THE INVESTIGATION BY DOPPLER ULTRASONOGRAPY OF BLOOD FLOW DYNAMICS OF TESTES AND LIVER IN MEN EXPOSED CHRONICALLY TO TOLUENE

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Abstract

Organic solvents used in various industrial processes may cause toxic effects in various biological tissues of human. Many previous studies have demonstrated, histopathologically, that toluene produced toxic effects in liver and testes. The aim of this study was to investigate the arterial and venous blood flow rate in the liver and testes of male workers who experienced occupational exposure to toluene.

The experimental group comprised 30 male painters who had experienced occupational exposure to toluene inhalation for a minimum of 10 years; a control group comprised 30 healthy, age-matched male volunteers. The blood flow rate of the testes and liver of both groups were determined by Doppler ultrasonography.

We determined that some arterial and venous blood flow rates of liver and testes changed in painters exposed occupationally to toluene ($p<0.05$). The results indicated significant changes in arterial and venous blood flow rate of right testes, left testes arterial end diastolic flow, left testes arterial flow and main hepatic venous blood flow rate of the right lobe of the liver. Other parameters showed no statistically significant difference.

We conclude that long-term occupational exposure to toluene can affect arterial and venous blood flow. The results indicate testes and liver tissue damage in these subjects.

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Introduction

Toluene (C_7H_8; methylbenzene, phenylmethane, and toluol) is a clear, colorless, volatile aromatic hydrocarbon and is an organic solvent. Approximately 92% of toluene produced is used in gasoline; the remaining 8%, purified as commercial toluene, is used in the production of industrial chemicals [1].

Organic solvents are used in various industrial processes, such as paint manufacturing, spray painting, shoe making, degreasing, metal processing, and auto manufacturing [2].

Toluene vapor is rapidly absorbed from the respiratory tract; oral and dermal absorption occur more slowly. The half-life elimination of toluene in human blood is approximately 3-4 hours [3]. Toluene is a significant social and public health problem in many countries. Because of its low cost and easy availability, toluene is a common source of substance abuse in adolescents and younger children.

Only limited research has been conducted on the effects of toluene on human fertility. The effect of toluene in men is even more difficult to evaluate. In an occupational study, Merck et al. reported sexual disturbances and an increase in plasma levels of follicle –stimulating hormone (FSH) in men exposed to toluene [4]. Toluene may influence the endocrine system of the developing

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fetus, and this effect could also influence the reproductive capacity in adulthood [3].

It was reported that, toluene may adversely effect male reproductive functions. Testicular atrophy and reduced spermatogenesis were observed in one case involving chronic toluene abuse [3]. Women whose husbands inhaled toluene-based solvents at work have an increased incidence of spontaneous abortion [5], while Rendon *et al*. showed that workers in rubber factories have elevated numbers of abnormal sperm [6]. Contrary to these findings, Ono *et al*. observed that exposure to 2000 ppm toluene for days (6h/day) resulted in decreased sperm counts and epididymal weight in male rats, although it did not affect fertility [7]. Murata *et al*. observed that toluene has reproductive toxic potential [8].

Exposure to hepatotoxic solvents can occur in 1) occupational setting, through either daily inhalation or skin absorption of solvents; 2) residential setting, during either accidental or intentional ingestion in food, or as a toxic contaminant of food, or exposure to toxic agents such as in the form of glue sniffing; 3) environmental setting, commonly residential, usually through groundwater contamination, which includes ingestion of the water, skin contact through bathing in the water, and absorption, and volatilization of the solvents through heated bathing water [2].

Several factors have been shown to affect the handling of solvents by the liver and testes final toxicity effects. The most important determining factors are 1) species difference; 2) liver blood flow; 3) protein binding; 4) points of binding inside the liver and testes intracellularly.

Various solvents were used for many years until they were found to cause liver tumors. Scientist and physicians have to keep an open mind and constantly evaluate exposures in either of the above settings to assess liver effects [2].

This study was designed to investigate effects on the testes and liver blood flow rate of subjects with chronic occupational toluene inhalation. In many studies, it was reported that toluene had a pathological effect on the liver and testes.

Materials and Methods

The present study included thirty volunteer males, all of whom worked as painters, and; a control group of thirty male volunteers. None of the subjects reported acute or chronic illnesses. The study was approved by the Human Subjects Research Committee of Harran University.

Measurements of arterial and venous blood flow rate of liver (V_p, V_{end}, V_m, RI) and right and left testes of all subjects were measured by Doppler ultrasonography. (Esaote, Technos MPX 796FDII, CHINA).

The results were analyzed using paired samples t-tests in SPSS (version 11.5 for Windows). The experimental group and control group were compared with one another. P-values below 0.5 were considered to be statistically significant.

	n	Mean±S.D	p
Venous flow of expose right testes	30	0,030±0,009	<0,05
Venous flow of control right testes	30	0,037±0,010	
Arterial peak diastolic flow of expose right testes	30	0,086±0,023	>0,05
Arterial peak diastolic flow of control right testes	30	0,079±0,029	
Arterial maximum diastolic flow of expose right testes	30	0,051±0,016	>0,05
Arterial maximum diastolic flow of control right testes	30	0,054±0,015	
Arterial peak diastolic flow of expose left testes	30	0,073±0,016	>0,05
Arterial peak diastolic flow of control left testes	30	0,086±0,038	
Arterial end diastolic flow of expose left testes	30	0,031±0,010	<0,01
Arterial end diastolic flow of control left testes	30	0,056±0,024	
Venous flow rate of expose left testes	30	0,031±0,007	>0,05
Venous flow rate of control left testes	30	0,034±0,010	
Arterial end diastolic flow rate of expose right testes	30	0,578±0,082	>0,05
Arterial end diastolic flow rate of control right testes	30	0,603±0,094	
Arterial flow rate of expose left testes	30	0,045±0,075	<0,01
Arterial flow rate of control left testes	30	0,581±0,079	
Arterial resistive index of expose left testes	30	0,577±0,084	>0,05
Arterial resistive index of control left testes	30	0,581±0,079	

Table 1. Arterial and Venous blood flow rate (m/s) of testes.

