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Original article

Substance use and sexual function in juvenile idiopathic arthritis



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ABSTRACT

Objective: To evaluate alcohol/tobacco/illicit drug use and sexual function in adolescent juvenile idiopathic arthritis (JIA) and healthy controls.

Methods: 174 adolescents with pediatric rheumatic diseases were selected. A cross-sectional study with 54 JIA patients and 35 controls included demographic/anthropometric data and puberty markers assessments, physician-conducted CRAFFT (car/relax/alone/forget/friends/trouble) screen tool for substance abuse/dependence high risk and a questionnaire that evaluated sexual function, bullying and alcohol/tobacco/illicit drug use. Clinical/laboratorial data and treatment were also assessed in JIA.

Results: The median current age was similar between JIA patients and controls [15(10–19) vs. 15(12–18) years, $p=0.506$]. Frequencies of alcohol/tobacco/illicit drug use were high and similar in both JIA and controls (43% vs. 46%, $p=0.829$). However, age at alcohol onset was significantly higher in those with JIA [15(11–18) vs. 14(7–18) years, $p=0.032$], particularly in polyarticular onset ($p=0.040$). High risk for substance abuse/dependence (CRAFFT score ≥ 2) was found in both groups (13% vs. 15%, $p=1.000$), likewise bullying ($p=0.088$). Further analysis of JIA patients regarding alcohol/tobacco/illicit drug use showed that the median current age [17(14–19) vs. 13(10–19) years, $p<0.001$] and education years [11(6–13) vs. 7(3–12) years, $p<0.001$] were significant higher in those that used substances. Sexual activity was significantly higher in the former group (48% vs. 7%, $p<0.001$). A positive correlation was evidenced between CRAFFT score and current age in JIA patients ($p=0.032$, $r=+0.296$).

Conclusion: A high risk for substance abuse/dependence was observed in both JIA and controls. JIA substance users were more likely to have sexual intercourse. Therefore, routine screening is suggested in all visits of JIA adolescents.

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Uso de substâncias e função sexual na artrite idiopática juvenil

R E S U M O

Palavras-chave:

Álcool
Tabaco
Drogas ilícitas
Bullying
Artrite idiopática juvenil

Objetivo: Avaliar o uso de álcool/tabaco/drogas ilícitas e a função sexual em adolescentes com artrite idiopática juvenil (AIJ) e controles saudáveis.

Métodos: Selecionaram-se 174 adolescentes com doenças reumatológicas pediátricas. Fez-se um estudo transversal com 54 pacientes com AIJ e 35 controles. Foram feitas avaliações de dados demográficos/antropométricos e marcadores da puberdade; a escala de triagem CRAFFT (carro/relaxar/sozinho/esquecer/amigos/problemas) foi aplicada por um médico para determinar o alto risco de uso abusivo/dependência de substâncias. Um questionário avaliou a função sexual, a ocorrência de *bullying* e o uso de álcool/tabaco/drogas ilícitas. Também foram avaliados dados clínicos/laboratoriais e de tratamento da AIJ.

Resultados: A idade média atual foi semelhante entre pacientes com AIJ e controles [15 (10 a 19) vs. 15 (12 a 18) anos, $p=0,506$]. As frequências de uso de álcool/tabaco/drogas ilícitas foram elevadas e semelhantes entre pacientes com AIJ e controles (43% vs. 46%, $p=0,829$). No entanto, a idade em que começou a usar álcool foi significativamente maior naqueles com AIJ [15 (11 a 18) vs. 14 (7 a 18) anos), $p=0,032$], em particular na doença de início poliarticular ($p=0,040$). Encontrou-se um alto risco de uso abusivo/dependência de substâncias (pontuação no CRAFFT ≥ 2) em ambos os grupos (13% vs. 15%, $p=1,000$), do mesmo modo que o *bullying* ($p=0,088$). Uma análise mais aprofundada dos pacientes com AIJ em relação ao uso de álcool/tabaco/drogas ilícitas mostrou que a idade média atual [17 (14 a 19) vs. 13 (10 a 19) anos, $p<0,001$] e os anos de escolaridade [11 (6 a 13) vs. 7 (3 a 12) anos, $p<0,001$] foram significativamente maiores naqueles que usaram substâncias. A atividade sexual foi significativamente maior no primeiro grupo (48% vs. 7%, $p<0,001$). Foi evidenciada correlação positiva entre a pontuação na escala CRAFFT e a idade atual dos pacientes com AIJ ($p=0,032$, $r=+0,296$).

