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Alcohol, smoking and illicit drug use in pediatric systemic lupus erythematosus patients



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ABSTRACT

Objective: To evaluate alcohol, smoking and/or illicit drug use, and history of bullying in adolescent childhood-onset systemic lupus erythematosus and healthy controls.

Methods: 174 adolescents with pediatric rheumatic diseases were selected. All of the 34 childhood-onset systemic lupus erythematosus patients and 35 healthy controls participated in this study. A cross-sectional study included demographic/anthropometric data and puberty markers assessments; structured questionnaire and CRAFFT screening interview.

Results: McNemar tests indicated an excellent test-retest reliability of the structured questionnaire ($p = 1.0$). The median current age was similar between childhood-onset systemic lupus erythematosus patients and controls [15 (12–18) vs. 15 (12–18) years, $p = 0.563$]. The median of menarche age was significantly higher in childhood-onset systemic lupus erythematosus patients compared to controls [12 (10–15) vs. 11.5 (9–15) years, $p = 0.041$], particularly in those that lupus had occurred before first menstruation [13 (12–15) vs. 11.5 (9–15) years, $p = 0.007$]. The other puberty marker and sexual function parameters were similar in both groups ($p > 0.05$). Alcohol use was similar in both childhood-onset systemic lupus erythematosus patients and controls (38% vs. 46%, $p = 0.628$). A trend of lower frequency of CRAFFT score ≥ 2 (high risk for substance abuse/dependence) was evidenced in childhood-onset systemic lupus erythematosus patients compared to controls (0% vs. 15%, $p = 0.053$). Bullying was reported similarly for the two groups (43% vs. 44%, $p = 0.950$). Further analysis in lupus patients regarding alcohol/smoking/illicit drug use showed no differences in demographic data, puberty markers, history of bullying, sexual function, contraceptive use, disease activity/damage scores, clinical/laboratorial features and treatments ($p > 0.05$).

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Conclusion: This study showed high frequencies of early alcohol use in lupus adolescents and healthy controls, despite of a possible low risk for substance abuse/dependence in childhood-onset systemic lupus erythematosus patients.

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Uso de álcool, tabaco e drogas ilícitas por pacientes com lúpus eritematoso sistêmico pediátrico

R E S U M O

Palavras-chave:

Álcool

Tabagismo

Bullying

Puberdade

Lúpus eritematoso sistêmico de início na infância

Objetivo: Avaliar o uso de álcool, tabaco e/ou drogas ilícitas e a história de bullying entre adolescentes com lúpus eritematoso sistêmico pediátrico (LES-p) e controles saudáveis.

Métodos: Selecionaram-se 174 adolescentes com doenças reumatológicas pediátricas. Todos os 34 pacientes com LES-i e 35 controles saudáveis participaram deste estudo. Um estudo transversal incluiu avaliações de dados demográficos/antropométricos e marcadores da puberdade, um questionário estruturado e a entrevista de triagem Crafft.

Resultados: Testes de McNemar indicaram uma excelente confiabilidade teste-reteste do questionário estruturado ($p = 1,0$). A mediana da idade atual foi semelhante entre pacientes com LES-i e controles [15 (12 a 18) vs. 15 (12 a 18) anos, $p = 0,563$]. A mediana da idade na menarca foi significativamente maior em pacientes com LES-i em comparação com os controles [12 (10 a 15) vs. 11,5 (9 a 15) anos, $p = 0,041$], particularmente naquelas em quem o lúpus ocorreu antes da primeira menstruação [13 (12 a 15) vs. 11,5 (9 a 15) anos, $p = 0,007$]. Os outros marcadores da puberdade e parâmetros de função sexual foram similares nos dois grupos ($p > 0,05$). O uso de álcool foi semelhante entre pacientes com LES-i e controles (38% vs. 46%, $p = 0,628$). Evidenciou-se uma tendência de menor frequência de pontuação ≥ 2 no Crafft (alto risco para uso abusivo/dependência de substâncias) em pacientes com LES-i em comparação com os controles (0% vs. 15%, $p = 0,053$). O bullying foi relatado em frequência semelhante nos dois grupos (43% vs. 44%, $p = 0,950$). Uma análise mais aprofundada em relação ao uso de álcool/tabaco/drogas ilícitas em pacientes com lúpus não mostrou diferenças nos dados demográficos, marcadores da puberdade, história de bullying, função sexual, uso de anticoncepcionais, escores de atividade/danos da doença, características clínicas/laboratoriais e tratamentos ($p > 0,05$).

