2859 children to study the impact of calcium supplementation on children of varying ethnicity, physical activity, pubertal stage, type of supplementation (milk extract or other), duration of supplementation, and whether the calcium threshold was exceeded significantly that modified the effects on bone density at any site before they came to the conclusion that the impact was clinically insignificant in women, particularly after puberty.

Earlier studies also indicate that populations that consume the most cows' milk and other dairy products have among the highest rates of osteoporosis and hip fracture in later life (World Health Organization report, September 1998). Winzenberg and his associates (2006) study showed that although exercise significantly increased bone density and bone strength, calcium intake alone (Between 500 and 1500 mg) had no effect on the outcome

in adolescent girls studied prospectively for 12 years as they passed into young adulthood. (Lloyd et al, 2002)

A few major limitations with the Winzenberg (2006) study however were that: (a) It was limited only to the study of fractures and not generalized osteopenia and in particular AIS, therefore the results of this study cannot be extrapolated to girls with such conditions and (b) Calcium supplementation (300-1200 mg per day) in this study came from calcium citrate malate, calcium carbonate, calcium phosphate, calcium lactate gluconate, calcium phosphate milk extract, or milk minerals. The study did not directly use dairy foods as a supplement. Meanwhile, there have been older studies that show that supplementation with 1200 mg calcium/d is associated with increases in bone mineral measures in premenarcheal females. One particular study with young adults who bore stress fractures found a significantly high co-relation between low bone mineral densities in the femur and lumbar spine and low intakes of calcium and dairy products (Myburgh, Hutchins, Fataar, Hough, & Noakes, 1990).

Low bone mass and Adolescent Idiopathic Scoliosis (AIS)

Osteoporosis is a major public health issue, especially in women. (Jones, Nguyen, Sambrook, Kelly, Gilbert, Eisman, 1994; Cooley and Jones, 2001; Woolf and Pflieger, 2003). Meanwhile, multivariate analysis showed that AIS in girls was associated with lower bone mass. (Warren et al, 2005). This study found that AIS girls have lower body weight and BMI, longer segmental lengths and generalized low bone mass. In addition, inadequate calcium intake and weight-bearing physical activity were significantly associated with low bone mass in AIS girls during the peripubertal period. (Warren et al, 2005).

Peak bone mass is the maximal lifetime amount of bone tissue that is accrued in the skeleton during growth. Low peak bone mass is now considered an important determinant of low bone mineral density (Ott, 1991). Maximizing peak bone mass during the first few decades of life is currently seen as a potentially major strategy in osteoporosis prevention. The most rapid period of skeletal development occurs over several years in childhood and adolescence, accounting for 40–50% of the total accrual of skeletal mass (Bonjour et al, 1991; Slemenda, Reister, Hui, Miller, Christian, Johnston et al, 1994).

Thus this period may provide the best opportunity to maximize peak bone mass. Calcium is the major mineral in bone, and increasing dietary calcium intake has been proposed as an effective way of increasing peak bone mass. (Warren, Cheung, Tse, Xia Guo, Ling Qin, Ho Lee, Lau and Cheng, 2005). A significant increase in calcium requirements has been demonstrated during periods of most rapid growth and skeletal consolidation (particularly during infancy and adolescence, followed by childhood and young adulthood) (Matkovic, 1991).

A number of studies have assessed the effect on bone of increased dietary calcium (as supplements) in children between the ages of 7 and 14 yr (Nowson, Green, Hopper, Sherwin, Young, Guest, Smid, Larkins, Wark, 1997; Johnston, Miller, Slemenda, Reister, Hui, Christian, Peacock, 1992; Lloyd, Martel, Rollings, Andon, Kulin, Demers, Eggli, Kieselhorst, Chinchilli, 1996; Bonjour et al, 1997). These studies have all demonstrated increases in bone density with increased calcium intake. This positive effect on bone density, ranging from 1.6–5.1% gain compared with controls has been seen when total calcium intake is increased to 1200–1600 mg/d.

The complex clinical picture in AIS

Scoliosis represents a complex 3-dimensional deformity (Asher, 1999). A researcher, JIP James is credited with classifying idiopathic scoliosis according to the age of the patient at the time of diagnosis (James, 1954). Using his classification system, children diagnosed when they are younger than three years have infantile idiopathic scoliosis. Children diagnosed when they are aged 3-10 years have juvenile idiopathic scoliosis, and those older than 10 years have adolescent idiopathic scoliosis. These age distinctions, though seemingly arbitrary, have prognostic significance. For instance, Robinson and McMaster reviewed 109 patients with juvenile idiopathic scoliosis and found that nearly 90% of curves progressed, and almost 70% of these patients went on to require surgery (Robinson, 1996). These rates are much higher than the rates associated with other categories of idiopathic scoliosis. A real challenge is to predict which curves would progress significantly and which ones would not (Peterson, 1995).

