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ORIGINAL ARTICLE

Changes in lung function in adolescents with substance use disorders: an exploratory study

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ABSTRACT

Objective: To compare lung function between adolescents with and without substance use disorder (SUD). **Methods:** This was an observational, cross-sectional exploratory study. The sample consisted of 16 adolescents with SUD and 24 age-matched healthy controls. The adolescents in the clinical group were recruited from a psychiatric inpatient unit for detoxification and rehabilitation; their primary diagnosis was SUD related to marijuana, cocaine, or polysubstance use. Questionnaires and pulmonary function tests were applied for clinical evaluation. **Results:** We found that FVC, FEV_1, and their percentages of the predicted values were significantly lower in the adolescents with SUD than in those without. Those differences remained significant after adjustment for BMI and the effects of high levels of physical activity. The largest effect size (Cohen's d = 1.82) was found for FVC as a percentage of the predicted value (FVC%), which was, on average, 17.95% lower in the SUD group. In addition, the years of regular use of smoked substances (tobacco, marijuana, and crack cocaine) correlated negatively with the FVC%. **Conclusions:** This exploratory study is innovative in that it demonstrates the early consequences of smoked substance use for the lung health of adolescents with SUD.

Keywords: Adolescent; Substance-related disorders; Lung/physiopathology; Respiratory tract diseases/etiology; Cocaine; Cannabis.

INTRODUCTION

Experimentation with psychoactive substances, licit or illicit, frequently occurs during adolescence. Global epidemiological data indicate that approximately 20% of individuals between 16 and 24 years of age report using at least one illegal drug in the last year.[1] It has also been estimated that 19.33% of adolescents between 13 and 15 years are already cigarette smokers, which is alarming.[2] In addition, data from the U.S. Centers for Disease Control and Prevention indicate a similarly high prevalence (17.6%) of tobacco use during the transition from adolescence to adulthood (from 18 to 24 years of age).[3] In recent years, there has also been an increase in the estimated rates of marijuana use among adolescents.[4,5]

Early patterns of substance use are linked to an increased likelihood of developing a substance use disorder (SUD).[6] Individuals with an SUD present a persistent, compulsive pattern of substance use, which leads to significant impairment in various aspects of their life, including physical and mental health, as well as relationships and daily functioning. Although SUD is a significant public health concern worldwide, particularly regarding the consequences for mental health, little is known about its effects on respiratory and pulmonary function in the adolescent population.[7]

It has been reported that the long-term use of inhaled psychoactive substances has adverse pulmonary effects such as bronchial inflammation,[8] acute lung injury, and COPD.[7,9] Studies suggest that smoking crack cocaine results in multiple pulmonary alterations,[10] including lung lesions that may be worsened because of the toxicity caused by a pattern of polysubstance use which often occurs among people with problems related to cocaine use.[11] There is also evidence suggesting that most heroin users have some degree of airway obstruction and that frequent inhalation of the substance is one of the risk factors for developing COPD.[12,13] Pulmonary emphysema and asthma have been linked to the chronic

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use of heroin[14,15] and crack cocaine.[16] However, compromised lung function, as assessed by tests such as spirometry, is also evident after a prolonged period of marijuana use, as indicated by significantly lower FEV_1.[9,17] Pulmonary function tests have also shown that the measures associated with restrictive lung disease are 50% lower among heroin smokers than among tobacco smokers and nonsmokers, as well as that there is a high prevalence of COPD among heroin smokers.[14]

The impact that smoking tobacco, marijuana, crack cocaine, and heroin has on lung function has primarily been studied in adults, particularly in chronic users with an extensive consumption history. However, there remains a significant gap in our understanding of how SUD affects adolescents and their lung health. In addition, investigating this age group is relevant for identifying which spirometric parameters might be more affected by early substance misuse. Therefore, the aim of this study was to compare lung function measures between adolescents with and without SUD. Our exploratory findings may better characterize pulmonary alterations resulting from substance use, even during adolescence.

METHODS

Ethics

The study was performed in accordance with the principles stated in the Declaration of Helsinki. Before the research protocol, including the study procedures and questionnaires, was submitted for ethical committee review and project appreciation, approval was sought from both the school and the hospital. Ethical consent was then obtained for all protocols from the local institutional review board and appropriate ethics committees to confirm that the study met national and international guidelines for research on humans (Ethical approval numbers and dates: 4.128.393 / July 1, 2020; 5.223.468 / February 3, 2022). Written informed consent was obtained from parents or legal guardians, as well as from the participants themselves.

