Complementary and Alternative Medicine Use in a Large Pediatric Autism Sample

AUTHORS: James M. Perrin, MD,[a] Daniel L. Coury, MD,[b] Susan L. Hyman, MD,[c] Lynn Cole, PNP,[c] Ann M. Reynolds, MD,[d] and Traci Clemons, PhD[e]

[a]Department of Pediatrics, Harvard Medical School, MassGeneral Hospital for Children, Boston, Massachusetts; [b]Nationwide Children's Hospital, The Ohio State University School of Medicine, Columbus, Ohio; [c]Golisano Children's Hospital, University of Rochester School of Medicine, Rochester, New York; [d]Children's Hospital Colorado, University of Colorado, Aurora, Colorado; and [e]EMMES Corporation, Rockville, Maryland

KEY WORDS

autism spectrum disorders, complementary and alternative medicine

ABBREVIATIONS

ADOS—Autism Diagnostic Observation Schedule
ASD—autism spectrum disorder
ATN—Autism Treatment Network
CAM—complementary and alternative medicine
CBCL—Child Behavior Checklist
CSHQ—Child Sleep Health Questionnaire
DSM-IV—*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*
GI—gastrointestinal
OR—odds ratio
PDD-NOS—pervasive developmental disorder not otherwise specified

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Address correspondence to James M. Perrin, MD, Department of Pediatrics, Harvard Medical School, MassGeneral Hospital for Children, 100 Cambridge St, #1542, Boston, MA 02114. E-mail: jperrin@partners.org

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abstract

BACKGROUND AND OBJECTIVE: Children and adolescents with autism spectrum disorder (ASD) often use complementary and alternative medicine (CAM), usually along with other medical care. This study aimed to determine associations of ASD diagnostic category, co-existing conditions, and use of medications with use of CAM.

METHODS: We used the Autism Speaks Autism Treatment Network patient registry, which collects information on CAM use, medical conditions, and psychotropic medication at enrollment. CAM was categorized as special diets versus "other" CAM; ASD was defined as autism, pervasive developmental disorder (PDD), or Asperger's. Gastrointestinal symptoms, seizure disorders, sleep problems, and medication use were determined from parent report. Child Behavior Checklist (CBCL) scores were used to measure behavioral symptoms. Logistic regression was used to determine associations of diagnostic category, other medical conditions, and medication use with CAM treatments, controlling for demographic characteristics.

RESULTS: Of 3413 subjects in the registry as of April 2011, 3173 had complete data on CAM use: 896 (28%) reported any use; 548 (17%), special diets; and 643 (20%), other CAM. Higher rates of CAM use were associated with gastrointestinal symptoms (odds ratio [OR] = 1.88), seizures (OR = 1.58), and CBCL total score >70 (OR = 1.29). Children with PDD (OR = 0.62), Asperger's (OR = 0.66), or using medications (0.69) had lower rates.

CONCLUSIONS: Children with ASD use more CAM when they have co-existing gastrointestinal symptoms, seizure disorders, and behavior problems. This study suggests the importance of asking about CAM use in children with ASD, especially those with complex symptoms. *Pediatrics* 2012;130:S77–S82

Complementary and alternative medicine (CAM) treatments are widely used to promote health, often as adjuncts to conventional medical treatment. CAM may be defined as a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine.[1] Parents often use CAM in the care of children who have autism spectrum disorder (ASD), most typically in combination with conventional medical treatments, a practice sometimes labeled as integrative medicine. Data from the National Health Interview Survey indicate that 38.3% of US adults and 12% of US children use CAM,[2] although a 2008 review indicated higher rates, with 20% to 40% of children using some CAM.[3] Use of CAM is higher in children and adults who have chronic health conditions. Among families represented in the Interactive Autism Network, more than one-half of children and youth who have ASD receive supplements. Families who choose to use CAM for their children who have ASD report an average of 7 CAM therapies.[4] At the time of a diagnostic visit for ASD, almost one-third of children were already treated with a dietary intervention.[5]

Most previous work on CAM in children/youth with autism has come from small samples or large national data sets lacking substantial clinical data. Earlier work has associated increased CAM use among children with chronic conditions, higher socioeconomic status, and parental use of CAM for themselves.[3]

Valicenti-McDermott et al[6] examined the associations of CAM with parent stress and clinical symptoms of gastrointestinal (GI), sleep, and behavioral problems. They found higher use of CAM among families of children with ASD compared with children with other developmental disabilities. Higher rates of CAM use were associated with higher parenting stress, reports of food allergies, and child behavioral problems.

