A 3-year physical activity intervention program increase the gain in bone mineral and bone width in prepubertale girls but not in boys - the prospective Copenhagen School Child Interventions Study – CoSCIS

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Abstract

Introduction: The aim of this study was to evaluate the effect of increasing the amount of time spent in physical education lessons on bone mineral accrual and gain in bone size in pre-pubertal Danish children.

Materials and methods: 135 boys and 108 girls, aged 6 to 8 years, were included in a school-based curriculum intervention program where the usual time spent in physical education classes was doubled to four lessons (180 min) per week. The control group were age matched children (62 boys and 76 girls) recruited from a separate community who completed the usual Danish school curriculum of physical activity (90 min/week). Dual energy X ray absorbtiometry (DXA) evaluated bone mineral content (BMC; g), bone mineral density (BMD; g/cm^2) and bone width at calcaneus and distal forearm before and after 3 years of intervention. Anthropometrics and Tanner stages were evaluated on the same occasions. General physical activity was measured with an accelerometer (MTI) worn for four days.

Results: In girls, the intervention group had a 12.5 % increase (p=0.04) in distal forearm BMC and a 13.2 % increase (p=0.005) in distal forearm scanned area in comparison with the girls in the control group. No differences were found between the intervention and control groups in the boys.

Conclusion: Increasing the frequency of physical education lessons for pre-pubertal children is associated with a higher accrual of bone mineral and higher gain in bone size after three years in girls but not in boys.

Keywords: Exercise intervention, bone mineral density, bone size, children, population based

Introduction

Osteoporosis is a major public health problem and even though the clinical consequences are mostly seen in old age, evidence is accumulating that predisposing factors arise in childhood (1). One approach to reducing the prevalence of osteoporosis could be to increase the peak bone mass laid down during childhood and adolescence, as it has been estimated that a 10% increase in peak bone mass will reduce the osteoporotic fracture risk in elderly people by 50% (2). Although as much as 60-80% of the variance in bone mineral density (BMD) may be explained by genetic factors, modifiable environmental factors such as diet and physical activity are also important determinants of BMD (3). One of the key determinants of skeletal development during growth is mechanical load (4-8). For example, cross-sectional studies have reported higher BMD in physically active compared to physically inactive children (9-11) and a higher BMD in the dominant arm of both tennis and squash players compared with the non-dominant arm (12). Prospective controlled and uncontrolled exercise intervention studies in volunteers (13;14) and in school based exercise interventions, including pre-pubertal and early pubertal children, have reported a higher bone mineral acquisition in the intervention group than in the control group (15-20). However, all but three (21-23) of these studies have modified the existing physical education curriculum and replaced this with specifically designed bone stimulating activities. In addition, the studies using the ordinary school curriculum in the intervention group have had a maximum duration two years. A longer duration of the study could capture additive beneficial effects a shorter intervention study may miss. This study was designed to investigate the effect of three years of increased physical education classes delivered as part of the usual school curriculum on bone health in pre-pubertal Danish children.

Methods

All children (n=1024) in all 18 preschool classes in two suburbs of Copenhagen (Ballerup and Taarnby) were invited to participate in a three-year non-randomised controlled intervention trial of physical activity, the Copenhagen School Child Intervention Study (CoSCIS). The local ethical committee at the University of Copenhagen approved the study (reference KA00011gm). Written informed consent from the parents or guardian was mandatory before inclusion.

The intervention consisted of the standard physical education lessons (PE lessons) used within the Danish school curriculum, with the volume increased to the equivalent of four school lessons per week (180 min/week) delivered as two weekly lessons. The control group continued to receive the usual two lessons per week (90min/week). In the Danish school curriculum the PE lessons take place every week though the whole school year from August to June, and are mandatory for every child. The physical education lessons were supervised by the usual teachers in both suburbs and were not modified in any way. In addition to the increased volume of physical education, the intervention schools were modernised with new playgrounds and gym facilities, and the teachers participated in additional re-education in physical education 3-4 times each year.

The city council of Ballerup decided in 1999 that the intervention should be carried out in all schools in the community from preschool to 3rd grade. Hence children from Ballerup served as non-randomised intervention group and children from Taarnby as control group. Taarnby was selected because the community by comparison of social economic status and other community statistic was similar to Ballerup.