Conclusão: Observou-se um alto risco de uso abusivo/dependência de substâncias em pacientes com AIJ e controles. Os usuários de substâncias que têm AIJ são mais propensos a ter relações sexuais. Portanto, sugere-se a triagem de rotina em todas as consultas de adolescentes com AIJ.

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Introduction

Adolescence is an important phase to develop a positive body image, to establish social relationships, to achieve independence and sexual identity. Some of the biggest problems during this period in healthy adolescents are substance misuse,^{1,2} precocious sexual activity, reduced use of contraceptive methods and higher risk of sexually transmitted infections.³

In addition, the use of alcohol, tobacco and illicit drugs seems to be relevant in adolescents with chronic conditions, that may lead to addiction¹ and high-risk sexual behavior.^{2,3} Smoking provoke cardiovascular disease and alcohol intake can induce liver damage in patients with autoimmune diseases under methotrexate therapy.³ The substance use in chronic conditions may also induce poor adherence to medical treatment, resulting in disease activity and decrease health-related quality of life.

Adolescents may also suffer from bullying victimization, particularly those with chronic diseases.⁴ However, these issues have not been investigated simultaneously in an adolescent juvenile idiopathic arthritis (JIA) population.

Therefore, the aims of the present study were to evaluate alcohol, tobacco and/or illicit drug use in adolescent JIA patients and healthy controls. The possible associations between the use of the aforementioned substances in JIA patients and: demographic data, puberty markers, sexual function, bullying, JIA clinical parameters and treatments were also assessed.

Materials and methods

Patients and controls

We included all 174 adolescent outpatients (current age 10–19 years according to World Health Organization criteria) with pediatric rheumatic diseases followed at the Pediatric Rheumatology Unit of our University Hospital. These patients were selected between February to June 2014. Out of them, 55 JIA adolescents were approached and recruited for this study. The exclusion criterion was refusal to participate in this study. Both patients and controls had no apparent psychiatric disorders according the physician evaluation. One patient was excluded due to autism. Therefore 54 adolescents with JIA according to International League Against

Rheumatism criteria⁵ were eligible to participate. The control group included 35 healthy adolescents, without chronic diseases, referred from the primary and secondary health care services to the Adolescent Unit of our teaching University Hospital. This cross-sectional study was approved by the Local Ethics Committee of our University Hospital.

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

This study included demographic/anthropometric data and puberty markers assessments. The Portuguese CRAFFT (mnemonic acronym of car, relax, alone, forget, friends and trouble) screen (CRAFFT/CEASER) version was performed for both groups.^{2,6} A modified questionnaire evaluated sexual function,⁷ alcohol/tobacco/illicit drug use and bullying. These aspects were carried out blinded to JIA clinical, laboratorial and treatment data conducted by a single investigator.

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.⁷ Age at first menstruation (menarche) and first ejaculation (spermarche) were registered based on memory recollection.

CRAFFT screening

The validated Portuguese version of physician-conducted CRAFFT (CRAFFT/CEASER) screen was used and consisted of nine questions developed to screen adolescents for high-risk alcohol and drug 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. B-part contained six questions, which are signs of problematic substance use. One point was given to each “yes” answer in the B-part of the questionnaire. The score ranged from 0 to 6. A total score of ≥ 2 indicated high risk for substance abuse/dependence and a need for additional assessment.^{2,6}