Incidence of AIS

Although no demographic studies have been conducted, scoliosis is usually discussed in terms of its prevalence (i.e., the total number of existing cases within a defined population at risk). Rates may vary quite significantly based on what particular definition of scoliosis is used and what patient population is being studied. Stirling and his coauthors studied almost 16,000 patients aged 6-14 years in England and found the point prevalence of idiopathic scoliosis (Cobb angle $>10^\circ$) to be 0.5% (76 of 15,799 patients) (Stirling, 1996). The prevalence of scoliosis was highest (1.2%) in patients aged 12-14 years (Stirling, 1996).

Data such as these have helped reiterate the idea that the focus of screening efforts should be on children in this age group. When smaller Cobb angle measurements have been accepted (e.g., 6° or greater), a significantly higher sclerotic rate may be identified, such as the 4.5% rate reported by Rogala, Drummond and Gurr (1978). Other studies using the 10° definition of scoliosis have placed the overall prevalence in the 1.9-3.0% range (Albanese, 2002). Scoliosis has been suggested to develop more frequently in children born to mothers who are aged 27 years or older (Henderson, 1990).

Etiology of the disorder

The precise etiology of idiopathic scoliosis remains unknown. A primary muscle disorder has been postulated as a possible etiology of idiopathic scoliosis. The contractile proteins of platelets resemble those of skeletal muscle and calmodulin is an important mediator of calcium-induced contractility. Kindsfater and his colleagues from Denver studied the level of platelet calmodulin in 27 patients with adolescent idiopathic scoliosis (Kindsfater and Lawellin, 1994). Using indirect measurement methods, these researchers had conducted previous work indicating that increased levels of platelet calmodulin were associated with increasingly severe idiopathic scoliosis (Cohen, 1985). Using a direct measurement technique, they showed that patients with a progressive curve ($>10^\circ$ progression) had a statistically higher platelet calmodulin levels (3.83 ng/mcg vs 0.60 ng/mcg, $P<.01$) (Kindsfater, 1994). If such data is reproduced in larger studies, they hold the potential to allow clinicians to identify patients at higher risk of curve progression. An elastic fiber system defect (abnormal fibrillin metabolism) has been offered as one potential etiological explanation for idiopathic scoliosis (Hadley-Miller, 1994). However, such abnormal connective tissue has not been found universally in patients with idiopathic scoliosis. No clear cause and effect relationship has been established. Further research in this area is clearly warranted.

Pathophysiology of AIS

A lot has been written in recent years regarding the potential influence of melatonin on the development of idiopathic scoliosis. This has largely originated from studies in which the pineal gland was removed in chickens and scoliosis developed. These same studies suggested that the melatonin deficiency following pinealectomy might be the underlying

reason for the development of scoliosis. Bagnall and his coauthors studied pinealectomized chickens to which they administered therapeutic doses of melatonin (Bagnall, Raso and Moreau, 1999). They were unable to demonstrate any ability of the melatonin to prevent the development of scoliosis.

Nutritional and environmental factors related to AIS

Despite these studies, the interaction between calcium supplementation and pubertal status remains controversial, as the mechanism of the impact of augmented calcium intake during bone development is not very well understood. One view is that low bone mass and microarchitectural deterioration of bone tissue often leads to enhanced bone fragility and a consequent increase in fracture risk (WHO Study Group, 1994). According to genetic-environmental modeling (Flicker, Hopper, Rogers, Kaymakci, Green, Wark, 1995) up to 80% of population variability in bone mass is genetically determined, and 20% is explained by environmental factors, such as nutrition and physical activity.

In another study on twin girls (Nowson et al, 1997) with a mean age of 14 yr, calcium supplementation increased both hip (1.3%) and spine (1.5%) bone density significantly compared with co-twin controls over six months, despite 74% of our subjects having achieved menarche. In this experiment, the bone density difference was maintained during calcium supplementation to 18 months. However, a later, more recent review (Wosje and Specker, 2000) found the bone density results of several calcium supplementation trials in younger and older children to be inconsistent and unclear, with some trials observing significant effects at different pubertal ages and at some bone sites, but not others.

