Inhalants are a group of substances that have mind-altering or psychoactive effects when inhaled. The intoxicating effect makes them liable to abuse. Volatility is the common physical characteristic shared by all inhalants. Inhalant abuse is a worldwide problem. The substances abused are numerous, cheap, legal and easily available (Table 1). They are usually emptied into a plastic bag or a used drinks can and then inhaled through the mouth or nose to produce a high. Glue sniffing, solvent and volatile abuse are synonymous terms. The lifetime prevalence in the US is approximately 2%-4%. At our hospital, inhalant abuse was estimated to rank second to alcohol abuse among inpatients. The reason for this scale of inhalant abuse is not certain. The problem is best exemplified by the abuse of inhalers beyond medication by asthma sufferers.

Current understanding of the toxic effects of substance inhalation has come from documented cases of massive exposure to substances. The lipid-rich organs are particularly vulnerable (Table 2), and the nervous system is affected at many levels (Table 3). Clinical manifestations may be diffuse. As a rule, acute high-level exposure produces reversible changes, while chronic exposure results in permanent impairment. This is substantiated by MRI, autopsy and neurophysiological studies.

Toxicity is determined by the metabolic processes. Inhalants are rendered harmless by detoxication. Bioactivation can result in the production of toxic metabolites, but this process is normally limited by the concentration of P450 cytochrome enzymes present in the body. Massive exposure induces enzyme induction or saturation of detoxication processes with spillover in the bioactivation pathways. This results in increased toxic metabolite production and cell damage. Harmful free radicals are also generated during metabolism that bind cellular macromolecules in a manner different from toxic metabolites. Other determinants are hypoxia, acidosis, amino acids (excessive glutamate), competitive inhibition, hepatic and respiratory perfusion and antioxidant levels in the body.

 Clinically, inhalant abusers are of three types: juvenile experimenters in whom abuse is a fleeting phase; polydrug users who use inhalants as well as, but not in preference to, other drugs; and adults with an established inhalant abuse pattern. It is this last category who are at risk of serious
toxic effects. Paint, glue and gasoline are the most common inhalants abused.15-17 Toluene is the main toxic agent in paints. It is widely used in industry and has the highest potential for abuse. It is a white matter toxin affecting the nervous system, resulting in distal axonopathy. Petrol is a complex mixture of organic solvents and metal. Toxicity can result from either constituent. It affects both peripheral and central nervous systems.18-20

Case Reports

Case 1

A 33-year-old male was admitted with an 18-year history of paint spray inhalation. He regularly inhaled 5 cans a day and last inhaled on the day of admission. He was a smoker but denied abuse of other drugs. He had no significant past or family history. On examination, he strongly smelt of paint. He was confused and unable to follow a three-step command. He was disoriented to time. Attention, concentration, recent memory and calculations were impaired. In the primary position of gaze, he had rapid, horizontal to-and-fro movements of the eyes past the point of fixation. Eye movements were full, with coarse bilateral horizontal nystagmus. He reported inconsistently of impaired touch and pinprick sensation on the face. Speech was slurred and hearing was impaired. Reflexes were hyperactive and plantars equivocal. Finger, nose and heel shin tests were grossly abnormal. The patient had marked action tremor with head titubation. Romberg’s sign was positive. Gait was unsteady and wide based. Routine tests, including drug screen, were normal except for weakly reactive VDRL and TPHA. CT scan of the head revealed prominent ventricles but no other abnormality. EEG showed diffuse bilateral cerebral dysfunction. IQ score was 67.

Cognition, ocular abnormalities, impaired hearing, hyperreflexia and tremor disappeared completely during hospitalization, while neurological signs of dysarthria, nystagmus and ataxia remained unchanged. These cerebellar signs were first noticed during admission four years earlier, and had remained unchanged since then. He denied any abstinence from inhalants during this time.