Questionnaire administration

A pilot study was carried out in 30 consecutive healthy and JIA adolescents, who were tested and retested after 1–2 months. The pretest evaluated the subjects’ comprehension of the questions, the consistency and coherence of the answers and the time taken to answer the questionnaire. The questionnaire

included 14 questions with the option of answer “yes/no” or age/number of times about sexual function, bullying and alcohol/tobacco/illicit drugs use. Sexual function assessment included: age at first sexual intercourse, sexual intercourse in the last month, use of male contraceptive (condom) in the first sexual activity, current use of oral and emergency contraceptive, knowledge of sexual activity by parents and total number of sexual partners. Alcohol/tobacco and drugs [illicit inhalants drug (glue sniffing, aerosol and solvents) and illicit drugs [marijuana, stimulants (cocaine, crack and speed), poppers, LSD, opiates, heroin, crystal meth and ecstasy] use were also assessed: age at alcohol initiation, number of days of alcohol used 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. Bullying, which is defined as a recurrent exposure to emotional and/or physical aggression, was obtained by a “yes/no” answer to the question “Have you ever suffered bullying?”. The questionnaire was strictly confidential and was performed in the absence of legal guardians, relatives and friends.

JIA clinical, laboratorial and treatment assessments

Clinical assessments of JIA patients were assessed at the study entry and included: number of active joints (swelling within a joint, or limitation in the range of joint movement with joint pain or tenderness), number of limited joints, patient and physician global assessment of arthritis activity measured in a 10 cm horizontal visual analog scale (VAS), morning stiffness duration and Brazilian version of Childhood Health Assessment Questionnaire (CHAQ).⁹ Laboratorial assessment included erythrocyte sedimentation rate (ESR > 20 mm/1st hour) (Westergren method) and C-reactive protein (CRP > 5 mg/L) (nephelometry). Data concerning the use and current dosage of non-steroidal anti-inflammatory drugs (NSAIDs), prednisone, DMARDs (methotrexate, sulphasalazine and leflunomide), immunosuppressive drugs (cyclosporine) and biological agents (adalimumab, etanercept, tocilizumab and abatacept) were also determined.

Statistical analysis

The test-retest reliability of the modified questionnaire was verified using the Kappa index. 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 or Mann-Whitney tests in continuous variables to evaluate differences between JIA and controls, and between JIA subgroups. For categorical variables, differences were assessed by Fisher’s exact or Pearson chi-square tests. Spearman rank correlation coefficient was used for correlations between CRAFFT score and age. The level of significance was set at 5% ($p < 0.05$).

Results

The kappa index for test-retest was 0.850, demonstrating excellent reliability for the adolescents’ responses.

Table 1 – Demographic data, puberty markers, sexual function, alcohol, tobacco and illicit drug use, and bullying in adolescents with juvenile idiopathic arthritis (JIA) and controls.

