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The Effect of Menstrual Issues on Young Women with Angelman Syndrome

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Abstract

Study Objective—To characterize menstrual health issues and their effect in young women with Angelman syndrome (AS). Our secondary objective was to compare them with young women with autism spectrum disorders (ASDs).

Design—Cross-sectional convenience sample survey.

Setting—An institutional review board–approved Web-based survey of young female members of the Angelman Syndrome Foundation.

Participants—Caregivers of young women with AS, aged 12–25 years.

Interventions—None.

Main Outcome Measures—Symptom characterization and effect of menses on young women with AS.

Results—Menstrual and premenstrual symptoms were common among young women with AS, but infrequently caused problems at home or school. Less than half of the subjects used hormones to control their flow. Of those who used hormones, 75% used them continuously. Caregivers were satisfied with their method to control periods. Girls with seizures were more likely to use hormonal methods to control menses than those without seizures. Menstrual-associated morbidity in young women with ASD and AS was fairly similar, but with greater morbidity in the ASD group than in the AS group. However, girls with AS had more problems with menstrual hygiene with almost all of them requiring full assistance for managing hygiene.

Conclusion—In this group of young women with AS, who have moderate to severe neurodevelopmental disabilities and cannot manage their own hygiene, menstruation is not associated with significant problems. Menstrual management by hormones is used by less than half. When hormonal therapy is used, it is most commonly used continuously to suppress menses.

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Keywords

Angelman syndrome; Developmental delay; Menstruation; Menses; Menstrual hygiene; Menstrual changes with seizures; Catamenial epilepsy; Dysmenorrhea; Premenstrual syndrome

Introduction

Puberty is a time of mental, physical, and emotional change and, therefore, a time of transition for adolescents and their families. It might pose additional challenges for families of young women with developmental disabilities. Menarche might be accompanied by an increased need for support for activities of daily living including hygiene issues and catamenial influences on associated medical problems, such as seizures. In addition, families need to consider how evolving sexuality might affect their daughters and to plan for reproductive health care needs. Families and teens need education to help guard against inappropriate advances and exploitation, and to protect young women from pregnancy and sexually transmitted infections. The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics suggest that providers counsel families and patients with disabilities and offer ongoing support and education regarding sexuality and reproductive health needs.^{1,2} There is evidence that some populations of women with developmental disabilities have particular difficulties with menstrual issues, including pain control, hygiene, and behavior issues.^{3–5} It is not known if women with more significant cognitive impairment have greater difficulty with menstruation or experience a greater negative effect on home and school life.

Angelman syndrome (AS) is a neurogenetic disorder affecting 1 in 12,000–20,000 of the population, characterized by developmental delay, speech and motor impairment, epilepsy, and frequent lack of verbalization.^{6,7} Pubertal development progresses normally, but little is known regarding menstrual issues in young women with AS. It is possible that their specific characteristics predispose them to increased morbidity with puberty and menses. This study was designed with 2 goals. The first aim was to characterize menstrual health issues and the effect on the lives of young women with AS. The secondary aim of this study was to compare these young women with an historical cohort of young women with Autism spectrum disorder (ASD). ASD is another neurogenetic disorder characterized by impairments in social interactions and communication.⁸ This historical cohort was chosen for comparison because a subset of individuals diagnosed with AS have enough deficits in social affect and repetitive and/or stereotyped behaviors to meet the diagnostic criteria for ASD.⁹ In addition, in the study of young women with ASDs and this study characterizing menstrual issues for young women with AS, predominantly the caregivers functioned as the respondents to survey questions.

Materials and Methods

A University of Michigan institutional review board–approved Web-based survey, used previously in a study on teens with autism,⁸ was e-mailed to the membership of the Angelman Syndrome Foundation (ASF). Two hundred sixty caregivers of menstruating young women, aged 12–25 years, with AS were invited to participate through the ASF

listserv. Data were collected on participant hygiene, associated symptoms, effect on daily life, previous treatments, demographic characteristics, menstrual history, and seizure history. Standard criteria for dysmenorrhea and premenstrual syndrome (PMS) were used with specific AS criteria incorporated from the literature.^{10,11} A comparison was done with the results of a previously published study, using the same survey.⁸ This is a nonvalidated survey, however, it was developed from a literature review, clinical experience, was subjected to expert subject matter review, and was used in the ASD study. Statistical analyses were done using descriptive statistics, χ^2 comparisons, and 2-tailed *t* tests (IBM SPSS, version 21; and Statistics Calculator, version 3, StatPac, Inc). The ASD historical cohort was a convenience sample recruited through ASD and provider networks including support groups, electronic newsletters, community events, and pediatric, adolescent, psychiatric, developmental disability, and gynecologic clinics to identify parents and/or caregivers of girls with ASDs between the ages of 10 and 25 years who had had at least 1 menstrual cycle.⁸ Both surveys were filled out by caregivers of the girls. It provided a counterpoint for another group of young women with developmental delay.

