

Effects of volatile substance abuse on the respiratory system in adolescents

Effetti dell'abuso di sostanze volatili sull'apparato respiratorio degli adolescenti

Halime SC Büker¹, Esen Demir¹, Zeki Yüncü², Figen Gülen¹, Levent Midyat¹, Remziye Tanaç¹

¹Ege University Faculty of Medicine, Department of Pediatrics, Division of Pulmonology-Allergy, Izmir, Turkey

²Ege University Child and Adolescent Addiction Investigation and Practice Center (EGBAM), Izmir, Turkey

ABSTRACT

Aim: Inhalant abuse is a prevalent and often overlooked form of substance abuse in adolescents. Chronic inhalant abuse can damage respiratory, cardiac, renal, hepatic, and neurologic systems. This study aims to determine the physiologic effects of inhaling solvents on the respiratory functions.

Methods: The general health status of the subjects was assessed by history taking, physical examination and a questionnaire which was designed to show the severity of respiratory symptoms. Spirometry, ventilation/perfusion scintigraphy, and high resolution computed tomography (HRCT) were performed to assess pulmonary functions and anatomy.

Results: Thirty-one male volatile substance abusers and 19 control subjects were included in the study. The mean age of onset of inhalant use was 14.6 ± 2.2 (9-18) years and duration of drug use was 3.7 ± 1.7 years. The most common respiratory symptoms in volatile substance abusers were nasal congestion (45.2%), sputum (38.7%), exercise intolerance (32.3%) and cough (22.6%). Results of spirometric studies showed 12 (41.4%) subjects with low FVC values < 80% of predicted, indicative of restrictive ventilatory pattern in the study group. Although the difference was not statistically significant, restrictive ventilatory pattern was higher in the study group. There was no statistically significant correlation between restrictive ventilatory pattern and the age of onset/duration/frequency of inhalant abuse, respiratory symptoms and scintigraphic abnormalities. Subjects who had restrictive pattern in their pulmonary function tests were more likely to have abnormal findings at HRCT ($p < 0.01$).

Conclusion: This study has shown a positive correlation between volatile substance abuse and the development of restrictive ventilatory pattern, but more comprehensive studies are needed for more precise conclusions.

Keywords: Abuse, adolescent, inhalant, respiratory system.

RIASSUNTO

Scopo: Negli adolescenti l'abuso di inalanti è una forma ad alta prevalenza di abuso di sostanze, ma spesso è trascurato. Può danneggiare l'apparato respiratorio, cardiaco, renale, epatico ed il sistema nervoso. Questo studio cerca di determinare gli effetti fisiologici dell'inalazione di solventi sull'apparato respiratorio.

Metodi: Le condizioni generali dei soggetti sono state valutate con l'anamnesi, l'esame obiettivo ed un questionario progettato per identificare la gravità dei sintomi respiratori. Per valutare la funzionalità respiratoria e gli aspetti morfologici sono state effettuate spirometria, scintigrafia ventilo/perfusoria ed una TAC toracica ad alta risoluzione (HRCT).

Risultati: Sono stati inclusi nello studio 31 maschi che abusavano di sostanze volatili e 19 soggetti di controllo. L'età media dell'inizio dell'abuso di inalanti era $14,6 \pm 2,2$ (9-18) anni e la durata dell'uso di droga era $3,7 \pm 1,7$ anni. I sintomi più comuni dell'abuso di sostanze volatili erano: congestione nasale (45,2%), espettorato (38,7%), intolleranza allo sforzo (32,3%) e tosse (22,6%). I risultati degli studi spirometrici hanno identificato 12 (41,4%) soggetti con bassi valori di capacità vitale forzata (< 80% del teorico), suggestivi per un pattern restrittivo. Nonostante la differenza non fosse significativa il pattern ventilatorio restrittivo era maggiore nel gruppo oggetto dello studio. Il pattern ventilatorio restrittivo non era statisticamente correlato con l'età di inizio, la durata o la frequenza dell'abuso di inalanti, con i sintomi respiratori e con le anomalie scintigrafiche. I soggetti con deficit restrittivo avevano tuttavia una maggiore frequenza di reperti patologici alla HRCT ($p < 0,01$).

Conclusioni: Questo studio mostra una correlazione positiva tra abuso di sostanze volatili e sviluppo di un deficit respiratorio restrittivo, ma sono necessari studi più approfonditi per ottenere dati conclusivi più accurati.

✉ Levent Midyat

Ege University, Faculty of Medicine, Department of Pediatrics, Division of Pulmonology-Allergy

Cocuk Sagligi ve Hastaliklari AD

35100, Bornova, Izmir, Turkey

email: midyatlev@yahoo.com

Data di arrivo del testo: 28/10/2010 – Accettato dopo revisione: 06/12/2010

Multidisciplinary Respiratory Medicine 2011; 6(3): 161-168

Parole chiave: Abuso di sostanze, adolescenza, apparato respiratorio, inalanti.