Study design and sampling procedures

This was an observational, cross-sectional exploratory study. The sample, recruited between September of 2021 and December of 2022, comprised 16 adolescents with SUD and 24 age-matched healthy controls. The inclusion criteria were being male and being between 15 and 18 years of age. Individuals with chronic psychotic disorders were excluded, as were those who were categorized as illiterate, mainly because illiteracy and psychosis could introduce biases in the completion of questionnaires and the collection of clinical data.

The participants in the SUD group were recruited from a psychiatric inpatient unit for alcohol and drug detoxification at a hospital in the city of Porto Alegre, Brazil. Over 21 days of hospitalization, they were treated by a multidisciplinary team of clinical physicians, psychiatrists, psychologists, nurses, nursing technicians, occupational therapists, and physical educators. The patients also followed a diet plan, together with a medication protocol for detoxification and management of withdrawal symptoms. The protocol comprised mostly chlorpromazine, at doses ranging from 50 mg/day to 125 mg/day. All participants in the clinical group had an SUD (related to marijuana, powder cocaine, crack cocaine, or polysubstance use) as their primary diagnosis. The diagnosis was confirmed by psychiatric evaluation according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition criteria. It is noteworthy that our data were collected during the COVID-19 pandemic and that all patients admitted to the unit therefore underwent mandatory SARS-CoV-2 testing. None of the patients included in our study had a current diagnosis of COVID-19. The participants in the control group were recruited from private schools in the same city. A questionnaire about drug use behavior was applied in order to determine their eligibility. None of the control group participants had a history of regular use of substances such as alcohol, tobacco, marijuana, and cocaine.

Two questionnaires were utilized in the study: a basic sociodemographic questionnaire; and the sixth version of the Addiction Severity Index (ASI-6). The sociodemographic questionnaire covered level of education, age, socioeconomic status, and frequency of physical activity, high levels of physical activity being defined as engaging in moderate- to high-intensity exercise more than three times a week, each session lasting for at least one hour. The ASI-6 consists of a semi-structured interview assessing the history of alcohol and other drug use, including information such as the age at initiation, duration, frequency, and quantity of consumption.[18] A year of regular use is defined as that during which a substance was used at least three times a week. We analyzed data from years of regular use of alcohol, tobacco, marijuana, powder cocaine, and crack cocaine. We generated an additional variable—years of regular use of smoked substances—estimated for the inhaled substance most regularly used by the participant (tobacco, marijuana, or crack cocaine). For example, if the participant reported five years of regular marijuana use and three years of regular tobacco use, their score on this variable was five years. In addition, all variables related to years of regular consumption were adjusted for the age of participants by calculating the ratio between years of regular consumption and current age. Medical records were reviewed to collect data on medication use and previous illnesses. We checked vital signs, weight, and height, as well as calculating BMIs, for which the data were standardized to Z-scores.

Spirometry was carried out according to the acceptability and reproducibility criteria of the American Thoracic Society/European Respiratory Society.[19] All measurements were corrected for the local barometric pressure and temperature on the day of the tests. Initial weight and height were measured

using a scale and a tape measure. The tests were performed individually, with the subjects standing, without the use of a nose clip, and with a KOKO spirometer (Longmont, CO, USA). The parameters assessed were FVC, FEV_1, the FEV_1/FVC ratio, and $FEF_{25-75\%}$. For better visualization of the results, the spirometric parameters are expressed as absolute values and as percentages of the predicted values according to international reference equations.[20] In the SUD group, spirometry was performed in the second week of detoxification, to avoid the effects of acute withdrawal.

Statistical analysis

Quantitative variables were tested concerning data distribution, and no evidence of non-normality was found. Therefore, quantitative variables are expressed as means and standard deviations. The Shapiro-Wilk test was chosen for normality analysis of data distribution because it is better suited for use with small sample sizes. Qualitative variables are expressed as absolute values and percentages. The groups were compared by using the t-test for independent samples. The effect size for t-tests was estimated by calculating Cohen's d statistic, which categorizes the effect size as small (0.2-0.4), medium (0.5-07), or large (≥ 0.8), particularly for spirometric measures. Qualitative variables were compared between groups by using the chi-square test. For spirometric variables with significant intergroup differences, we performed analysis of covariance (ANCOVA), adjusting for possible confounding factors. To assess potential associations between spirometric data and clinical data, we performed a Spearman correlation analysis restricted to the SUD group. All analyses were performed with the SPSS Statistics software package, version 17.0 (SPSS Inc., Chicago, IL, USA). Values of $p < 0.05$ were considered statistically significant.