Results

E-mail invitations for the survey were sent to 260 families of young women aged 12–25 years with AS twice and 78 surveys (30%; 78 of 260) were returned. The demographic data are outlined in Table 1. Of the parents who reported their daughter's level of cognition, 77% (47 of 61) were severely or profoundly cognitively impaired. Seventy-nine percent of the girls were nonverbal (48 of 61). Their periods were of average duration (3–7 days; 76%; 38 of 50) with only 10% reporting periods lasting more than 7 days. They reported normal frequency of periods (10 or more per year; 43%; 23 of 53) and flow (88% not heavy; 44 of 50).

Menstrual and Premenstrual Morbidity

The morbidity of the menstrual symptoms are outlined in Table 2. Most families reported at least 1 menstrual or premenstrual symptom, many of which were reported to be “severe.” These symptoms caused approximately 20% of the girls to “often” have problems at home or to miss school. The most common premenstrual symptoms were irritability, aggression, crying, and anxiety; the most common menstrual symptoms were pain and cramps, back pain, diarrhea, headaches, and thigh pain. The most frequently used medications to control pre- and menstrual symptoms were nonsteroidal anti-inflammatory drugs (NSAIDs; 60%; 27 of 45). Thirty-one percent used hormones to control their symptoms and 9% did not use any medication. Menstrual hygiene issues often caused problems at home in 6% (2 of 47), often prevented school attendance in 8% (4 of 46), and often negatively affected their ability to learn in 9% (4 of 47).

Hormone Use

More than half of subjects (53%; 25 of 48) did not use any hormonal management to control their menstrual cycle or flow. Forty percent (19 of 48) of girls used a hormonal method to control their menstrual flow and 75% (9 of 12) of those used it in a continuous fashion. Of those using hormonal methods (total = 19), 74% used combined oral contraceptives (14 of

19) and 24% used progesterone-only methods (5 of 19) including depot medroxyprogesterone acetate injections and progesterone-only pills. Two percent each used mefenamic acid (1 of 48), hysterectomy (1 of 48), or endometrial ablation (1 of 48). No intrauterine devices, implants, patches, or rings were used in this population. The reasons for using hormones were: eliminate menses (70%; 12 of 17), make periods less painful (12%; 2 of 17), regulate menses (12%; 2 of 17), and lighten periods (6%; 1 of 17). Most of the caregivers (88%; 15 of 17) were satisfied with their method to control periods. Two girls (4% of total population) had undergone surgical procedures to stop menstruation, because of uncontrollable menses; 1 with an endometrial ablation and 1 with a hysterectomy.

Seizures

Most of this study population (81%; 48 of 59) had epilepsy. Seizure frequency varied between rare (42%; 25 of 59), infrequent (<1 per month; 25%; 15 of 59), and frequent (>1 per month; 14%; 8 of 59). Of the girls who had seizures, 58% (28 of 48) had no change in their seizures with menstruation, 38% (18 of 48) had increased seizure frequency, and 4% (2 of 48) had decreased seizure activity. The girls who used medications to control cyclical seizures (total = 14) were split between using increased doses of seizure medications (57%; 8 of 14) and using a hormonal method (43%; 6 of 14). Girls with seizures were more likely to use hormonal methods to control their menses than those without seizures ($\chi^2 = 12.106$; $P = .017$).

Comparison with Young Women with ASDs

One hundred sixty-two surveys were initiated in the ASD group and 124 completed surveys were returned. Demographic characteristics are reported in Table 1. Our sample of young women with AS were significantly less likely to communicate verbally than the young women with ASDs ($t = 8.031$; $P < .00001$). Their periods were similar in duration. Menstrual hygiene issues were different in the 2 populations, with most of those with AS needing help with all aspects (89%; 42 of 47) and those with ASD needing assistance with only specific aspects of menstrual hygiene, such as help with blood-stained clothing and/or bedding (63%; 78 of 124), reminders to change a pad or tampon (48%; 60 of 124), or disposing of used menstrual products (44%; 55 of 124).

