Nutrition and Bone Density in Boys with Autism Spectrum Disorder

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ABSTRACT

Background Boys with autism spectrum disorder (ASD) have lower bone mineral density (BMD) than typically developing controls. Differences in diet and exercise may contribute to low BMD.

Objective Our aim was to examine macro- and micronutrient intakes and self-reported physical activity in boys with ASD compared to TDC and the relationship of these variables with BMD.

Design/methods We conducted a cross-sectional study of 49 boys (25 ASD, 24 typically developing controls) assessed for 3-day food records and physical activity records, and BMD of the whole body less head, hip, and spine using dual-energy x-ray absorptiometry. Fasting levels of 25(OH) vitamin D and calcium were obtained.

Participants Participants were adolescent boys, aged 8 to 17 years, recruited from a clinic population (ASD) or community advertisements (ASD and typically developing controls) matched for age.

Results ASD participants were approximately 9 months younger than typically developing control participants on average. Body mass index and serum vitamin D and calcium levels were similar. Boys with ASD consumed 16% fewer calories, with a larger percentage obtained from carbohydrates, and 37% less animal protein and 20% less fat than typically developing controls. A lower proportion of ASD participants were categorized as "very physically active" (27% vs 79%; $P<0.001$). BMD z scores were 0.7 to 1.2 standard deviations lower in ASD than typically developing controls at all locations. Higher animal protein, calcium, and phosphorus intakes were associated positively with bone density measures in boys with ASD.

Conclusions Compared to typically developing controls, boys with ASD had lower protein, calcium, and phosphorus intakes, activity levels, and BMD z scores at the lumbar spine, femoral neck, total hip, and whole body less head. Protein, calcium, and phosphorus intakes were associated positively with BMD.
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AUTISM SPECTRUM DISORDER (ASD) IS A NEURO-developmental disorder characterized behaviorally by impairments in social interactions and communication and atypical, restricted, and repetitive patterns of behaviors, with rates of up to 1 in 68 children in the United States.[1] Nutrition management of children with

ASD is a challenge because children frequently have a restricted diet, often self-imposed, limited by taste or texture.[2] Their diet may also be limited by medical illness or parent choice of a restricted food type, such as gluten-free and/or casein-free diets.[3,4] Furthermore, concurrent gastrointestinal diseases in children with ASD may affect absorption of nutrients.[5]

Peak bone mass is an important determinant of future bone health.[6] The childhood years are critical for development of bone mass, which depends on many factors, including genetics, nutrition, weight-bearing activity, hormonal status, medication use, and medical disease.[7] Because of a restricted diet, insufficient vitamin D intake,[8-10] gastrointestinal disease,[5,11] chronic use of medications including anti-epileptics,[12,13] antipsychotics,[14] and selective serotonin reuptake inhibitors,[15] as well as hypotonia[16] and lower physical activity levels,[17] children with ASD have many risk factors for low

bone mineral density (BMD). In cross-sectional studies examining BMD in ASD and typically developing age-matched controls, we have previously reported decreased BMD at the spine, hip, and femoral neck in peripubertal boys with ASD compared to typically developing controls,[10,18] and other authors have also described low BMD z scores and low bone cortical thickness in ASD.[19-22] Low peak bone mass could lead to increased fracture risk. Further, studies report higher odds of hip and spine fractures in children and adults with ASD.[23,24] In a secondary analysis of the primary study, we now seek to learn whether differences in diet and activity contribute to lower BMD in boys with ASD.

SUBJECTS AND METHODS

Subjects

A total of 38 males (19 ASD and 19 typically developing controls) between the ages of 8 to 17 years were enrolled at study initiation for the cross-sectional study in 2011[10] and returned for a follow-up outpatient visit in 2015. At the time of the second visit, 13 additional participants (6 ASD and 7 typically developing controls) were enrolled. Upon analysis, two typically developing control siblings were excluded due to abnormally low levels of serum 25-hydroxy vitamin D (25 [OH]D) (<15 ng/mL [<36 pmol/L]), suggesting that they were no longer typically developing controls and had a possible condition with the potential to affect bone metabolism. Therefore, a total of 49 participants (25 ASD and 24 typically developing controls, including two to three siblings from each of five families) were available for cross-sectional analyses. Data for this secondary analysis were primarily obtained from participants' 2015 outpatient study visit (n=38). If data were not available at the 2015 visit, but were available from the 2011 visit, data from their 2011 visit (n=11) were used.