Individual clinical trials of calcium supplementation (Jones et al, 1994; Chan, Hoffman and McMurry, 1995; Lanou, Berkow, Barnard, 2005; Jadad, Moore, Carroll, Jenkinson, Reynolds, Gavaghan, 1996) and dairy products (Chan et al, 1995) have shown increases in bone mineral density in children, although the increases may not be maintained.(Lanou et al, 2005)

Narrative reviews have concluded that overall calcium supplementation seems to have a modestly favorable effect on bone outcomes at the end of the treatment period (French and Fulkerson, 2000; Wosje and Specker, 2000; Lanou et al, 2005). However, a latter day meta analysis by Winzenberg, et al (2006) indicates that calcium supplementation has limited impact on bone mineral density. The only site where they did find an impact was the upper limb and even here the effect was small, equivalent to about a 1.7 percentage point greater in the supplemented group compared with the control group, which persisted even after supplementation stopped.

Nonetheless, the authors concluded that this small increase in upper limb bone mineral density is unlikely to result in a clinically important decrease in the risk of fracture.

Importantly, the researchers found no effects at other sites where fracture is common—namely, the femoral neck and lumbar spine.

Meanwhile, milk-based and other kind of supplementation has also been assessed to determine if dairy products are better for promoting bone integrity than other forms of calcium supplementation. (Lanou et al, 2005). The authors of this study also concluded that literature did not support recommendations for consumption of dairy products for bone health end points in children and young adults. They also called into question the public health importance of the modest benefits of high dose calcium.

Treatment options in AIS

From the previous discussion, it is clear that adequate calcium supplementation can reduce the chances of AIS in prepubertal women. There is however considerable debate as to how much supplementation is enough for the target group.

How much supplementation is adequate?

The study done by Winzenberg, et al (2006) found that during supplementation, the magnitude of changes in bone density outcomes was similar (i.e., negligible) even when the total calcium intake exceeded the threshold of 1400 mg/day estimated in scientific literature (Matkovic and Heaney, 1992; Jackman, Millane, Martin, Wood, McCabe, Peacock, 1997).

A study by Warren et al (2005) for instance shows that calcium intake in AIS is too low (< 400 mg/day) to be sufficient for optimal bone mineralization. Osteopenia in AIS may therefore result from sub-optimal bone-mineralization qualitatively and quantitatively. Such subjects fail to catch-up with abnormally escalated bone growth during peripubertal period.

Meanwhile, results of longitudinal data produced by the same authors showed that BMD accretion in AIS was persistently reduced throughout adolescence when compared with age-matched controls. In effect, AIS with severe curve-severity appeared to have lower BMD.

The impact of calcium supplementation in identical twins

In a study conducted by Johnston et al. (1992), the researchers found no impact of increased calcium intake on bone density in female twins who were either postmenarcheal or who passed through puberty during the study. However, those twins

who were premenarcheal showed significant BMD increases in the lumbar spine and distal radius.

In this study, Johnston et al. (1992) examined the effect of calcium supplements on bone mineral density in pairs of identical twins. One twin received the calcium supplement while the other received a placebo. After three years of supplementation, the prepubertal twin who received calcium increased his or her bone mass significantly more than his or her twin who received the placebo at most of the bone sites examined.

However when the twins entered puberty or were postpubertal at the end of three years, there were no significant differences in bone mass between the calcium supplemented and placebo twins. This indicates that nutritional deficiencies can be made good for only up to a certain age, in adolescent girls at least. Thereafter the impact is more difficult to neutralize. Other studies using calcium isotopes have also found that girls retain more of the absorbed calcium before puberty and during early puberty (Abrams & Stuff, 1994).

This may explain why the calcium supplements had less of an effect on bone mass in the pubertal and postpubertal twins.

Is there a correlation between age, sex and calcium supplementation?

Due to paucity of scientific research in this area, the developmental stage at which calcium supplementation produces the greatest bone effects remain a controversial subject. Experts meanwhile continue to recommend adequate intake of calcium for youth ages nine to 18 years. For girls it is generally 1,300 milligrams per day. Several studies of adolescent female subjects have found that girls participating in aesthetic sports such as gymnastics and ballet consume far less than this recommended amount (Benardot,

Schwarz, & Heller, 1989; Benson, Gillien, Bourdet, & Loosli, 1985; Moen, Sanborn, & Dimarco, 1992).