RESULTS

Table 1 shows the demographic and clinical characteristics of the sample. We observed that the groups did not differ in age, BMI, height, or weight, although the proportion of individuals with a high level of physical activity was greater in the control group, as was that of those with a high monthly family income (> 5,000 Brazilian reals). The proportion of individuals with a low monthly family income (< 1,000 Brazilian reals) was greater in the SUD group. In addition, we observed differences in the level of education, the mean number of years of schooling being higher in the control group than in the SUD group.

Regarding years of substance use in the SUD group, tobacco and marijuana were used for the longest times (approximately three years of regular use). Regarding the estimated variable of years of regular use of smoked substances, the mean was approximately four years. For each participant in the SUD group, we also calculated the ratio between the years of regular consumption of each substance and the current age. The mean ratios were as follows: 2.75 ± 7.5 for lifetime regular alcohol use; 22.8 ± 18.8 for lifetime regular tobacco use; 23.1 ± 15.4 for lifetime regular marijuana use; 16.1 ± 15.4 for lifetime regular powder cocaine use; 3.75 ± 7.6 for lifetime regular crack cocaine use; and 27.1 ± 17.4 for lifetime regular use of any smoked substance.

Spirometry

When comparing lung function data (Table 2), we found that the absolute FVC, FVC as a percentage of the predicted value (FVC%) and FEV_1 as a percentage of the predicted value (FEV_1%) were significantly lower in the SUD group than in the control group. The absolute FEV_1/FVC ratio was significantly higher in the SUD group than in the control group. Effect sizes

Table 1. Anthropometric, demographic, and clinical characteristics of the sample.

Variable	Group		Statistic	p
	SUD (n = 16)	Control (n = 24)		
Age (years), mean ± SD	15.37 ± 1.02	15.33 ± 0.96	t = 0.13	0.632
BMI (Z-score), mean ± SD	23.3 ± 3.63	20.7 ± 2.36	t = 1.59	0.119
Height (cm), mean ± SD	170.3 ± 4.86	171.8 ± 7.42	t = 0.71	0.480
Weight (kg), mean ± SD	67.6 ± 11.44	62.2 ± 8.10	t = 1.66	0.105
High physical activity level, n (%)	0 (0.0)	13 (54.2)	x^2 = 12.84	< 0.001
Family income (< R$1,000/month), n (%)	13 (81.2)	0 (0.0)	x^2 = 28.88	< 0.001
Family income (R$1,000-5,000/month), n (%)	3 (18.8)	1 (4.2)	x^2 = 2.26	0.132
Family income (> R$5,000/month), n (%)	0 (0.0)	23 (95.8)	x^2 = 36.07	< 0.001
Years of schooling, mean ± SD	7.68 ± 1.57	10.33 ± 1.57	t = 6.59	< 0.001
Years of alcohol use, mean ± SD	0.37 ± 1.08	-	-	-
Years of tobacco use, mean ± SD	3.37 ± 2.62	-	-	-
Years of marijuana use, mean ± SD	3.37 ± 2.30	-	-	-
Years of powder cocaine use, mean ± SD	2.12 ± 2.27	-	-	-
Years of crack cocaine use, mean ± SD	0.50 ± 1.09	-	-	-
Years of smoked substance use, mean ± SD	4.00 ± 2.52	-	-	-

SUD: substance use disorder; χ^2: chi-square test; and R$: Brazilian reals (1 real currently equals 0.20 US dollars).