INTRODUCTION

Volatile substance abuse (VSA) is an especially important problem, because inhalants are daily-used substances, the age of onset of VSA is early, and acts as a gateway toward abuse of more dangerous substances. Inhalants are thought to be the first substances which children abuse; especially because inhalants are cheap, easily accessible, legally freely sold, in a packaging suitable for use, and have a quick impact [1,2]. Inhalants are volatile hydrocarbons such as toluene, n-hexane, methyl butyl ketone, trichlorethylene, trichlorethane, dichloromethane, gasoline and butane.

In Turkey, the most widely used inhalants are paint thinners, and glues [3]. Because of the highly lipophilic character of inhalants, their use exerts harmful effects on various systems, and primarily on the nervous system. The most important acute effect of volatiles is sudden death, which is thought to develop as a result of vagal inhibition, anoxia, respiratory failure, and cardiac arrhythmia [3,4]. Long-term low-dose volatile substance abuse may cause nervous system damage, such as muscle weakness, tremor, peripheral neuropathy, cerebellar dysfunction, chronic encephalopathy, and dementia [5-8]. In addition, there are also non-neurologic complications such as congestive heart failure, distal renal tubular acidosis, metabolic acidosis with high anion gap, Fanconi syndrome, nephrolithiasis, glomerulonephritis, Goodpasture's syndrome, toxic hepatitis, reversible hepatorenal failure, leukemia, and aplastic anemia [8].

VSA is a problem which is gaining importance in children and young adults of developed nations, along with developing nations. A research conducted by the United Nations Office on Drugs and Crime (UNODC) found the age of onset to be 11 for inhalants, 16 for cannabis, and 17 for ecstasy [9]. Therefore, it is necessary to investigate the effects of abuse of inhalants on health, and to inform and educate these children, their families, and society in general. Inhalants are widely abused and have many known adverse effects; but there are few published clinical research studies in the literature to date investigating the long-term pulmonary toxicity of volatile inhalants. In this study, we aimed to determine the physiologic effects of inhaling solvents on the respiratory functions of the adolescent inhalant abusers.

MATERIALS AND METHODS

This is a case-control study, conducted between November 2006 and November 2007, as a joint collaboration between Ege University Faculty of Medicine, Department of Pediatrics, Division of Pulmonology and Allergy, and Ege University Child and Adolescent Addiction Investigation and Practice Center (EGBAM). The approval of the Institutional Ethics Committee of Ege University

Faculty of Medicine was obtained before the initiation of study.

Study group

The subject group of this study were the individuals undergoing inpatient treatment at the Ege University Child and Adolescent Addiction Investigation and Practice Center (EGBAM). Criteria for inclusion in the study were that subjects: i) met the diagnostic criteria of DSM-IV-TR inhalant-related disorders; and ii) were able to cooperate in the study, by responding to questions, and undergoing the necessary examinations. Exclusion criteria were: i) a history of chronic systemic illness, or assuming a pharmaceutical drug for this type of illness, in the period before the development of substance abuse; ii) presence of a psychological disorder, at a level which would not allow participating in, or continuing with the study.

A total of 31 volatile substance abusers were admitted to the study. The age range of the patient group was 13-21 years. The control group comprised 19 subjects, selected from adolescents who had no health problem and who did not abuse any substance. All of the subjects who met the criteria for inclusion in the study, and their parents, were informed both verbally and in writing. After this, a questionnaire was administered that probed their sociodemographic characteristics, and respiratory system complaints. Detailed physical examination of all the subjects was performed. The severity of inhalant abuse was assessed, by a psychiatrist experienced in substance abuse disorders, by administering YUKUD (Yeniden Adolescent Inhalant Use Severity Scale), which consists of 18 questions. Subjects underwent a pulmonary function test, ventilation-perfusion scintigraphy, and high-resolution computerized tomography (HRCT).

Statistical evaluation

Statistical analyses were performed using "SPSS (Statistical Package for Social Sciences) 15.0 for Windows" software. The results were evaluated with a 95% confidence interval, and $p < 0.05$ was accepted as statistically significant.

RESULTS

Sociodemographic characteristics

A total of 31 subjects took part in the study. All subjects were males, with an average age of 17.9 ± 1.5 (13.3-20.1) years. Applicants who were resident within Izmir were 81.1%, those coming from outside of Izmir were 12.9%. The mothers of 96.8%, and fathers of 93.5%, were alive; mothers' cigarette smoking rate was 58.1%, while fathers' was 41.9%, and fathers' rate of consuming both alcohol and cigarettes was 41.9%. Only 16.2% of the fathers were not using a substance. The percentage of subjects living at home with their family was 96.8%. The rate of running away from home without informing their family was 90.3%. The length of time these subjects had lived on the street varied be-

tween 1 to 45 days, with a mean of 8.6 ± 12.4 days. Upon investigating their educational status, 90.3% of the subjects were found to be not attending school. The years of education that the subjects had had were between 1 and 13, with a mean of 7.8 ± 2.8 years. Until the time of admission to EGEBAŞ, 93.5% of the subjects had worked in an occupation related to some volatile substance. The family income of 16% of subjects was 0-400 euros/month, of 67% was 400-700 euros/month, and of 16.1% was ≥ 700 euros/month.

