

Investigation of The Liver Functions in Abusers of Volatile Substances

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- ✓ Glue sniffing is a frequent problem among teenagers. Various chemical substances, especially toluene and benzene, contained in glues have been reported to be hepatotoxic. The liver functions of 39 healthy teenagers who used to be chronic glue sniffers were investigated to detect any subclinical hepatic damage. No abnormalities could be determined by the conventional laboratory tests. We suggest that the incidence of the hepatotoxicity of sniffing is low and reversible, and that the early detection of these probable hepatotoxic effects by conventional laboratory tests is not possible to detect.

Key words: Volatile substance abuse, hepatotoxicity, teenagers

- ✓ **Uçucu Madde Bağımlılarında Karaciğer Fonksiyonlarının Araştırılması**

Yapıştırıcıların uygunsuz kullanımı adolesanlarda sık karşılaşılan bir problemdir. Yapıştırıcılar içerisinde bulunan çeşitli kimyasal maddeler, özellikle toluen ve benzen'in hepatotoksik olduğu bildirilmiştir. Eskiden kronik yapıştırıcı bağımlısı olan 39 adolesanın karaciğer fonksiyonları, subklinik karaciğer hasarı tespit etmek üzere araştırıldı. Rutin laboratuvar testlerinde herhangi bir anormallik bulunamadı. Bu bağımlılığın hepatik hasar yapma ensidansının düşük ve reversibl olduğu ve muhtemel hasarın erken dönemde rutin tetkiklerle ortaya çıkarılamayacağı kanısına varıldı.

Anahtar kelimeler: Uçucu madde suiistimali, hepatotoksisite, adolesan

INTRODUCTION

The use of volatile substances are very commonly abused by children and adolescents. The desired effects appear to be euphoria, tranquility, relaxation and hallucination. These substances are different from other drugs in that they are not sold illegally on street corners. The purchase and possession of these substances are illegal. They are cheap and are usually available in our homes^(1,2).

The abuse of volatile substances is an important social problem especially among teenagers. It is estimated that 3 to 4% of teenagers engage in this activity on a regular basis⁽³⁻⁵⁾. Glue/adhesives and paint sniffing are the most common forms of substance

abuses. Their commercial products contain toluene, benzene, xylene, trichloroethylene, tetrachloroethylene, methylene chloride, trichlorethane, carbon tetrachloride, acetone, naphtha, n-hexane.

Although the other volatile solvents may be effective, toluene (methyl benzene) is usually considered the major active agent⁽⁶⁾. The acute toxic effects of toluene include death due to cardiac arrhythmia or pulmonary or cerebral edema, renal and hepatic failure. Chronic toluene exposure can lead to muscle weakness, gastrointestinal disturbances, neuropsychiatric abnormalities, peripheral neuropathy, some hematological, renal and hepatic damage⁽⁷⁻⁹⁾.

In this study, 39 teenagers who were

abusing solvent substances and have recently quitted this addiction were investigated by the conventional liver function tests to detect in advance any cryptogenic hepatic disease and the results were discussed.

MATERIALS AND METHODS

The present study was conducted in 39 boys who were chronic paint and glue vapour sniffers in the past for a while and treated in the governmental rehabilitation center where inpatient and outpatient chemical dependency treatment and prevention program is applied. All of the participants had quitted the habit at least one month prior to the study. Subjects who had a current or prior history of diseases that could have affected the liver function were not included in the study. Peripheral blood samples were collected in the morning after fasting overnight, and serum aspartate aminotransferase (AST); serum alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), alkaline phosphatase (ALP), total and direct bilirubin concentrations levels were measured in all cases. Ultrasonographic examinations of the livers could be performed in 19 (48%) cases.

An appropriate institutional review board approved the project and informed consent was obtained from both parents or legal guardian after the nature of the procedures had been explained fully.

RESULTS

Seven of the subjects abused paint thinner, and the others abused glue vapor. Their age ranged from 13 to 21 years (mean, 14.9 ± 2.1 years). The duration of the abuse before rehabilitation ranged from two to five years, with a mean of 3.2 ± 1.0 years. None were drug dependent. All of them are smokers and consume alcohol rarely (when they have the possibility). All subjects had no sign or symptom of any disease, and were healthy at the time of sampling. Serum liver enzyme activities, total and direct bilirubin concentrations of all subjects were within the normal range (The data are summarized in Table). No abnormalities could be detected by means of ultrasonography either.