Table 2. Comparison of spirometry variables.[a]

Variable	Group		Statistic	p	Cohen's d
	SUD (n = 16)	Control (n = 24)			
FVC (absolute)	4.31 (0.56)	4.92 (0.84)	t = 2.54	0.015	0.85 (large)
FVC (pred%)	92.00 (11.16)	109.95 (16.26)	t = 3.84	< 0.001	1.28 (large)
FEV_1 (absolute)	3.88 (0.46)	4.25 (0.65)	t = 1.94	0.059	0.65 (medium)
FEV_1 (pred%)	96.25 (9.86)	110.33 (15.36)	t = 3.24	0.002	1.09 (large)
FEV_1/FVC ratio (absolute)	0.92 (0.12)	0.86 (0.44)	t = 2.18	0.036	0.18 (small)
FEV_1/FVC ratio (pred%)	104.37 (8.11)	100.20 (5.04)	t = 2.00	0.052	0.61 (medium)
$FEF_{25-75\%}$ (absolute)	4.56 (0.69)	4.72 (0.85)	t = 0.61	0.544	0.20 (small)
$FEF_{25-75\%}$ (pred%)	100.43 (14.63)	114.70 (34.07)	t = 1.57	0.123	0.54 (medium)

SUD: substance use disorder; pred%: and percentage of the predicted value [a]Values expressed as mean ± SD.

ranged from small to large. The largest effect size was for FVC%, corresponding to the most significant difference between the two groups: 17.95% lower in the SUD group. We found no significant differences between the two groups in terms of the absolute FEV_1, the FEV_1/FVC ratio as a percentage of the predicted value, absolute $FEF_{25-75\%}$, or $FEF_{25-75\%}$ as a percentage of the predicted value.

We utilized ANCOVA to determine whether the group effect on specific lung function parameters persisted even after adjustment for the influences of BMI and a high physical activity level. The significant group effects persisted for all variables: absolute FVC ($F = 6.67$, $p = 0.014$); FVC% ($F = 10.80$, $p = 0.002$); FEV_1% ($F = 5.60$, $p = 0.023$); and the absolute FEV_1/FVC ratio ($F = 5.74$, $p = 0.022$). The BMI also had a significant effect ($p < 0.05$) in the ANCOVAs referring to the two FVC variables (FVC and FVC%). No significant effects were found for the high level of physical activity variable.

Finally, we performed correlation analyses restricted to data from the SUD group, in order to determine whether age, BMI, height, weight, chlorpromazine dose, and years of substance use correlated with the measures of lung function (Table 3). We found that BMI correlated positively with the absolute FVC, FVC%, and the absolute FEV_1/FVC ratio. The years of regular use of smoked substances/age ratio correlated negatively with FVC%. None of the spirometric parameters were found to correlate significantly with age, height, weight, chlorpromazine dose, or the years of regular consumption/age ratio for tobacco, marijuana, powder cocaine, crack cocaine, or alcohol.

Considering the positive correlation between BMI and the spirometric variables, we repeated this analysis across our entire sample, including the control group. This second analysis showed no significant association between BMI and spirometric variables ($p > 0.05$ for all).

DISCUSSION

This study compared lung function between adolescents with and without SUD. We found differences in specific measures of FVC and FEV_1, the percentages of their predicted values, and the FEV_1/FVC ratio. These changes remained significant after adjustment for the effects of covariates such as BMI and physical activity level. The largest effect size was found for the FVC%, suggesting that adolescents with SUD have less air that can be exhaled forcefully. In addition, the years of regular use of smoked substances correlated negatively with the FVC%. This exploratory study is innovative in that it demonstrates the early pulmonary consequences of SUD in an adolescent population, whose trajectory of chronic substance use is still unfolding. Although we found lung function to be lower in the SUD group, it is noteworthy that the percentages of the predicted values for the spirometric parameters FVC and FEV_1 were within the normal range (above 80%) in both groups, suggesting that there is no lung function impairment associated with SUD during adolescence. Nevertheless, our study partially corroborates the growing body of evidence showing a clinically relevant loss of lung function related to the chronic smoking of tobacco, marijuana, crack cocaine, and heroin.

There is growing evidence that marijuana use can promote pulmonary changes associated with COPD, most commonly characterized by decreases in FEV_1 and FVC.[21,22] The recurrent use of marijuana in combination with tobacco increases the alterations and pulmonary impairment, as assessed by pulmonary function tests. That is because cigarettes are smoked more frequently than is marijuana, especially by adults.[22] In the case of the association between marijuana and COPD, data indicate that individuals who smoke marijuana and tobacco are twice as likely to develop severe respiratory symptoms of the disease.[23,24] These findings are relevant given the profile of our clinical sample, in which tobacco and marijuana were the substances that were consumed most commonly and for the longest periods.[24] In addition, because of the mechanisms of injury potentiated by the toxicity of the substances, their regular use can worsen the clinical presentation of lung diseases such as asthma and COPD.[25,26] For example, evidence suggests that cocaine use exacerbates asthma, as well as increasing symptom severity and the length of the hospital stays due to lung disease.[27]

Table 3. Correlation analyses in the substance use disorder group (n = 16).