In the study group, 5 subjects (16.1%) reported having had a suicide attempt. There were 26 (64.5%) subjects with a criminal record, and 6 of these (19.3%) had done time in prison because of substance abuse. 74.2% of the subjects reported previously having gotten medical help because of substance abuse. Occurrence of inpatient treatment because of substance addiction was between 1 and 6 times, with a mean of 1.9 ± 1.4 . Except for glue (trademark: Bally) and paint thinner, no other inhalant abuse was found. The rate of Bally abuse was 80.6%, paint thinner 6.5%, and those who abused both were 12.9% (Table I).

Cigarette smoke was the substance most used along with inhalants. After cigarettes, followed hashish, ecstasy, benzodiazepine, alcohol and cocaine addictions. Cigarette abuse rate was 3.2%, addiction rate 87.1%; hashish abuse rate 29%, addiction rate 54.8%; ecstasy abuse rate 25.8%, addiction rate 29%; benzodiazepine abuse rate 19.4%, addiction rate 19.4%; alcohol abuse rate 51.6%, addiction rate 16.1%, cocaine abuse rate 9.7%, and addiction rate 3.2% (Table II). The mean age of onset of VSA was 14.2 ± 2.2 (9-18) years. The age of onset of abuse of the other substances was: 11.8 ± 2.7 (7-16) years for cigarettes, 14.2 ± 2.0 (10-18) years for alcohol, 14.5 ± 2.1 (10-19) years for hashish, 14.7 ± 1.6 (12-17) years for benzodiazepine, 15.0 ± 2.6 (12-18) years for cocaine, and 15.2 ± 1.4 (12-17) years for ecstasy.

The duration of VSA varied between 1 and 9.2 years, with a mean of 3.7 ± 1.7 years. In terms of the duration of abuse, and the amount of substance abused daily, the subjects with an abuse history of 1-2 years were daily abusing a mean of 4.0 ± 1.4 tubes of inhalants, those with 2-3 years were abusing a mean of 4.1 ± 6.8 tubes, those with 3-4 years

TABLE I: THE DISTRIBUTION OF INHALANTS BEING ABUSED AMONG THE STUDY SUBJECTS

Volatile Substance Abuse	n (%)
Paint thinner	2 (6.5%)
Glue (trademark, Bally)	25 (80.6%)
Thinner + Bally	4 (12.9%)

were abusing a mean of 5.6 ± 2.3 tubes, those with 4-5 years were abusing a mean of 5.7 ± 4.0 tubes, and those with 5 years were abusing 6.1 ± 5.6 tubes.

Evaluation with Yeniden Inhalant Abuse Severity Scale (YUKUD)

YUKUD scale points ranged between 10 and 50, with a mean of 31.0 ± 9.7 . Although YUKUD scale points had a weak negative correlation with the age of onset of VSA (as YUKUD scale points increase, age of onset decreases), this was not statistically significant ($p > 0.05$). There was no significant relationship between the duration of attending school, the length of time of living on the streets, and the YUKUD scale points ($p > 0.05$). Although the YUKUD scale points of those whose mothers smoked cigarettes were found to be higher than for those with non-smoker mothers, that was not a statistically-significant difference ($p > 0.05$). Father's substance/use status was not significantly related to the YUKUD scale points ($p > 0.05$). Although the YUKUD scale points of the subjects who had run away from home were higher than for those who had not run away, that was not statistically significant ($p > 0.05$). Also no significant difference was detected in YUKUD scale points for subjects with respect to having suicide attempts or having a criminal record ($p > 0.05$).

Respiratory system findings

As shown in Table III, the most frequent symptom among the subjects was nasal congestion (45.2%). Following this was: sputum (38.7%), exercise intolerance (32.3%), cough (22.6%), chest pain (16.1%), shortness of breath (9.7%), tachypnea (9.7%), wheezing (6.4%), sneezing (6.4%), and runny nose

TABLE II: THE AGE OF ONSET, AND THE RATES OF ABUSE AND ADDICTION, FOR EACH SUBSTANCE

Substance name	Age of onset (years) Mean \pm SD	Abuse n (%)	Addiction n (%)
Cigarette smoke	11.85 ± 2.69	1 (3.2%)	27 (87.1%)
Inhalant	14.16 ± 2.16	0	31 (100%)
Alcohol	14.23 ± 1.97	16 (51.6%)	5 (16.1%)
Hashish	14.46 ± 2.06	9 (29.0%)	17 (54.8%)
Benzodiazepine	14.75 ± 1.65	6 (19.4%)	6 (19.4%)
Cocaine	15.0 ± 2.58	3 (9.7%)	1 (3.2%)
Ecstasy	15.17 ± 1.42	8 (25.8%)	9 (29.0%)

TABLE III: DISTRIBUTION OF RESPIRATORY-RELATED COMPLAINTS AMONGST GROUP (N = 31) OF VOLATILE SUBSTANCE ABUSERS

	N	%
Nasal congestion	14	45.16
Sputum	12	38.71
Exercise intolerance	10	32.26
Coughing	7	22.58
Chest pain	5	16.13
Shortness of breath	3	9.68
Tachypnea	3	9.68
Wheezing	2	6.45
Sneezing	2	6.45
Runny nose	2	6.45

(6.4%). No symptoms were present amongst the control group, as this group was selected from adolescents without health problems.

