SHORT REPORT

Bone density in asthmatic children treated with inhaled corticosteroids

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Abstract

Volumetric trabecular bone mineral density of the lumbar spine (vTBMD) and distal radius (rTBMD) were measured in 20 prepubertal white asthmatic children treated with moderate to high doses of inhaled corticosteroids. The median standard deviation score for vTBMD (0.20, −0.56 to 2.09) and rTBMD (−0.04, −0.82 to 1.39) were within the normal range.

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The British Thoracic Society (BTS)[1] asthma treatment guidelines recommend treatment with inhaled corticosteroids (ICS) in children with moderate to severe asthma. While ICS agents are safer than oral corticosteroids, there is concern that these agents in high doses might have potential for systemic side effects such as adrenal suppression, poor growth, cutaneous atrophy, and possibly reduced bone mineral density (BMD).[2] The aim of this study was to investigate the effect of moderate to high doses of ICS on volumetric trabecular BMD of lumbar spine and distal radial BMD in prepubertal asthmatic children.

Subjects and methods

Twenty prepubertal (Tanner stage 1) white children (11 girls, 9 boys; aged 4–9 years, median age 7.6 years) with chronic asthma were recruited to the study from two specialist paediatric asthma clinics. All were taking moderate to high dose ICS as defined by the current BTS asthma treatment guidelines[1] (greater than than 400 µg/day beclomethasone dipropionate or budesonide, or greater than 200 µg/day fluticasone propionate). Children with chronic illnesses, apart from asthma and a history of fractures or immobilisation in the last three years, were excluded from the study. Information on the average daily dose of ICS and the total dose of oral prednisolone over the 12 month period prior to BMD measurements was collected from the clinic and general practitioner records. Five children were treated with beclomethasone dipropionate, nine with budesonide, and six with fluticasone propionate, administered either by hand held dry powder devices or pressurised metered dose inhalers used with large volume spacer devices. The study was approved by Manchester Ethics Committee and written consent was obtained from parents. Weight was measured to the nearest 0.1 kg and height to the nearest mm. Volumetric trabecular BMD of T12 to L3 vertebrae (vTBMD) was measured by quantitative computed tomography (QCT; Philips Tomoscan SR 4000 scanner, Philips Medical Imaging, Best, Netherlands) using a single energy, low dose scanning technique, and expressed as mineral equivalents of K_2HPO_4 in water. Precision in healthy adults is 1.3%. Distal radial volumetric trabecular BMD (rTBMD) was measured by peripheral quantitative computed tomography (pQCT; Stratec-Norland XTC 2000, Stratec-Norland, Medizintechnik, Pforzheim, Germany). Measurements were made proximal to the distal radial epiphysis at 4% of the forearm length. Precision in healthy adults is 0.78%. The BMD values were transformed into standard deviation scores using the in house rTBMD data from healthy white children and published vTBMD values in children from the USA.[3] Height standard deviation scores were calculated using the 1990 UK growth reference data.[4]

All data are expressed as median and range. A single group Wilcoxon signed rank test was used to determine if median standard deviation scores for vTBMD, rTBMD, and height were significantly different from zero. The Mann–Whitney U test was used to compare the differences in the median values of height,

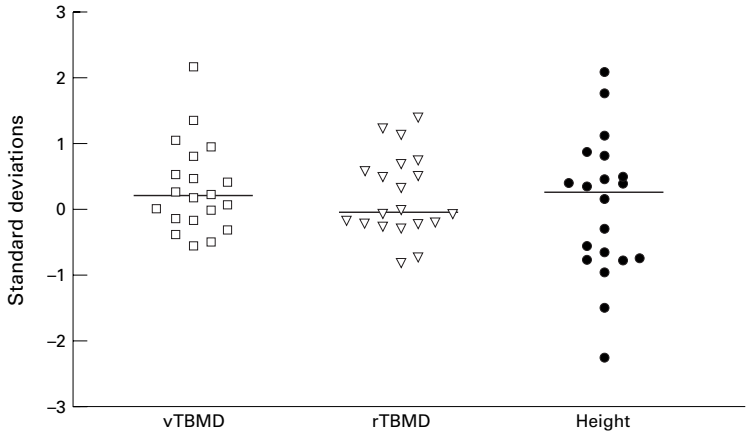

Figure 1 Scatter plot of standard deviation scores of lumbar spine trabecular BMD, distal radial trabecular BMD, and height for the whole group. The horizontal bars represent median values, which were not significantly different from zero.