Seven hundred and four children (69%) with a mean age of 6.7 ± 0.4 (SD) (range 5.6 - 8.2) years agreed to participate; 224 boys and 190 girls from Ballerup and 144 boys and 146 girls from Taarnby. Anthropometric, bone measurement and habitual physical activity (accelerometer) data were collected at baseline. Accelerometer data was collected from 642 children. Of these, 16 files were lost in the download process and accelerometers were not returned from six participants. A further fifty-eight children failed to meet the criteria of at least 8 hours of recording for three days out of four registered, giving a final number of 297 boys and 265 girls with complete data to be included in the baseline evaluation. Three years later the children were re-tested. Fifty-one children had withdrawn their consent to participate, 28 had moved from the two districts and 11 did not attend the testing, leaving 614 children to participate in the follow-up examination. At follow-up, anthropometrics, bone measurement and physical activity data were once more collected. Among the participants at follow-up, 20 children were not scanned due to a fault with the DXA scanner at the test occasion, leaving 594 children to be scanned. Physical activity data were not obtained from 64 children, as they did not use the accelerometers due to sickness, holidays or technical problems with the instruments. Only children with complete data at baseline and follow-up were included in the present analysis. Complete data were collected in 379 children, 135 boys and 108 girls from the intervention group and 62 boys and 76 girls from the control group. Testing of schools alternated between the two areas; all baseline measurements were performed between December 2001 and June 2002 in preschool and follow-up measures were completed between September 2004 and May 2005 with the children now in 3rd grade. Measures were completed in a gym or in a classroom at the schools.

Bone mineral content (BMC; g) and bone mineral density (BMD; g x cm^{-2}), scanned area of calcaneus of distal forearm were evaluated by peripheral dual energy X ray absorbtiometry (DXA; LUNA PIXI ®, software version: 1.4 CD_{MDD}) in the distal end of the left and right forearm and the left and right os calcanei. The region of interest (ROI) in os calcaneus was automatically positioned and based on predefined anatomical landmarks and the ROI in the forearm was automatically positioned 30 mm proximal to the site of the radius and ulna junction. With this equipment and software, the scanned area is proportional to the size of the scanned bone. The choice of ROI, the analysis of scan was made exactly in the same way in both scans, in all children both in preschool and at follow up. In this report we present the average value from right and left extremities.

The level of habitual physical activity (PA) was measured by the MTI 7164 activity monitor (Manufacturing Technology Inc., Fort Walton Beach, Fl). The MTI activity monitor samples acceleration at 10 Hz and integrates this over an epoch defined by the user. As children's habitual physical activity is characterised with short bursts (less than 10 seconds) of activity (21) the epoch was set at 10 seconds. The choice of epoch gave a registration time of 4 days; two weekdays, and the weekend. The children attached the MTI one day before it was set to record the activity, to accustom the child to the monitor and prevent artificially elevated measurements at the beginning of data recording. The MTI was secured as close as possible to the centre of gravity (i.e., lower back) using an elastic belt. The children were instructed to wear the monitor at all times except during water-based activity and when sleeping. All parents received a letter describing how the monitor should be worn. In order to distinguish true zeros from zeros recorded when the MTI was not worn, the data were cleaned as follows: all MTI files were screened for sustained periods of zero activity. Periods of 10 minutes or more with only zero counts were interpreted as the MTI not being worn and thus were removed from the file. Given these criteria, the data were included if the child had accumulated more than 8 hours of activity per day for at least three days. All units were frequently tested in a motor-driven device creating a known vertical acceleration, and all measurements were adjusted with a unit specific factor found in the test. Data were then adjusted for MTI unit using the calibration factor for each unit. A mean count per 10 seconds of observation was calculated for each child. The MTI variables were adjusted for total time that the monitor was worn by dividing number of monitored minutes per day and defined as the daily physical activity (PA counts/minutes).