Variables	JIA (n = 54)	Healthy controls (n = 35)	p
Demographic data			
Current age, yrs	15 (10–19)	15 (12–18)	0.506
Female gender	38 (70)	26 (74)	0.688
BMI, kg/m ²	20.79 (13.2–35.6)	19.53 (16.4–25.9)	0.205
Social economic class B and C	51 (94)	34 (97)	1.000
Education, yrs	9 (3–13)	10 (6–12)	0.826
Puberty markers			
Tanner 3	7 (13)	4 (11)	1.000
Tanner 4	10 (19)	12 (34)	0.102
Tanner 5	30 (57)	19 (54)	0.830
Menarche	32/38 (84)	26/26 (100)	0.073
Menarche age, yrs	12 (9–15)	11.5 (9–15)	0.528
Spermarche	10/16 (63)	7/9 (78)	0.661
Spermarche age, yrs	13 (10–15)	13 (12–14)	0.959
Sexual function			
Sexual activity	13 (24)	9 (26)	0.861
First sexual activity age, yrs	15 (13–17)	15 (12–17)	0.606
Sexual intercourse in last month	8/13 (62)	4/9 (44)	0.666
Condom at the first sexual activity	13/13 (100)	8/9 (89)	0.409
Oral contraception use in females	5/11 (46)	3/10 ^a (30)	0.659
Emergency contraceptive use	4/11 (36)	4/9 (44)	1.000
Knowledge of sexual activity by parents	9/13 (69)	6/8 (75)	1.000
Total number of sexual partner, number	2.5 (1–5)	1 (1–2)	0.071
Alcohol, tobacco and/or illicit drug use			
Alcohol use	23 (43)	16 (46)	0.829
Alcohol use	23 (43)	16 (46)	0.829
Age at onset alcohol, yrs	15 (11–18)	14 (7–18)	0.032
Polyarticular onset JIA, n = 17	15 (13–17)	14 (7–18)	0.040
Systemic onset JIA, n = 19	15 (11–17)	14 (7–18)	0.188
Drinking alcohol in past 30 days, number	0 (0–7)	0 (0–5)	0.505
Tobacco use	4 (7)	5 (14)	0.308
Age at onset smoking, yrs	16 (13–18)	15 (7–15)	0.250
Smoking in past 30 days, number	0	0 (0–30)	0.180
Illicit drug use	1 (2)	2 (6)	0.559
Age at onset illicit drug, yrs	14	14	1.000
Illicit drug use in past 30 days, number	0 (0–0)	1.5 (0–3)	0.480
CRAFFT score (0–6)	0 (0–3)	0 (0–5)	0.836
CRAFFT score ≥ 2	7 (13)	5 (15)	1.000
CRAFFT item			
Car	14/54 (26)	5/34 (15)	0.213
Relax	4/16 (25)	2/11 (18)	1.000
Alone	1/16 (6)	1/11 (9)	1.000
Forget	2/16 (13)	5/11 (46)	0.084
Friends	5/16 (31)	5/11 (46)	0.687
Trouble	1/16 (6)	0 (0)	1.000
Bullying	11/43 (26)	15/34 (44)	0.088

CRAFFT, car, relax, alone, forget, friends, trouble in the last 12 months; screening test.

The results are presented in n (%) and median (range) or mean ± SD.

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

The median current age was similar between JIA patients and controls [15 (10–19) vs. 15 (12–18) years, $p = 0.506$], likewise the frequency of female gender ($p = 0.688$), years of education ($p = 0.826$), social economic classes ($p = 1.000$) and Tanner 5 ($p = 0.830$). The median menarche age and spermarche age were also alike [12 (9–15) vs. 11.5 (9–15) years, $p = 0.528$ and 13 (10–15) vs. 13 (12–14) years, $p = 0.959$], respectively, as well as frequency of sexual activity ($p = 0.861$) and age of the first

sexual intercourse [15 (13–17) vs. 15 (12–17) years, $p = 0.606$] (Table 1).

The frequencies of alcohol, tobacco and/or illicit drug use were high and similar in both JIA patients and controls (43% vs. 46%, $p = 0.829$). However, the age at alcohol onset was significantly higher in those with JIA compared to healthy controls [15 (11–18) vs. 14 (7–18) years, $p = 0.032$], especially in polyarticular JIA onset ($n = 17$) [15 (13–17) vs. 14 (7–18) years, $p = 0.04$].

Table 2 – Demographic data, puberty markers, bullying and disease parameters in adolescents with juvenile idiopathic arthritis (JIA) according to alcohol, tobacco and illicit drug use.