Variable	FVC (absolute)		FVC (pred%)		FEV_1 (pred%)		FEV_1/FVC ratio (absolute)	
	r	p	r	p	r	p	r	p
Age	0.286	0.283	0.200	0.458	0.271	0.310	−0.091	0.736
BMI Z-score	0.580	0.018	0.733	0.001	0.322	0.223	−0.668	0.005
Height	0.422	0.104	−0.073	0.788	−0.089	0.742	−0.302	0.256
Weight	0.016	0.953	0.120	0.659	0.025	0.926	−0.053	0.846
Chlorpromazine use	−0.317	0.231	−0.401	0.124	−0.157	0.560	0.408	0.116
Tobacco use*	−0.138	0.610	−0.331	0.210	−0.143	0.598	0.335	0.205
Marijuana use*	0.211	0.433	−0.153	0.572	−0.156	0.564	−0.163	0.547
Crack cocaine use*	−0.358	0.174	−0.494	0.052	−0.231	0.389	0.458	0.075
Smoked substance use*	−0.519	0.039	−0.370	0.158	−0.261	0.328	0.450	0.080
Powder cocaine use*	−0.134	0.621	−0.119	0.661	−0.043	0.874	0.177	0.513
Alcohol use*	0.031	0.910	−0.161	0.551	−0.173	0.522	−0.225	0.403

pred%: percentage of the predicted value. *Years of regular use/age ratio.

We found no associations between spirometric parameters and the years of regular smoking of tobacco, marijuana, or crack cocaine, as well as no associations between spirometric parameters and the regular use of substances that are not smoked, such as alcohol and powder cocaine. This should be interpreted cautiously, considering our small sample size. However, when estimating a variable that considered the prolonged use of marijuana, crack cocaine, or tobacco, we found an inverse correlation between years of regular use and FVC%. That finding partially corroborates the results of a cohort study conducted by Sherrill et al., who showed progressive reductions in FEV_1 and the FEV_1/FVC ratio in marijuana smokers over a six-year follow-up period, suggesting that the substance is associated with a continuous decline in lung function over the years, which can be accelerated in the case of concurrent cigarette smoking.[28]

Our study has significant limitations. First, the sample size was small and the study was exploratory in nature. However, considering that few studies have investigated lung function in an adolescent population with SUD, we have contributed to expanding a little-explored field. Second, participants in the SUD group had been admitted to a detoxification treatment program, including the prescription of psychotropic drugs, especially chlorpromazine. Nevertheless, our correlation analyses between the dose of chlorpromazine and the spirometry variables revealed no significant associations. Third, we found significant differences in socioeconomic indicators such as level of education and family income, suggesting that there are major differences between adolescents with and without SUD in terms of life trajectory, family background, and psychosocial factors. However, many studies indicate that poverty, a low level of education, and other markers of social vulnerability are risk factors for SUD,[29,30] making it more challenging to match the SUD group with a healthy reference group of socioeconomic peers. Fourth, because SUD was the primary health problem of the patients, no clinical lung assessment was performed during the treatment program. Lastly, the adolescents with SUD who were enrolled in the study were recruited from among a group of inpatients and were therefore representative of adolescents with relatively severe disease.

Despite its limitations, our study suggests that lung function is impaired in adolescents with SUD. Therefore, clinicians need to be aware of the history of substance use in patients with airway alterations, and our data suggest that lung function changes can start in adolescence. Future studies with fewer limitations may generate more robust evidence on pulmonary alterations in this population and suggest paths for the clinical applicability of these findings.

AUTHOR CONTRIBUTIONS

DBK: drafting of the manuscript. DBK, MM, MG, and LEWS: data collection. JHC: data curation. JHC, MM, MG, LEWS, MVFD, FF, MHJ, and TWV: revision of the manuscript. MVFD, MHJ, and TWV: study design. FF: data analysis. TWV: supervision. All authors read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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