Pulmonary function tests

The groups' age, weight, and height distributions were not statistically significantly different ($p > 0.05$) (Table IV). The mean FEV_1 value was 3.8 ± 0.6 L in the patient group, while 4.2 ± 0.6 L in the control group, and there was a statistically significant difference between them ($p < 0.05$). Calculated as a percentage of the predicted value, the mean FEV_1 of the patient group was $97.7 \pm 13.8\%$, while the control group's was $103.4 \pm 10.7\%$, and there was no statistically significant difference between them ($p > 0.05$).

The mean FVC values were 3.90 ± 0.62 L in the patient group compared to 4.3 ± 0.7 L in the control group, the difference between the two groups being statistically significant ($p < 0.05$). Calculated as a percentage of the predicted value, the mean FVC was $84.0 \pm 11.7\%$ in the patient group vs. $88.7 \pm 10.9\%$ in the control group, and there was no statistical significance between the two ($p > 0.05$). The mean FEV_1/FVC ratio was 97.1 ± 4.7 in the study group vs. 97.6 ± 3.3 in the control group. Calculated as a percentage of the predicted value, the mean FEV_1/FVC was $117.0 \pm 5.5\%$ in the patient group vs. $117.4 \pm 4.5\%$ in the control group. None of the numerical or percentage values showed a significant difference ($p > 0.05$). The average peak expiratory flow (PEF) value, was $6.85 \pm$

1.08 L/sec in the patient group, compared to 9.5 ± 0.8 L/sec in the control group. Calculated as a percentage of the predicted value, the average PEF was $80.4 \pm 17.0\%$ in the patient group vs. $110.2 \pm 17.9\%$ in the control group. Both numerical and percentage values were found to be lower in the study group, with a high level of statistical significance ($p < 0.01$). The average mean expiratory flow (MEF)₂₅₋₇₅ value was 4.9 ± 1.2 L/sec in the study group compared to 6.3 ± 1.2 L/sec in the control group. Calculated as a percentage of the predicted value, the average MEF₂₅₋₇₅ was $114.6 \pm 22.9\%$ in the study group, and $138.9 \pm 32.1\%$ in the control group. Both numerical and percentage values were found to be lower in the study group, with a high level of statistical significance ($p < 0.01$) (Table V).

Twelve (41.4%) subjects in the study group and 2 (15.4%) subjects in the control group had a reduction of 20% or more in FVC levels which was not statistically significant ($p > 0.05$). There was no statistically significant relationship ($p > 0.05$) between a reduction of $\geq 20\%$ in FVC, and the age of onset, nor duration of VSA, nor total amount of abused substances. There was no statistically significant relationship between pulmonary system complaints and a reduction of $\geq 20\%$ FVC (Table VI).

The study group was divided into two subgroups, according to their predicted FVC values being below (group 1) vs. above (group 2) 80%. The HRCT findings of the two subgroups showed no statistically significant difference in the rates of small airways disease, nor subpleural nodules ($p > 0.05$); but centrilobular nodule and atelectasis rates were significantly higher in the first group ($p < 0.05$). There was statistically a highly significant difference ($p < 0.01$) between having an abnormal finding in HRCT and having a reduction of $\geq 20\%$ in FVC. Comparing the scintigraphy findings, there was no significant difference concerning perfusion or ventilation disorders ($p > 0.05$) (Table VII).

DISCUSSION

A "substance" is any chemical which is consumable by various means, and influences sensations, perceptions, cognition, or other brain functions with a likelihood of abuse and addiction. "Substance abuse" is the recurring use of a substance within a year, which may cause probable social and/or legal problems or physical risk. "Substance addiction" is a broad concept of addiction, which reflects the

TABLE IV: DEMOGRAPHIC CHARACTERISTICS OF THE GROUPS

	Study group (n = 31)	Control group (n = 13)	P*
	Mean \pm SD	Mean \pm SD	
Age (years)	17.94 ± 1.52	18.78 ± 0.64	0.066
Weight (kg)	67.88 ± 14.16	64.61 ± 8.54	0.455
Height (cm)	173.61 ± 8.92	176.30 ± 4.95	0.315

*: Student's t-test.