Conclusão: Este estudo mostrou uma alta frequência de uso precoce de álcool em adolescentes com lúpus e controles saudáveis, apesar de um possível baixo risco para uso abusivo/dependência de substâncias em pacientes com LES-i.

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Introduction

Childhood-onset systemic lupus erythematosus (c-SLE) is a rare disease that occurs mainly in adolescents. Adolescence is a transitional period of physical and psychological development that may be associated with high-risk behaviors.¹

In this regard, alcohol, smoking and illicit drug use is a relevant public health issue in healthy adolescents with high risk for substance abuse/dependence² and sexual dysfunction.³ Furthermore, adolescents may suffer from bullying victimization with poorer health status and psychological distress.⁴ However, the concomitant assessment of these adolescent health problems was not performed in c-SLE population.

Therefore, the objective of our study was to assess alcohol, smoking and/or illicit drug use in adolescent c-SLE patients

and healthy controls. We also evaluated the possible associations between alcohol, smoking and/or illicit drug use and: demographic data, bullying, clinical features, puberty markers, sexual function, contraceptive use, disease parameters and treatments in lupus population.

Materials and methods

Patients and controls

From February to June 2014, 174 adolescents (current age varying from 10 to 19 years according to World Health Organization criteria for adolescents) with pediatric rheumatic diseases were followed at the Pediatric Rheumatology Unit of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Brazil. Out of them, 34 adolescents had c-SLE. The exclusion criteria were current psychiatric disorders or unwilling

to participate. All of them participated in this cross-sectional study and fulfilled the American College of Rheumatology classification criteria for SLE.⁵ The control group included 35 healthy female adolescents followed-up in our University Hospital at the educational and preventive group of the Adolescent Unit. These control volunteers were subjected to the same exclusion criteria. Local Ethics Committee of our university hospital approved this study.

Puberty markers, sexual function and alcohol/smoking/illicit drug use, and bullying

This study included demographic/anthropometric data and puberty markers assessments; a structured questionnaire evaluated sexual function and alcohol, smoking and illicit drug use, bullying and the Portuguese CRAFFT (mnemonic acronym of car, relax, alone, forget, friends, trouble) screen (CRAFFT/CEASER) version.^{6,7} These aspects were performed blinded to clinical, laboratorial and treatment assessments.

Socio-demographic and anthropometric data

Current age, gender, years of education, weight and height were evaluated. Body mass index (BMI) was defined by the formula: weight in kilograms/height in square meters.

The Brazilian socio-economic classes were classified according to the ABEP (Associação Brasileira de Empresas de Pesquisa).⁸

Puberty markers assessments

Secondary sexual characteristics were classified according to Tanner pubertal changes in both genders.⁹ Age at first menstruation (menarche) and first ejaculation (spermarche) were registered based on memory recollection.

Structured questionnaire

A pilot study was carried out in 30 consecutive adolescents who were tested and then retested 1–2 months later in February and April 2014, to evaluate response reliability of the aforementioned questionnaire, covering the following features: sexual function and alcohol/smoking and illicit drugs use.

Sexual function evaluation included: presence and age at first sexual intercourse, sexual intercourse in the last month, use of male contraception (condom) in the first sexual activity, oral and emergency contraceptive use, knowledge of sexual activity by parents and number of sexual partners in life. Both healthy controls and c-SLE patients have a routine orientation about sexual function and birth controls, emotional problems and drugs issues in the Adolescent and Pediatric Rheumatology Units of our University Hospital. Barrier methods are encouraged for our entire male and female sexually active c-SLE patient. Although its long-term use is associated with decreased bone mineral density, depot medroxyprogesterone acetate injection (every three months administered in our Day Hospital) is our preferable method indicated for

all sexually active c-SLE patient, due to adequate adherence. Progestin-only pills may be also used, although the main issue related to its use by adolescents is poor compliance due to menstrual irregularity. Oral levonorgestrel is also indicated as an emergency contraception method in female c-SLE.

