Pharmacological Action of Xylocaine on Trichloroethylene in Terms of E. C. G. Findings

by

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KAZUYA HIROTA of our Department has published some time ago his findings on the toxicity of trichloroethylene, used in the dental field as a local anesthetic agent [1]. It has been known that this drug sometimes brings about a serious cardiac disturbance and BORNES and IVES [2] reported that trichloroethylene promotes the sensitivity of adrenalin and is responsible for the irregular pulsation. MORRIS [3] also pointed out that it even brings about the ventricular fibrillation.

The present paper is another contribution to the toxicity of trichloroethylene and it will be of interest when our findings are compared with those of HIROTA here and there.

Experimental Materials and Method

By way of materials, use was made of ripe male and female rabbits, weighing about 2 kg, indiscriminately. With the use of a specially designed syringe, trichloroethylene (a British product, Trilene) was infused into a wad of gauze, 10×20 cm in eight folds, which was directly placed on the nose of animals with the aid of retaining plates. A fixed amount of trichloroethylene was infused into the wad at regular intervals.

ME-50 ink-type 3-channel electrocardiographic apparatus, manufactured by Japan Optical Co., was linked to the electrocardiometer electrodes and it was used for secondary derivation with the time register of 1 second.

Experimental Results

1. Repetitive infusion of trichloroethylene.

In the first phase of our experiments, a fairly minute quantity of 0.1 ml of trichloroethylene was inhaled by the rabbits 5 times in succession at intervals of 10 minutes, 0.2 ml being dosed at the sixth time finally. As a result, till three doses lengthening between R and R took place immediately after the administration and the elevation of R and the reduction of S were more or less in parallel to one another, this tendency disappearing from the fourth time downward. On the whole, electrocardiographic changes in the rabbits were transient in that those changes which took place till three doses restored themselves to the normalcy in about 90 seconds (Fig. 1).

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Fig. 1. Administration of 0.1 ml Trichlorethylene at an Interval of 10 Minutes

In the next phase, 0.2 ml was administered in 4 doses at intervals of 10 minutes, 0.1 ml being dosed at the fifth time finally. As a results, till two dose there took place similar lengthening between R and R, disappearance of P, lengthening of ST, elevation of T and sometimes there was recorded something which might be the ventricular fibrillation. On the other hand, there was no change at all at the fifth administration of 0.1 ml (Fig. 2).

Fig. 2. Administration of 0.2 ml Trichlorethylene at an Interval of 10 Minutes (1)

In some rabbits, there were electrocardiographic changes which failed to return to the normalcy even after 90 seconds, where remarkable descending curves were registered between S and T. Similarly, here the lengthening between R and R was also attested to till the fourth dose (Fig. 3).

From these findings, it seemed possible to establish an indicator that when an introduction of some drug cause some changes between the boundaries set by three successive E. C. G. changes owing to the inhalation of 0.1 ml trichlorethylene on the one hand and four successive E. C. G. changes owing to the inhalation of 0.2 ml trichlorethylene on the other, we may ascribe any changes beyond these boundaries to that drug in question.

Fig. 3. Administration of 0.2 ml Trichloroethylene at an Interval of 10 Minutes (2)

2. Infusion of trichlorethylene in different doses.

Although it was made clear enough from the tests above that the inhalation of trichlorethylene in the amount of 0.1 to 0.2 ml brought about changes, we had the idea that when a dosage was much larger, possible effect of a drug to be administered during the intervals of repetitive inhalation might not be perceived. In a similar vein, when a dosage was too small to effect changes in E. C. G. current, possible effect of a drug might not be also perceived. Therefore, with a view to establishing what would be considered an adequate dosage of trichlorethylene, it was administered in differing dosages within a range of 0.05 ml and 0.5 ml.

As a result, no changes took place with dosages of 0.05 ml and 0.1 ml but, on the other hand, with 0.5 ml it seemed to be too strong and more or less stable changes were secured with a dosage around 0.15 ml. With other test animals, an optimal dosage was found to be within a range of 0.15 and 0.2 ml. Fig. 4 gives this part of our tests in which the same animals were subjected to different dosages.

Fig. 4. Administration of Various Dosages of Trichlorethylene at an Interval of 20 Minutes

3. Premedication of xylocaine prior to the inhalation of trichlorethylene.

It is not definitely known as yet whether trichlorethylene changes by means of the electrocardiogram are due to the central or peripheral nervous system. However, as a matter of fact, the incidence of some cardiac disturbance in man owing to trichlorethylene is sometimes encountered. Based on this fact, an effort was made to see how the intravenous injection of xylocaine, a commonly employed local narcotic agent, would reflect on the E. C. G. changes because of trichlorethylene.

Consequently, the E. C. G. changes attendant on a repetitive inhalation of 0.1 ml trichlorethylene were inhibited for some time by the intravenous injection of 2% xylocaine in the amount of 0.1 ml 1/2 kg. This finding made us assume that, aside from the fact whether the action of xylocaine may be attributed to the central or peripheral nervous system, this local narcotic agent does not work adversely on trichlorethylene (Fig. 5).

Conclusions

When rabbits were made to inhale trichlorethylene, reduction between R-R took place down to 1/4 when 3.0 ml was dosed, with the pronounced heart beat and ventricular fibrillation in the intervals (HIROTA). In our present study, however, much less amount of trichlorethylene was used.

Fig. 5. Premedication of Xylocaine before the Inhalation of Trichlorethylene

When small dosages within a range of 0.1 to 0.2 ml were administered for repetitive cycles, more or less the same changes took place in E. C. G. findings each time, e. g., lengthening between R-R. We have found xylocaine to be inhibitive of these changes.

This fact will assume more interest from a point of view of eliminating injurious by-effect of trichlorethylene, when it is considered in connection with the finding of HIROTA that the premedication of amisalin, a drug believed to cure the irregular pulsation, intravenously before the inhalation of trichlorethylene aggravates the E. C. G. changes attendant upon trichlorethylene.

References

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