The greatest acquisition of skeletal mass occurs over several years in late childhood and adolescence (accounting for 40–50% of adult total body bone mineral) (Bonjour et al, 1991; Slemenda et al, 1994). This period provides a window of opportunity when interventions may have their maximal effect to increase peak bone mass and reduce fractures later in life. These results indicate that calcium supplementation by an average of 914 mg/d in females before menarche is effective in enhancing bone accrual, at both the TH and LS and TB BMC after 12 months of intervention.

In one particular study (Melissa et al, 2004) a significant increase in TH aBMD (adjusting for age, height, and weight) was maintained after 18 months, but not after 24 months of intervention. Further TB BMC remained 3.7% higher in the twins taking calcium after 24 months. Although the dropout rate at 18 and 24 months did not enable the researchers to detect sustained effects at the spine, yet they did detect effects on TB BMC.

They observed that the effect of calcium supplementation waned over time. One possible explanation for this is that the administered calcium dose diminished over time in relation to body mass and skeletal mass due to rapid growth at this stage of life (for example, total body bone mineral increased by 38% over the 24 months of the trial).

As discussed earlier, a few calcium intervention studies have demonstrated significant differences in outcomes between pre- and postpubertal subjects (Johnston et al, 1992; Lloyd et al, 1996).

Later studies also report a 1.9% greater increase with calcium at 6 months rising to 2.4% at 18 months, compared with our previous study with a 1.3% effect after 12 months

(Nowson, 1997). Johnston et al. (1992) also found a significant effect on BMD with increased calcium intake (average, 719 mg calcium/d as citrate malate) in 22 prepubertal monozygotic twin pairs. Significant increases of 5.1% at the distal radius (cortical bone) and 2.8% at the lumbar spine (more trabecular bone) were observed, but there was no effect of calcium in the 23 pairs of monozygotic twins who were postpubertal or who passed through puberty during the study period.

Meanwhile, Molgaard and his associates (Molgaard, Thomsen and Michaelsen, 1999) and Bailey and associates (Bailey, Martin, McKay, Whiting, Mirwald, 2000) indicated that a significant relationship of bone accretion with pubertal stage occurs in boys and girls, with the peak annual accretion occurring earlier in girls (13 yr) than boys (14 yr). Further tanner stage (Einhorn, 1992) has been found to be a significant determinant of BMD in girls, but not in boys. Therefore, the underlying rates of change in bone mineral measures may well differ between girls and boys of the same age, and responsiveness to interventions may differ. Bonjour and co-workers (1997) found that supplementation with 804 mg calcium/d added to foods in prepubertal females for 48 wk resulted in a 1.6–2.4% increase in bone density compared with controls at various sites. They also reported that gains in BMD were more pronounced in girls on a low calcium intake before the study. Lloyd *et al.* (1996) reported similar results but with a substantially smaller level of calcium dose (360 mg/d). Approximately 32% of their female population had reached menarche compared with 5% of our female twins at the end of the first 12 months. Lloyd *et al.* (1996) reported that among subjects with above-median Tanner score; the calcium-supplemented girls had higher rates of bone acquisition than the placebo group. Dairy products like milk, cheese, and yogurt are the richest food sources of calcium in the diet.

Other good sources include tofu, broccoli, turnip greens, and orange juice and fruit drinks that have been fortified with calcium.

Is there a link between vitamin D deficiency and idiopathic scoliosis?

Besides calcium, Vitamin D deficiency has also been found to be linked with idiopathic scoliosis. A team of scientists at the All India Institute of Medical Sciences (AIIMS), New Delhi, India, has done a recent study linking low vitamin D levels to bone disorders. (www.live.mint.com, July 11, 2008) The research led by Ravinder Goswami of the department of endocrinology and metabolism at AIIMS lends credence to the fact that vitamin D deficiency can lead to life threatening emergencies in young population that has not developed protective bio-adaptation over time.

After their first systematic study of blood serum in 2000, which showed more than 75% of healthy people studied in northern India had vitamin D deficiency; this group of researchers has shown that though our skin has darkened while adapting to tropical climate, there is no bio-adaptation to this deficiency. In other words, the dark skin, which prevents ultraviolet rays mediated vitamin D to be formed in the body, does not lead to over-expression of vitamin D receptor, a hormone that regulates calcium levels in the body. As a result, say researchers they suffer from bone disorders like rickets, osteomalacia and osteoporosis, which are widely prevalent in the subtropics.