Variables	Use alcohol, tobacco and/or illicit drug (n = 23)	Non use alcohol, tobacco and/or illicit drug (n = 31)	p
Demographic data			
Current age, yrs	17 (14–19)	13 (10–19)	<0.001
Disease duration, yrs	6 (1–17)	4 (0.25–15)	0.063
Female gender	16 (70)	22 (71)	0.911
BMI, kg/m ²	21.15 (18–27)	20.09 (13–30)	0.132
Social economic class B and C	22 (96)	28 (90)	0.628
Education, yrs	11 (6–13)	7 (3–12)	<0.001
Puberty markers			
Tanner 3	1 (4)	6 (20)	0.123
Tanner 4	3 (13)	7 (23)	0.484
Tanner 5	19 (83)	11 (37)	0.001
Menarche	16 (100)	16 (73)	0.030
Menarche age, yrs	12 (9–15)	12 (9–14)	0.861
Spermarche	7 (100)	3 (33)	0.011
Spermarche age, yrs	13 (12–15)	11 (10–13)	0.082
Sexual function			
Sexual activity	11 (48)	2 (7)	<0.001
First sexual activity age, yrs	16 (13–17)	14 (14)	0.227
Sexual intercourse in last month	7/11 (64)	1/2 (50)	1.000
Condom at the first sexual activity	11/11 (100)	2/2 (100)	1.000
Oral contraception use in females	4/9 (44)	1/2 (50)	1.000
Emergency contraceptive use	4/9 (44)	0	0.491
Knowledge of sexual activity by parents	7/11 (64)	2/2 (100)	1.000
Total number of sexual partner, number	3 (1–5)	1 (1)	0.074
Bullying	5/18 (28)	6/25 (24)	1.000
JIA parameters			
Morning stiffness	7 (30)	2/29 (7)	0.061
Morning stiffness, min	30 (10–120)	20 (10–30)	0.492
Active joints	7 (30)	10 (32)	0.887
Number of active joints	1 (1–8)	1 (1–9)	0.956
Limited joints	16 (70)	20 (65)	0.697
Number of limited joints	2 (1–11)	3.5 (1–61)	0.165
ESR, mm/1st h	14.5 (2–60)	20 (2–47)	0.809
ESR, >20 mm/1st h	10/22 (46)	11/27 (41)	0.740
CRP, mg/L	2.23 (0–76)	1.23 (0–155)	0.847
CRP, >5 mg/L	6/22 (27)	7/26 (27)	0.978
Patient's VAS, cm	1 (0–9)	1 (0–5)	0.748
Physician's VAS, cm	0 (0–4)	1 (0–4)	0.307
CHAQ	0.56 (0–2.6)	0.63 (0–1.5)	0.779
Current treatment			
NSAID	19 (83)	29 (94)	0.384
Naproxen	7 (30)	16 (52)	0.120
Glucocorticoids	2 (9)	6 (19)	0.443
Dose, mg/day	3 (13)	8 (26)	0.319
Methotrexate	11.3 (2.5–40)	5 (2.5–25)	0.214
Dose, mg/week	4 (17)	6 (19)	1.000
Leflunomide	25 (10–50)	25 (10–37.5)	0.731
Dose, mg/day	3 (13)	5 (16)	1.000
Sulfasalazine	20 (20)	20 (10–20)	0.094
Cyclosporine	0	1 (3)	1.000
Dose, mg/day	2 (9)	3 (10)	1.000
Biological agents	190 (180–200)	150 (100–200)	0.584
Abatacept	12 (52)	10 (32)	0.141
Etanercept	1 (4)	2 (7)	1.000
Adalimumab	5 (22)	3 (10)	0.217
Tocilizumab	4 (17)	3 (10)	0.443
	2 (9)	2 (7)	1.000

The results are presented in n (%) and median (range) or mean ± SD, CRAFTT (car, relax, alone, forget, friends, trouble) screening test.

Illicit drugs were used by one JIA patient (marijuana and cocaine) and two controls (marijuana) ($p=0.559$) and no difference was observed in the frequency of tobacco use. CRAFFT score ≥ 2 was similar in both groups (13% vs. 15%, $p=1.000$). Of our 7 JIA patients with CRAFFT score ≥ 2 , 4 had polyarticular onset, 5 used methotrexate and 6 biological agents. The frequency of bullying was lower in patients with JIA vs. controls, however it did not reach statistical significance (26% vs. 44%, $p=0.088$) (Table 1).