TABLE V: EVALUATING THE PULMONARY FUNCTION TESTS FOR THE STUDY AND CONTROL GROUPS

	Study group (n = 29) Mean ± SD	Control group (n = 13) Mean ± SD	P*
FEV ₁ (L)	3.78 ± 0.59	4.23 ± 0.59	0.029*
FEV ₁ (%)	97.75 ± 13.85	103.38 ± 10.75	0.202
FVC (L)	3.90 ± 0.62	4.35 ± 0.71	0.046*
FVC (%)	84.03 ± 11.66	88.69 ± 10.88	0.229
PEF (L/sec)	6.85 ± 1.08	9.54 ± 0.85	0.001**
PEF (%)	80.44 ± 16.97	110.23 ± 17.88	0.001**
FEV ₁ /FVC	97.10 ± 4.75	97.61 ± 3.30	0.727
FEV ₁ /FVC (%)	117.00 ± 5.55	117.37 ± 4.53	0.866
MEF ₂₅₋₇₅ (L/sec)	4.94 ± 1.22	6.35 ± 1.21	0.001**
MEF ₂₅₋₇₅ (%)	114.65 ± 22.95	138.92 ± 32.15	0.008**

*: Student's t-test.

*p < 0.05.

**p < 0.01.

substance having taken a central role in the person's life, the individual's having lost the control over his/her own substance use, and the existence of substance-related physical and psychological problems [10]. Both in Turkey and in the rest of the world, the rates of use of stimulants and sedatives are increasing fast, and the age of onset of VSA is becoming terrifyingly younger. A long-term use of inhalants is known to have harmful effects on many systems, and primarily on the central nervous system. But the literature on the effects on the respiratory system has been limited to a few case reports. In this study, all of the subjects were males with an age range of 13-21 years. This selection was because of the policy of the Ege University Child and Adolescent Addiction Investigation and Practice Center (EGBAM), that admits only males for inpatient treatment. Investigating the literature also points to males as the more likely to abuse volatile substances [11,12]. EGBAM started its service in September 2003. Listing the applications to the EGBAM outpatient service between September 2003 and September 2005, 88.5% of the subjects are found to be males [13].

In Turkey, the widely used volatile substances are paint thinner and glue [3]. Glues contain less toluene than paint thinner, and the abusers report that glue gives more euphoria and hallucinogenic effects, while paint thinner has more sedative and anesthetic effects [14]. In conducted studies, it was found that those who live on the streets prefer paint thinner, while those who live with their family prefer glue [15,16]. This situation may be explained by the different motivation behind the abuse: leisurely pursuit in the case of those who live with their family, while for those who live on the streets the purpose is to stay alive, enduring the cold and danger of the streets, and to lessen the pain of hunger. In this study, the volatile substances which were reported to be abused were only Bally and thinner, Bally abuse rate being 80.6%, thinner 6.5%, and their being used together 12.9%. This marked difference between Bally and thinner usage might be due to the fact that almost all of the subjects were living with their families.

Vega et al. [11] have stated that, in the development of volatile substance addiction, a history of substance abuse in the family and parents' smoking

TABLE VI: COMPARING THE REDUCTION IN FVC WITH THE PULMONARY SYSTEM COMPLAINTS IN THE STUDY GROUP

	FVC ≤ 80 % (n = 12)		FVC > 80 % (n = 17)		P*
	n	%	n	%	
Coughing	2	16.7	4	23.5	1.000
Shortness of breath	3	25.0	0	0	0.060
Tachypnea	0	0	2	11.8	0.498
Wheezing	0	0	1	5.9	1.000
Chest pain	2	16.7	2	11.8	0.706
Sputum	4	33.3	6	35.3	0.913
Exercise intolerance	5	41.7	4	23.5	0.298
Sneezing	0	0	2	11.8	0.498
Runny nose	0	0	2	11.8	0.498
Nasal congestion	5	41.7	8	47.1	0.774

*: Fisher's Exact test, where Chi-Square test would be necessary.

TABLE VII: COMPARING THE REDUCTION IN FVC, WITH HRCT AND SCINTIGRAPHY FINDINGS

	FVC		P
	≤ 80% (n = 8)	> 80 % (n = 15)	
HRCT			
Small airways disease	0	2 (13.3%)	0.280
Subpleural nodule	4 (50.0%)	2 (20.0%)	0.136
Centrilobular nodule	2(25.0%)	0	0.043*
Atelectasis	2 (25.0%)	0	0.043*
Normal	1 (12.5%)	11 (73.3%)	0.009**
Scintigraphy			
Perfusion disorder	3 (33.3%)	4 (28.6%)	1.000
Ventilation disorder	1 (11.1%)	3 (25.0%)	0.603

Definition of abbreviations: FVC, forced vital capacity; HRCT, high resolution computerized tomography.

*: Chi-square test.

*p < 0.05.

**p < 0.01.

cigarettes have an important influence. Volatile substance abusers have quite high rates of substance use in their family. In our study there were no substances used in the subjects' families except for mothers smoking cigarettes and fathers both smoking cigarettes and consuming alcohol. Alcohol consumption rate was 41.9%, while cigarette smoking rate was 58.1% for mothers, and 83.8% for fathers. Only 16.2% of the fathers were not using any substances.