Both populations had at least 1 menstrual symptom, but those with ASD were significantly more likely to have frequent symptoms (>50% of the time), during menses ($t = 5.206$; $P < .0001$) and also before menses ($t = 6.655$; $P < .0001$). Girls with ASDs had greater rates of severe symptoms before their menses ($t = 7.308$; $P < .0001$), but not more severe symptoms during menses. Neither group often missed school because of menstrual issues, nor did they often cause problems at school, but the ASD group's symptoms were statistically significantly more likely to often cause problems at home than were those of the AS group ($t = 2.552$; $P = .0117$). Both groups were similar in their predominant use of NSAIDs for symptom control. NSAIDs were similarly effective in the 2 groups for menstrual ($t = 0.257$; $P = .7977$) and premenstrual symptoms ($t = 0.660$; $P = .5109$).

Similar proportions of girls used hormones in the 2 groups (AS, 41%; $n = 45$ and ASD, 28%; $n = 124$; $t = 1.633$; $P = .1044$). Most participants in both groups took combined oral

contraceptive pills (AS, 71%; $n = 19$ and ASD, 86%; $n = 30$; $t = 1.334$; $P = .1879$), with more in the AS group taking them continuously (75% vs 35; $t = 2.474$; $P = .0175$). There were no reported surgical cases of hysterectomy or endometrial ablation in the ASD group, compared with 2 girls in the AS group.

Discussion

Menstruation in girls with AS is in the normal range for onset of menarche and duration of flow. There is considerable symptomatology with menses but a negative effect on the home environment and school attendance was reported in approximately 20% of the respondents. There were only a few for whom menstrual hygiene, PMS, or menstrual symptoms caused frequent problems at home or substantively affected school attendance. More than half of the young women and their families were coping with menstrual issues without intervention. This is in keeping with a recent study by Kirkham et al¹² from Canada, who found that most cognitively or physically impaired young women at their clinic did not experience dysmenorrhea, heavy periods, or menstrual-related behavior or mood changes. Menstrual issues were also studied in a population of girls with Rett syndrome, who were commonly found to have dysmenorrhea and PMS, but did not routinely limit activities.⁵ This will help care providers with anticipatory guidance, because many families of young women with developmental disorders are very concerned about menses and frequently seek care with the onset of pubertal signs, and before menarche because of these worries.^{13,14} Because so many teens in this study were doing well without interventions, the common practice that puberty and menstruation should be allowed to progress naturally is supported. When menses start, the effect can then be assessed after several cycles have been experienced. Clinicians can provide reassurance and let patients and their families know that menses might not be the burden they fear and might not require any menstrual management intervention.¹⁵ However, many parents might wish to use hormones for uses other than menstrual management, for protection against pregnancy.

In this population with moderate to severe disabilities, hormone use is limited and less frequent than in the general population of women with developmental disabilities.¹⁶ This group with AS uses combined oral contraceptives predominantly, with a progesterone-only method use much less frequent. This is consistent with other studies in which combined oral contraceptives were the most commonly used method of cycle control.^{5,12} However, in this study in girls with AS, there was no usage of any long-acting reversible contraception for menstrual management, as has recently become more common in other groups of adolescents with developmental delay.¹² Young women with AS would need a general anesthetic to have an intrauterine device placed, which can be a barrier to initiation of use. There were no comments from caregivers about individuals with side effects from hormonal treatment but many comments about how much hormonal treatment had improved girls' symptoms. Most caregivers were satisfied with medications to control menstrual symptoms and only 2 caregivers were dissatisfied.

Although approximately 80% of all young women with AS had a seizure disorder, seizure activity was infrequent (<1 per month) in approximately two-thirds. There was no change in seizure activity with menses in more than half of the respondents. Young women with

seizures were more likely to use hormones to suppress their menses and caregivers were overall satisfied with their method. Although this was a small study, it can be helpful to reassure families that in this population with epilepsy, only 38% had an increase in seizures related to their menstrual cycle and that hormonal and antiepileptic medications were found helpful by care givers to help control this increase in seizures.