We examined CAM use in a large and diverse population of children who have ASD for whom a clinical database documented medical diagnosis and care. Given previous work in this area, we were particularly interested in the associations of CAM use with diagnostic categories of ASD, co-occurring conditions including other mental health conditions, and use of other treatments, while controlling for child demographic characteristics.

METHODS

This study was a cross-sectional analysis of data from a large multisite registry of children and adolescents with ASD involved in a North American collaborative to improve health care for children who have ASD. The Autism Speaks Autism Treatment Network (ATN), a collaboration among 17 academic health centers in the United States and Canada, has developed a common registry protocol for children enrolled in all sites. Main registry inclusion criteria are age 2 to 18 years as well as an Autism Diagnostic Observation Schedule (ADOS) -supported and *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) diagnosis of ASD. Sites enroll new patients and collect data on returning patients who have continuing care at the site. Enrollment (based on the date of consent) for the registry began in December 2007. We included all children enrolled in the ATN registry as of the end of April 2011.

Variables

CAM Usage

The medical history questionnaire completed by the parent at entry to the registry includes a series of questions about CAM use, addressing both special diets and other CAM treatments. Parents were queried as to whether their children use various treatments such as acupuncture, chelation, chiropractic, or hyperbaric oxygen therapy; dietary supplements (vitamin supplements, probiotics, antifungal agents, digestive enzymes, glutathione, sulfation, amino acids, or essential fatty acids); and special diets (classified as gluten free, casein free, Feingold, no processed sugars, no salicylates, or other). Because of the infrequent endorsement of most of the CAM therapies, the variables were collapsed into a primary outcome of any CAM use versus no CAM use and 2 subgroup outcomes of (1) special diets versus no CAM use; and (2) "other" CAM use versus no CAM use.

Clinical Diagnosis

All children entered into the registry had clinical diagnoses of ASD with documentation of DSM-IV criteria and completion of the ADOS. ADOS and DSM-IV criteria scores were used to define categories of ASD (autism, pervasive developmental disorder not otherwise specified [PDD-NOS], or Asperger's).

Co-occurring Conditions

The initial medical history questionnaire queried GI symptoms, specifically constipation, diarrhea, abdominal pain, and GI allergy. We dichotomized children into those with reported GI symptoms and those without. To determine presence of sleep disorders, the Child Sleep Health Questionnaire (CSHQ), a 33-item parent questionnaire, was used.[7] Insofar as the CSHQ has been studied well only to age 10 years, we limited analyses of sleep disorder associations with CAM use to children $<$11 years old.[8] Total CSHQ scores $>$41 have been reported as a sensitive cutoff for clinically significant sleep problems. Presence or absence of seizures according to parent report was also included. The Child Behavior

Checklist (CBCL) was used to determine presence of co-existing mental health symptoms, using cutoff scores of 70 on the CBCL internalizing, externalizing, and total scores denoting risk for behavioral problems.[9] Finally, we used parent report of use of medication, specifically for behavior problems.

Previous research has documented relations of age, race, and parental education with use of CAM.[3] Thus, these variables were included as control variables in our analyses. We categorized age as 2 to 5 years, 6 to 11 years, and 12 to 18 years. Maximum education level, collected from the child's primary and secondary caregivers, was grouped as follows: high school graduate or less, some college, college graduate, or postgraduate work. Race and ethnicity came from parent report. Race was categorized as white, black, Asian-American, or other; ethnicity was categorized as Hispanic or non-Hispanic origin.

Analyses

We determined associations with the use of any CAM through a 3-stage process by using logistic regression (SAS procedure LOGREG). In all analyses, use of any CAM was compared with the referent control group (no CAM usage). In stage 1, each factor (diagnostic category, co-occurring conditions, and use of medications) was included separately in bivariate analyses. Variables associated with CAM use at a level of $P < .20$ or less were retained as factors for further analysis. Multilevel categorical variables were retained if any of the comparisons (eg, high versus low, top versus bottom) were significant. Parent education and race/ethnicity were included as controls in the multivariable analyses.

In stage 2, all variables retained from stage 1 analyses were entered as a group into a multivariable model, along with the control variables (age, race/ethnicity, and parental education). In stage 3, model simplification consistent with χ^2 tests of change in deviance was performed. Variables not statistically significant were excluded from the model. Model simplification continued until the reduced model yielded a significant ($P \leq .05$) worsening of fit according to the likelihood ratio criterion.