In the case histories of inhalant abusers, a characteristic that is reported in the literature is trouble in their education, such as truancy, failure in school, and/or dropping out without completing their education [17,18]. In a study by Ögel et al. [19], 86.2% of the subjects reported having dropped out of school, and the average length of education was 7.3 years. In a study conducted by Altenkirch and Kinderman [20], 38% of the volatile substance abusers had attendance to a lower grade, and 90% dropped out of school, without completing their 9-year education toward a diploma. In our study, investigating educational status, 90.3% of the subjects were found to be not attending school. The years of education completed by the subjects varied between 1 and 13, similar to the rates reported in the literature, and the average length of education was 7.80 ± 2.79 years.

Shoemakers (production or repair), furniture producers, printers, coiffeurs, painters, personnel of gas-oil stations, car/motorcycle/bicycle repairers, dry-cleaners, those working in petroleum refineries and related industries, personnel of factories using or producing inhalant-solvents, personnel of drug factories, and personnel working in medical fields constitute the increased-risk groups for volatile substance addiction and abuse [21]. A comprehensive study conducted in Mexico by Conyer et al. [22] found male gender, low socio-economic status, and work conditions as the primary risk factors toward VSA. Likewise, in our study, 93.5% of the subjects had previously worked in a job where there was a high risk of encountering volatile substances. And

this suggests a solution against the problem of volatile substance addiction, pointing out the importance of prohibiting children from working in workplaces where they might encounter inhalants. Substance addicts have high rates of attempting and committing suicide [11,23]. Ögel et al. [19] found that 16.7% of inhalant abusers had suicide attempts in their history. In our study, this rate was similar: 16.1%.

There are a few fundamental characteristics which differentiate inhalant abusers from the abusers of other substances. Aggressiveness, committing substance-abuse related crimes, running away from home, harming oneself, and truancy, are more prevalent among these subjects than in adolescents who abuse other substances [24-29]. Concerning the effects of inhalants on the brains of addicts, cognitive problems are generally seen [30,31]. Tolerance against inhalants develops fast and easily, and clinically-significant withdrawal symptoms do not occur [31]. To this list, when the adolescents living on the streets are added, there surfaces the need for questionnaire forms and scales to assess the addiction intensities of inhalant abusers [14]. Therefore, in 2005, Ögel et al. [32] developed YUKUD (Yeniden Inhalant Abuse Severity Scale). In that study, which was conducted with 50 volatile substance addict adolescents, the mean scale total score of the subjects was 61.4 ± 10.4 . Similarly, in our study, the YUKUD scale was used to investigate the substance abuse intensity of the subjects. Obtained total scores varied between 10 and 50, and the average was 31.1 ± 9.7 . No relationship was found between abuse intensity, and the age of onset of VSA, school attendance duration, or father's substance abuse. As the duration of living on the streets increases, the abuse intensity also increases, and these correlate almost at a statistically significant level. The YUKUD scores for those who had run away from home, had suicide attempts, had trouble with the law, and whose mothers were smoking cigarettes, were found to be higher, although not significantly so.

Coughing, shortness of breath, and wheezing are the most frequent complaints of inhalant abusers [6]. In a study conducted in the Philippines with 31 street children, the most frequently observed respiratory system complaints were listed as shortness of breath (38.7%), coughing (35.5%), and runny nose (29%) [33]. Hellquist et al. [34], after analysing histopathologically the nasal biopsies taken from 10 painters who had occupational exposure to toluene and isobutyl acetate, reported that they encountered no normal mucosa. In a study conducted in Turkey, animals which were subjected to thinner inhalation had mucosal deformation, including inflammation and cilia loss in their nasal and larynx mucosa. In our study, the most frequently observed symptom was nasal congestion (45.2%). Following this came, in descending order of prevalence: sputum (38.7%), exercise intolerance (32.3%), coughing (22.6%), chest pain (16.1%), shortness of breath (9.7%), tachypnea (9.7%), wheezing (6.4%), sneezing (6.4%), and runny nose (6.4%).

In the literature, studies investigating the pulmonary functions of inhalant abusers are quite rare. Studies which investigate VSA-related morbidity and mortality are mostly limited to investigating the occupational exposure to solvents in industrial settings [8]. According to the U.S. Occupational Health and Safety Administration (OSHA), the safe limit allowable for solvents is 200 parts per million (ppm) for toluene, and 100 ppm for trichlorethylene. But, the concentration of toluene inhaled from a bag which contains Bally might reach 10,000 ppm [3,8]. Schikler et al. [35], compared the pulmonary function tests of 42 inhalant addicts between the age of 11-31 years, and 20 healthy controls aged between 10-26 years, and found that the residual volumes of the addicts were significantly higher than those of the controls. Panacinar emphysema was observed in the lung tissues obtained from 3 subjects who were known as inhalant addicts and who had died because of trauma or accident, and this finding was proposed to explain the increase in residual volume [35].