Body height was measured by a portable Harpenden stadiometer to the nearest 0.5 cm with the child in bare stockinged feet standing upright against the stadiometer. Body weight was measured with the subjects lightly dressed to the nearest 0.1 kg using an electronic scale (Seca 882). Bicipital, tricipital, subscapular and suprailiac skinfolds were measured with a Harpenden skinfold calliper in the children by two experienced scientists according to conventional criteria and measuring procedures (22). A questionnaire used to report gender and physical activity during school breaks, active transport and playing outside in leisure time was completed by 586 children at baseline.

Identification of pubertal stage is assessed from a scale of pictures according to Tanner (Tanner 1962). Girls are staged according to breast development (b1-b5) and pubic hair growth (ph1- ph5). B1 means no development of breasts and b5 means full/finished development of breasts. Ph1 means no pubic hair yet, Ph5 means fully grown pubic hair.

For boys genital development (g1-g5) and pubic hair growth (ph1-ph5) are used. G1 means that the growth and development of the genitals has begun, G5 means fully-grown and mature development of the genitals. Pubic hair is rated as in girls.

The identification took place at the same day the other tests took place in 3rd grade. The children were asked to rate their stage of sexual maturity by comparison with the photographs and drawing of Tanner (Tanner 1962). The girls did that together with our female laboratory technician and the boys together with our male staff. This was done with respect to the children's privacy after a careful explanation of the procedures and purpose, which also was given to the parents whom was invited to "participate" in the assessment.

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 12.0. Descriptive statistics are presented as mean ± standard deviation (SD). Data that did not have a Gaussian distribution such as sum of four skin folds, were logarithmically transformed and the means of the log-transformed data were back-transformed to a geometric mean as described by Altmann (24). Group differences at baseline, at follow-up and when comparing the changes, were tested by an independent Student's t-test. Group differences in the changes of the bone variables during the follow-up was tested by analyses of covariance (ANCOVA) with baseline height, weight, bone mass (BMC or BMD) and changes in height (as to adjust for any difference in growth) as covariates. In order to avoid mass significance Bonferroni correction was used. All the children were finally divided into quartiles of baseline PA as to test if the least active had the greatest benefits of the intervention program. Sex differences in activity during school breaks and leisure time were analysed using the Chi-square test. A difference of $p < 0.05$ was regarded as statistically significant.

Results

Drop out analyses were carried out to compare height, weight and body mass index (BMI; kg/m^2) in the 31% non-participants and the 69% participants (out of the initial 1024 children). This examination was performed approximately one year after study start, when the first general, systematic medical examination of children in Denmark took place. This examination included 612 participants (out of the 704 baseline participants) and 277 non-participants (out of the at baseline 318 non-participants), a comparison that revealed no significant differences between participants and non-participants in age, height, weight or BMI, in neither boys nor girls (data not shown).

Tables 1 and 2 report demographic, physical activity and bone parameter measurements for boys and girls respectively, for both groups at baseline and at follow-up. In girls, the intervention group had a 12.5 % increase (p=0.04) in distal forearm BMC and a 13.2 % increase (p=0.005) in distal forearm scanned area in comparison with the girls in the control group. This was found despite a 4.1% (p=0.046) increase in body height in the control group compared with the intervention group (table 2) and no difference in mean physical activity level between the groups. No differences were found at baseline, at follow-up or in the changes over 3 years when comparing the boys in the intervention and control groups (table 1). It is of note that general physical activity measured by accelerometry did not differ between the groups despite of the doubling of PE lessons in the intervention group.

Questionnaire data reported that ninety-eight out of 281 girls (35%) preferred to play indoors during school breaks, whereas only 66 out of 289 boys (23%) did the same (p=0.001) (Figure 1). In addition, 148 out of 292 boys (51%) played more than five times per week outdoors during leisure time, compared to 118 out of 282 girls (42%) (p=0.02).

Discussion

This non-randomised controlled exercise intervention trial suggests that an increase in PE lessons in 6-8 years old children over 3 years is associated with skeletal benefits in girls but not in boys. Several previous school based prospective intervention (training) studies have demonstrated that exercise induces positive skeletal effects in pre-pubertal girls (25-27). These trials have reported 1.5 - 29 % greater bone mineral accrual in the intervention groups compared to controls. Similar, but smaller magnitude, beneficial effects of exercise on bone health have also been reported in boys (28;29). However, most published studies have modified the PE lessons by including specific osteogenic activities, such as jumping and skipping, and only a few studies have increased the duration of the ordinary school curriculum (30;31). This is an attractive approach when trying to evaluate a population based prevention program, as PE lessons are mandatory in Denmark, a fact that makes it possible to include all children, not only those who volunteer to exercise. Children with a minimal interest in PE and a minimal participation in other physical activities are perhaps those who will achieve most benefits from an intervention program, as the relative increase in the level of physical activity in these children will be greater than in their more active peers. This is why we chose the school as the intervention arena.