Goswami's two new studies were recently published in the *British Journal of Nutrition* and *European Journal of Clinical Nutrition*. (www.live.mint.com, July 11, 2008)

This study elaborates that in the early stage of vitamin D deficiency, our body adapts by increasing the parathyroid hormone in the blood, which helps in maintaining the normal

calcium levels, and, hence, the deficiency is not easily detectable. However, in the long run, this leads to bone re absorption (bone breaks down to release calcium in the blood) and osteoporosis (reduction in bone density which enhances risks of fracture).

When it comes to bone health, vitamin D and calcium go hand in hand, as the former helps in the absorption of the latter. The prevalent dietary calcium intake is 307 -340mg in urban population and 263-280mg in rural population, which is less than a third of the required calcium (1 gm/day). As a consequence, even though these people live in the sunniest part of the globe, they remain deficient in vitamin D.

All this calls for a national policy on vitamin D fortification of food, just as is common in the West. The overarching claim for fortification comes from Goswami's other study which shows that 60,000 units (IU) of vitamin D taken once a week for eight weeks along with 1g of elemental calcium every day restored the baseline vitamin D level of 5-7 nanogram/millilitre to the ideal level of 32ng/ml. The sufficient level is 20ng/ml. But the levels dropped to 9.6ng/ml one year after vitamin D supplements were stopped.

Therefore, direct exposure to sunlight, at least for half-an-hour a day, is what researchers suggest for good vitamin D intake.

In this context, a Japanese study (Masatoshi, 2000) found a definite link between vitamin D receptor (VDR) gene polymorphisms and idiopathic scoliosis. The purpose of this study was to determine whether DNA polymorphisms in the VDR gene were related to the pathogenesis of adolescent idiopathic scoliosis. The results based on a study of 217 girls with adolescent idiopathic scoliosis suggested that there was an association between curve severity and menarcheal age and that growth in girls with adolescent idiopathic scoliosis differed from that in normal girls, but this cannot be attributed to the VDR gene.

Two hundred and seventeen girls with adolescent idiopathic scoliosis were selected, and lymphocytes DNAs were extracted from peripheral blood, and the VDR gene, which contains the endonuclease Fok I and the Apa I sites was amplified by PCR. The mean. \pm .SD Cobb's angle of the highest magnitude was 30.6 ± 12.9 degrees. Stature was 158.3 ± 5.6 cm, arm span was 160.0 ± 13.4 cm, while age at menarche was 12.3 ± 1.1 years (mean. \pm .SD). The distribution of the VDR genotypes for the Fok I site was FF: 45.6%, Ff: 46.5%, and ff: 7.8%, and that for the Apa I site was AA: 10.4%, Aa: 47.5%, and aa: 42.1%.

The frequency of the VDR genotypes for the Fok I and Apa I sites was not statistically different from that of normal girls. Neither height, arm span, nor menarcheal age was associated with the Fok I and Apa I site polymorphisms. There was an association between curve severity and menarcheal age, however, curve severity was not associated with the Fok I and Apa I site polymorphisms. VDR gene polymorphisms were not related to height and puberty in girls with idiopathic scoliosis.

Nonetheless, the authors did suggest that growth in girls with adolescent idiopathic scoliosis differed from that in normal girls, and that some other factor (other than VDR gene) could be responsible for pathogenesis of idiopathic scoliosis in adolescent girls that needs to be studied. Till date, no conclusive link has been scientifically established between Vitamin D deficiency and the progression of idiopathic scoliosis in adolescent girls.

Is AIS related to culture and poor nutritional habits?

The endemic nature of AIS suggests that here could indeed be such a link. There have been no controlled demographical studies of this nature.

Limitations and future recommendations

From the above discussion, it is clear that there is continuing uncertainty about the impact of calcium and Vitamin D deficiency on optimal accrual of bone mass. Although there is no denying that dietary calcium does appear to have some fundamental role in the development of growing bones, this role has not yet been scientifically studied.

What is clear from the available research is that this calcium must be absorbed in sufficient quantities in order to adequately provide for periods of rapid growth (such as infancy and adolescence) and to offset daily excretory losses that would otherwise deplete previously obtained skeletal reserves (Ilich and Kerstetter, 2000).

In this sense, there could be threshold requirement for dietary calcium and possibly for Vitamin D as well that are determined predominantly by the skeletal needs. This implies that the skeletal response will occur when calcium intake is increased from deficiency levels to a threshold zone. This implies that calcium intake above this threshold will probably not produce additional gains in bone mass (Ilich and Kerstetter, 2000) although this conclusion too needs the support of further investigation.