Alcohol/smoking and illicit drugs use assessment involved: age at alcohol initiation, number of days of alcohol use in the last 30 days, age at smoking initiation, number of days using cigarettes in the last 30 days, age at illicit drug initiation and number of days using illicit drugs in the last 30 days. Use of illicit inhalants drug (glue sniffing, aerosol and solvent) and illegal drugs [marijuana, stimulants (cocaine, crack and speed), LSD, opiates, heroin and ecstasy] were systematically assessed. Bullying, which is defined as recurrent exposure to emotional and/or physical aggression, was registered based on memory recollection. The questionnaire was given in the absence of legal guardians, relatives and/or friends.

CRAFFT screening

The Portuguese version of physician-conducted CRAFFT (CRAFFT/CEASER) screen was used and consists of 9 questions developed to screen adolescents for high-risk alcohol and drugs use.⁶ This questionnaire is divided in two parts. Part A includes three questions regarding the use of alcohol, marijuana, hashish or another substance in the last twelve months. If the adolescent responded “no” to all three questions, only the question related to “Car” of the B-part should be asked. If the adolescent answered “yes” to one of the opening questions, all of the questions of part B should be asked. The B-part contained six questions, which are signs of problematic substance use, such as: 1. “Have you ever ridden in a car driven by someone (including yourself) who was “high” or had been using alcohol or drugs?”, 2. “Do you ever use alcohol or drugs to relax, feel better about yourself, or fit in?”, 3. “Do you ever use alcohol or drugs while you are by yourself, or alone?”, 4 “Do you ever forget things you did while using alcohol or drugs?”, 5. “Do your family or friends ever tell you that you should cut down on your drinking or drug use?”, 6. “Have you ever gotten into trouble while you were using alcohol or drugs?”. One point was related to each answer “yes” in the B-part of the questionnaire. A total score of ≥ 2 indicated high risk for substance abuse/dependence and a need for additional assessment.⁷

c-SLE clinical, laboratorial and treatment assessments

SLE clinical manifestations were defined as: articular involvement (non-erosive arthritis), mucocutaneous lesions (malar or discoid rash, oral ulcers or photosensitivity), serositis (pleuritis or pericarditis), neuropsychiatric diseases (seizure or psychosis), renal involvement (proteinuria ≥ 0.5 g/24 h, presence of cellular casts, and/or persistent hematuria ≥ 10 red blood cells per high power field), and hematologic abnormalities (hemolytic anemia, leukopenia with a white blood cell count $<4000/\text{mm}^3$, lymphopenia $<1500/\text{mm}^3$ on two or more occasions and thrombocytopenia with platelet count $<100,000/\text{mm}^3$ in the absence of drugs or infection).

Erythrocyte sedimentation rate (ESR) was performed by Westergreen method and C-reactive protein (CRP) by nephelometry. Anti-double-stranded DNA (anti-dsDNA) autoantibody was detected by indirect immunofluorescence using *Crithidia luciliae* as substrate.

Disease activity was evaluated according to SLE Disease Activity Index 2000 (SLEDAI-2K).¹⁰ Cumulative damage was measured by SLE International Collaborating Clinics/ACR Damage Index (SLICC/ACR-DI).¹¹

Data concerning the use and current dosage of prednisone, hydroxychloroquine, methotrexate, azathioprine, intravenous cyclophosphamide, mycophenolate mofetil and intravenous immunoglobulin were also determined.

Statistical analysis

The test-retest reliability of the structured questionnaire was verified using the McNemar test. Results were presented as the mean \pm standard deviation (SD) or median (range) for continuous and number (%) for categorical variables. Data were compared by t test or Mann-Whitney test in continuous variables to evaluate differences between c-SLE and controls, and between SLE subgroups. For categorical variables, differences were assessed by Fisher's exact test or Pearson chi-square test. Spearman rank correlation coefficient was used for CRAFFT score and age correlations. The level of significance was set at 5% ($p < 0.05$).

Results

McNemar tests indicated an excellent test-retest reliability of the structured questionnaire ($p = 1.0$).

Table 1 includes demographic data, puberty markers, sexual function, alcohol, smoking and illicit drug use, and bullying in c-SLE and controls. The median current age was similar between c-SLE patients and controls [15 (12-18) vs. 15 (12-18) years, $p = 0.563$], likewise the frequency of female gender (76% vs. 74%, $p = 0.833$). BMI was significantly higher in c-SLE patients compared to controls [22.11 (16.4-36.6) vs. 19.53 (16.4-25.9) kg/m², $p = 0.002$].