A similar staged modeling approach was also used for the 2 subgroup comparisons of interest: (1) any special diet usage versus no CAM usage; and (2) "other" CAM usage versus no CAM usage.

Prevalence odds ratios (ORs) and 95% confidence intervals, which describe the association between use of any CAM, special diets, or other CAM and the risk factors, were computed relative to the control group of no CAM usage.

RESULTS

A total of 3413 participants were enrolled in the ATN registry as of April 28, 2011. A total of 3173 had available data on CAM usage. Children with no available CAM data were more likely to have a diagnosis of autism (73% vs 67%; $P = .01$) and be of Hispanic ethnicity (15% vs 6%; $P = .02$). The demographic characteristics of the 3173 participants who were included in the analysis are shown in Table 1, grouped according to usage of CAM (any CAM usage versus no CAM usage). A total of 896 (28%) participants reported use of any CAM; 548 (17%) reported use of a special diet; and 643 (20%) reported use of other CAM treatment (Table 2). As with other research regarding CAM use in children and adolescents,[3] wealthier households had higher rates of reported CAM usage in their children, as did white families compared with African-American or Latino families. ORs for each risk factor according to the 3 outcomes from the stage 1 bivariate analyses are given in Table 3. ORs significant at $P < .20$ are noted.

The stage 3 reduced multivariable logistic regression model had acceptable fit. Estimated ORs and significant associations ($P \leq .05$) from the stage 3 final models are given in Table 4. We report here associations that remained significant in multivariable analyses.

Differences in CAM Use by Autism Diagnostic Category

Children and adolescents with a diagnosis of Asperger's or PDD-NOS had significantly decreased use of any CAM compared with children with a diagnosis of autism (OR = 0.62 for Asperger's and OR = 0.66 for PDD-NOS). Those with PDD-NOS or Asperger's had significantly lower reports of use of special diets than those with autism (ORs = 0.44 and 0.65, respectively), whereas those with PDD-NOS had significantly lower reports of use of other CAM than those with autism (OR = 0.67).

CAM Use and Co-occurring Conditions

Parents of children in the ATN registry reported significantly higher rates of CAM use when they also reported GI problems (OR = 1.88 for CAM use in general; OR = 2.38 for special diets; OR = 1.82 for other CAM). Similarly, children whose parents reported a history of seizures also reported higher CAM use (OR = 1.58 for CAM use in general; OR = 1.97 for special diets; OR = 1.664 for other CAM). We found no significant association of CAM use with presence or absence of sleep problems.

CAM Use and CBCL Scores

Children with CBCL scores (internalizing, externalizing, and total) above the cutoff of 70 had significantly higher rates of CAM and special diet usage than children with lower scores. After controlling for other factors, this association remained only for the CBCL total problem score (OR = 1.29 for CAM; OR = 1.34 for special diets).

TABLE 1 Characteristics of ATN Participants According to CAM Usage

Characteristic	No CAM Usage[a]	Any CAM Usage	Total
Age, y			
2–5	1274 (56)	514 (57)	1788
6–11	765 (34)	297 (33)	1062
12–18	238 (10)	85 (9)	323
Gender			
Male	1924 (85)	747 (83)	2671
Female	353 (15)	149 (17)	502
ASD			
Autism	1481 (65)	633 (71)	2114
Asperger's	215 (9)	74 (8)	289
PDD-NOS	581 (26)	189 (21)	770
Caregiver(s)' highest level of education			
High school graduate or less	360 (17)	69 (8)	429
Some college	619 (29)	197 (23)	816
College graduate	598 (28)	311 (36)	909
Postgraduate work	573 (27)	275 (32)	848
Missing	—	—	171
Race			
White	1738 (76)	732 (82)	2470
Black/African American	195 (9)	31 (3)	226
Asian	116 (5)	46 (5)	162
Other	228 (10)	87 (10)	315
Ethnicity			
Hispanic or Latino origin	243 (11)	64 (7)	307
Not of Hispanic or Latino origin	1984 (89)	811 (93)	2795
Missing	—	—	71
Parent-reported GI problems			
No	1151 (52)	305 (35)	1456
Yes	1064 (48)	568 (65)	1632
Missing	—	—	85
Parent-reported sleep problems as measured by using the CSHQ (age <11 y)			
No	566 (33)	219 (31)	924
Yes	1156 (67)	477 (69)	1882
Missing	—	—	367
CBCL internalizing *t* score			
<70	1632 (76)	602 (71)	2234
≥70	523 (24)	249 (29)	772
CBCL externalizing *t* score			
<70	1796 (83)	688 (81)	2484
≥70	359 (17)	163 (19)	522
CBCL total score			
<70	1488 (69)	538 (63)	2026
≥70	667 (31)	313 (37)	980
Missing CBCL data	—	—	167
Parent-reported history of seizures			
No	1916 (85)	678 (76)	2594
Yes	336 (15)	206 (24)	545
Missing			34
Reported psychotropic medication usage			
No	1387 (73)	547 (73)	1934
Yes	516 (27)	206 (27)	722
Missing	—	—	517