Heaney (2001) has however estimated that calcium threshold levels for optimally nourished children and adolescents are approximately 1400–1600 mg/d. It has been observed that during periods of rapid growth, calcium absorption is up-regulated to meet the body's needs. Mean height velocity has been shown to peak at approximately 12 yr of age in females (Matkovic, 1991).

The use of female twins is good in the sense that it can account for many genetic and environmental confounders (Wark and Nowson, 2003), in contrast to a host of earlier studies based on unrelated individuals. In any case, the co-twin design also has greater

statistical validity than a comparable study of unrelated individuals with a similar sample size, in part due to the matching of subjects for age, genetic and environmental factors, skeletal maturity, and anthropometric factors (Hopper, Green, Nowson, Young, Larkins, Wark, 1998).

The only potential problem with the co-twin intervention design is the possibility of crossover, particularly when the co-twins cohabit. However, even in this case, each crossover would be predicted to reduce rather than exaggerate any treatment effect.

Conclusion

The importance of preventing generalized osteopenia in the control of AIS progression during the peripubertal period cannot be overemphasized. Since the incidence of Adolescent Idiopathic Scoliosis (AIS) remains high in certain far eastern communities, an environmental cause for the spinal disorder cannot be overruled.

As of now, there are few, scientifically controlled studies performed on children with low baseline calcium intakes. Studies with purely postpubertal and peripubertal sample of children are even fewer. Given that calcium accumulation in the skeleton accelerates during puberty (Bonjour et al, 1991; Abrams, O'Brien, Stuff, 1996) the paucity of data in the peripubertal period is an important gap.

Needless to say, more research is required in children with low calcium intakes and in peripubertal children. Given the small treatment effects seen with calcium supplementation, however, it may be appropriate to explore possible alternative nutritional interventions, such as increasing vitamin D concentrations (Moyer-Mileur, Xie, Ball, Pratt, 2003; Zhu Greenfield, Ma, Zhang, Hu, 2004) and intake of fruit and vegetables (Jones, Riley and Whiting, 2001)

Given the multi-causal nature in the progression of this disorder, an overemphasis on calcium supplementation represents a simplified approach to improving the bone health of children and adolescents. In my opinion, an excessive focus on calcium recommendations in nutrition policy and research draws attention away from a more comprehensive research on how to promote long-term bone health among young people. Public health would be better served by researching how other dietary and lifestyle factors, such as exercise and switching to a more natural (less processed) pattern of food

intake would benefit children's bones. Promising areas for further research include understanding the impact of regular exercise, vitamin D status, increasing raw fruit and vegetable consumption, limiting salt intake, limiting or avoiding animal protein, and avoiding smoking. Because the course of scoliosis did not seem to correspond with much published work, or with current hypotheses of etiology, a rethinking of the whole subject is advocated.

In the final analysis, it needs to be observed that other than its cosmetic benefit the promotion of a higher bone-mass in AIS may be important to strengthen the bone strength of the sclerotic spine, which may modify the natural course of scoliosis progression, and to reduce the risk of osteoporosis and bone fractures in future.

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Appendix

List of Abbreviations

Bone Mineral Density: BMD is a measure of bone density, reflecting the strength of bones as represented by calcium content. The BMD test detects osteopenia (mild bone loss, usually without symptoms) and osteoporosis (more severe bone loss, which may cause symptoms)

Adolescent Idiopathic Scoliosis (AIS): This is a lateral (side) curvature of the spine that can occur in children aged 10 to maturity. The spine may curve to the left or right. Sometimes AIS may start at puberty or during an adolescent growth spurt. Idiopathic means the abnormal curve develops for unknown reasons. There could be a genetic predisposition for some adolescents to develop AIS.

DXA: Dual energy x-ray absorptiometry

FA: Forearm

FN: Femoral neck

LS: Lumbar spine

TB BMC: Total body bone mineral content

TH: Total hip

Vitamin D receptor (VDR) gene: It plays a key role in interacting with vitamin D receptors and occurs in at least two different genetic types. Individuals who inherit the "weak" type of VDR gene from both parents may be at increased risk of several disorders.

Vitamin D: A fat-soluble vitamin occurring in several forms, especially vitamin D₂ or vitamin D₃, required for normal growth of teeth and bones, and produced in general by ultraviolet irradiation of sterols found in milk, fish, and eggs.