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OCCUPATIONAL
SOLVENT EXPOSURE
ASSOCIATED WITH
DEVELOPMENTAL
TOXICITY

Case studies

Keywords

Organic solvent
Toluene
Xylene,
Teratogen
Children

JEL Classification

I10, I13, I19

Abstract

Organic solvent is a broad term that applies to many classes of chemicals. The solvent (benzene, toluene etc.) aspects of occupational exposure are reviewed via the examination of the use, occurrence, and disposition as well as population's potential of risk. The general public can be exposed to solvent in ambient air as a result of its occurrence in paint process. Solvents are primarily irritants to the skin and mucous membranes and have narcotic properties at high concentrations. Published epidemiological data identified various types of birth defects in certain occupations.

Introduction

There are many solvents therefore will focus on those organic solvents usually found in the workplace or at home, or are frequently abused. Teratology is the study of environmentally induced congenital anomalies. A teratogen is an agent, which by acting on the developing embryo or foetus, can cause a structural anomaly (Diav-Citrin & Koren, 2000)

Common occupational solvents are paint thinner (toluene, benzene, xylene etc.) or glue solvents (acetone, methyl acetate, ethyl acetate etc.) (Table I) (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?GENETOX>). Inhalation is the most common route of human exposure.

Published epidemiological data identified various types of birth defects in certain occupations such as furniture making, manufacturing industrial equipment, plastic and textile industry, shoe manufacturers, painting, printing and adhesive industries, demonstrating a general relationship with the teratogenic potency of the solvents.

The chemicals presented during the furniture production are volatile aromatic compounds as toluene, ethylbenzene, xylenes, acetone, butan-2-one, ethyl, isobutyl and methoxypropyl acetate and 4-methylpentan-2-on (Pośniak *et al.*, 2005). Exposure to solvents in work-related settings or through inhalant abuse is possible for women of reproductive age but some data suggest that the high levels of toluene exposure typical with inhalant abuse are more detrimental to fetal development than typical occupational exposure (Hannigan & Bowen, 2010).

Animal studies demonstrate that brief, repeated, prenatal exposure to high concentrations of solvent can cause growth restriction, malformation and impairments of biobehavioral development in laboratory animals (Bowen, 2005). There is no question that animal teratology studies are helpful in human teratology, but negative animal studies do not guarantee that these agents are free from reproductive effects. Observations from human occupational or non-occupational/ incidental exposure in the home to volatile organic compounds were closely related with increased risk for spontaneous abortion or new-born with congenital malformations (McMartin *et al.* 1989)

Occupational exposure is a chronic expose characterized by critical parameters such as duration of exposure, route of exposure, and dosage of exposure. Abuse of solvents refers to intentional inhalation of solvent vapors in order to obtain a feeling of ecstasy and the air concentration of the solvent is more likely to be higher than an occupational or accidental exposure with a greater risk of teratogenic effects (Hersh *et al.* 1985; McMartin *et al.* 1989).

Case report

Patient 1 is a white male who was evaluated at 3 years age because of developmental delay. He was born at 26 weeks gestation age to a woman who had history of regular occupational solvent inhalation. During pregnancy she did not use alcohol or other substance abuse but she did not stop occupational exposure until second trimester of pregnancy. The father was young, healthy and there is no consanguinity. Developmental delay was identified in infancy. Other aetiological tests were normal (TORCH test, EEG and thyroid function). At three years age he revealed failure to thrive (height = -2.34 SD, weight = -2.96 SD), microcephaly (OFC = -3.41 SD), facial dysmorphism (short palpebral fissures, deep set eyes, epicanthic folds, flat nasal bridge, thin upper lip), cryptorchidism, attentional deficits and severe intellectual disability. Renal ultrasound was normal.

Discussions

In this case there was a chronic maternal exposure to solvents before and for the first three months of pregnancy without other teratogen substance abuse recording. The most frequent manifestation of toluene/xylene fetopathy are microcephaly, craniofacial dysmorphism, developmental and intellectual impairment (attentional deficits and hyperactivity) and variable growth deficiency. Maternal solvent abuse by inhalation is reported to cause an embryopathy similar to fetal alcohol syndrome (Hersh *et al.* 1985).

Toluene, xylene and other solvents exposures as perchloroethylene, have been associated with an increased risk of spontaneous abortion in women (Donald *et al.* 1991).

The pathogenesis of solvent embryopathy has not been clarified. Previously studies suggested that facial and brain anomalies could be explained by abnormal proliferation and migration of neural crest cells.

Variable clinical features of patients with solvent embryopathy could be defined by the duration and intensity of exposure, gestational age at the time of exposure, nature of the solvent, interaction with other teratogen substances and especially the genetic predisposition of the fetus (Mattison, 1992). Genetic variations that result in deficiency of ALDH2, an enzyme involved in toluene metabolism, may increase the risks of toluene teratogenicity in at-risk individuals at lower levels of exposure (Wilkins-Haug, 1997).

Conclusions

Our study aimed to emphasize the importance of occupational teratogens recognition. Clinical

findings of the patient support chronic solvent exposure in utero as a potential human teratogen cause. There are some solvent occupational, non-occupational/ incidental exposure in the home, or exposure as the result of solvent abuse for which we can draw strong conclusions about the potential to cause congenital anomalies. In order to prevent congenital anomalies it should be emphasized that the exposure to potential teratogens must be reduced before pregnancy and especially in the first few weeks of pregnancy. Wearing gloves, masks and protective clothing, reducing the airborne concentration of a solvent by providing good ventilation is also recommended.

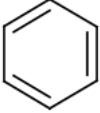
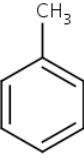
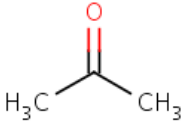
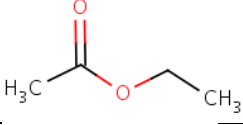
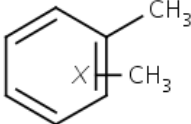
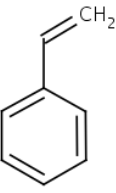
Acknowledgments

Alina Luca and Elena Braha contributed equally to this work. We thank the patient and his family for participating in the study.

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Table I. Common occupational solvents

Solvent	Chemical formula		Taxonomic Name and Assay
Benzene	C_6H_6		Prokaryotes - gene mutation Plants - gene mutation In vivo mammalian somatic cells - chromosome effects
Toluene	$C_6H_5-CH_3$		In vivo mammalian somatic cells - chromosome effects In vivo mammalian, sperm morphology - other genotoxic effects In vitro mammalian - cell transformation, viral enhancement
Acetone	$CH_3-C(=O)-CH_3$		Prokaryotes - gene mutation Plants - gene mutation In vitro mammalian - chromosome effects In vivo mammalian somatic cells - chromosome effects
Ethyl acetate	$CH_3-C(=O)-O-CH_2-CH_3$		In vivo mammalian somatic cells - chromosome effects Prokaryotes - other genotoxic effects
Xylene	C_8H_{10}		In vivo mammalian somatic cells - chromosome effects In vitro mammalian, SCE - other genotoxic effects
Styrene	$C_6H_5CH=CH_2$		Prokaryotes - gene mutation Lower eukaryotes - gene mutation Insects - gene mutation In vitro mammalian - gene mutation Plants - chromosome effects In vitro mammalian - chromosome effects In vivo mammalian somatic cells - chromosome effects In vitro mammalian - cell transformation, viral enhancement
After Genetic Toxicology Data Bank (GENE-TOX) http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?GENETOX			