In the literature, we found a single study addressing the relationship between VSA and respiratory functions. This study by Pogoy et al. [33] observed low FVC values indicating restrictive ventilatory pattern in 13 (41.9%) of the 31 street children between ages of 7-18 (mean age 14 ± 2) years, and with a mean duration of drug use of 2.6 ± 2.5 years. The FEV₁ values of all of their subjects were normal. In our study, the highest obtained FEV₁ and FVC values of the inhalant addicts were significantly lower than those of the control group ($p < 0.05$). PEF and MEF₂₅₋₇₅ values of the study group were lower than in the control group, at a high level of statistical significance ($p < 0.01$). FEV₁/FVC ratio was not different between the groups ($p > 0.05$). Calculating the percentage of reduction relative to the predicted values, 12 (41.4%) subjects in the study group were found to have low FVC values, indicating restrictive ventilatory pattern. FEV₁ of 2 subjects (6.89%) was reduced 20% or more. Restrictive ventilatory pattern was more prevalent in the study group, but not

at a statistically significant level. Therefore, VSA might be causing decreases in lung volumes and flow velocities and, similar to the case of Pogoy et al.'s study, this might be related to a restrictive ventilatory pattern. In our study, relations between a reduction of $\geq 20\%$ in FVC and age of onset of VSA, duration of abuse, total amounts of abused inhalants, and respiratory system complaints were not statistically significant ($p > 0.05$).

In the literature, we found no study evaluating the radiological findings of inhalant abusers. Dividing the study group into two subgroups according to their reduction in FVC, i.e. those who have vs. do not have restrictive ventilatory pattern, and then comparing their HRCT findings, small airways disease and the observed subpleural nodules rates we found no statistically significant differences between the two subgroups ($p > 0.05$), while the rates of observed centrilobular nodules and atelectasis were significantly higher in the first subgroup ($p < 0.05$). Restrictive ventilatory pattern was correlated with abnormal findings in HRCT, with a high level of statistical significance ($p < 0.01$). In view of the findings observed in the lung scans of all of our inhalant addicted subjects, those who have a low FVC at spirometry should undergo HRCT.

In a study which compared the ventilation scintigraphies of 28 car painters who had occupational exposure to toluene, and 13 healthy controls, it was stated that Tc-99m diethylenetriaminepentaacetate (DTPA)'s clearance from lungs was slower in car painters than in controls [36]. In another study, which was conducted with 10 painters and 10 healthy controls, occupational exposure/subjection to toluene was shown not to influence bronchoalveolar epithelial permeability. In our study, we performed ventilation scintigraphy in 21 volatile substance addicts, and 3 (14.2%) of the subjects were found to have hypoventilation in the right apical region, while 1 (4.7%) had retention in central airways. No relationship was found between a reduction in FVC, and perfusion and ventilation disorders.

Inhalation of volatile substances for their psychoactive properties has a very long history and has been widely detected all around the world in different age groups, including very young people. As volatile substance abuse is a social problem, it requires a social response. VSA will best be addressed by addressing the social problems facing young people. Respiratory complications of volatile substances are well noted to clinicians as a clinical observation, but have not been documented or studied adequately in clinical research. This study has shown a positive correlation between volatile substance abuse and the development of restrictive ventilatory pattern. But further evaluation of long-term effects (more than 10 years) of volatile substances, and more comprehensive studies are needed to enable more precise conclusions to be drawn.

CONFLICT OF INTEREST STATEMENT: None of the authors has any conflict of interest to declare in relation to the subject matter of this manuscript.