Data are presented as number (%).

[a] Percentages may not add to 100 due to rounding.

TABLE 2 Rates of Specific CAM Usage

Characteristic	*N*
Any CAM	896
Special diets	548
Gluten-free diet	249
Casein-free diet	289
No processed sugars	69
No sugars or salicylates	28
Feingold diet	14
Other specified special diet	293
Other CAM	643
Other vitamin supplements	413
Probiotics	274
Essential fatty acids	171
Digestive enzymes	116
Higher dosing vitamin B_6 and magnesium	99
Chiropractic	77
Amino acids	59
Antifungals	58
Glutathione	33
Chelation	19
Hyperbaric oxygen	12
Acupuncture	10
Sulfation	7
Other specified CAM	173

Use of Psychotropic Medications

Children with reported psychotropic medication use had significantly lower current use of special diets (OR = 0.69).

DISCUSSION

We found substantially higher rates of CAM use in children who have classic autism compared with children and youth who have Asperger's or PDD-NOS. Parents also reported higher rates of CAM use if their child had certain co-existing conditions, specifically GI symptoms, seizures, or evidence of behavior problems, although children taking psychotropic medications had lower use of special diets. This report extends previous work related to CAM usage among children and adolescents who have ASD[4–6] by documenting associations of CAM use with co-existing medical conditions.

The CAM use in this clinical population is similar to that of children and adolescents who have other chronic health conditions, although the rates reported are somewhat lower than in other studies reporting on children with ASD.[4,5] Our findings may better reflect the prevalence of CAM use in similar populations because interest in the topic may bias samples of volunteers for online surveys. Furthermore, our sample is fairly young, with less exposure to CAM. Kemper et al[3] reported rates varying from 30% to 70% among children who have chronic conditions. In another study, 74% of 112 children with ASD in a referral practice reportedly use

TABLE 3 Associations (ORs) Between Use of Any CAM and Subgroup Categories of Special Diets and "Other" CAM

Factor	Exposure		Any CAM (n = 896)	Special Diets (n= 548)[a]	Other CAM (n = 643)[a]
	A Versus B				
Gender	Male	Female	0.92	0.96	0.88
ASD	Asperger's	Autism	0.81*	0.51*	0.91
	PDD-NOS	Autism	0.76*	0.70*	0.77*
Parent-reported GI problems	Yes	No	2.01*	2.46*	1.91*
Parent-reported sleep problems as measured by using the CSHQ	Yes	No	1.07	1.08	0.96
Parent-reported history of seizures	Yes	No	1.76*	2.16*	1.71*
CBCL internalizing T score	Yes	No	1.29*	1.39*	1.19*
CBCL externalizing T score	Yes	No	1.19*	1.29*	1.01
CBCL total score	Yes	No	1.30*	1.42*	1.14*
Reported psychotropic medication usage	Yes	No	1.01	0.79*	1.14

[a] Compared with the no CAM usage group.

* Nominally significant, $P < .20$.

CAM, especially dietary supplements and additions.[10] In 2 pediatric practices, 95% of children used CAM, mainly dietary treatments, melatonin, chiropractic therapy, antifungal agents, and sensory integration.[11] The initial medical history regarding CAM use did not specify melatonin or sensory integration as CAM treatments, thus leading to lower rates of identification in this population. More than 30% of 284 newly diagnosed children with ASD used CAM; 9% of them used potentially harmful CAM, such as chelation, antibiotics, or excessive amounts of vitamins.[5] In our population, a small percentage reported using CAM treatments that have been identified as potentially harmful (chelation reported in <4% of children). In the report by Levy et al, surprisingly, Latino children had much higher rates of CAM use than did white or African-American children. Our findings are similar to those of Valicenti-McDermott et al,[6] in a much smaller sample, in which reports of food allergies and behavior problems were associated with increased CAM use.