The difference in the outcome in the boys and the girls could be the result of the boys in general being more active than the girls. This is supported by the MTI data, where boys are approximately 10% more active than girls both at baseline and at follow up (table 1 and 2). This observation is also supported by previous reports (32-36). In addition as previously reported (29), the boys spent approximately 15% more time in high intensity activity than the girls. An increase in the school curriculum will thus confer a relatively lower increase in the total level of physical activity in boys than in girls. The underlying reason for this gender discrepancy in the level of physical activity is not known, but may be the result of habitual differences in children’s play activities. Data from the CoSCIS population at baseline support this view (Figure 1), reporting that boys prefer to play outside to a greater extent than girls. This may be one of the reasons why the boys are more physically active than the girls. In contrast, the girls in this study preferred to play indoors more than the boys, a place where sedentary activities are possibly more predominant. This hypothesis is not opposed by the current accelerometer data in this trial (Table 1 and 2). Another explanation for the differences in the outcome between the boys and girls could be the gender differences in BMC and BMD at age 6-8 years (at baseline). As previously reported (37), the boys in this cohort had a higher distal forearm BMC and BMD than the girls at baseline, while there was no difference in the calcaneus. Thus the girls and boys could show different timing in the accrual of bone mineral and bone size in early ages and thus also react differently at the same age to exposure to physical activity. It seems that the skeleton is most prone to react to environmental factors during periods with fast growth (38).

Finally, the differences in the outcome between the boys and girls could also be the result of gender discrepancies in maturation. Girls are in general more mature than boys in the same chronological age (39). In this study the girls are more mature than the boys evaluated by Tanner stage ($p<0.05$) (data not shown). A variety of studies have also reported that the skeleton is most responsive to mechanical load in the late pre- or early peri-pubertal period (13;14;40-44). That is, the girls in this study were probably closer to puberty than the boys, thus also probably more prone to respond to mechanical load than the boys.

The study by Valdimarssons et al. (45) reported even greater benefits from exercise in the girls than in this trial, with up to 29% greater changes in the intervention group after 12 months of intervention compared to up to 13% greater changes in this study. There could be several explanations for this. We introduced physical activity for four lessons per week given as two double lessons compared to one lesson five times per week in the studies by Valdimarsson et al and Linden et al. (31;46) Due to practical reasons, the intervention group had double lessons (1.5 hour) twice per week. One can therefore speculate that an impact on the skeleton every day is more prone to stimulate bone formation than a less frequent load. This is supported by animal studies which infer that the same load presented as everyday activity gives a higher skeletal response than the same load given during few session per week (6;47-49).

It was slightly unexpected to identify skeletal benefits in the forearm, since this is a non-weight bearing region and it is well known that mechanical load confers benefits only in the loaded regions (14;50-53). A possible explanation for this finding was that the school gymnastics included a lot of activities such as climbing ropes and ladders where arm strength was important and probably conferred a substantially higher relative load at the upper extremities in the intervention group. The larger accrual of distal forearm bone mineral and bone size than the similar accrual of calcaneal bone mineral and bone size do not oppose this hypothesis. An alternative explanation could be that the calcaneus was repeatedly loaded by everyday activities, other than the intervention, so that the extra physical activity in school did not induce substantial extra osteogenic stimulus in this region. The fact that these results only are seen in the girls could again be due the difference in play pattern with boys perhaps performing more “arm activities” than the girls. But this is only speculative and we have no data to support this.