All children had a body mass index z score between −1.88 and +1.88 for age, based on standard charts.[25] Children with ASD met *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition criteria[26] and Autism Diagnostic Observation Schedule criteria for an ASD.[27,28] The control group was recruited through advertisement in primary care providers' offices, the Internet, advertisement within the hospital, and word of mouth. Exclusion criteria for all participants included use of medications that affected bone metabolism, including testosterone, estrogen/progesterone, or glucocorticoids (except inhaled glucocorticoids); and use of anticonvulsant medications, such as diphenylhydantoin, phenobarbital, topiramate, carbamazepine, and valproic acid. Children with a known disease affecting bone, such as Crohn's disease, celiac, thyroid and renal disease, or evidence of impaired vitamin D metabolism based on laboratory results, were also excluded. Studies were performed at a clinical research center as outpatients. The Institutional Review Board of Partners Health-Care System approved this study. Informed assent and consent were obtained from subjects and their parents, respectively.

Experimental Protocol

All participants had a history and physical examination performed at the outpatient visit at the clinical research center, including self-report of pubertal (Tanner) stage using standardized pictures. Parents helped with collection of food records and puberty and exercise assessments during the week before the visit. Daily nutrient intake and average food group

RESEARCH SNAPSHOT

Research Question: Do differences in diet and activity contribute to lower bone mineral density in boys with autism spectrum disorder?

Key Findings: In this cross-sectional study of 49 boys (24 of which are controls), study participants were assessed for bone mineral density, 3-day food records, and physical activity. Boys with autism spectrum disorder consumed 16% fewer calories and 37% less animal protein than controls, were less active and had lower bone mineral density z scores. Protein, calcium, and phosphorus intake were lower in autism spectrum disorder than typically developing controls and were associated positively with bone mineral density.

serving count were assessed by Clinical Research Center dietitians using a 3-day food record and the Minnesota Nutrition Data System for Research software, versions 2009 and 2014,[29,30] which parents completed on the week before visit. Food records were collected from 79% of subjects on 2 weekdays and 1 weekend day and from 13% on 3 weekdays and 5% from 2 weekend days and 2 weekday. Final calculations were completed using Nutrition Data System for Research, version 2014[30] for all visits. Two activity questionnaires were utilized: The Oxford Physical Activity Questionnaire and the Youth Physical Activity Survey. The Oxford Physical Activity Questionnaire is validated for adolescents, and while the Youth Physical Activity Survey is not validated, it contains activities that are more appropriate to the ASD population (eg, rocking, spinning, full body tantrums).[31,32]

BMD was measured using dual-energy x-ray absorptiometry (Hologic Discovery A software, version APEX 4.0.2)[33] at the total hip, femoral neck, and lumbar spine (L1-4). During the 2015 visit, whole body and whole body less head BMD was also measured (not available for participants assessed in 2011). The z scores based on age-, sex-, and race-specific pediatric norms from Hologic were reported. Dual-energy x-ray absorptiometry was also used for measures of body composition (lean and fat mass). Additional anthropometric measurements were completed at this outpatient visit using standardized techniques (Lohman). Height (cm) was measured without shoes in triplicate using a wall-mounted Harpenden stadiometer (Holtain, Ltd) and weight (kg) was measured in light clothing, without shoes, using a calibrated Tanita BWB 800S digital scale (Tanita Corporation of America Inc).

Statistical Analysis

Data were analyzed using Statistical Analysis Software (version 9.4, SAS Institute).[34] Continuous variables were assessed for normality, and transformations were performed to approximate normality as appropriate. Generalized estimating equations were used to compare ASD vs typically developing control participants to account for correlation among siblings, as our sample included five sets of two to three siblings. Separate models were used to adjust for age and age plus physical activity. Estimates are reported for the mean age and log-transformed Oxford Physical Activity Questionnaire physical activity levels. Generalized estimating equations was also used to test linear associations of