Of JIA subtypes, systemic onset was observed in 19 patients, polyarticular in 17, pauciarticular in 13, enthesitis-related arthritis in 3 and psoriatic arthritis in 2. Further analysis of JIA patients regarding alcohol/tobacco/illicit drug use showed that the median current age [17 (14–19) vs. 13 (10–19) years, $p<0.001$] and education years [11 (6–13) vs. 7 (3–12) years, $p<0.001$] were significantly higher in those that used the aforementioned substances. The frequencies of Tanner 5 ($p=0.001$), menarche ($p=0.030$) and spermarche ($p=0.011$) were also significantly higher in the former group, likewise sexual activity (48% vs. 7%, $p<0.001$). No differences were evidenced between alcohol/tobacco/illicit drug use and disease parameters and current treatment in both groups ($p>0.05$, Table 2).

A positive correlation was evidenced between CRAFFT score and current age in JIA patients ($p=0.032$, $r=+0.296$), with no correlation in controls ($p=0.571$). No correlations were evidenced between CRAFFT score and age of alcohol onset ($p=0.751$), onset of sexual intercourse ($p=0.606$) and education years ($p=0.066$) in JIA patients.

Discussion

To the best of our knowledge, this was the first study that assessed simultaneously adolescent health issues in JIA population and controls, and evidenced a higher age at alcohol onset in patients, mainly in polyarticular subtype. In the JIA adolescent group, substance users were more likely to have sexual intercourse. We also found a higher risk for substance abuse/dependence at later age in JIA adolescents.

The advantage of the present study was the evaluation of physician-conducted CRAFFT (CEASER) screening tool. This score is used to determine the high-risk of alcohol and drug dependence in adolescents.^{2,6} A questionnaire with excellent test-retest reliability that evaluated sexual function, bullying and licit/illicit drug consumption was also used. A healthy control group with similar age, academic background, gender and socio-economic class was pertinent herein, since these data were related with bullying and drug use.^{1,2} However, the main weaknesses of this study was the cross sectional analysis, as well as the small sample studied and the lack of the evaluation of different forms of bullying.

Alcohol use was previously reported in 36% of adolescent and young adults with pediatric rheumatic diseases.¹⁰ In addition, Nash et al. reported a 19% of alcohol experimentation in 52 JIA adolescents,¹¹ contrasting to 43% observed herein. This finding may be related to an increased alcohol intake in adolescents during the nineties¹² and the economic growth in our country,¹³ thus enabling middle socio-economic class to consume. Therefore, restriction strategies are required to decrease alcohol use.

Of note, the age at alcohol onset was higher in JIA patients, especially in polyarticular onset under methotrexate and biological agents. Our patients ignored the information to avoid substance use concomitant to biological and non-biological DMARDs, with a high risk to adverse events, particularly hepatotoxicity.¹¹ We used a screening procedure for substance use.^{2,6} Indeed, CRAFFT score ≥ 2 in our JIA patients indicated higher risk for substance abuse/dependence.² Based on that, additional assessment and therapeutic intervention with a multidisciplinary and multiprofessional team is required.

Importantly, JIA substance users engaged more in sexual activity, with possible unsafe sexual relations, sexually transmitted diseases and pregnancy. This finding may be also related to the fact that the patients were older with higher sexual maturity. Despite JIA is a painful, chronic and disability disease, and may influence sexual function,^{14,15} our patients presented their first sexual activity earlier.

A delay of puberty markers was not evidenced in JIA patients, which is a distinct pattern in our adolescent with juvenile systemic lupus erythematosus¹⁵ and juvenile dermatomyositis.¹⁶ In addition, bullying was frequently reported in JIA and controls that may cause depression, anxiety and interfere with proper adherence of medication use.⁴ A prospective study, recruiting larger sample of JIA and evaluating these aspects, will be necessary.

In conclusion, high risk for substance abuse/dependence was observed in both JIA and controls. JIA substance users were more likely to have sexual intercourse. Our study reinforces that JIA adolescents should be systematically screened by pediatricians for sexual, alcohol and drugs health behavioral patterns, as part of Pediatric Rheumatology service visits. Alcohol and contraception education to JIA patients, especially those treated with methotrexate and biologic agents, should be included in the routine care.

Conflicts of interest

The authors declare no conflicts of interest.

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