ABNORMAL MOTOR MOVEMENTS DURING DIVINYL ETHER ANESTHESIA

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SINCE the review of Martin and Rovenstine (1) in 1941 comparatively little has been written about divinyl ether. This report is intended to call attention to a property of this volatile liquid which perhaps has not been sufficiently emphasized. We refer to the occurrence of muscular twitchings or generalized convulsions when divinyl ether has been or is being administered to infants and children. The incidence, description and etiology of abnormal motor movements observed in 1,418 patients receiving this drug at the Hospital of the University of Pennsylvania will be described.

METHOD

Divinyl ether was used either for induction to diethyl ether anesthesia or as the sole anesthetic agent for surgical procedures of less than ten minutes duration. It was administered by an open technique by medical students, interns, or resident anesthetists under supervision. The liquid was dropped upon a mask covered with a gauze of eight layers thickness until the patient was in the first or second plane of surgical anesthesia, a period which varied from two to five minutes. In most instances 100 per cent oxygen, flowing at a rate of 0.5 to 1.0 liter per minute, was delivered beneath the mask as gauze side-pieces were added after changing to diethyl ether. In a small number of cases, the oxygen was begun shortly after the start of anesthesia.

Ethyl chloride was administered by the same technique in a control series of patients.

The temperature in the induction and anesthesia rooms was controlled by air conditioning units at 70 to 74 F.

Description of the Abnormal Motor Movements Following Divinyl Ether. Voluntary or purposeful movements occurring during the first and second stages of anesthesia with divinyl ether have not been included in this study. We were concerned here only with the involuntary, purposeless movements in the different planes of the third stage. The types of muscular response were variously described but can be fitted into two groups as follows:

1. Jerky, violent movements, commonly called "twitchings" by the anesthetist, were limited to specific regions of the body in 22 patients

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but progressed to generalized clonic convulsions in 14 additional instances.

2. Gross, slow, less violent, more automatic and rhythmical movements were noted in 10 patients. Some observers classed these as athetoid movements. The shoulder girdle alone was involved in two cases, the hands alone in one, and the hands and arms in three. "Running movements" were listed as such only once. In the remaining three patients there were claw-like movements of the fingers as the arms were pulled up across the chest toward the face.

RESULTS

The data are listed in table 1. Of the 1418 patients, 46 reacted with abnormal motor movements, an over-all incidence of 3.2 per cent. This compares unfavorably with other series of generalized convulsions under divinyl ether reported in the literature (2–8) where the

INCIDENCE OF ABNORMAL MOTOR MOVEMENTS FOLLOWING DIVINYL ETHER

Age Group	Number of Patients		Patients with Abnormal Motor Movement		Percentage of Group	
	Male	Female	Male	Female	Male	Female
Up to 12 mos.	41	16	1	0	2.4	0
1–3 years	138	96	2	5	1.5	5.2
4–6 years	289	226	7	19	2.4	8.4
7–11 years	293	198	7	4	2.4	2.0
12–20 years	56	44	1	0	1.8	0
Over 20 years	3	13	0	0	0	0
No age recorded	0	5	0	0	0	0
Total	820	598	18	28	2.2	4.7

incidence ranged from 0.08 to 1.3 per cent except for the one case of Ruth (9) which occurred during the first ten administrations of the drug. For some as yet unexplained reason, convulsive seizures during inhalation anesthesia are more prone to occur in females. This predominance appeared in our series, with an incidence among females of 4.7 per cent as compared to 2.2 per cent for males. In the four to six year age group, the incidence of seizures was 8.4 per cent among females.

Forty-eight per cent of the convulsions were manifested while divinyl ether was being administered. The remainder appeared one to five minutes after it had been discontinued and diethyl ether was being given. This has been noted by others (3–5).

Treatment of the 46 patients consisted solely of assisting respirations with positive pressure 100 per cent oxygen. This resulted in cessation of the movements, usually within one minute.

To study the possibility that these movements might be related to

the dosage of divinyl ether, the agent was administered rapidly so that maximum quantities were delivered per unit time. Nine children (none of whom are included in the over-all statistics) received between 22 and 40 cc. in from four to eight minutes. Blood levels of the drug were not determined. In this group there were three localized and three generalized convulsive seizures. Two of these six children had a respiratory rate of 60–80 per minute during divinyl ether anesthesia.