DISCUSSION

In a study conducted in 24 patients who were abusing substances in which the only solvent was toluene, ALP was elevated in 13 patients, and the other liver function tests were abnormal in 8 patients⁽¹⁰⁾. Severe liver cell injury was detected in a case who developed acute oliguric renal failure following repeated toluene sniffing for about 8 hours⁽¹¹⁾. Jaundice and abnormal liver function was observed in another case who inhaled toluene⁽¹²⁾. AST and ALT were elevated in a 26-year-old male after reingested 100 ml of toluene (about 70% toluene)⁽¹³⁾.

Table. Liver Function Tests in The Volatile sSubstances Abusers.

	The results (Means \pm standard deviations)	Normal range according to the age
AST (U/L)	25.35 ± 9.34	(8-40 U/L)
ALT (U/L)	26.37 ± 11.54	(5-40 U/L)
GGT (U/L)	15.11 ± 4.83	(< 40 U/L)
ALP	170.16 ± 97.36	(100-390 U/L)
Total bilirubin/direct bilirubin	$0.95 \pm 0.46 / 0.29 \pm 0.17$	(< 1.2 mg/dl) / (< 0.4 mg/dl)

The conditions of the subjects above were so serious to be hospitalized, and these toxic effects were reversible after the exposure was stopped.

As toluene is one of the most commonly used organic solvents in the various industries, its hepatotoxic effects were investigated in workers exposed to organic solvents; in one study conducted in 180 workers exposed to organic solvents in which the major components were xylene and toluene, gama-glutamyl transferase activity was found to be associated with severity of exposure to the mixture of solvents⁽¹⁴⁾. It has been reported that workers with jaundice that had developed two to four months after beginning work at a chemical plant recovered within a few weeks of stopping the work, and one worker who resumed work at the plant developed clinical and biochemical evidence of relapse of liver damage⁽¹⁵⁾. In another study conducted in 120 workers, hyperenzymia, hyperlipaemia and significant reduction of glutathion in certain percentage of the workers (from seven to 31% at different indices) were found⁽¹⁶⁾. Other studies also reported abnormal liver function tests in chemical workers exposed to organic solvents⁽¹⁷⁻¹⁹⁾.

On the other hand, in a study performed on 33 workers, no dose-response relationship was found between exposure to solvent mixtures in ambient air, reaching and sometimes even exceeding the threshold limit values for mixtures, and liver enzyme activities⁽²⁰⁾. Moreover, in two cases in coma due to toluene exposure, liver function tests were normal. No reason could be found to explain the lack of impairment of hepatic function in these two severe cases of acute intoxication⁽²¹⁾. Several investigators also reported that organic solvent exposure usually do not produce damage to the liver⁽²²⁻²⁴⁾. In

our investigation, conventional laboratory examinations of 39 toluene sniffers were also normal. It can be suggested that liver functions is not affected by toluene exposure in any one of these subjects.

The other important agent in the glues is benzene. One of the sources of benzene in our subjects was smoking. In an investigation performed in mice, a large and dose dependent effect was seen in the liver after 5 days of exposure with almost complete repair within 48 hours⁽²⁵⁾. Contrasting results have been reported; AST, ALT, ALP, and GGT were found normal in workers exposed to benzene⁽²⁶⁾.

Most toxic effects induced by toluene and benzene reported above resulted in complete recovery after the exposure has been stopped. In the present study, the subjects had quitted the addiction at least one month ago. They might have recovered from the possible hepatotoxic effects of the glue sniffing.

The role of ethanol in organic solvent toxicity has been extensively studied, and controversial findings have been reported. We believe that our subjects did not have the possibility to consume enough alcoholic beverage to affect the hepatotoxicity of glue vapors, due to the poverty.

Metabolic interaction between toluene and benzene had been considered. It has been shown that toluene is a competitive inhibitor of benzene⁽²⁷⁾. This interaction might be effective in our cases.

In another investigation, serum bile acid (SBA) concentrations in comparison with conventional liver function tests were determined in a selected group of workers occupationally exposed to a mixture of organic solvents and in a reference group. It has been found that the mean levels of AST, ALT, ALP, GGT and direct bilirubin

concentrations in the two groups were similar, whereas mean SBA levels were increased in the exposed group. It has been suggested that conventional liver function tests are insensitive for early liver damage detection⁽²⁸⁾. In another study conducted in 45 workers who had been chronically exposed to xylene-toluene-benzene mixture in the atmosphere, it has been reported that radioisotopic investigations of the liver functions detected some damage while biochemical parameters remained within the normal range⁽²⁹⁾. In our study, routine laboratory tests might not be sensitive enough to detect any subclinical hepatic damage.

In conclusion, hepatic damage may occur as a consequence of the inhalation. But, the incidence of this toxicity seems to be low, and most of this toxicity may be reversible after the cessation of the exposure, and it is not possible to detect earlier these hepatotoxic effects by conventional laboratory tests.

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