The median of menarche age was significantly higher in c-SLE patients compared to controls [12 (10-15) vs. 11.5 (9-15) years, $p = 0.041$], particularly in those that lupus had occurred before menarche [13 (12-15) vs. 11.5 (9-15) years, $p = 0.007$] (Table 1).

The frequencies of alcohol, smoking and/or illicit drug use were high and similar in both c-SLE patients and controls (38% vs. 46%, $p = 0.628$). Marijuana was used by two healthy controls and none in c-SLE patients (0% vs. 6%, $p = 1.000$). The median of CRAFFT score was alike in both groups [0 (0-1) vs. 0 (0-5), $p = 0.721$], whereas a trend of lower frequency of CRAFFT score ≥ 2 was evidenced in c-SLE patients compared to controls (0% vs. 15%, $p = 0.053$). Bullying was reported similarly in the two groups (43% vs. 36%, $p = 0.572$) (Table 1).

Further analysis of lupus patients that used alcohol, smoking and/or illicit drug compared to those that did not use these substances showed no differences in demographic data, puberty markers, sexual function parameters, contraceptive use, history of bullying, lupus clinical manifestations,

SLEDAI-2K, SLICC/ACR-DI, ESR, CRP and anti-dsDNA autoantibodies ($p > 0.05$). Current use and current dose of prednisone, hydroxychloroquine, methotrexate, azathioprine, intravenous cyclophosphamide and mycophenolate mofetil were also similar in both groups ($p > 0.05$).

No correlations were evidenced between CRAFFT score in both c-SLE and healthy controls groups ($n = 69$) and: current age ($p = 0.249$), age of alcohol onset ($p = 0.800$) and age onset of sexual intercourse ($p = 0.297$).

Discussion

Our study showed high frequencies of early alcohol use in adolescents with c-SLE and in healthy controls, despite of a possible low risk for substance abuse/dependence in the former group.

The major advantage of this study was the assessment of a structured questionnaire with high test-retest reliability that evaluated sexual function, licit and illicit substance use and bullying. CRAFFT score, which is a screening tool for high-risk alcohol or drugs use in teenagers, was also applied.¹² Furthermore, a healthy control group with similar age, gender and socio-economic class was relevant, since these data were associated with bullying, alcohol and illicit drugs in adolescents.^{2,12-15} However, the major limitations of this study were the small number of subjects recruited in only one Pediatric Rheumatic service, a cross sectional design and non use of a standardized self-completion questionnaire for different types of bullying.⁴ In addition, there was no sample size calculation for this study, which does not allow generalizing of these results, especially in a research that was based only on the questionnaire and not for medical tests or a more detailed history.

Alcohol consumption was high in the present study, as expected in adolescents with c-SLE and healthy controls. Prevalence of alcohol use in adolescents varied from 23% to 68%, using distinct methodological procedures, such as questionnaires or structured interviews.^{14,16} This finding is probably related to low-cost and easy access to adolescents in our country, in spite the efforts of Brazilian healthy public policy. The age of alcohol onset was also early in our c-SLE patients (14 years), different from a national survey performed in Brazilian adolescents (15.8 years).¹⁴

In contrast to alcohol intake, smoking and marijuana were rarely used by lupus and healthy adolescents, probably due to the predominance of females. Indeed, male gender was associated with an increased risk for illegal drug use.¹⁴ The illicit or licit drug use did not influence sexual function parameters and contraceptive use, differently from another study.³ These substances seemed not to interfere with disease markers and treatments in c-SLE patients.

Importantly, our study showed a low risk for problematic/hazardous substance pattern of use in c-SLE patients, probably due to complex disease and overprotection by parents and families. However, adolescent experimentation has a potential risk for later development of substance use disorders in adulthood.¹⁶ Therefore, prevention is a more cost-effective intervention than curative approaches. Indeed, American Academy of Pediatrics recommends that

Table 1 – Demographic data, puberty markers, sexual function, alcohol, smoking and illicit drug use, and bullying in childhood-onset systemic lupus erythematosus (c-SLE) and controls.