Case 2

A 38-year-old male was admitted with a 20-year history of petrol inhalation. He used half a liter/day and had last inhaled two days before admission. He was a smoker but denied abuse of any other substance. He had a 6-month history of weakness and numbness in the legs that had gradually progressed to involve the hands. There was no significant past or family history. Neurological examination revealed bilateral foot drop. Muscles of the hands, feet and anterior compartment of legs were wasted. He had distal motor weakness. Ankle and supinator jerks were absent, knee jerks were diminished and the plantars were going down. Touch and pin prick were impaired in the glove-and-stocking distribution. Vibration and joint position sense were intact. The patient walked with assistance and had a high-stepping gait. Apart from elevated gamma-glutamyl transferase (GGT) and positive hepatitis C serology, all other investigations, including drug screening, were unremarkable. He denied any periods of abstinence. He was discharged with no neurological improvement.

Case 3

A 23-year-old male was admitted with a history of inhalant dependence. He started inhaling glue at the age of 15 but switched to paint spray four years later. He used one can/day and last inhaled one day before admission. He was a smoker but denied abuse of any other substance. The only neurological abnormality was a stumbling, wide-based gait. Routine investigations, including drug screening, were normal. His IQ score was 87. He reported similar problems in a maternal uncle (Case 1). Gait ataxia was first diagnosed on his previous admission 18 months earlier. It had remained unchanged since then. He had had no periods of abstinence during this time.

Discussion

Each of the above cases had a long history of inhalant abuse. Inhalants contain chemicals that are used in industry for dissolving lipids. It is logical to assume that prolonged use would result in CNS damage. Two patients were inhaling paint that contained toluene. This neurotoxic chemical is known to produce a full-blown cerebellar syndrome and gait ataxia in chronic users.15,21 Case 1 had findings consistent with CNS dysfunction at multiple levels, e.g., cranial nerves, corticospinal tract, and cerebellum. There was also evidence of diffuse neurological damage, e.g., abnormal EEG and CT scan of the head. Most of the neurological deficits recovered on cessation of the inhalant during hospitalization, except cerebellar syndrome. This was persistent and had remained unchanged for the previous four years. The case manifested features of both acute high-level inhalant exposure with reversible neurological impairment and chronic exposure with persistent deficits.

Case 3 had a similar neurological problem. He had abnormal gait that had remained unchanged for almost 2 years. Case 2 had sensorimotor neuropathy. Sensory findings were less marked and restricted to small fiber loss. Motor weakness was severe, and serum lead levels were unavailable. Lead causes pure motor neuropathy of the upper extremities. Features inconsistent with lead toxicity were absence of CNS findings, normal blood count and RBC morphology and sensorimotor peripheral nerve involvement. Although symptoms of lead toxicity can occur with low lead levels, solvent-induced neuropathy was the most likely explanation. Elevated liver enzymes further substantiated this. Chlorohydrocarbons in the solvents are known hepatotoxins (Table 2). Case 1 and Case 3 were blood relatives, and had somewhat similar neurological deficits. Genetic make-up of an individual determines the
concentration of cytochrome P450 enzymes present in the body and the likelihood of harm. It would therefore be correct to infer that vulnerability to neurological damage in inhalant users may, to some extent, depend upon familial and genetic factors. Inhalant abuse is associated with academic difficulties and lack of success at school. Both these cases had low to borderline IQ scores. IQ is a good measure of academic success, but besides this, has limited value. IQ probably constitutes a premorbid characteristic. Its relationship to inhalant-induced neurological damage is unclear.

Whether the neurological impairment would be permanent or reversible cannot be known with certainty until complete and sustained remission from inhalants has been achieved. The issue of irreversibility of neurotoxicity remains unresolved, as studies that clarify this question are few and compounded by methodological flaws. Inhalant abusers are noncompliant and resistant to treatment, and total abstinence is difficult to attain. How much recovery of neurological function would ultimately occur and the factors that influence this remain undetermined.

The exact prevalence or incidence of neurotoxicity is difficult to establish, as the rates vary with each involved chemical, and there are too many chemicals to consider, making the task difficult. In one study on substance abuse, two-thirds of the subjects were on paint inhalers. This was a small sample of unselected individuals. Harmful effects are not seen in all cases, and some individuals are more prone to these effects than the rest of the population. A better understanding of the risk factors is required. Inhalant toxicity in adults is under researched. Studies identifying responsible chemicals, predisposing factors and outcome of specific toxic effects are needed. Neurophysiological markers (BAER) of toxic brain damage are known. There is a need to develop biological markers that would quantify exposure, provide evidence of harmful effects and identify sensitive individuals.

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References