Ethyl chloride was administered by an open technique as the induction agent prior to administration of ethyl ether to 204 children. There were no generalized convulsions and only a single instance of clonic movements of the hands and feet in this group of patients.

DISCUSSION

The interesting fact of this clinical study was the difference between divinyl ether and ethyl chloride as far as the production of abnormal motor movements was concerned. Both volatile liquids were administered in an essentially similar manner yet the former agent was associated with a sixfold greater incidence of such movements.

Lundy (10) has listed thirty-three possible contributing factors in his discussion of convulsions occurring during inhalational anesthesia. The majority of these would have been operating presumably equally in both series of patients and cannot, therefore, be used to explain the marked difference between the two anesthetic drugs. It will also be recalled that only 14 of the 46 abnormal motor reactions of the divinyl ether group progressed to generalized convulsions, so that one must consider factors responsible for reactions of a far less serious nature than a convulsive seizure. This is particularly true for the slow, more automatic, rhythmical movements noted in ten of the patients receiving divinyl ether.

Impurities in divinyl ether have been implicated (10). Adriani (11) examined fifty specimens of this drug and concluded that the container could be resealed after opening and used again within ten days without fear of deterioration of the contents. During the latter part of this study, if a seizure occurred, the divinyl ether remaining in the bottle was used in as many as two or three subsequent anesthetizations without recurrence of the abnormal movements.

In 1940, Orth and his colleagues (12) studied the action of divinyl ether on the central nervous system of the dog. A quotation from their paper is pertinent, "In each of 108 surgical Vinethene anesthetizations to 46 dogs, there was some degree of aberrant, muscular movement which ranged from twitches to coordinated activity of all four extremities, simulating running movements. This type of coordinated muscular response *has never occurred* in over 400 anesthetizations with chloroform, cyclopropane or diethyl ether."

Divinyl ether appears to be unique among the commonly used inhalational agents as far as the production of automatic, coordinated

movements in the dog is concerned. This type of rhythmical response suggests involvement of subcortical regions. That the locus might be in the basal ganglia of man is suggested by the resemblance of the movements described in group II to those noted in diseases of the extrapyramidal system.

The ability to produce abnormal movements in two-thirds of the small series of nine children by deliberate overdosage suggests that studies of the relationship between jugular vein blood concentrations of divinyl ether and the onset of seizures might be worth while. Electoencephalographic tracings would also be of interest. We have no explanation for the rapid respiratory rate noted in two of the nine patients.

One is tempted to implicate hypoxia as an etiologic factor for several reasons: (1) The technique of administering volatile liquids on a gauze mask reduces the inspired oxygen concentration considerably below normal unless additional oxygen is supplied; (2) the tachypnea of two of the patients in the "overdosage" series might have shifted (through hypocapnia) the oxygen dissociation curve of hemoglobin sufficiently to the left to make tissue hypoxia a possibility (13); (3) all seizures responded with the inhalation of 100 per cent oxygen. Some force is removed from these arguments, however, when it is realized that item (1) above would have applied to the ethyl chloride series; that the hypocapnia of item (2) might have been more important in producing cerebral vasoconstriction than a shift in oxyhemoglobin dissociation; and the value of 100 per cent oxygen might have been related to the associated increased pulmonary ventilation (use of assisted respiration) and consequent reduction in divinyl ether concentration in the blood stream and tissues. Arterial oxygen tension determinations might cast some light on this, but tissue oxygen tensions would be of even greater interest.

SUMMARY AND CONCLUSIONS

The incidence of abnormal motor movements noted in a series of 1,418 patients receiving divinyl ether was 3.2 per cent. Females were affected more than males. Two distinct types of abnormalities were observed. The concentration of the drug appears to have a bearing upon the production of the convulsive movements, although hypoxia as an additional contributing factor cannot be excluded. Inhalation of 100 per cent oxygen proved effective in treatment. Ethyl chloride administered by the same technique rarely caused abnormal motor responses.

No deaths occurred in this series. Despite the high incidence of abnormal motor movements associated with administration of this drug, on the basis of a long clinical experience with divinyl ether we believe it to be a useful anesthetic agent.

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