References

1. Espeland K. Identifying the manifestations of inhalant abuse. *Nurse Pract* 1995;20:49-50.
2. McHugh MJ. The abuse of volatile substances. *Pediatr Clin North Am* 1987;34:333-340.
3. Demirbek B. Türkiye'de uçucu madde bağımlılığı profili. Uzmanlık Tezi, İstanbul. Bakırköy Ruh ve Sinir Hastalıkları Hastanesi. 1991.
4. Shepherd RT. Mechanism of sudden death associated with volatile substance abuse. *Hum Toxicol* 1989;8:287-291.
5. Lorenc JD. Inhalant abuse in the pediatric population: a persistent challenge. *Curr Opin Pediatr* 2003;15:204-209.
6. Brouette T, Anton R. Clinical review of inhalants. *Am J Addict* 2001;10:79-94.
7. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989;8:293-300.
8. Meadows R, Verghese A. Medical complications of glue sniffing. *South Med J* 1996;89:455-462.
9. Birlesmis Milletler Uyusturucu ve Suç Ofisi. Türkiye'de Sağlık Hizmetleri, Eğitim ve Toplumsal Girişimle Madde Kullanımının Önlenmesi, Madde Kullanımı Üzerine Ulusal Değerlendirme Çalışması 2003;68.
10. Rinaldi RC, Steindler EM, Wilford BB, Goodwin D. Clarification and standardization of substance abuse terminology. *JAMA* 1988;259:555-557.
11. Vega WA, Zimmerman RS, Warheit GJ, Apospori E, Gil AG. Risk factors for early adolescent drug use in four ethnic and racial groups. *Am J Public Health* 1993;83:185-189.
12. Ashton CH. Solvent abuse. *BMJ* 1990;300:135-136.
13. Yüncü Z, Aydin C, Coskunol H, Altintoprak E, Bayram AT. Çocuk ve ergenlere yönelik bir bağımlılık merkezinin 2 yıllık poliklinik kayıtlarının değerlendirilmesi. *Bağımlılık Dergisi* 2006;7:31-37.
14. Ögel K, Aksoy A, Liman O, et al. Sokakta yaşayan çocukların ve madde kullanımını. İstanbul: Ek-Bil yayıncılık. 2003.
15. Ögel K. Ergen Uçucu Madde Bağımlılılarının Özellikleri, UMATEM Verileri. 2004.
16. Ögel K, Taner S, Tosun M, Gürol DT, et al. Yatarak Tedavi Gören Ergen Uçucu Madde Kullanıcılarında Madde Kullanım Özellikleri: Cinsiyet Ve Yasadığı Yere Göre Karşılaştırma. *Bağımlılık Dergisi* 2005;6:76-83.
17. Öztürk KE, Altinoğlu I, Atasoy N, et al. Ergenlerde uçucu madde kullanımında rol oynayan faktörler. 5. Anadolu Psikiyatri Günleri Program ve Bildiri Özeti Kitabı 1996;39.
18. Aytaçlar S, Ertekin G, Türkcan A, et al. UMATEM'de yatan hastaların sosyodemografik özelliklerini ve yaşam alanlarındaki sorunlarını değerlendirmeye. 33. Ulusal Psikiyatri Kongresi Bildiri Özeti Kitabı. Bakırköy Ruh ve Sinir Hastalıkları Hastanesi ve Psikiyatri Derneği 1997;125.
19. Ögel K, Tamar D, Evren C, Çakmak D. Uçucu madde kullanımının yaygınlığı: Çok merkezli bir araştırmmanın verilerinin değerlendirilmesi. *Anadolu Psikiyatri Dergisi* 2000;1:220-224.
20. Altenkirch H, Kindermann W. Inhalant abuse and heroin addiction: a comparative study on 574 opiate addicts with and without a history of sniffing. *Addict Behav* 1986;11:93-104.
21. Bukstein O. Practice parameters for the assessment and treatment of children and adolescents with substance use disorders. American Academy of Child and Adolescent Psychiatry. *J Am Acad Child Adolesc Psychiatry* 1997;36:140S-156S.
22. Tapia-Conyer R, Cravioto P, De La Rosa B, Velez C. Risk factors for inhalant abuse in juvenile offenders: the case of Mexico. *Addiction* 1995;90:43-49.
23. Kuğu N, Akyüz G, Ersan E, Doğan O. Sanayi bölgesinde çalışan çıraklıarda madde kullanımı ve etkileyen etkenlerin araştırılması. *Anadolu Psikiyatri Dergisi* 2000;1:19-25.
24. Mackesy-Amiti ME, Fendrich M. Inhalant use and delinquent behavior among adolescents: a comparison of inhalant users and other drug users. *Addiction* 1999;94:555-564.
25. White HR, Loeber R, Stouthamer-Loeber M, Farrington DP. Developmental associations between substance use and violence. *Dev Psychopathol* 1999;11:785-803.
26. Farrington DP, Loeber R. Epidemiology of juvenile violence. *Child Adolesc Psychiatr Clin N Am* 2000;9:733-748.
27. Howard MO, Jenson JM. Inhalant use among antisocial youth: prevalence and correlates. *Addict Behav* 1999;24:59-74.
28. Inciardi JA, Surratt HL. Children in the streets of Brazil: drug use, crime, violence, and HIV risks. *Subst Use Misuse* 1998;33:1461-1480.
29. Noto AR, Nappo SA, Galduróz JC, Mattei R, Carlini EA. Use of drugs among street children in Brazil. *J Psychoactive Drugs* 1997;29:185-192.
30. Ron MA. Volatile substance abuse: a review of possible long-term neurological, intellectual and psychiatric sequelae. *Br J Psychiatry* 1986;148:235-246.
31. Richardson H. Volatile substance abuse: evaluation and treatment. *Human Toxicol* 1989;8:319-322.
32. Ögel K, Aksoy A, Topuz A, Liman O, et al. Ergenlerde Uçucu Madde Kullanımı Siddetini Değerlendirme Ölçeği Uygulama Kılavuzu. Yeniden yayınları, İstanbul. 2005.
33. Pogoy FB, de Guia TS. Lung function test of toluene abusers among urban street children ages 7 to 18 years old. *Chest* 2005;128:351S.
34. Hellquist H, Irander K, Edling C, Ödkvist LM. Nasal symptoms and histopathology in a group of spray-painters. *Acta Otolaryngol* 1983;96:495-500.
35. Schikler KN, Lane EE, Seitz K, Collins WM. Solvent abuse associated pulmonary abnormalities. *Adv Alcohol Subst Abuse* 1984;3:75-81.
36. Cerci SS, Öztürk O, Sütçü R, Özbeş FM, Baydar CL, Yıldız M, Akkaya A, Delibas N. Evaluation of the effects of toluene inhalation on alveolar epithelial permeability by ^{99m}Tc-DTPA inhalation scintigraphy in automobile painters. *Nucl Med Commun* 2008;29:45-52.