The strengths of this study include the large population based sample size, the narrow age span and the longest prospective controlled exercise intervention study in children published to date looking at the effect on bone health. The population-based design is of particular importance when we, as in this study, try to evaluate if an exercise intervention program could be used as a prevention strategy to minimise the proportion of individuals with low bone mass in the society. Another study strength is the evaluation of bone size. There are previous cross-sectional studies indicating that highly intense exercise increases bone size (54;55), but this study suggest that this could be achieved with a more modest level of physical activity. This is of clinical relevance, as bone strength is not only dependent on BMD but also on skeletal geometry, architecture and bone size (56-59). For example, women with spine fractures have smaller lumbar spine vertebrae but normal femoral neck size while women with hip fractures have a smaller femoral neck size but normal vertebral body size compared to controls (60). Also, straight mechanical calculations reveal the importance of bone size for resistance to fractures as bone strength increases by the fourth power of the radius of a tubular structure (61-64). Limitations include the non-randomised study design, a design that could include selection bias at baseline. However, there was no difference between the intervention and the control group at baseline in any of the measured variables. We had preferred a randomisation at individual level, but this was not possible to perform as the level of physical education in each region was decided by the city council, not by us. In addition, randomization within the classes would through time have led to enormous problems with children crossing over between the groups. Therefore we accepted that all schools from one specific region were chosen as the intervention schools, without individual randomization.

In summary, a moderate intensity school based exercise intervention program carried out over three years seems to induce positive skeletal effects in girls but not in boy, possibly due to boys having such a high level of physical activity independent of achieving extra training or not. Future studies must reveal whether an extension of the program closer to puberty, if a more intense exercise intervention program scattered throughout all weekdays and an intervention program in a more sedentary population could confer benefits also in boys.

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Table 1 Age, anthropometrics, physical activity (PA; count per minutes), bone mineral content (BMC), bone mineral density (BMD), bone size and pubertal development in boys at baseline, after 3 years and with the changes during the follow-up period. Differences between the intervention group and the control group at baseline, at follow-up and the delta values of the anthropometrics were tested by independent t-test. Differences in the delta values of the bone measurements were tested by ANCOVA with baseline height, weight, bone mass (BMC or BMD) and changes in height as covariates. Data presented as mean with SD and p-values.

Table 1	**Baseline**			**Follow-up (after 3 years)**			**Changes during the 3-years period**		
Boys	Inter-vention group (n=135)	Control group (n=62)	p-value	Inter-vention group (n=135)	Control group (n=62)	p-value	Inter-vention group (n=135)	Control group (n=62)	p-value
Age (years)	6.8 ± 0.4	6.8 ± 0.4	0.95	9.6 ± 0.4	9.6 ± 0.4	0.75	2.8 ± 0.1	2.8 ± 0.1	0.49
Height (cm)	124.2 ± 4.5	123.6 ± 5.2	0.39	140.3 ± 5.3	139.6 ± 6.0	0.45	16.1 ± 1.8	16.0 ± 2.5	0.66
Weight (kg)	24.4 ± 3.0	24.7 ± 3.6	0.54	33.6 ± 5.6	34.2 ± 6.2	0.49	9.3 ± 3.1	9.5 ± 3.4	0.60
Sum of 4 skinfolds (mm)[a]	22.5 ± 7.2	23.6 ± 8.8	0.26	26.9 ± 13.5	28.6 ± 16	0.28	4.4 ± 8.2	5.0 ± 9.8	0.51
PA (counts/min)	776.8 ± 213	804.9 ± 268	0.43	718.1 ± 201	698.0 ± 178	0.50	-58.6 ± 251	-106.9 ± 283	0.23
BMC Calcaneus (g)	0.75 ± 0.24	0.80 ± 0.23	0.19	1.38 ± 0.25	1.35 ± 0.26	0.40	0.63 ± 0.23	0.55 ± 0.20	0.16
BMC Distal forearm (g)	1.92 ± 0.30	1.97 ± 0.31	0.27	2.33 ± 0.38	2.35 ± 0.45	0.72	0.41 ± 0.31	0.39 ± 0.39	0.94
BMD Calcaneus (g/cm^2)	0.32 ± 0.04	0.31 ± 0.04	0.35	0.41 ± 0.05	0.40 ± 0.06	0.34	0.09 ± 0.04	0.09 ± 0.04	0.50
BMD Distal forearm (g/cm^2)	0.29 ± 0.03	0.29 ± 0.03	0.60	0.31 ± 0.04	0.31 ± 0.04	0.72	0.02 ± 0.03	0.02 ± 0.03	0.40
Scanned area Calcaneus	2.38 ± 0.67	2.53 ± 0.61	0.12	3.38 ± 0.40	3.38 ± 0.44	0.99	1.0 ± 0.63	0.85 ± 0.57	0.90
Scanned area Distal forearm	6.66 ± 0.68	6.78 ± 0.59	0.23	7.49 ± 0.82	7.58 ± 0.84	0.49	0.83 ± 0.79	0.80 ± 0.73	0.60
Tanner - Pubic hair				1.0 ± 0.1	1.0 ± 0.1	0.98			