Variables	c-SLE (n = 34)	Healthy controls (n = 35)	p
<i>Demographic data</i>			
Current age, yrs	15 (12–18)	15 (12–18)	0.563
Female gender	26 (76)	26 (74)	0.833
BMI, kg/m ²	22.11 (16.4–36.6)	19.53 (16.4–25.9)	0.002
Social economic class B and C	32 (94)	34 (97)	0.614
Education, yrs	9 (6–12)	10 (6–12)	0.516
<i>Puberty markers</i>			
Tanner 3	4 (12)	4 (11)	1.000
Tanner 4–5	27 (79)	31 (89)	0.299
Menarche	24/26 (92)	26/26 (100)	0.490
Menarche age, yrs	12 (10–15)	11.5 (9–15)	0.041
Lupus before menarche, yrs	13 (12–15)	11.5 (9–15)	0.007
Lupus after menarche, yrs	12 (10–14)	11.5 (9–15)	0.595
Spermarche	5/8 (62)	7/9 (78)	0.620
Spermarche age, yrs	12 (12–13)	13 (12–14)	0.240
Lupus before spermarche, yrs	12 (12–13)	13 (12–14)	0.257
Lupus after spermarche, yrs	12.5 (12–13)	13 (12–14)	0.513
<i>Sexual function</i>			
Sexual activity	7 (21)	9 (26)	0.614
First sexual activity age, yrs	15.5 (14–17)	15 (12–17)	0.427
Sexual intercourse in last month	1/7 (14)	4/9 (44)	0.308
Condom at the first sexual activity	6/7 (86)	8/9 (89)	1.000
Oral contraception use in females	1/6 (17)	3/10 ^a (30)	1.000
Emergency contraceptive use	2/6 (33)	4/9 (44)	1.000
Knowledge of sexual activity by parents	2/7 (29)	6/8 (75)	0.132
Sexual partner in life, number	1 (1–2)	1 (1–2)	0.529
<i>Alcohol, smoking and/or illicit drug use</i>			
Alcohol use	13 (38)	16 (46)	0.628
Alcohol use	13 (38)	16 (46)	0.628
Age at onset alcohol	14 (10–17)	14 (7–18)	0.887
Drinking alcohol in past 30 days, number	0 (0–2)	0 (0–5)	0.242
Tobacco smoking use	1 (3)	5 (14)	0.198
Age at onset smoking	11	15 (7–15)	–
Smoking in past 30 days, number	0	0 (0–30)	–
Illicit drug use	0	2 (6)	1.000
Age at onset illicit drug	0	14 (14–14)	–
Illicit drug use in past 30 days, number	0	1.5 (0–3)	–
CRAFFT score (0–6)	0 (0–1)	0 (0–5)	0.721
CRAFFT score ≥2	0	5 (15)	0.053
<i>CRAFFT item</i>			
Car	8 (24)	5 (15)	0.355
Relax	1 (14)	2 (18)	1.000
Alone	0	1 (9)	1.000
Forget	0	5 (45)	0.101
Friends	0	5 (45)	0.101
Trouble	0	0	1.000
<i>Bullying</i>	13/30 (43)	15/34 (44)	0.950

The results are presented in n (%) and median (range).

CRAFFT, car, relax, alone, forget, friends, trouble; screening test.

^a One healthy control used oral contraception before sexual activity.

adolescents be screened for both high-risk sexual behavior, as well as for drugs and alcohol use as part of routine visit.¹⁷

Of note, bullying is unwished, repeated and aggressive behavior in school adolescents that involves a real or perceived power imbalance. Adolescents with chronic diseases have an increased risk of peer victimization, reinforcing the relevance of the quality of an inclusive education system.⁴ Furthermore, bullying may cause higher rates of depression and anxiety,¹⁸ and may influence adherence in patients.¹⁹ Future prospective study, recruiting larger sample and evaluating these aspects, will be necessary in c-SLE population.

We have confirmed our previous observations of late menarche age^{20,21} and normal spermarche age²² in c-SLE patients compared with healthy Brazilian adolescents. Endocrine-disrupting effects of alcohol and smoking use may influence pubertal development,²³ however this aspect was not evidenced in the present study.

In conclusion, this study showed high frequencies of early alcohol use in lupus adolescents and healthy controls, with a possible low risk for substance abuse/dependence in c-SLE patients. Therefore, our study emphasized a routine screening for substance use in all c-SLE adolescents.²⁴

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Conflict of interests

The authors declare no conflict of interests.

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