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EFFECT OF STYRENE ON LEVELS OF SEROTONIN, NORADRENALINE, DOPAMINE AND ACTIVITY OF ACETYL CHOLINESTERASE AND MONOAMINE OXIDASE IN RAT BRAIN

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SUMMARY

Oral intubation of styrene (1 ml/kg body weight daily) in adult male albino rats for 15 days produced a significant increase in serotonin and noradrenaline but no change in dopamine contents in brain. The brain of treated animals also showed a significant decrease in monoamine oxidase (MAO) but no change in acetyl cholinesterase (AChE) activity. The neurotoxic effects of styrene may be mediated through alterations in levels of these biogenic amines in the brain tissue.

INTRODUCTION

Styrene (vinyl benzene) is widely used in the manufacture of plastics and rubbers. Application of polystyrene is rapidly increasing in a variety of household items, food utensils and packaging materials. Reports of migration of monomer styrene into food material, stored in polystyrene containers, have caused great concern due to their toxic properties [1]. The workers handling this monomer are reported to suffer from neurological disorders, involving both the central and peripheral nervous system [2—4]. The hepatic effects of styrene have been extensively studied in man and experimental animals [2, 3] but little is known about the biochemical mechanism by which styrene exerts its neurotoxicity. Attempts have, therefore, been made to see if styrene interferes with the metabolism of neurotransmitters. The effect of styrene on serotonin, noradrenaline and dopamine levels and on MAO and AChE activity in whole brain of rats is reported in the present investigation.

Abbreviations: AChE, acetylcholinesterase; MAO, monoamine oxidase.

MATERIALS AND METHODS

Two groups, each of 12 male albino rats (225—250 g) (Industrial Toxicology Research Centre colony) received ad lib. pellet diet (Hind Lever Animal Feed, India). Group 1 was given 1.0 ml styrene/kg body weight daily for 15 days by oral intubation, and the controls (Group 2) received an equal volume of saline. All the animals were killed by decapitation on day 16. Brain tissue was rapidly removed, blotted on filter paper and processed for the estimation of biogenic amines and enzyme activity.

Assay of biogenic amines. The whole brain tissue from 6 treated and 6 control animals was homogenized individually in acidified butanol using a Potter—Elvehjem type homogenizer fitted with a teflon pestle. The homogenate was transferred to glass-stoppered tubes and centrifuged at 3000 rev/min for 5 min in a refrigerated centrifuge. Dopamine, noradrenaline and serotonin contents were measured in the supernatant, fluorometrically, using an Aminco-Bowman Spectrophotofluorometer [5, 6].

Assay of enzyme activity. The whole brain tissue from 6 treated and 6 control animals was homogenized in ice cold 0.25 M sucrose to yield 10% (w/v) homogenates for assay of enzyme activity. Activities of AChE (EC 3.1.1.7) and MAO (EC 1.4.3.4) were determined by the method of Hestrin [7] and Tabor et al. [8], respectively.

Determination of protein. Protein contents were estimated by the method of Lowry et al. [10] using bovine serum albumin as standard.

RESULTS AND DISCUSSION

The general condition of control and styrene-treated animals was normal and there was no significant difference in body or brain weights.

Table I shows the effect of styrene on levels of serotonin, noradrenaline and dopamine in brain. Styrene treatment significantly increased the levels of serotonin (62.5%) and noradrenaline (50%) but had no effect on dopamine content. The increase in the levels of these biogenic amines may

TABLE I

EFFECT OF ORALLY ADMINISTERED STYRENE (1 ml/kg) ON LEVELS OF NORADRENALINE, DOPAMINE AND SEROTONIN (μg/g FRESH TISSUE)

	Noradrenaline	Dopamine	Serotonin
Control	0.30 ± 0.03	0.39 ± 0.08	0.48 ± 0.02
Experimental	0.45 ± 0.04[a] (50)	0.44 ± 0.10	0.78 ± 0.04[a] (62.5)

All values are expressed as mean ± S.E. from six animals.
Values in parentheses indicate percent increase in amine concentration.
[a] $P < 0.001$ when compared with corresponding controls.

result from an effect of styrene on their synthesis or breakdown in brain tissue. To see whether styrene increased the level of these biogenic amines by affecting MAO, which plays a significant rôle in the oxidative deamination of these neurotransmitter substances, activity of this enzyme was measured in brain tissue. Activity of AChE was estimated to see whether styrene mediates its effect through acetylcholine. The results (Table II) show the effect of styrene on the activities of MAO and AChE. The activity of MAO was significantly decreased in the treated animals, while AChE remained unaltered. However, styrene, when incubated in vitro with rat brain homogenates up to a concentration of $1 \cdot 10^{-2}$ M, did not show any effect on MAO activity.

Serotonin and catecholamines play a significant role in the physiological function of brain. Alterations in their levels have been shown to cause

TABLE II

ACETYLCHOLINESTERASE AND MONOAMINE OXIDASE ACTIVITY IN BRAIN TISSUE OF CONTROL AND STYRENE-TREATED RATS

	Acetylcholinesterase (nmol acetylcholine hydrolysed/min/mg protein)	Monoamine oxidase (nmol benzaldehyde formed/min/mg protein)
Control	92.2 ± 2.9	1.7 ± 0.20
Experimental	95.5 ± 3.1	0.75 ± 0.04[a]

All values are mean ± standard error of six animals.
[a] $P < 0.001$ when compared with corresponding controls.

abnormal mental behaviour and mood [9, 11]. The present studies show that styrene increases the levels of serotonin and noradrenaline by inhibiting their metabolic disposition. That there were no significant differences in AChE between the control and treated animals suggests that the effects of styrene are not mediated through acetylcholine. An increase in serotonin and noradrenaline concentration may be due to stress, as observed for lithium and other xenobiotics [9, 11]. Although the exact biochemical mechanism of the neurotoxic effect of styrene remains to be elucidated, the present results suggest an impairment of neurotransmission.

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