How these clinical characteristics of children affect the use of CAM is unclear, and our data do not directly address mechanisms underlying use. Parents of children who have classic autism may view their child's condition as more severe and seek alternative treatments to complement other care the child receives. Families seek to address problematic behaviors or symptoms by using CAM; therefore, parents whose children have GI symptoms may particularly try both dietary changes and other CAM treatments to improve their child's nutrition and symptoms. Dietary and nutritional concerns are among the most prominent questions that parents ask about their children who have autism. Families whose children experience the feeding problems and food aversion that are common among children with autism might tend toward nutritional supplementation either to compensate for perceived dietary deficiencies or as a primary treatment. Why children who have seizures have higher rates of CAM use is unclear, although the presence of seizures may also indicate more clinical severity to parents, encouraging them to seek alternative therapies. Parents whose children use psychotropic medications, conversely, may feel that they have active and somewhat effective treatments and turn to alternative treatments less than other families.

This study has several limitations. Essentially all information comes from parent report, without having confirmatory information from other observers or measures of the child's findings or health status. The registry questions

TABLE 4 Multivariable Associations (ORs) Between Use of Any CAM, Special Diets, or Other CAM

Factor	Exposure		Any CAM[a] (n = 896)	Special Diets[a,b] (n = 548)	Other CAM[a,b] (n = 643)
	A Versus B				
ASD	Asperger's	Autism	0.62 (0.46–0.84)	0.44 (0.28–0.69)	0.72 (0.52–1.00)
	PDD-NOS	Autism	0.66 (0.54–0.82)	0.65 (0.49–0.85)	0.67 (0.53–0.84)
Parent-reported GI problems	Yes	No	1.88 (1.57–2.25)	2.38 (1.86–3.05)	1.82 (1.50–2.22)
CBCL total score	Yes	No	1.29 (1.06–1.56)	1.34 (1.04–1.72)	NS[c]
Parent-reported history of seizures	Yes	No	1.58 (1.27–1.96)	1.97 (1.50–2.59)	1.66 (1.30–2.10)
Reported psychotropic medication usage	Yes	No	NS[c]	0.69 (0.52–0.91)	NS[c]

[a] ORs (95% confidence intervals) from stage 3 model, comparing the outcome with no CAM usage.

[b] Compared with the no CAM usage group.

[c] Non significant differences.

regarding CAM did not include a number of commonly used CAM therapies, such as melatonin, herbal remedies, massage, or sensory integration. Thus, this study may have underestimated CAM use. Families participating in the ATN registry represent a population with generally more access to large medical centers in large metropolitan areas and may not be as representative as those with transportation barriers to receiving care. Families participating in the ATN registry may also represent a group more willing to participate in clinical research and more oriented toward conventional medicine, which may not be as representative of CAM users in general. Several of the measures used indicate symptoms rather than provide actual indicators of specific conditions (eg, the GI symptom questionnaire and the CBCL). As a cross-sectional study, the data do not allow any determination of cause and effect. For example, the study cannot determine whether GI symptoms in children led to higher rates of CAM use or alternatively whether higher rates of CAM use caused more GI symptoms. It will help to develop better longitudinal measures that will allow determination of the effects of CAM use on key child outcomes.

This study provides strong evidence associating certain medical conditions with differential use of CAM among families raising children with ASD. As with other CAM use, it will help to determine more about the potential synergistic effects of CAM with medical treatments as well as ways that CAM use may interfere with improvement in medical conditions. The review by Huffman et al[12] also documents the need for substantially more study of the efficacy of CAM among children who have neurodevelopmental disabilities. The common CAM treatments (ie, special diets, vitamin and nutrient supplements) have the potential to affect conventional treatments recommended by practitioners operating in the medical home model, and primary care providers should inquire about and be aware of CAM use in their patients and families.[13] The American Academy of Pediatrics has called for pediatricians to establish a dialogue with families surrounding CAM, encouraged education of both consumers and clinicians regarding CAM, and sought better evidence of CAM treatments to guide clinical practice.[14] Our study points out the importance of understanding more about parents' motivations to use CAM and especially how their children's other health conditions influence those motivations.

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