Table 1 Height, weight, and trabecular BMD of lumbar spine and distal radius in children treated with different inhaled corticosteroids (ICS)

	Beclomethasone dipropionate	*Budesonide*	*Fluticasone propionate*
Number of subjects	5	9	6
ICS dose (μg/m^2/day)	778 (367–1164)	819 (382–2381)	444 (316–1034)
Total dose of oral steroids (mg) in the previous year	40*	360 (90–1000)	408 (165–460)
Height (cm)	121 (114.5–135.5)	120 (110–142)	128 (111–135)
Standard deviation score	0.41 (−0.78 to 1.14)	−0.72 (−2.2 to 2.1)	0.67 (−0.65 to 1.8)
Weight (kg)	22.8 (19–31)	22.0 (21–35)	27.6 (19–46)
Lumbar spine volumetric TBMD (mg/cm^3)	174 (148–228)	164 (146–179)†	190 (158–204)
Standard deviation score	0.34 (−0.49 to 2.16)	0.02 (−0.56 to 0.54)†	0.89 (−0.16 to 1.35)
Distal radial volumetric TBMD (mg/cm^3)	180 (154 to 213)	187 (182 to 210)	215 (164 to 233)
Standard deviation score	−0.19 (−0.73 to 0.75)	−0.07 (−0.25 to 0.68)	0.83 (−0.82 to 1.39)

All data are expressed as median and range.
The median vTBMD and vTBMD standard deviation scores in the fluticasone propionate treated children were higher than in those treated with budesonide ($p < 0.05$).
*Only one patient received oral steroids in the beclomethasone dipropionate treated group.
†$p<0.05$ compared to fluticasone propionate group.

weight, vTBMD, and rTBMD in the three ICS groups. Significance was based on two tailed tests; $p < 0.05$ was considered to be significant.

Results

For the whole group, the median standard deviation scores for vTBMD, rTBMD, and height were 0.20 (−0.56 to 2.09), −0.04 (−0.82 to 1.39), and 0.26 (−2.24 to 2.09) respectively (fig 1), which were not significantly different from zero. Table 1 shows the results for individual ICS. Fluticasone propionate is generally considered to be twice as potent as budesonide and beclomethasone dipropionate, which is reflected in the lower median prescribed dose of this ICS, as shown in table 1. The median vTBMD and vTBMD standard deviation scores in fluticasone propionate treated children were higher than in those treated with budesonide.

Discussion

While reduced BMD has been reported in asthmatic adults treated with ICS,[5] results of studies in children suggest that these agents do not have adverse effects on BMD measured using dual energy *x* ray absorptiometry (DXA).[6] DXA provides a measure of areal bone mineral density (aBMD, mg/cm^2) that is calculated by dividing the total (cortical and trabecular) bone mineral content by the projected area of the region of skeleton scanned. As the volume of the scanned bone is not measured, aBMD fails to distinguish between changes in the mineral density and bone size in growing children. This is an important consideration, as chronic childhood asthma may lead to delay in growth and puberty, whereas treatment with high dose of ICS might impair both the growth[5] and mineralisation of the skeleton. Finally, DXA does not allow selective measurement of the trabecular bone, which is more likely to be affected by corticosteroids than the cortical bone.

In this study, we used QCT and pQCT to selectively measure volumetric BMD of the metabolically active trabecular bone component of the spinal vertebral bodies and distal radius, respectively. Unlike aBMD, volumetric BMD is not affected by bone size and in prepubertal children, its values change very little with age.[3] We found that volumetric vTBMD and rTBMD of prepubertal asthmatic patients treated with moderate to high doses of ICS were within the normal range. There are several limitations of our cross sectional study, including the effect of the different inhaler devices used, inhaler technique, and compliance on the amount of drug actually inhaled by patients. We were not able to obtain accurate data on lifetime dose of ICS and oral corticosteroids from patient records. Finally, our conclusions cannot be extended to the pubertal period, when there is a significant increase in volumetric trabecular BMD.[3] Nevertheless, our results should reassure parents and health professionals that ICS do not adversely affect trabecular BMD of the axial and appendicular skeleton in prepubertal asthmatic children. A prospective, randomised controlled trial is required to confirm our finding that fluticasone propionate is less likely to affect trabecular BMD in prepubertal children than budesonide or beclomethasone dipropionate.

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