Results

No significant difference was observed between the groups in terms of the dimensions of liver, right and left testes (p>0.05; table 1). Arterial and venous blood flow rate were measured in both groups. Right testes venous flow rate, left testes arterial end diastolic flow rate, and left testes arterial flow rate differed significantly between the experimental and control groups (p<0.05, p<0.01, p<0.01; table 2).

Other parameters were not significantly different between the experimental and control groups (table 3).

	n	Mean±S.D	p
Main hepatic venous maximum flow rate of expose group	30	0,148±0,066	>0,05
Main hepatic venous maximum flow rate of control group	30	0,130±0,050	
Main hepatic venous flow rate of expose right lobe	30	0,084±0,025	<0,05
Main hepatic venous flow rate of control right lobe	30	0,111±0,035	
Main hepatic venous flow rate of expose left lobe	30	0,114±0,054	>0,05
Main hepatic venous flow rate of control left lobe	30	0,113±0,023	
Vena porta flow rate of expose group	30	0,099±0,025	>0,05
Vena porta flow rate of control group	30	0,117±0,040	
Vena cava inferior flow rate of expose group	30	0,133±0,059	>0,05
Vena cava inferior flow rate of control group	30	0,141±0,049	

Table 2. Arterial and Venous blood flow rate (m/s) of liver.

	n	Mean	p
Liver of exposed group	30	143,11±15,07	>0,05
Liver of control group	30	139,11±10,25	
Left testes of exposed group	30	907,82±237,54	>0,05
Left testes of control group	30	853,14±167,09	
Right testes of exposed group	30	889,60±259,36	>0,05
Right testes of control group	30	860,57±173,80	

Table 3. Dimensions of liver as milimeter, right and left testes as milimeter square.

Discussion

Several studies have reported that toluene exposure produces adverse effects on the testes, sperm morphology, and both liver function and morphology. In published studies, it was claimed that toluene did not induce adverse effects on fertility of rats [9] or human males (American Petroleum Institute). Roberts *et al*. reported that the effects on the 2-regeneration reproductive toxicity of toluene did not adversely affect fertility and reproductive [1].

Toluene is metabolized by the liver; however, the liver does not appear to be primary target for toluene toxicity. In study of Guzelian et al. seven of the patients had liver biopsies, which showed some centrally lobular and periportal fat accumulation, and Kupffer cell hyperplasia [10]. A study by Swensson *et al*. has looked at 47 rotogravure workers occupationally exposed to toluene and showed elevation of liver enzymes and chemical hepatitis [11].

Experimental animals exposed to toluene at concentrations of 500 to 800 ppm for 7 days showed increased liver weights, but no significant morphological changes by microscopy. Electron microscopical studies revealed ultrastructural changes which were compatible with changes in cytochrome p-450 concentrations. Other studies have shown no effect on liver size or liver function [12,13]. It is highly likely that, in predisposed individuals, toluene can cause liver damage, especially in those patients who have fatty liver changes from other causes.

Tomei *et al*. looked at liver damage among shoe repairers who use toluene, among other solvents [14]. Hepatotoxicity has been reported throughout the literature in individuals exposed to xylene and toluene [15].

Dalgaard *et al*. observed no effect on sperm parameters in rats which were exposed pre-and postnatally to 1200 ppm toluene; They found no significant differences in mating, fertility, or pregnancy indices [3]. Any differences in mating, fertility or pregnancy indices were found after *in utero* exposure to 1200 ppm toluene. This finding is in accordance with a study by Theil and Chahoud [16]. However, Ono et al. reported that two studies of rats exposed to high levels (2000 or 6000 ppm) of toluene resulted in direct toxic effects on the epididymis [17].

The findings of Ono et al. indicate that toluene inhalation may adversely affect male reproductive functions, although no exposure-related effects were noted on the weights or histopathological features of the male reproductive organs. They reported that epididymal sperm counts were significantly

reduced in rats exposed to 6000 ppm toluene [17]. At the same time, the sperm motion parameters were also suppressed on the whole in 600 ppm groups, although the differences were not significant. These findings reveal that toluene inhalation at 6000 ppm, 2h/day for 5 weeks, suppresses the number of sperm, the sperm quality and sperm activity. The results of their study emphasize that toluene exposure did not induce morphologic changes in testes or alter spermatogenesis within the testes. Their findings indicated that toluene does not directly affect spermatogenic cells within the testes, but may act on spermatozoa within the epididymis. These observations are consistent with our previous finding that inhalation of toluene (2000 ppm 6 h/ day) for 90 days decreases sperm counts and sperm motility in rats, but dose not affect the spermatogenesis in testes or *in vivo* fertility [6].

Conclusions

This study did not detect testicular atrophy, but found that males occupationally exposed to toluene experienced blood flow problems, especially within the testes. This study also found that Doppler ultrasonography may be used as a routine procedure to measure blood flow in workers occupationally exposed to toluene.

Declaration of Interest

The authors report no conflict of interest and the article is not funded or supported by any research grant.

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