a: geometric mean

Table 2. Age, anthropometrics, physical activity (PA; count per minutes), bone mineral content (BMC), bone mineral density (BMD), bone size and pubertal development in girls at baseline, after 3 years and with the changes during the follow-up period. Differences between the intervention group and the control group at baseline, at follow-up and the delta values of the anthropometrics were tested by independent t-test. Differences in the delta values of the bone measurements were tested by ANCOVA with baseline height, weight, bone mass (BMC or BMD) and changes in height as covariates. Data presented as mean with SD and p-values

Table 2	**Baseline**			**Follow-up (after 3 years)**			**Changes during the 3-years period**		
Girls	Inter-vention group (n=135)	Control group (n=76)	p-value	Inter-vention group (n=135)	Control group (n=76)	p-Value	Inter-vention group (n=135)	Control group (n=76)	p-value
Age (years)	6.7 ± 0.3	6.7 ± 0.4	0.37	9.5 ± 0.4	9.4 ± 0.4	0.29	2.8 ± 0.1	2.8 ± 0.1	0.53
Height (cm)	121.5 ± 4.9	122.5 ± 4.6	0.17	137.9 ± 6.6	139.6 ± 5.8	0.06	16.3 ± 2.6	17.1 ± 2.7	0.046
Weight (kg)	23.6 ± 3.2	23.9 ± 3.8	0.55	32.6 ± 5.7	33.3 ± 6.4	0.50	9.0 ± 3.1	9.3 ± 3.2	0.53
Sum of 4 skinfolds (mm)[a]	27.7 ± 6.4	28.2 ± 10.0	0.26	33.6 ± 13.0	33.2 ± 18.4	0.51	6.6 ± 9.2	5.0 ± 11	0.88
PA (counts/min)	696.2 ± 175	717.0 ± 143	0.39	640.4 ± 159	648.0 ± 167	0.75	-55.8 ± 196	-69.0 ± 182	0.64
BMC Calcaneus (g)	0.77 ± 0.23	0.77 ± 0.21	0.98	1.26 ± 0.27	1.29 ± 0.25	0.45	0.49 ± 0.20	0.51 ± 0.20	0.90
BMC Distal forearm (g)	1.75 ± 0.26	1.77 ± 0.29	0.59	2.14 ± 0.34	2.12 ± 0.40	0.61	0.40 ± 0.33	0.35 ± 0.27	0.04
BMD Calcaneus (g/cm^2)	0.32 ± 0.05	0.32 ± 0.05	0.87	0.41 ± 0.06	0.41 ± 0.06	0.52	0.09 ± 0.04	0.09 ±0.04	0.88
BMD Distal forearm (g/cm^2)	0.28 ± 0.03	0.28 ± 0.03	0.46	0.29 ± 0.03	0.29 ± 0.04	0.95	0.01 ± 0.03	0.01 ± 0.03	0.29
Scanned area Calcaneus	2.44 ± 0.64	2.43 ± 0.54	0.90	3.08 ± 0.44	3.11 ± 0.43	0.60	0.63 ± 0.52	0.68 ± 0.49	0.80
Scanned area Distal forearm	6.28 ± 0.71	6.31 ± 0.72	0.80	7.42 ± 0.82	7.29 ± 0.84	0.31	1.14 ± 0.76	0.99 ± 0.60	0.005
Tanner - Pubic hair				1.2 ± 0.4	1.2 ± 0.6	0.26			

a: geometric mean

Figure 1: Physical activity during school breaks and during leisure time in preschool. N = 574