Comparing this study population with adolescents with ASDs showed that the premenstrual symptoms were statistically more significant for girls with ASD, leading to significantly more issues at home, but not at school. Menstrual hygiene was much more complicated for girls with AS because of their greater dependence than girls with ASD. These differences might be related to the nature of the 2 conditions themselves; girls with ASD exhibit a wider spectrum of cognitive abilities than individuals with AS, reflecting a greater range of developmental level, self-care, and autonomy. Second, there is a significant difference in verbal ability between the 2 groups: 82% of the young women with ASD were verbal, however only 21% of the individuals with AS were verbal. In our study we therefore more heavily relied on caregivers to assess the needs or problems with menstruation in these young women with AS and ASD and report on these problems. We did not define other modes of communication for young women with either of these disabilities, although there are data to suggest that 55%-60% of individuals with AS use augmentative communication such as iPad or picture communication to express their needs.¹⁶ The language or communication barriers also make validation of our survey more complicated.

This study is the first of its kind to examine menstrual issues in girls with AS. The results also add to the discourse on menstrual issues in young women with developmental disabilities and the varying effects it might have. This study has several limitations. The survey was used to collect data from caregivers of a mostly nonverbal population rendering the data an approximation and parent interpretation of symptomatology. This indirect reporting inherently introduces error but this is the only way to survey this population with significant developmental delay. This study also relied on recollection of symptoms and not prospective charting, which limits the accuracy. The modest response rate of 30% decreases the generalizability to the overall population of women with AS. Because the data were only from girls with AS, a rare condition, the morbidity of menstrual issues in this population might not be generalizable to women with other moderate to severe cognitive developmental disabilities. Because it was a cross-sectional survey from a range of ages in which some subjects would be recently postmenarche, and others many years since menarche, we cannot comment about trends over time with menstrual symptoms. Future studies include a potential follow-up survey to compare symptomatology over time and assess uptake of newer methods for menstrual cycle control including long-acting methods.

Overall, the major clinical effect of this study was to provide information to care providers and parents of young girls with AS to understand and anticipate issues around puberty and menstruation. The cooperation of the ASF, a family and professional organization, allowed us to use a patient and family centered approach to gather data. By providing their e-mail list, they allowed us to reach a reasonable sample of families of young women with a rare condition that would have otherwise been difficult to find in a clinical setting.

This study and comparison with young women with ASD showed that girls with moderate to severe developmental delay tolerate their menstrual cycles relatively well. When treatment is needed, several methods are helpful to alleviate symptoms, limiting the effect of the cycles on school and home life. Premenarchal anticipatory guidance by care providers can reassure parents that most girls do quite well with puberty and menarche without intervention. The recommendation to let puberty run its course and use intervention only if menses and symptoms are severe enough to warrant medication use, was confirmed by this study.

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Study Population Characteristics

Table 1

Characteristic	AS	n	Range or %	ASD	n
Mean age, years	18	51	12–25	15.5	124
Mean age of menarche, years	12.4	55	8–17	12	124
Race	Caucasian	64	95 (61/64)	89% (110/124)	–
Developmental delay	Mild-moderate (IQ 40–70)	7	11 (7/61)	Borderline*	–
	Severe (IQ < 40)	23	38 (23/61)		
	Don't know	31	51 (31/61)		
Communication	Verbal	13	21 (13/61)	82% (102/124)	–
	Nonverbal	48	79 (48/61)		

AS, Angelman syndrome; ASD, autism spectrum disorder; MR, mental retardation

* IQ average for the group was reported solely as “borderline” without an “n.” It was per parent report of categorical options (gifted, above average, average, borderline, mild MR, moderate MR, severe MR).

Table 2

Symptom Frequency, Severity, and Effect

Symptom Variable	During Menses, %	Premenstrual Symptoms, %
Number of symptoms		
No response to periods	46 (21/46)	N/A
At least 1 symptom	84 (38/45)	98 (44/45)
Severity of symptoms		
Severe or moderate symptoms	68 (30/44)	21 (9/42)
Frequency of symptoms		
Never or rare symptoms	53 (24/45)	44 (20/45)
Frequent symptoms (>50% of the time)	19 (9/47)	31 (14/45)
Morbidity or effect of symptoms		
Symptoms never or rarely prevent attendance at school or activities	61 (27/44)	73 (32/44)
Symptoms almost always or often prevent attendance at school or activities	7 (30/43)	7 (30/43)
Symptoms never or rarely cause a problem at school or interfere with her ability to learn	55 (25/44)	56 (25/44)
Symptoms almost always or often cause a problem at school or interfere with her ability to learn	16 (7/44)	20 (9/45)
Symptoms never or rarely cause a problem at home	55 (25/45)	42 (19/45)
Symptoms almost always or often cause a problem at home	9 (4/44)	20 (9/45)

N/A, not applicable